Program Schedule from the 42nd American Society of Andrology Annual Meeting

April 21 – 25, 2017

Miami, Florida

JOINTLY PROVIDED BY:
Creighton University Health Sciences Continuing Education and the American Society of Andrology
Earn up to 19.25 AMA PRA Category 1 Credits™. See inside for details.
# SCHEDULE AT A GLANCE

## American Society of Andrology 42nd Annual Conference

***“New Concepts and Perspectives in Male Reproductive Health”***

**April 21 – 25, 2017**

**The Hilton Miami Downtown | Miami, Florida**

Program Chairs: Sylvie Breton, PhD and Joseph Alukal, MD

All sessions will be held in **Symphony Ballroom III/IV** unless otherwise noted.

Speakers and times are subject to change.

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### FRIDAY, APRIL 21, 2017

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>2:00 p.m. - 6:00 p.m.</td>
<td>Registration/Information Desk Open</td>
<td>Symphony Ballroom Registration</td>
</tr>
<tr>
<td>5:00 p.m. - 10:00 p.m.</td>
<td>Executive Council Meeting and Dinner</td>
<td>Concerto B</td>
</tr>
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### SATURDAY, APRIL 22, 2017

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Location</th>
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<tbody>
<tr>
<td>7:00 a.m. - 7:00 p.m.</td>
<td>Registration/Information Desk Open</td>
<td>Symphony Ballroom Registration</td>
</tr>
<tr>
<td>4:00 p.m. - 9:30 p.m.</td>
<td>Exhibit Hall Open</td>
<td>Symphony Ballroom Foyer</td>
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</tbody>
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### FRIDAY, APRIL 21, 2017

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Location</th>
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<tbody>
<tr>
<td>8:30 a.m. - 5:30 p.m.</td>
<td><em>ASA Andrology Lab Workshop</em></td>
<td>Concerto A</td>
</tr>
<tr>
<td>12:00 p.m. - 1:30 p.m.</td>
<td><strong>LAB SCIENCE FORUM LUNCHEON</strong></td>
<td>Concerto B</td>
</tr>
<tr>
<td>1:00 p.m. - 4:00 p.m.</td>
<td><strong>ASA Clinical Symposium</strong></td>
<td>Concerto D</td>
</tr>
<tr>
<td>6:00 p.m. - 6:10 p.m.</td>
<td>Welcome and Opening Remarks</td>
<td>Symphony Ballroom III/IV</td>
</tr>
<tr>
<td>6:10 p.m. - 6:30 p.m.</td>
<td>Updates from NIH, NICHD &amp; NIEHS</td>
<td>Symphony Ballroom III/IV</td>
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<tr>
<td>6:30 p.m. - 6:50 p.m.</td>
<td><strong>ANDROLOGY Journal Award</strong></td>
<td>Symphony Ballroom III/IV</td>
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<tr>
<td>6:50 p.m. - 7:45 p.m.</td>
<td><strong>EMIL STEINBERGER MEMORIAL LECTURE</strong></td>
<td>Symphony Ballroom III/IV</td>
</tr>
<tr>
<td>7:45 p.m. - 8:00 p.m.</td>
<td><strong>Distinguished Andrologist Award</strong></td>
<td>Symphony Ballroom III/IV</td>
</tr>
<tr>
<td>8:00 p.m. - 9:30 p.m.</td>
<td><strong>ASA Welcome Reception</strong></td>
<td>Symphony Ballroom Foyer</td>
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### SUNDAY, APRIL 23, 2017

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Location</th>
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<tbody>
<tr>
<td>6:30 a.m. - 8:00 a.m.</td>
<td>Past President’s Breakfast</td>
<td>Symphony Ballroom I/II</td>
</tr>
<tr>
<td>7:00 a.m. - 6:00 p.m.</td>
<td>Registration/Information Desk Open</td>
<td>Symphony Ballroom Registration</td>
</tr>
<tr>
<td>7:00 a.m. - 7:00 a.m.</td>
<td>Exhibit Hall Open</td>
<td>Symphony Ballroom Foyer</td>
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<tr>
<td>7:00 a.m. - 8:00 a.m.</td>
<td>Continental Breakfast in Exhibit Hall</td>
<td>Symphony Ballroom Foyer</td>
</tr>
<tr>
<td>8:00 a.m. - 9:00 a.m.</td>
<td><strong>LECTURE I</strong></td>
<td>Symphony Ballroom I/II</td>
</tr>
<tr>
<td>9:00 a.m. - 9:15 a.m.</td>
<td><strong>Distinguished Service Award</strong></td>
<td>Symphony Ballroom I/II</td>
</tr>
<tr>
<td>9:15 a.m. - 10:45 a.m.</td>
<td><strong>SYMPOSIUM I - New Insights into ART</strong></td>
<td>Symphony Ballroom I/II</td>
</tr>
<tr>
<td>10:15 a.m. - 10:45 a.m.</td>
<td><strong>Autism and Other Developmental Disorders in ART</strong></td>
<td>Symphony Ballroom I/II</td>
</tr>
<tr>
<td>12:30 p.m. - 2:00 p.m.</td>
<td><strong>MENTORING LUNCHEON</strong></td>
<td>Symphony Ballroom I/II</td>
</tr>
<tr>
<td>12:30 p.m. - 2:00 p.m.</td>
<td><strong>Editorial Board Luncheon</strong></td>
<td>Symphony Ballroom I/II</td>
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© 2017 American Society of Andrology and European Academy of Andrology
<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
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<tbody>
<tr>
<td>2:00 p.m. - 3:30 p.m.</td>
<td><strong>CONCURRENT ORAL SESSIONS</strong></td>
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<tr>
<td>2:00 p.m. - 3:30 p.m.</td>
<td>Oral Session I (Basic Science)</td>
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<tr>
<td>2:00 p.m. - 3:30 p.m.</td>
<td>Oral Session II (Clinical)</td>
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<tr>
<td>3:30 p.m. - 3:45 a.m.</td>
<td>Networking and Break in Exhibit Hall</td>
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<tr>
<td>3:45 p.m. - 4:30 p.m.</td>
<td><strong>EAA LECTURE</strong></td>
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<tr>
<td>4:30 p.m. - 5:15 p.m.</td>
<td><strong>LECTURE II</strong></td>
</tr>
<tr>
<td>5:15 p.m. - 6:30 p.m.</td>
<td><strong>3RD ANNUAL TRAINEE DIRECTED MINI-SYMPOSIUM</strong></td>
</tr>
<tr>
<td>6:30 p.m. - 7:30 p.m.</td>
<td>Presentation of Trainee Awards</td>
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<tr>
<td>7:30 p.m. - 8:30 p.m.</td>
<td>Trainee Forum and Mixer</td>
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<tr>
<td><strong>MONDAY, APRIL 24, 2017</strong></td>
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<tr>
<td>7:00 a.m. - 6:00 p.m.</td>
<td>Registration/Information Desk Open</td>
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<tr>
<td>7:00 a.m. - 8:00 a.m.</td>
<td>Continental Breakfast</td>
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<tr>
<td>8:00 a.m. - 9:00 a.m.</td>
<td><strong>WOMEN IN ANDROLOGY LECTURE</strong></td>
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<tr>
<td>9:00 a.m. - 9:15 a.m.</td>
<td>Young Andrologist Award</td>
</tr>
<tr>
<td>9:15 a.m. - 10:15 a.m.</td>
<td><strong>SYMPOSIUM II - Sex and Gender Identity and Reproductive Health</strong></td>
</tr>
<tr>
<td>9:15 a.m. - 9:35 a.m.</td>
<td>Advances in Transgender Surgery</td>
</tr>
<tr>
<td>9:35 a.m. - 9:55 a.m.</td>
<td>Guideline for the Endocrine Treatment of Transgendered Individuals</td>
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<tr>
<td>9:55 a.m. - 10:15 a.m.</td>
<td>Fertility Preservation in Transgendered Individuals</td>
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<tr>
<td>10:15 a.m. - 10:30 a.m.</td>
<td>Refreshment Break</td>
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<tr>
<td>10:30 a.m. - 11:15 a.m.</td>
<td><strong>DIVERSITY LECTURE</strong></td>
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<tr>
<td>11:15 a.m. - 12:30 p.m.</td>
<td><strong>Poster Session II</strong></td>
</tr>
<tr>
<td>12:30 p.m. - 1:45 p.m.</td>
<td><strong>WOMEN IN ANDROLOGY LUNCHEON &amp; DISCUSSION</strong></td>
</tr>
<tr>
<td>1:45 p.m. - 3:15 p.m.</td>
<td><strong>SYMPOSIUM III - Male Reproductive Tract</strong></td>
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<tr>
<td>3:15 p.m. - 3:30 p.m.</td>
<td>Refreshment Break</td>
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<tr>
<td>3:30 p.m. - 4:15 p.m.</td>
<td><strong>INTERNATIONAL LECTURE</strong></td>
</tr>
<tr>
<td>4:15 p.m. - 5:00 p.m.</td>
<td><strong>LECTURE III</strong></td>
</tr>
<tr>
<td>5:00 p.m. - 6:00 p.m.</td>
<td><strong>ASA Annual Business Meeting</strong></td>
</tr>
<tr>
<td>7:00 p.m. - 11:00 p.m.</td>
<td><strong>ANNUAL BANQUET</strong></td>
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**SCHEDULE AT A GLANCE**

**2:00 p.m. - 3:30 p.m.**

- **Concurrent Oral Sessions**
  - Oral Session I (Basic Science)
    - Location: Symphony Ballroom III/IV
  - Oral Session II (Clinical)
    - Location: Concerto A

**3:30 p.m. - 3:45 a.m.**

- Networking and Break in Exhibit Hall

**3:45 p.m. - 4:30 p.m.**

- EAA Lecture
  - Therapeutic Promise of Spermatogonial Stem Cells
    - (Introduced by Patricia S. Cuasnicu, PhD)
    - Stefan Schlatt, PhD
    - University of Muenster, Germany

**4:30 p.m. - 5:15 p.m.**

- Lecture II
  - Male Infertility as an Indicator of Overall Health
    - (Introduced by Joseph P. Alukal, MD)
    - Michael L. Eisenberg, MD
    - Stanford University School of Medicine

**5:15 p.m. - 6:30 p.m.**

- 3rd Annual Trainee Directed Mini-Symposium
  - "Finding Your BLISS: Careers in Andrology"
    - (see page 24 for full program schedule)
  - *Not CME Accredited

**6:30 p.m. - 7:30 p.m.**

- Presentation of Trainee Awards
  - Location: Symphony Ballroom III/IV
  - (All Trainee Travel and Onsite Poster Awards: Outstanding Trainee Investigator, Anna Steinberger Award, and Trainee Merit Awards will be distributed)

**7:30 p.m. - 8:30 p.m.**

- Trainee Forum and Mixer
  - Location: Upper Pool Terrace

**1:45 p.m. - 3:15 p.m.**

- Symposium III - Male Reproductive Tract
  - Moderator: Gail A. Cornell, PhD

**3:15 p.m. - 3:30 p.m.**

- Refreshment Break
  - Location: Symphony Ballroom Foyer

**3:30 p.m. - 4:15 p.m.**

- International Lecture
  - Fertility Restoration by Spermatogonial Stem Cell Transplantation
    - (Introduced by Patricia S. Cuasnicu, PhD)
    - Takashi Shinhara, PhD
    - Horizontal Medical Research Organization, Japan

**4:15 p.m. - 5:00 p.m.**

- Lecture III
  - Molecular Genetics of External Genitalia Development
    - (Introduced by Gail S. Prins, PhD)
    - Martin J. Cohn, PhD
    - Howard Hughes Medical Institute

**5:00 p.m. - 6:00 p.m.**

- ASA Annual Business Meeting

**7:00 p.m. - 11:00 p.m.**

- Annual Banquet
  - Off-Site Location: El Tucán
  - 1111 SW 1st Ave
  - Miami, FL 33130
  - Shuttle bus leaving from the valet entrance (street level) of the hotel at 6:15 p.m.
TUESDAY, APRIL 25, 2017

7:00 a.m. - 8:00 a.m. 2018 Program Committee Meeting

7:00 a.m. - 12:00 p.m. Registration/Information Desk Open
Location: Symphony Ballroom Registration

7:00 a.m. - 8:00 a.m. Continental Breakfast
Location: Symphony Ballroom Foyer

8:00 a.m. - 9:30 a.m. SYMPOSIUM IV - Testicular Somatic Cells / Spermatogenesis
Moderator: Kyle Orwig, PhD

8:00 a.m. - 8:30 a.m. Development and Validation of a Xenograft Model of Human Testicular Development
Rod T. Mitchell
MRC Centre For Reproductive Health

8:30 a.m. - 9:00 a.m. Genetic Causes of Human Azoospermia
Kenneth Aston, PhD
University of Utah Andrology and IVF Laboratories

9:00 a.m. - 9:30 a.m. Human Testicular Peritubular Cells
Artur Mayerhofer, PhD
BioMedizinisches Centrum - BMC LMU Muenchen

9:30 a.m. - 9:45 a.m. Refreshment Break
Location: Symphony Ballroom Foyer

9:45 a.m. - 11:15 a.m. SYMPOSIUM V - Sperm Function
Moderator: Pablo E. Visconti, PhD

9:45 a.m. - 10:15 a.m. Calcium Signaling in Sperm Motility Regulation and Male Fertility
Jean-Ju Chung, PhD
Yale School of Medicine Biological & Biomedical Sciences

10:15 a.m. - 10:45 a.m. An Ion Channel on Steroids: The Unconventional Pathway of Sperm Activation
Polina Lishko, PhD
University of California, Berkeley

10:45 a.m. - 11:15 a.m. Lipid Regulation of Sperm Function: From Basic Science to a Clinical Test of Male Fertility
Alexander J. Travis, VMD, PhD
Cornell University

11:15 a.m. - 12:15 p.m. AUA LECTURE
Regenerative Medicine for Genitourinary Organs
(Introduced by Joseph P. Alukal, MD)
Anthony Atala, MD
Wake Forest University School of Medicine

12:15 p.m. Meeting Adjourned
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Dear Colleagues,

I am excited to welcome you to our 42nd Annual Meeting, entitled “New Concepts and Perspectives in Male Reproductive Health.” The Program Committee, co-chaired by Drs. Joseph Alukal (NYU Medical School) and Sylvie Breton (MGH, Harvard University), have developed an outstanding program with new insights and emerging tools in genetics, genomics, immunology, molecular biology, clinical andrology, and environmental science that span many aspects of male reproductive and sexual health.

This exciting program showcases speakers and topics with the potential to alter our understanding of basic and clinical andrology that offer promise from medical advances and the development of innovative therapies for male contraception and preservation of testicular function and fertility. We hope to see you at the Mentoring Luncheon and the Trainee Symposium and the abstract sessions to hear about the accomplishments of our students, trainees, and other attendees.

Be sure to attend the cutting edge lectures, poster sessions, and symposia on topics such as “New Insights into ART,” “Sex and Gender Identity and Reproductive Health,” and the ASA Clinical Symposium entitled “Sexual Function and Fertility in the Spinal Cord Injured Male.”

Other highlights of the meeting are our honorary lectures, including:

- The Emil Steinberger Memorial Lecture: “Making a Good Genome for the Sperm” by Mary Ann Handel, PhD, The Jackson Laboratory
- WOMEN IN ANDROLOGY LECTURE: “Sperm Interactions with the Female Reproductive Tract” by Susan S. Suarez, MS, PhD, Cornell University
- INTERNATIONAL LECTURE: “Fertility Restoration by Spermatogonial Stem Cell Transplantation” by Takashi Shinohara, PhD, Horizontal Medical Research Organization, Japan
- EAA LECTURE: “Therapeutic Promise of Spermatogonial Stem Cells,” by Stefan Schlatt, PhD, University of Muenster, Germany
- AUA LECTURE: “Regenerative Medicine for Genitourinary Organs,” by Anthony Atala, MD, Wake Forest University School of Medicine

Kudos to our local organizing committee, Paul Cooke and Alan Scott Polackwich, for their help with local arrangements. Please join us at our annual banquet to be held at the swinging Cuban supper club, El Tucán, for a fun night of Latin dancing and food with your colleagues!

The ASA is a special society that brings together basic scientists, translational researchers, and clinicians in a stimulating and collegial environment. Enjoy the 42nd Annual Meeting where you can catch up with friends and colleagues, rejuvenate excitement about your science and care of patients with male reproductive disorders and learn about the latest scientific and therapeutic advances in male reproductive health.

Mary M. Lee, MD, FAAP
Professor and Stoddard Chair of Pediatrics
President, American Society of Andrology

PRESIDENT’S WELCOME

Past Presidents of the American Society of Andrology

<table>
<thead>
<tr>
<th>Year</th>
<th>President</th>
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<tr>
<td>1975-77</td>
<td>Emil Steinberger*</td>
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<tr>
<td>1977-78</td>
<td>Don W. Fawcett*</td>
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<tr>
<td>1978-79</td>
<td>C. Alvin Paulsen*</td>
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<td>1979-80</td>
<td>Nancy J. Alexander</td>
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<td>1980-81</td>
<td>Philip Troen</td>
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<td>1981-82</td>
<td>Richard M. Harrison</td>
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<td>1982-83</td>
<td>Richard J. Sherins</td>
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<td>1983-84</td>
<td>Andrzej Bartke</td>
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<td>1984-85</td>
<td>Rudi Ansbacher</td>
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<td>1985-86</td>
<td>Anna Steinberger</td>
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<td>1986-87</td>
<td>William D. Odell</td>
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<td>1987-88</td>
<td>Larry L. Ewing*</td>
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<td>1988-89</td>
<td>C. Wayne Bardin</td>
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<td>1989-90</td>
<td>Rupert Amann</td>
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<td>1990-91</td>
<td>Howard Nankin</td>
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<td>1991-92</td>
<td>David W. Hamilton</td>
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<td>Ronald S. Swerdloff</td>
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<td>1993-94</td>
<td>Bernard Robaire</td>
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<td>1994-95</td>
<td>Glenn R. Cunningham</td>
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<td>1995-96</td>
<td>Marie-Claire Orgebin-Crist</td>
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<td>1996-97</td>
<td>Arnold M. Belker</td>
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<td>Terry T. Turner</td>
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<td>1998-99</td>
<td>Richard V. Clark</td>
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<td>1999-2000</td>
<td>Barry T. Hinton</td>
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<td>J. Lisa Tenover</td>
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<td>Barry R. Zirkin</td>
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<td>2002-2003</td>
<td>Jon L. Pryor</td>
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<td>2003-2004</td>
<td>Gail S. Prins</td>
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<td>2004-2005</td>
<td>William J. Bremner</td>
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<td>2005-2006</td>
<td>Sally Perreault Darney</td>
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<td>2006-2007</td>
<td>Christina Wang</td>
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<td>2007-2008</td>
<td>Terry R. Brown</td>
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<td>Wayne J.G. Hellstrom</td>
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<td>Dolores J. Lamb</td>
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<td>2010-2011</td>
<td>Paul J. Turek</td>
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<td>2011-2012</td>
<td>Gail A. Cornwall</td>
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<td>2012-2013</td>
<td>Donna L. Vogel</td>
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<td>2013-2014</td>
<td>Erwin Goldberg</td>
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<td>2014-2015</td>
<td>Jay I. Sandlow</td>
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<tr>
<td>2015-2016</td>
<td>Vassilios Papadopoulos</td>
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</tbody>
</table>

*Deceased
OFFICERS
President
Mary M. Lee, MD, FAAP
Vice President
Susan A. Rothmann, PhD, HCLD
Secretary
Sylvie Breton, PhD
Treasurer
Rex A. Hess, PhD
Past President
Vassilios Papadopoulos, DPharm, PhD

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Elizabeth Snyder, PhD; Bar Harbor, ME (Chair)
Cristian O’Flaherty, PhD, DVM; Montreal, QC Canada (Vice Chair)
Bylaws Committee
Jannette Dufour, PhD; Lubbock, TX (Co-Chair)
Peter Liu, MBBS, PhD, FRACP; Torrance, CA (Co-Chair)
Clinical Symposium
Joseph P. Alukal, MD; New York, NY (Co-Chair)
Peter Stahl, MD; Scarsdale, NY (Co-Chair)
Communications and Media Committee
Sarah Kimmins, PhD; Ste-Ann-de-Bellevue, QC Canada (Chair)
Diversity Committee
George L. Gerton, PhD; Philadelphia, PA (Co-Chair)
Hooman Sadri-Ardekani, MD, PhD; Lewisville, NC (Co-Chair)
Endowment Committee
Susan A. Rothmann, PhD, HCLD; Cleveland, OH (Chair)
Gail S. Prins, PhD; Chicago, IL (Co-Chair)
Ethics Committee
Ronald W. Lewis, MD, FACS; Augusta, GA (Chair)
Finance Committee
Michael A. Palladino, PhD; West Long Branch, NJ (Chair)

Future Program Committee
Nina Sarah Davis, MD, FACS; Portland, OR (Co-Chair)
Steven M. Schrader, PhD; Cincinnati, OH (Co-Chair)

Future Meetings Committee
Nina Sarah Davis, MD, FACS; Portland, OR (Co-Chair)
John McCarrey, BS, MS, PhD; San Antonio, TX (Co-Chair)

Industrial Relations Committee
Joseph P. Alukal, MD; New York, NY (Chair)

International Liaison Committee
Patricia S. Cuasnicu, PhD; Buenos Aires, Argentina (Chair)

Journal Committee
Rex A. Hess, PhD; Urbana, IL (Chair)

Journal Editors
Douglas T. Carrell, PhD, HCLD; Salt Lake City, UT (Editors-In-Chief)
Manuela Simoni, MD, PhD; Modena, Italy (Editors-In-Chief)
Ewa Rajpert-De Meys, MD, PhD, DMSc; Copenhagen, Denmark (Editor-In-Chief through Dec. 31, 2016)

Laboratory Science Forum
David S. Karabinus, PhD, HCLD; Montpelier, VA (Chair)

Liaison Committee
Cristian O’Flaherty, PhD, DVM; Montreal, QC Canada (Chair)

Local Arrangements Committee
Paul S. Cooke, PhD; Gainesville, FL (Co-Chair)
Alan Scott Polackwich Jr., MD; Miami Beach, FL (Co-Chair)

Membership Committee
Alan Diekman, PhD; Little Rock, AR (Chair)
Mary K. Sampleski, MD; Los Angeles, CA (Co-Chair)

Nominating Committee
Vassilios Papadopoulos, DPharm, PhD; Los Angeles, CA (Chair)

Program Committee
Joseph P. Alukal, MD; New York, NY (Co-Chair)
Sylvie Breton, PhD; Boston, MA (Co-Chair)

Public Affairs and Policy Committee
Ajay K. Nangia, MBBS, FACS; Kansas City, KS (Chair)

Testis Workshop
Leslie Lynn Heckert, PhD; Kansas City, KS (Chair)
Vassilios Papadopoulos, DPharm, PhD; Los Angeles, (Vice Chair)

Trainee Affairs
Sophie La Salle, PhD; Downers Grove, IL (Co-Chair)
Mara Roth, MD; Seattle, WA (Co-Chair)

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Email: info@andrologysociety.org

NOTICE TO READERS
Every effort has been made to ensure the information printed here is correct; however, details are subject to change.
A natural charmer, Miami’s attractions range from the exotic wildlife of the Everglades to the exotic nightlife of South Beach, from a deep blue ocean to a shallow emerald bay, from the mangrove forests of watery Biscayne National Park to the sawgrass prairies of giant Everglades National Park.

More than 20 miles of beaches line the coast from Cape Florida down south to Golden Beach up north, with world-famous Miami Beach in between, offering easy access to swimming, sunning and other recreation. Miles of more secluded sands can be reached only by boat.

**MIAMI BEACH, BAL HARBOUR & SUNNY ISLES BEACH**

Miami’s world-famous beaches start in Miami Beach at South Pointe and run north for miles. By day, South Beach buzzes with shopping, sightseeing and dining, particularly on Lincoln Road, a pretty pedestrian promenade of boutiques, galleries, theaters, clubs and cafes. Nearby, Ocean Drive is the Art Deco icon of Miami Beach.

When the sun goes down, South Beach heats up. Trendy clubs and cafes hit their stride as celebrities, models, artists and tourists flood the streets to see and be seen. Up the coast, bygone glamour and modern renewal converge in North Beach, site of legendary resorts, tucked-away dining gems and a family-friendly beachside recreation area.

Beyond Miami Beach, the town of Surfside offers eclectic shopping and dining, and farther north awaits Bal Harbour, one of the world’s most elegant shopping, residential and vacation enclaves. Next, expansive Haulover Park enables seaside recreation with a marina, picnic facilities and a beach that includes a secluded clothing-optional section.

Last stop: Sunny Isles Beach, busily replacing mid-20th-century motels and diners with gleaming new high-rise resorts and fine dining restaurants, and uber-exclusive Golden Beach, where single-family houses still sit right on the ocean.

**COCONUT GROVE, LITTLE HAVANA, CORAL GABLES & BEYOND**

Nested on Biscayne Bay, Coconut Grove presents a bohemian village of posh boutiques, artsy galleries, eclectic shops, fine eateries, historical sites and thousands of boats. Modern Miami began in the Grove, where visitors can see the bayside home of pioneer Commodore Ralph Monroe. In Coconut Grove Village West, explore the area’s rich Bahamian heritage.

Little Havana remains the soul of the Cuban community. Its main drag, Calle Ocho (Southwest 8th Street), is a party for the senses – enjoy the rich aroma of handmade cigars, the strong taste of café cubano, the rhythmic sound of salsa, and the unique sight of grizzled men wearing guayaberas and playing dominoes. Every March, a million people descend on Calle Ocho for the world’s biggest block party.

South of Little Havana – and a world apart – is Coral Gables, conceived a century ago by George Merrick, who envisioned the Spanish Mediterranean as he planned his city of stately villas, flowing fountains, broad plazas and meandering waterways. Locals love to shop and dine along the city’s signature boulevard, Miracle Mile.

Near South Miami, recreational shoppers find a huge shopping center, Dadeland Mall. Fanning out in all directions are endless residential communities, which make the southwest the largest quarter, from suburban Kendall to agricultural South Miami-Dade and Homestead, including the gateway to the Everglades.
**Testis Workshop:**
*Location: Symphony Ballroom Registration Desk*
- Wednesday, April 19, 2017: 6:00 p.m. – 8:30 p.m.
- Thursday, April 20, 2017: 7:00 a.m. – 6:00 p.m.
- Friday, April 21, 2017: 7:00 a.m. – 6:00 p.m.
- Saturday, April 22, 2017: 7:00 a.m. – 2:00 p.m.

**ASA Annual Conference:**
*Location: Symphony Ballroom Registration Desk*
- Friday, April 21, 2017: 2:00 p.m. – 6:00 p.m.
- Saturday, April 22, 2017: 7:00 a.m. – 7:00 p.m.
- Sunday, April 23, 2017: 7:00 a.m. – 6:00 p.m.
- Monday, April 24, 2017: 7:00 a.m. – 6:00 p.m.
- Tuesday, April 25, 2017: 7:00 a.m. – 12:00 p.m.

**ASA EXHIBIT HALL HOURS**
*Location: Symphony Ballroom Foyer*
- Saturday April 22, 2017: 4:00 p.m. – 9:30 p.m.
- Sunday April 23, 2017: 7:00 a.m. – 4:00 p.m.

**OPTIONAL WORKSHOPS/SYMPHOSIA**

*ASA Andrology Lab Workshop*
“Restoring Strict Morphology Relevance: A Consensus Workshop”
*Date: Saturday, April 22, 2017*
*Time: 8:30 a.m. – 5:30 p.m.*
*Cost: $295 ASA Member (Active or Trainee) and $345 Non-Member*
*Please note the Lab Science Forum Lunch is included in ALW registration fee.
*Approved by ABB Laboratory Accreditation*

*ASA Clinical Symposium*
“Sexual Function and Fertility in the Spinal Cord Injured Male”
*Date: Saturday, April 22, 2017*
*Time: 1:00 p.m. – 4:00 p.m.*
*Cost: This event is complimentary to ASA Conference registered Attendees. However for those who would like to attend this program and are not registering for the ASA meeting, the rate is $75.00 for a Clinical Symposium Only Registration.*

*ASA 3rd Annual Trainee Directed Mini-Symposium*
“Finding Your BISSL: Careers in Andrology”
*Date: Sunday, April 23, 2017*
*Time: 5:15 p.m. – 6:30 p.m.*
*Cost: Included in the ASA Annual Meeting Registration fees - Requires RSVP.*

**SPECIAL EVENTS**

**Testis Workshop Welcome Reception**
*Date: Wednesday, April 19, 2017*
*Time: 8:15 p.m. – 9:30 p.m.*
*Location: Upper Pool Terrace*
*Dress: Business casual or casual attire is appropriate*
*Cost: One ticket included in TW registration; $25.00 for additional tickets.*

**ASA Luncheons**

**Lab Science Forum Luncheon**
“Discordance and the Lab: Evaluating and Processing Semen from Virus-Infected Patients”
*Date: Saturday, April 22, 2017*
*Time: 12:00 p.m. – 1:30 p.m.*
*Location: Concerto B*
*Speaker: Erma Z. Drobnis, PhD, HCLD*
*Cost: $35.00 for Attendees (Member/Non-Member).*
*Lab Science Forum Lunch included in ALW registration fee.*

**Mentoring Luncheon**
“Experiment With Your Career (Or Why You Can Do Almost Anything When Trained as a Scientist)“
*Sponsored by the Diversity and Trainee Affairs Committees*
*Date: Sunday, April 23, 2017*
*Time: 12:30 p.m. – 2:00 p.m.*
*Location: Concerto B*
*Speaker: Michael A. Palladino, PhD, Monmouth University*
*Cost: $25.00 for Trainees, $35.00 for Attendees (Member/Non-Member).*

**Women in Andrology Luncheon and Discussion**
*Date: Monday, April 24, 2017*
*Time: 12:30 p.m. – 1:45 p.m.*
*Location: Concerto B*
*Host: Jannette Dufour, PhD, Texas Tech University Health Sciences Center*
*Speakers: Susan Rothmann, PhD, HCLD & Jannette Dufour, PhD*
*Cost: $25.00 for Trainees, $35.00 for Attendees (Member/Non-Member).*
*The Women in Andrology of the American Society of Andrology was formed to promote women’s contributions to and representation in the activities of the ASA, specifically, and the field of Andrology in general.*

**ASA EVENING EVENTS**

**ASA Welcome Reception**
*Date: Saturday, April 22, 2017*
*Time: 8:00 p.m. – 9:30 p.m.*
*Location: Symphony Ballroom Foyer*
*Dress: Business casual or casual attire is appropriate*
*Cost: One ticket included in ASA registration; $25.00 for additional tickets.*

**ASA Trainee Forum and Mixer**
*Date: Sunday, April 23, 2017*
*Time: 7:00 p.m. – 8:30 p.m.*
*Location: Upper Pool Terrace*
*The ASA Trainee Forum and Mixer provides an opportunity for trainee members to meet other trainees, as well as more established members of the society. Senior members of the society will be present in this informal forum and discussion group setting to answer your questions about relevant topics such as grant writing, searching for a post-doctor job, alternative PhD career paths, succeeding in the clinic or lab, etc.*

**ASA Annual Banquet**
*Date: Monday, April 24, 2017*
*Time: 7:00 p.m. – 11:00 p.m.*
*Location: El Tucán, 1111 SW 1st Ave., Miami, FL 33130*
*Close your eyes, take a deep breath and be transported to the bygone era of glitz and glamour. El Tucán is a modern day cabaret that reinvigorates the lavish dinner and show concepts of the 1940’s Havana, Cuba. Nestled in the heart of Miami’s bustling Financial District, the ASA banquet will offer a note-worthy experience featuring a taste of Miami.*
*Cost: $80.00 for Attendees (Member/Non-Member), $40.00 for Trainees.*
*Includes dinner, cocktails and entertainment. Please sign up for this event on the registration form.*

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Andrology, 2017, Supplement, 8
MESSAGE FROM THE PROGRAM CO-CHAIRS

Friends and Colleagues:

On behalf of the ASA Program Committee, we are pleased to welcome you to the 42nd Annual Meeting of the American Society of Andrology. This year’s theme is “New Concepts and Perspectives in Male Reproductive Health.” This topic honors the history, commitment, and dedication of professionals who focus time and expertise to advance the reproductive health of men.

This year, we are bringing together the concepts of male reproductive health and men’s overall health. We have assembled an exciting program that features world-renowned scientific leaders, who will highlight recent advances in a variety of complementary andrology disciplines. The fields of both clinical andrology and reproductive medicine are constantly and rapidly evolving, thanks to fundamental, translational and clinical research in urology, reproductive molecular and cell biology, reproductive technologies, endocrinology, and genetics. The tradition of the Society’s meeting is to disseminate scientific knowledge and promote interactions between basic researchers and clinical scientists at all professional levels, from trainees to seasoned investigators and clinicians. We are thankful to our lecturers, symposium speakers, session chairs and trainee co-chairs for their contribution to this stimulating meeting. We would also like to thank the Program Committee members, who were instrumental in the selection of topics and speakers for this meeting, and we thank WJ Weiser & Associates for their expert handling of the many logistics associated with the organization of this meeting.

The ASA remains highly committed to the success of Andrology trainees, and we are pleased to mention that we are continuing to feature the trainee symposium as an integral part of the 2017 Annual Meeting – the symposium will be followed by a formal presentation of trainee awards. We also invite you to attend the lively Trainee Forum and Mixer that will take place immediately after the trainee award ceremony on Sunday.

We have seen significant advances in many areas of andrology, including testicular and male reproductive tract biology, spermatogenesis, genetics, immunology, cancer and environmental biology. Together we are, therefore, in a unique position to promote and develop novel diagnostics and therapeutic interventions aimed at preserving male reproductive health, fertility, and sexual function, in the context of men’s overall health.

Finally, we would like to extend our gratitude to the past and present presidents of the ASA, Vassilios Papadopoulos and Mary M. Lee for providing us with the opportunity to serve as program co-chairs for the 2017 ASA Annual Meeting.

We hope you will enjoy the meeting in warm and beautiful Miami!

Joseph Alukal, MD  Sylvie Breton, PhD

PROGRAM COMMITTEE

Joseph P. Alukal, MD; New York, NY (Co-Chair)
Sylvie Breton, PhD; Boston, MA (Co-Chair)
Robert Edward Brannigan, MD; Hinsdale, IL
Arthur L. Burnett II, MD, MBA; Baltimore, MD
Peter Chan, MD; Montreal, QC Canada
Gail A. Cornwall, PhD; Lubbock, TX
Kathleen Hwang, MD; Providence, RI
Ralph G. Meyer, PhD; Mendon, UT
Moira K. O’Bryan, BSc, PhD; Clayton South, VIC Australia
Kyle Orwig, PhD; Pittsburgh, PA
Gail S. Prins, PhD; Chicago, IL
Peter Stahl, MD; Scarsdale, NY
Cigdem Tanrikut, MD; Boston, MA
Robert S. Viger, PhD; Quebec City, QC Canada
Pablo E. Visconti, PhD; Amherst, MA
Thomas J. Walsh, MD, MS; Seattle, WA

CLINICAL SYMPOSIUM

Joseph P. Alukal, MD; New York, NY (Co-Chair)
Peter J. Stahl, MD; Scarsdale, NY (Co-Chair)
Mary Ann Handel

Dr. Handel received a BA degree from Goucher College in Baltimore, Maryland, and her PhD from Kansas State University. She conducted postdoctoral research on gamete differentiation at the Oak Ridge National Laboratory, in Oak Ridge, Tennessee. After many years on the faculty at the University of Tennessee, Knoxville, she assumed her present position as senior research scientist at The Jackson Laboratory. Her research interests are in the field of male reproductive biology, to which she brings an extensive and in-depth background in experimental investigation of the genetics of meiosis and male germ-cell biology, using the laboratory mouse as an experimental model. Her recent work focuses on the roles of chromosomal axis proteins in the early stages of meiotic recombination, chromosome homology recognition, and synopsis. More broadly, she has published on the genetic control of spermatogenesis, the meiotic cell cycle and meiotic nuclear domains. Additionally she has considerable experience analyzing male infertility phenotypes in mouse mutants and co-directed a mutagenesis program that identified many mouse models for reproductive genomics. Dr. Handel also has an extensive mentoring record, including mentoring of undergraduate, predoctoral and postdoctoral scholars, in both academic as well as private research institutional environments. Overall, she has mentored 11 postdoctoral fellows, 16 graduate students, 35 undergraduate research students and two teacher interns. Most of her postdoctoral fellows and PhD students have achieved independent academic teaching and/or research positions. Dr. Handel is active in reproductive sciences nationally. She is a fellow of the American Association for the Advancement of Science, and a member of the Society for the Study of Reproduction (SSR), Genetics Society of America, American Society for Andrology, and International Mammalian Genome Society. She participates frequently as a reviewer for NIH study sections and as a member of advisory boards and committees of federal and international funding agencies. She was editor-in-chief (2004 - 2009) and consulting editor (2009 - 2013) of Biology of Reproduction, served on the board of directors of the SSR, and currently serves as co-chair of the Publications Committee of the SSR.
Anthony Atala, MD  
*Wake Forest School of Medicine*

Dr. Atala is the director of the Institute for Regenerative Medicine, and chair of urology at Wake Forest University. He is editor in chief of *Stem Cells Translational Medicine and BioPrinting*.

Dr. Atala is a recipient of the US Congress funded Christopher Columbus Award, the World Technology Award in Medicine, the Samuel Gross Prize, the Innovation Award from the Society of Manufacturing Engineers, and the Edison Science/Medical Award. He was elected to the National Academy of Medicine in 2011, and to the National Academy of Inventors in 2014. His work was listed twice in *Time* magazine’s top 10 medical breakthroughs of the year. He was named by *Scientific American* as one of the world’s most influential people in biotechnology in 2015. He also received the Innovator of the Year Award from *R & D Magazine* in 2016.

Dr. Atala has led several NIH working groups and was the founder of the Regenerative Medicine Foundation. He heads a team of over 450 researchers, and 12 applications of technologies developed in his laboratory have been used clinically. He is editor of 14 books, has published over 500 articles and has applied for or received over 250 national and international patents.

The Outstanding Trainee Investigator Award is given to the ASA trainee member with the best abstract and research presentation at the annual meeting. The award encourages trainee members to submit and present their best work and contribute to the scientific excellence of the Society.

The recipient of the 2017 Outstanding Trainee Investigator Award will be announced during the Presentation of Trainee Awards on Sunday, April 23, 2017, at 6:30 p.m.

### NEW INVESTIGATOR AWARD RECIPIENTS

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<tr>
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<td>1983</td>
<td>Thomas T. Tarter</td>
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<td>1984</td>
<td>Peter S. Albertson</td>
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<td>1985</td>
<td>Randall S. Zane</td>
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<td>1986</td>
<td>Mark A. Hadley</td>
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<td>1987</td>
<td>Peter Grosser</td>
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<td>Stuart E. Ravnik</td>
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<td>1989</td>
<td>Tracy L. Rankin</td>
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<td>Donna O. Bunch</td>
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<td>1991</td>
<td>Robert Viger</td>
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<td>1992</td>
<td>John Kirby</td>
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<td>Michael A. Palladino</td>
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<td>1994</td>
<td>Linda R. Johnson</td>
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<td>Mehdi A. Akhondi</td>
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<td>Wei Gu, Daniel B. Rudolph</td>
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<td>Loren D. Walensky</td>
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<td>Dolores D. Mruk</td>
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<td>Jacques J. Tremblay</td>
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<td>Jeffrey J. Lysiak</td>
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<td>Alexander T.H. Wu</td>
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<td>2002</td>
<td>Ebtesam Attaya</td>
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<td>2003</td>
<td>Mustafa Faruk Usta</td>
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### OUTSTANDING TRAINEE INVESTIGATOR AWARD RECIPIENTS

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<tr>
<td>2004</td>
<td>Darius Paduch</td>
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<td>Tara Barton</td>
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<td>2014</td>
<td>Andrew Midzak</td>
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<td>2015</td>
<td>Qi Fu</td>
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<td>2016</td>
<td>Namarata Khurana</td>
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DISTINGUISHED ANDROLOGIST AWARD

This is the highest award of the Society, presented annually to an individual who has made an outstanding contribution to the progress of Andrology.

Masaru Okabe, PhD
Osaka University

Dr. Masaru Okabe received his PhD from Osaka University and has spent the entirety of his career researching at that institution, with the exception of 1.5 years at the National Institute of Environmental Health Sciences in Research Triangle Park, North Carolina.

He is a Professor Emeritus of the Research Institute for Microbial Diseases at Osaka University. He was the director of the Animal Resource Center for Infectious Diseases in that Institute from 2002 - 2013. He has published over 250 original articles. His general research area is reproduction, with specific research interests including the mechanism of sperm-egg interaction. He published the first fusion factor of mouse sperm and mouse egg in Nature and Science, respectively. He believes in the power of gene manipulated animals and utilizes many transgenic and knockout mouse lines in his research. He is also known as the scientist who made the world’s first “green mice.”

DISTINGUISHED ANDROLOGISTS

1976  Roy O. Greep & M.C. Chang
1977  Robert E. Mancini
1978  Robert S. Hotchkiss
1979  Thaddeus Mann
1980  John MacLeod
1981  Alexander Albert
1982  Eugenia Rosemberg
1983  Kristen B.D. Eik-Nes
1984  Mortimer B. Lipsett
1985  Robert H. Foote
1986  Alfred D. Jost
1987  Emil Steinberger
1988  Yves W. Clermont
1989  C. Alvin Paulsen
1990  Marie-Claire Orgebin-Crist
1991  Philip Troen
1992  C. Wayne Bardin
1993  Anna Steinberger
1994  Richard J. Sherins
1995  Rupert P. Amann
1996  J. Michael Bedford
1997  Brian P. Setchell
1998  Ryozi Yanagimachi
1999  Richard D. Amelar
2000  Bayard T. Storey
2001  Frank S. French
2002  Geoffrey M. H. Waites
2003  David M. de Kretser
2004  Ronald Swerdloff
2005  Mitch Eddy
2006  Norman Hecht
2007  Eberhard (Ebo) Nieschlag
2008  Bernard Robaire
2009  William Bremner
2010  Dolores Lamb
2011  Barry Zirkin
2012  Erwin Goldberg
2013  Christina Wang
2014  Gail S. Prins
2015  Deborah A. O’Brien
2016  Barry T. Hinton

The Distinguished Andrologist Award is sponsored by the Eugenia Rosemberg Endowment Fund

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DISTINGUISHED SERVICE AWARD

This award is bestowed annually to recognize an individual who has provided distinguished service to The American Society of Andrology.

Janice P. Evans, PhD  
Johns Hopkins University

Janice Evans, PhD, is a professor in the Department of Biochemistry and Molecular Biology in the Bloomberg School of Public Health at Johns Hopkins University. She graduated cum laude from Davidson College, majoring in biology, and then went on to earn her PhD from the University of North Carolina at Chapel Hill. She did post-doctoral fellowships at Scripps Research Institute, in the Department of Cell Biology, and at the University of Pennsylvania, in the Center for Research on Reproduction and Women’s Health. She joined the Johns Hopkins faculty in 1998. Her research program examines mammalian gamete biology and fertilization, with one current focus being the oocyte’s progression through meiosis. She also has been very active in her scientific community, including having been the chair or co-chair of the 2011 Gordon Research Conference on Fertilization and Activation of Development, the 2012 meeting of the American Society of Andrology (ASA), and the 2013 meeting of the Society for the Study for Reproduction (SSR). In these two societies in which she has been most active, the ASA and SSR, she has chaired seven different committees, served on both societies’ governing bodies (the Executive Council and Board of Directors, respectively), served as treasurer of the ASA, and currently is vice president-elect of the SSR, to serve as president in 2018-2019. At Johns Hopkins, she was selected for participation in the SOURCE [Student Outreach Resource Center] Faculty Fellows program for 2014-2015, and the Johns Hopkins Leadership Program for Women Faculty in 2015-2016, and won the Service-Learning Award for Faculty Excellence in Teaching in 2016.

DISTINGUISHED SERVICE AWARD RECIPIENTS

1994 C. Alvin Paulsen  
1995 Andrzej Bartke  
1996 Philip Troen  
1997 Marie-Claire Orgebin-Crist  
1998 Rupert P. Amann  
1999 David W. Hamilton  
2000 Bernard Robaire  
2001 Gail S. Prins  
2002 Terry T. Turner  
2003 Arnold M. Belker  
2004 J. Lisa Tenover  
2005 Barry Hinton  
2006 Barry Zirkin  
2007 Sally Perreault Darney  
2008 Matthew P. Hardy  
2009 Erwin Goldberg  
2010 Joel L. Marmar  
2011 Christina Wang  
2012 Terry R. Brown  
2013 Rex A. Hess  
2014 Susan Rothmann  
2015 Steven M. Schrader  
2016 Donna L. Vogel

Distinguished Service Award is sponsored by the American Society of Andrology.
MATTHEW P. HARDY
YOUNG ANDROLOGIST AWARD

This annual award is bestowed upon an Active Member of the American Society of Andrology who at the time of the award, is less than forty-five (45) years of age and who has made significant contributions to the field of Andrology.

Polina V. Lishko, PhD

Polina V. Lishko, PhD, received a doctorate in biophysics in 2000 from the Bogomoletz Institute of Physiology of the National Academy of Sciences of Ukraine, where she worked with Dr. Oleg Krishtal on regulation of ion channels in hippocampal neurons. She engaged in postdoctoral research with Dr. Vadim Arshavsky of Harvard Medical School working on molecular mechanisms of phototransduction in mammalian retina. From 2005, she worked as postdoctoral researcher in Dr. Rachelle Gaudet at Harvard University, and studied structure function relation of TRPV channels. From 2006 to 2011, Dr. Lishko was an instructor at the University of California, San Francisco (UCSF), where she studied regulation of sperm physiology by ion channels. In 2012, she joined the faculty of the University of California, Berkeley, as an assistant professor of molecular and cell biology.

MATTHEW P. HARDY YOUNG ANDROLOGIST AWARD RECIPIENTS

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<thead>
<tr>
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<td>L.J.D. Zaneveld</td>
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<td>William B. Neaves</td>
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<td>Barry T. Hinton</td>
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<td>Luis Rodriguez/Rigau</td>
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<td>Patricia M. Saling</td>
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<td>Gary R. Klinefelter</td>
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<td>Robert Chapin</td>
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<td>Matthew P. Hardy</td>
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<td>Jacquetta Trasler</td>
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<td>Christopher L.R. Barratt</td>
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<td>Joanna E. Ellington</td>
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<td>Kate Loveland</td>
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<td>John K. Amory</td>
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<td>Moira K. O’Bryan</td>
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<td>Michael A. Palladino</td>
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<td>Peter Liu</td>
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<td>Jacques J. Tremblay</td>
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<td>2014</td>
<td>Sarah Kimmins</td>
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<td>Jon M. Oatley</td>
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<td>2016</td>
<td>Lee B. Smith</td>
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</table>

The Matthew P. Hardy Young Andrologist Award is sponsored by the Matthew P. Hardy Endowment Fund
THANK YOU TO DONORS & SPONSORS

The American Society of Andrology, Inc. gratefully acknowledges these lifetime contributions to the various ASA Endowment or Asset Funds

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July 1, 2016 - January 31, 2017

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Thank You to Our 2017 Educational Grant Supporters
American Urological Association, Inc.

Please Be Sure to Attend the Following Industry Satellite Symposium

SATURDAY, APRIL 22, 2017

12:00 p.m. - 1:00 p.m.  Industry Satellite Symposium Lunch
Location: Concerto D
“Managing and Minimizing IPP Complications”

Doron Stember, MD
New York, NY
EDUCATIONAL NEEDS AND OBJECTIVES

42nd Annual ASA Conference
“New Concepts and Perspectives in Male Reproductive Health”

COURSE DESCRIPTION
The diagnosis and management of many conditions in andrology have been greatly influenced by recent pharmacological, surgical and basic science advances. One of the greatest challenges in this discipline is to keep abreast of the many dynamic changes in this field. An internationally acclaimed faculty has been assembled to provide this update, with presentations on topics such as Transgender Surgery, Genitourinary Tissue Regeneration, Male Sexual Dysfunction, Male Infertility, Reproductive Biology, and Stem Cell Biology. During the plenary sessions, attendees will have the opportunity to participate in question and answer sessions.

TARGET AUDIENCE
Practicing community and academic urologists, PhD researchers, PhD candidates, andrology lab personnel, physician extenders in fertility and urology practices, DVM practitioners and candidates with reproductive focus

EDUCATIONAL NEEDS
There have been many recent advances in both the basic science and clinical understanding of male reproductive health. Urologists and basic scientists should be up-to-date on the latest advances, research efforts, and treatment recommendations regarding conditions such as azoospermia, intersex conditions, and the specific concerns of transgendered individuals. Reproductive urologists treat conditions such as varicocele, obstructive and non-obstructive azoospermia, and gender disorder as well as buried penis, and complications of transgender surgery. These practitioners need to be updated on the advances in diagnostic modalities and treatment options for these conditions. Many collaborating PhD researchers working in reproductive biology and cell biology do not have an awareness of the clinical management of these conditions, their relatively high prevalence, and the need for an increased understanding of underlying biology of these conditions. Researchers will benefit from awareness of the epidemiology of these conditions, both in terms of their commonality and their predisposition to other urologic and general disease. Furthermore, an understanding of the epidemiologic impact of the treatment for these conditions (in terms of risk to offspring) is vital.

An awareness of future directions for research is useful to the audience as well; updated reviews of spermatogenesis and sperm-cell interactions will help identify future targets for contraceptive treatments and novel treatments in fertility medicine. Finally, new frontiers in clinical medicine including cell culture techniques for spermatogonial stem cells and tissue engineering of urological organs will be explored.

A review of these topics will prove hugely useful to urologists and other MDs, PhD researchers, DVMs and trainees as well as physician extenders in andrology and laboratory professionals working in fertility medicine.

EDUCATIONAL OBJECTIVES
At the conclusion of the ASA 42nd Annual Conference, participants should be able to:

- Review the latest guidelines on the management of male infertility.
- Discuss the epidemiologic importance of male infertility.
- Discuss the epidemiologic impact of treatments for male infertility such as intracytoplasmic sperm injection (ICSI).
- Review the current understanding of spermatogonial stem cell biology.
- Apply lessons regarding appropriateness of transgender surgery to urologic practice.
- Discuss the current understanding of appropriate development of external genitalia in the context of intersex conditions.
- Review the new opportunities for tissue engineering in the management of urological disease.
- Discuss the current understanding of sperm-cell interactions (in the male epididymis, the female reproductive tract, etc.) with the goal of identifying opportunities for modification of sperm function.
- Review the advances in understanding of human and animal spermatogenesis.

2017 ASA CLINICAL SYMPOSIUM
“Sexual Function and Fertility in the Spinal Cord Injured Male”

EDUCATIONAL NEEDS
Education and training are lacking for clients and practitioners in the management of infertility in men with SCI. Most infertility specialists do not evaluate the male partner of an infertile couple and often do not even refer the men for fertility evaluations. Most urologists have not had much training or exposure in the techniques of sperm retrieval via assisted ejaculation.

EDUCATIONAL OBJECTIVES
At the conclusion of the ASA Clinical Symposium, attendees should be able to:

- Explain causes of infertility in men with spinal cord injury.
- Distinguish the unique characteristics of infertility in men with spinal cord injury.
- Explain methods of semen retrieval in men with spinal cord injury.
- Assess the fertility status of a man with spinal cord injury and formulate a plan of management appropriate for his sperm quality.
ACCREDITATION STATEMENT

Category 1
Creighton University Health Sciences Continuing Education designates this live activity for a maximum of 19.25 AMA PRA Category 1 Credit(s)™. Physicians should claim only credit commensurate with the extent of their participation in this activity.

AAPA accepts AMA category 1 credit for the PRA from organizations accredited by ACCME.

Accreditation Statement
This activity has been planned and implemented by Creighton University Health Sciences Continuing Education (HSCE) and the American Society of Andrology for the advancement of patient care. Creighton University Health Sciences Continuing Education is accredited by the American Nurses Credentialing Center (ANCC), the Accreditation Council for Pharmacy Education (ACPE), and the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing education for the healthcare team.

Nurses and other healthcare professionals will receive a Certificate of Attendance. For information on the applicability and acceptance of Certificates of Attendance for educational activities certified for AMA PRA Category 1 Credit™ from organizations accredited by the ACCME, please consult your professional licensing board.

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Special Assistance
We encourage participation by all individuals. If you have a disability, advance notification of any special needs will help us better serve you. Call (847) 619-4909 if you require special assistance to fully participate in the meeting.
# SCHEDULE OF EVENTS

**The XXIV North American Testis Workshop**  
**“From Testis Differentiation to Sperm Production”**  
**April 19 – 22, 2017**

**The Hilton Miami Downtown**

Program Chairs: Leslie L. Heckert, PhD and Vassilios Papadopoulos, DPharm, PhD  
All sessions will be held in *Symphony Ballroom III/IV* unless otherwise noted.

## WEDNESDAY, APRIL 19, 2017

<table>
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<tr>
<th>Time</th>
<th>Event</th>
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<tr>
<td>6:00 p.m. - 8:30 p.m.</td>
<td>Registration/Information Desk Open</td>
<td><em>Symphony Ballroom Registration</em></td>
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<tr>
<td>7:00 p.m. - 7:15 p.m.</td>
<td>Welcome and Opening Remarks Program Chair: Leslie L. Heckert, PhD University of Kansas Medical Center</td>
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</tbody>
</table>
| 7:15 p.m. - 8:15 p.m. | **KEYNOTE ADDRESS:**  
Comparison Between Human and Rodent Spermatogonial Renewal and Differentiation  
Dirk De Rooij, PhD  
Universiteit Utrech, the Netherlands |  

**8:15 p.m. - 9:30 p.m.** Testis Workshop Welcome Reception  
*Location: Upper Pool Terrace*

## THURSDAY, APRIL 20, 2017

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<th>Time</th>
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<td>7:00 a.m. - 6:00 p.m.</td>
<td>Registration/Information Desk Open</td>
<td><em>Symphony Ballroom Registration</em></td>
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<td>7:15 a.m. - 8:00 a.m.</td>
<td>Continental Breakfast Location: <em>Symphony Ballroom Foyer</em></td>
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<tr>
<td>8:00 a.m. - 8:55 a.m.</td>
<td>Benchmark Lecture I</td>
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**8:00 a.m. - 8:05 a.m.** Chair and Introduction  
Michael D. Griswold, PhD  
*Washington State University*

**8:05 a.m. - 8:55 a.m.** Uniting the Genome: Multifaceted Roles of piRNAs during Spermatogenesis  
Haifan Lin, PhD  
*Yale University Stem Cell Center*

## SESSION I: GERMLINE ESTABLISHMENT & HOMEOSTASIS

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<th>Time</th>
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| 8:55 a.m. - 9:00 a.m. | Chair and Introduction to Session I  
Jon M. Oatley, PhD |  

**9:00 a.m. - 9:40 a.m.** Dynamics of Stem Cell Replacement in the Drosophila Testis Niche  
Erika Matunis, PhD  
*Johns Hopkins University*

**9:40 a.m. - 10:20 a.m.** Defining Spermatogonial Stem Cell Transcriptomes at the Single-Cell Level  
Brian P. Hermann, PhD  
*University of Texas at San Antonio*

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<tr>
<td>10:20 a.m. - 10:40 a.m.</td>
<td>Break Location: <em>Symphony Ballroom Foyer</em></td>
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| 10:40 a.m. - 11:20 a.m. | Differential Requirements for the ‘Mechanistic Target of Rapamycin’ (mTOR) and mTORC1 Component Raptor in Spermatogonial Development in the Mouse  
Christopher Geyer, PhD  
*East Carolina University*

## SESSION II: GERM CELL DIFFERENTIATION AND MAINTENANCE - THE ROLE OF RNA & RBP’S

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<th>Time</th>
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| 11:35 a.m. - 11:50 a.m. | Short Talk #2  
Conservation of a Gene Expression Barcode that Defines Spermatogonial Stem Cells in Mice and Humans  
Presented by: Anukriti Singh, BTech  
*University of Texas* |  

**1:10 p.m. - 1:15 p.m.** Chair and Introduction to Session II  
Wei Yan, PhD  
*University of Nevada*

**1:15 p.m. - 1:55 p.m.** Distinct Functions of Nanos2 and Nanos3 During Spermatogenesis  
Yumiko Saga, DSc  
*National Institute of Genetics Japan*

**1:55 p.m. - 2:35 p.m.** GASZ Interacts with Mitofusins to Regulate Spermatogenesis  
Yuan Wang, PhD  
*East China Normal University*

**2:35 p.m. - 2:55 p.m.** Break  
*Location: Symphony Ballroom Foyer*

**2:55 p.m. - 3:35 p.m.** Regulation of Testis Transcriptome by the MOV10 RNA Helicase  
Jeremy Wang, MD, PhD  
*University of Pennsylvania*  

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Andrology, 2017, Supplement, 19
SCHEDULE OF EVENTS

FRIDAY, APRIL 21, 2017

7:00 a.m. - 6:00 p.m.  Registration/Information Desk Open
Location: Symphony Ballroom Registration

7:15 a.m. - 8:00 a.m.  Continental Breakfast
Location: Symphony Ballroom Foyer

8:00 a.m. - 8:55 a.m.  Benchmark Lecture II

8:00 a.m. - 8:05 a.m.  Chair and Introduction
Dolores J. Lamb, PhD, HCLD

8:05 a.m. - 8:55 a.m.  New Insights into the Causes and Consequences of Male Infertility
John R. Aitken, PhD, ScD, FRSE, FSRB
University of Newcastle Australia

8:55 a.m. - 9:00 a.m.  Chair and Introduction to Session III
Jannette Dufour, PhD
Texas Tech University Health Sciences Center

9:00 a.m. - 9:40 a.m.  Control of Post-Natal Testis Development by the Sertoli Cells
Peter O'Shaughnessy, PhD
University of Glasgow Veterinary School, Ireland

9:40 a.m. - 10:20 a.m.  New Insights into Fate Deamination and Maintenance of the Testis
Humphrey H. Yao, PhD
NIEHS/NIH

10:20 a.m. - 10:40 a.m.  Break
Location: Symphony Ballroom Foyer

10:40 a.m. - 11:20 a.m.  Evidence that Nucleocytoplasmic Transport Proteins Mediate Environmental Cues Required for Male Fertility
Kate Loveland, PhD
Monash University and Hudson Institute of Medical Research

SESSION III: TESTIS DEVELOPMENT & DIFFERENTIATION

1:10 p.m. - 1:15 p.m.  Chair and Introduction to Session IV
Ralph Meyer, PhD
Utah State University

1:15 p.m. - 1:55 p.m.  Spermatogenesis Requires Classical and Nonclassical Testosterone Signaling
William H. Walker, PhD
University of Pittsburgh

1:55 p.m. - 2:35 p.m.  The CAMKI-MEF2-NUR77-AMPK Cascade in the Regulation of Leydig Cell Steroidogenesis
Jacques J. Tremblay, PhD
Laval University, Canada

2:35 p.m. - 2:50 p.m.  Short Talk #7
ADCY2 is a Candidate Gene for the Development of Congenital Genitourinary Anomalies Through Partial Disruption of Steroidogenesis
Presented by: Marisol O’Neill, MS
Baylor College of Medicine

SESSION IV: TRANSCRIPTIONAL & ENDOCRINE REGULATION IN THE TESTIS

3:10 p.m. - 3:15 p.m.  Chair and Introduction to Session V
Vassilios Papadopoulos, DPharm, PhD
University of Southern California

3:15 p.m. - 3:35 p.m.  Spermatogenesis as a Model System to Define Katanin Function
Moira K. O’Bryan, BSc, PhD
Monash University, Australia

3:35 p.m. - 4:35 p.m.  Intercellular Networks and Luminal Acidification in the Epididymis
Sylvie Breton, PhD
Massachusetts General Hospital

4:35 p.m. - 4:50 p.m.  Short Talk #8  
Mutation of a Single Amino Acid of Meiosis-Expressed Gene 1 by CRISPR/CAS9 System Results in Impaired Spermiogenesis and Male Infertility in Mice  
Presented by: Shiyang Zhang  
Virginia Commonwealth University

4:50 p.m. - 6:50 p.m.  Poster Session II  
Location: Symphony Ballroom I/II

SATURDAY, APRIL 22, 2017

7:00 a.m. - 2:00 p.m.  Registration/Information Desk Open  
Location: Symphony Ballroom Registration

7:15 a.m. - 8:00 a.m.  Continental Breakfast  
Location: Symphony Ballroom Foyer

8:00 a.m. - 9:00 a.m.  Benchmark Lecture III

8:00 a.m. - 8:05 a.m.  Chair and Introduction  
Prabhakara Reddi, PhD  
University of Illinois Urbana Champaign

8:05 a.m. - 8:55 a.m.  Daddy Issues: Effects of the Paternal Environment on Future Generations  
Oliver J. Rando, PhD, MD  
University of Massachusetts

SESSION VI: GENETICS & EPIGENETICS OF MALE REPRODUCTION

8:55 a.m. - 9:00 a.m.  Chair and Introduction to Session VI  
Jacquetta Trasler, MD, PhD  
McGill University Health Centre

9:00 a.m. - 9:40 a.m.  Humanized Infertility Alleles in Mice Reveal Novel Gene Activities  
John Schimenti, PhD  
Cornell University

9:40 a.m. - 10:00 a.m.  Break  
Location: Symphony Ballroom Foyer

10:00 a.m. - 10:40 a.m.  Environmental Programming of the Sperm Epigenome  
Sarah Kimmins, PhD  
McGill University, Canada

10:40 a.m. - 11:20 a.m.  Niacin: A Dietary Factor Influencing Sperm Quality and Epigenetic Information  
Mirella Meyer-Ficca, PhD  
Utah State University

11:20 a.m. - 11:35 a.m.  Introduction to the NICHD Contraceptive Research Program  
Daniel S. Johnston, PhD  
NIH, NICHD

11:35 a.m. - 11:50 a.m.  Concluding Remarks & Acknowledgments  
Vassilios Papadopoulos, DPharm, PhD

11:50 a.m. - 12:00 p.m.  Announcement of the 25th North American Testis Workshop

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Andrology, 2017, Supplement, 21
## SCHEDULE OF EVENTS

American Society of Andrology 42nd Annual Conference  
“New Concepts and Perspectives in Male Reproductive Health”  
April 22 – 25, 2017  

Program Chairs: Sylvie Breton, PhD and Joseph Alukal, MD  
All sessions will be held in **Symphony Ballroom III/IV** unless otherwise noted.

### FRIDAY, APRIL 21, 2017

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<th>Time</th>
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<tr>
<td>2:00 p.m. - 6:00 p.m.</td>
<td>Registration/Information Desk Open</td>
<td>Symphony Ballroom Registration</td>
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<tr>
<td>5:00 p.m. - 10:00 p.m.</td>
<td>Executive Council Meeting and Dinner</td>
<td>Concerto B</td>
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### SATURDAY, APRIL 22, 2017

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<th>Time</th>
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<td>7:00 a.m. - 7:00 p.m.</td>
<td>Registration/Information Desk Open</td>
<td>Symphony Ballroom Registration</td>
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<tr>
<td>4:00 p.m. - 9:30 p.m.</td>
<td>Exhibit Hall Open</td>
<td>Symphony Ballroom Foyer</td>
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<tr>
<td>8:30 a.m. - 5:30 p.m.</td>
<td><em>ASA Andrology Lab Workshop</em> (See page 26 for full program schedule)</td>
<td>Concerto A</td>
</tr>
<tr>
<td>12:00 p.m. - 1:30 p.m.</td>
<td>LAB SCIENCE FORUM LUNCHEON “Disordance and the Lab: Evaluating and Processing Semen from Virus-Infected Patients”</td>
<td>Concerto B</td>
</tr>
<tr>
<td>12:00 p.m. - 1:00 p.m.</td>
<td>Industry Satellite Symposium Lunch</td>
<td>Concerto D</td>
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<tr>
<td>1:00 p.m. - 4:00 p.m.</td>
<td>ASA Clinical Symposium</td>
<td>Symphony Ballroom III/IV</td>
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### SUNDAY, APRIL 23, 2017

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<tr>
<th>Time</th>
<th>Event</th>
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<tr>
<td>6:30 a.m. - 8:00 a.m.</td>
<td>Past President's Breakfast</td>
<td>Concerto D</td>
</tr>
<tr>
<td>7:00 a.m. - 6:00 p.m.</td>
<td>Registration/Information Desk Open</td>
<td>Symphony Ballroom Registration</td>
</tr>
<tr>
<td>7:00 a.m. - 4:00 p.m.</td>
<td>Exhibit Hall Open</td>
<td>Symphony Ballroom Foyer</td>
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</table>
| 8:00 a.m. - 9:00 a.m. | LECTURE I: The Importance and Strategy for Placing Male Reproductive Health in the Centre Stage in the Political and Research Agenda  
(Introduced by Sylvie Breton, PhD)  
Christopher Barratt, PhD  
University of Dundee, United Kingdom | Symphony Ballroom III/IV          |
| 9:00 a.m. - 9:15 a.m. | Distinguished Service Award  
(Introduced by Janice L. Bailey, PhD)  
2017 Recipient: Janice P. Evans, PhD | Symphony Ballroom III/IV          |
| 9:15 a.m. - 10:45 a.m. | SYMPOSIUM I - New Insights into ART  
Moderator: Peter Chan, MD | Symphony Ballroom III/IV          |
| 9:15 a.m. - 10:45 a.m. | Childhood Outcomes Following Infertility and Infertility Treatment  
Mary Croughan, PhD  
University of California San Francisco | Symphony Ballroom III/IV          |
| 9:45 a.m. - 10:15 a.m. | Implications of the Aging Male Gamete on ART Outcome  
Gianpiero Palermo, MD  
Weill Cornell Medical, Reproductive Medicine | Symphony Ballroom III/IV          |
| 10:15 a.m. - 10:45 a.m. | Autism and Other Developmental Disorders in ART  
Sven Sandin, PhD  
Mount Sinai School of Medicine | Symphony Ballroom III/IV          |
| 10:45 a.m. - 11:00 a.m. | Quick Break                                                           | Symphony Ballroom III/IV          |
| 11:00 a.m. - 12:30 p.m. | *Poster Session I  
*Not CME Accredited | Symphony Ballroom III/IV          |
| 12:30 p.m. - 2:00 p.m. | Lunch (on your own)                                                    | Concerto B                        |
| 12:30 p.m. - 2:00 p.m. | MENTORING LUNCHEON  
“Experiment With Your Career (Or Why You Can Do Almost Anything When Trained as a Scientist)”  
Sponsored by the Diversity and Trainee Affairs Committees  
Location: Concerto B  
Michael A. Palladino, PhD | Concerto B                        |

### SUNDAY, APRIL 23, 2017

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<td>8:00 a.m. - 9:30 p.m.</td>
<td>ASA Welcome Reception</td>
<td>Symphony Ballroom Foyer</td>
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<td>12:30 p.m. - 2:00 p.m.</td>
<td>Editorial Board Luncheon</td>
<td>Concerto D</td>
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Andrology, 2017, Supplement, 22
2:00 p.m. - 3:30 p.m.  | CONCURRENT SESSIONS  
Oral Session I (Basic Science)  
Moderator: Clemence Bellecaneen, PhD  
Location: Symphony Ballroom III/IV

2:00 p.m.  
DIFFERENTIAL TOLEROGNIC CAPACITY OF THE EPIDIDYMIS AND TESTIS IN MICE WITH CONDITIONAL DELETION OF TGFBR2 IN DENDRITIC CELLS  
Presented By: Fernando Pierucci-Alves, DVM  
Kansas State University

2:15 p.m.  
HUMANIN TRANSGENIC MICE ARE PROTECTED FROM CYCLOPHOSPHAMIDE-INDUCED MALE GERG CELL APOPTOSIS  
Presented By: YanHe Lue, MD  
LABioMed at Harbor-UCLA

2:30 p.m.  
PATERNAL EXPOSURE TO ENVIRONMENTAL CONTAMINANTS ALTERS THE SPERM PROTEOME AND INDUCES NEGATIVE PREGNANCY OUTCOMES TRANSGENERATIONALLY  
Presented By: Janice L. Bailey, PhD  
Universite Laval

2:45 p.m.  
DEVELOPMENT OF SPERM IN VITRO FROM SPERMATOGONIAL CELLS OF PREPUBERTAL CANCER PATIENTS  
Presented By: Mahmoud Huleihel, PhD  
Ben-Gurion University

3:00 p.m.  
REGULATION OF CYP26B1 EXPRESSION IN THE SPERMATOGONIAL STEM CELL NICHE  
Presented By: Parag Parekh PHD  
University of Texas MD Anderson Cancer Center

3:15 p.m.  
HIGH-RESOLUTION PHENOTYPING OF SPERMATOGONIC DEFECTS USING SINGLE-CELL SEQUENCING  
Presented By: Min Jung  
Washington University in St. Louis

2:00 p.m. - 3:30 p.m.  | CONCURRENT SESSIONS  
Oral Session II (Clinical)  
Location: Concerto A

2:00 p.m.  
ISOTRETINOIN IMPROVES TOTAL MOTILE SPERM COUNT IN SOME MEN WITH IDIOPATHIC OLIGOASTHENOSPERMIA  
Presented By: John Amory, MD, MPH  
University of Washington

2:15 p.m.  
GNRH-ANTAGONIST TREATMENT BEFORE ALLOGENEIC SPERMATOGONIAL STEM CELL TRANSPLANTATION ENHANCES SPERMATOGENIC RECOVERY IN RHESUS MONKEYS  
Presented By: Gunapala Shetty, PhD  
University of Texas MD Anderson Cancer Center

2:30 p.m.  
SPERM MITOCHONDRIAL COPY NUMBER AND DELETIONS: ASSOCIATIONS WITH URINARY-ISOPROSTANE AND PHTHALATE METABOLITES IN MALE PARTNERS UNDERGOING ASSISTED REPRODUCTIVE TECHNOLOGIES (ART)  
Presented By: Alexandra Olmsted  
University of Massachusetts Amherst

2:45 p.m.  
EFFECTS OF LONG-TERM TESTOSTERONE THERAPY (TTH) WITH TESTOSTERONE UNDECANOATE INJECTIONS (TU) ON ANTHROPOMETRIC AND METABOLIC PARAMETERS IN HYPOGONADAL MEN AND AN UNTREATED CONTROL GROUP: REAL-LIFE REGISTRY DATA FROM A UROLOGY/ANDROLOGY OFFICE  
Presented By: Farid Saad, DVM, PhD  
Bayer HealthCare

3:00 p.m.  
IMPLICATIONS OF ANDROGEN RECEPTOR ACTIVATION ON THYROID CANCER PHENOTYPE  
Presented By: Anvita Gupta BE  
New York Medical College

3:15 p.m.  
TARGETED DEGRADATION OF ANDROGEN RECEPTOR (AR) AND ITS SPICLED VARIANT AR-V7 BY THE PHYTOCHEMICAL SULFORAPHANE: NEW THERAPEUTIC OPPORTUNITY FOR CASTRATION RESISTANT PROSTATE CANCER (CRPC)  
Presented By: Namrata Khurana MTECH  
Tulane University
MONDAY, APRIL 24, 2017

7:00 a.m. - 6:00 p.m.  Registration/Information Desk Open
Location: Symphony Ballroom Registration

7:00 a.m. - 8:00 a.m.  Continental Breakfast
Location: Symphony Ballroom Foyer

8:00 a.m. - 9:00 a.m.  WOMEN IN ANDROLOGY
LECTURE: Sperm Interactions with the Female Reproductive Tract
(Introduced by Jannette Dufour, PhD)
Susan S. Suarez, MS, PhD
Cornell University

9:00 a.m. - 9:15 a.m.  Young Andrologist Award
2017 Recipient: Polina Lishko, PhD
(Introduced by Pablo E. Visconti, PhD)

9:15 a.m. - 10:15 a.m. SYMPOSIUM II - Sex and Gender Identity and Reproductive Health
Moderator: Cigdem Tanrikut, MD

9:15 a.m. - 9:35 a.m.  Advances in Transgender Surgery
Lee C. Zhao, MD
NYU School of Medicine

9:35 a.m. - 9:55 a.m.  Guideline for the Endocrine Treatment of Transgendered Individuals
Wylie C. Hembree, MD
Columbia University Medical Center

9:55 a.m. - 10:15 a.m. Fertility Preservation in Transgendered Individuals
Courtney A. Finlayson, MD
Ann & Robert H. Lurie Children's Hospital of Chicago

10:15 a.m. - 10:30 a.m. Quick Break

10:30 a.m. - 11:15 a.m. DIVERSITY LECTURE:
Transgender Surgery: Crossing Disciplines and Changing Minds
(Introduced by George Gerton, PhD)
Marci L. Bowers, MD
Trinidad Reproductive Health

11:15 a.m. - 12:30 p.m. *Poster Session II
Location: Symphony Ballroom I/II
*Not CME Accredited

12:30 p.m. - 1:45 p.m. Lunch (on your own)

12:30 p.m. - 1:45 p.m.  WOMEN IN ANDROLOGY
LUNCHEON & DISCUSSION
(Hosted by Jannette Dufour, PhD, WIA Chair)
Speakers: Susan Rothmann, PhD, HCLD
& Jannette Dufour, PhD, Texas Tech University
Location: Concerto B

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Andrology, 2017, Supplement, 24
1:45 p.m. - 3:15 p.m.  SYMPOSIUM III - Male Reproductive Tract
Moderator: Gail A. Cornwall, PhD

1:45 p.m. - 2:15 p.m.  Relevance of CRISP Proteins for Fertilization and Fertility
Patricia S. Cuasnicu, PhD
Instituto de Biologia y Medicina Experimental, Argentina

2:15 p.m. - 2:45 p.m.  (DICER)-phering Extracellular MicroRNA Communication in the Epididymis
Clemence Belfeane, PhD
CRCHUQ-Laval University, Canada

2:45 p.m. - 3:15 p.m.  New Emerging Role for β-Defensins: Players During Epididymal Development
Maria Christina W. Avellar, PhD
Universidade Federal de São Paulo

3:15 p.m. - 3:30 p.m.  Refreshment Break
Location: Symphony Ballroom Foyer

3:30 p.m. - 4:15 p.m.  INTERNATIONAL LECTURE:
Fertility Restoration by Spermatogonial Stem Cell Transplantation
(Introduced by Patricia S. Cuasnicu, PhD)
Takashi Shinohara, PhD
Horizontal Medical Research Organization, Japan

4:15 p.m. - 5:00 p.m.  LECTURE III: Molecular Genetics of External Genitalia Development
(Introduced by Gail S. Prins, PhD)
Martin J. Cohn, PhD
Howard Hughes Medical Institute

5:00 p.m. - 6:00 p.m.  ASA Annual Business Meeting

7:00 p.m. - 11:00 p.m.  Annual Banquet
Location: El Tucán
1111 SW 1st Ave.
Miami, FL 33130
Shuttle Bus Available

TUESDAY, APRIL 25, 2017

7:00 a.m. - 8:00 a.m.  2018 Program Committee Meeting

7:00 a.m. - 12:00 p.m.  Registration/Information Desk Open
Location: Symphony Ballroom Registration

7:00 a.m. - 8:00 a.m.  Continental Breakfast
Location: Symphony Ballroom Foyer

8:00 a.m. - 9:00 a.m.  SYMPOSIUM IV - Testicular Somatic Cells / Spermatogenesis
Moderator: Kyle Orwig, PhD

8:00 a.m. - 8:30 a.m.  Development and Validation of a Xenograft Model of Human Testicular Development
Rod T. Mitchell
MRC Centre For Reproductive Health, United Kingdom

8:30 a.m. - 9:00 a.m.  Genetic Causes of Human Azoosperma
Kenneth Aston, PhD
University of Utah Andrology and IVF Laboratories

9:00 a.m. - 9:30 a.m.  Human Testicular Peritubular Cells
Artur Mayerhofer, PhD
BioMedizinisches Centrum - BMC LMU Muenchen, Germany

9:30 a.m. - 9:45 a.m.  Refreshment Break
Location: Symphony Ballroom Foyer

9:45 a.m. - 11:15 a.m.  SYMPOSIUM V - Sperm Function
Moderator: Pablo E. Visconti, PhD

9:45 a.m. - 10:15 a.m.  Calcium Signaling in Sperm Motility Regulation and Male Fertility
Jean-Ju Chung, PhD
Yale School of Medicine
Biological & Biomedical Sciences

10:15 a.m. - 10:45 a.m.  An Ion Channel on Steroids:
The Unconventional Pathway of Sperm Activation
Polina Lishko, PhD
University of California, Berkeley

10:45 a.m. - 11:15 a.m.  Lipid Regulation of Sperm Function: From Basic Science to a Clinical Test of Male Fertility
Alexander J. Travis, VMD, PhD
Cornell University

11:15 a.m. - 12:15 p.m.  AUA LECTURE: Regenerative Medicine for Genitourinary Organs
(Introduced by Joseph P. Alukal, MD)
Anthony Atala, MD
Wake Forest University

12:15 p.m.  Meeting Adjourned
ASA Andrology Lab Workshop
"Restoring Strict Morphology Relevance: A Consensus Workshop"
SATURDAY, APRIL 22, 2017

Location: Concerto A
Program Chair: Erma Z. Drobnis, PhD, HCLD

The ALW has been approved by the American Board of Bioanalysis (ABB) Professional Enrichment Educational Renewal (PEER) for 8.85 CEU’s or 8.5 contact hours of continuing education activity.

8:30 a.m. - 8:35 a.m. Welcome from ALW Committee
   Session Chair: Erma Z. Drobnis, PhD, HCLD

8:35 a.m. - 8:45 a.m. Purpose of the Workshop and Ground Rules

8:45 a.m. - 8:55 a.m. Connecting Devices and Data Input
   Faculty: Anna-Marie Bort, MLT, (ASCP)CME

8:55 a.m. - 9:20 a.m. Classification I: Participants

9:20 a.m. - 9:50 a.m. Classification II: Participants

9:50 a.m. - 10:20 a.m. Classification III: Participants

10:20 a.m. - 10:35 a.m. Break

10:35 a.m. - 10:55 a.m. WHO's on Fifth: How Morphology Lost Predictive Value
   Faculty: Susan A. Rothmann, PhD, HCLD

10:55 a.m. - 11:10 a.m. Results of Classification Sessions

11:10 a.m. - 11:30 a.m. Algorithm Rationale
   Faculty: Susan A. Rothmann, PhD, HCLD

11:30 a.m. - 12:00 p.m. Algorithm Mechanics
   Faculty: Anna-Marie Bort, MLT, (ASCP)CME

12:00 p.m. - 1:30 p.m. LAB SCIENCE FORUM LUNCHEON
   "Discordance and the Lab: Evaluating and Processing Semen from Virus-Infected Patients"
   Location: Concerto B
   Erma Z. Drobnis, PhD, HCLD

1:30 p.m. - 1:50 p.m. Algorithm Worked Examples
   Faculty: Anna-Marie Bort, MLT, (ASCP)CME

1:50 p.m. - 2:00 p.m. Keyword Exercise
   Faculty: Anna-Marie Bort, MLT, (ASCP)CME

2:00 p.m. - 2:40 p.m. Classification I: Participants

2:40 p.m. - 3:20 p.m. Classification II: Participants

3:20 p.m. - 3:30 p.m. Break

3:30 p.m. - 4:10 p.m. Classification III: Participants

4:10 p.m. - 5:30 p.m. Results of Classification: Discussion of Controversial Classifications
   Discussion of Controversial Classifications by Faculty

5:30 p.m. Adjourn
SCHEDULE OF EVENTS

ASA Clinical Symposium
“Sexual Function and Fertility in the Spinal Cord Injured Male”
SATURDAY, APRIL 22, 2017
1:00 PM – 4:00 PM

Program Chairs: Joseph Alukal, MD and Peter J. Stahl, MD
Location: Symphony Ballroom III/IV

1:00p.m. – 2:45 p.m. Infertility and Ejaculatory Dysfunction in Spinal Cord Injured Men
Series of lectures given by:
The Miami Project to Cure Paralysis, Lois Pope Life Center
University of Miami Miller School of Medicine

Faculty: Nancy L. Brackett, PhD, HCLD
Charles Lynne, MD
Emad Ibrahim, MD

1:00 p.m. – 1:14 p.m. Effect of Spinal Cord Injury on Erection and Ejaculation
Emad Ibrahim, MD
Lois Pope Life Center

1:15 p.m. – 1:29 p.m. Assisted Ejaculation Procedures in Spinal Cord Injured Men
Emad Ibrahim, MD
Lois Pope Life Center

1:30 p.m. – 1:44 p.m. Causes of Abnormal Semen Quality in Spinal Cord Injured Men
Nancy L. Brackett, PhD, HCLD
University of Miami Miller School of Medicine

1:45 p.m. – 1:59: p.m. Assisted Reproduction in Spinal Cord Injured Men
Charles M. Lynne, MD
University of Miami

2:00 p.m. – 2:30 p.m. Video Demonstrating Penile Vibratory Stimulation and Electroejaculation Procedures in Spinal Cord Injured Men
Charles M. Lynne, MD
University of Miami

2:30 p.m. – 2:45 p.m. Q&A Session

2:45 p.m. – 3:00 p.m. Break

3:00 p.m. – 3:20 p.m. Medical Management of Erectile Dysfunction in Spinal Cord Injured Men
Alan Scott Polackwich, MD
Mount Sinai Medical Center

3:20 p.m. – 3:40 p.m. Surgical Management of Erectile Dysfunction in Spinal Cord Injured Men
Doron Stember, MD
Beth Israel Medical Center

3:40 p.m. – 3:45 p.m. Quick Break

3:45 p.m. – 4:00 p.m. Costs, Billing, Reimbursement – Practical Aspects of Integrating SCI Patients into a Clinical Practice
Dana Alan Ohl, MD
University of Michigan

Funding: Supported by grants from the NIH.

SUNDAY, APRIL 23, 2017
8:00 a.m. - 9:00 a.m.

LECTURE I
THE IMPORTANCE AND STRATEGY FOR PLACING MALE REPRODUCTIVE HEALTH IN THE CENTRE STAGE IN THE POLITICAL AND RESEARCH AGENDA
Christopher Barratt, PhD
University of Dundee, United Kingdom

Men's Health Issues are of increasing importance from a public health standpoint; questions such as the safety of testosterone replacement or prostate cancer screening risk/benefit analysis are being asked in increasing numbers of patients yearly with an increasing burden on health care systems. At the same time, men (especially reproductive age males) continue to utilize health care providers at a lower rate than any other demographic. This talk hope to outline the beneficial impact of increasing awareness of male reproductive health issues from a public health standpoint.

Funding: This research was funded by the National Institute for Child Health and Human Development Program Project “Individual, Family, and Societal Outcomes of Infertility”(1-P01-HD3707-07) and the University of California, San Francisco.

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SPEAKER ABSTRACTS

SUNDAY, APRIL 23, 2017
9:45 a.m. - 10:15 a.m.

SYMPOSIUM I - New Insights into ART
IMPLICATIONS OF THE AGING MALE GAMETE ON ART OUTCOME
Gianpiero D. Palermo, MD, PhD
Stephanie Cheung, BSc, Nigel Pereira, MD, Gianpiero D. Palermo, MD, PhD
Reproductive Medicine, Weill Cornell Medicine, New York, NY

Objectives: To assess the occurrence of spermatogenic meiotic errors, copy number variants (CNV), mutations in relation to advancing paternal age and consequent contribution to proper embryo development. The epigenetic aspect of the aging male gamete in relation to DNA integrity and targeted gene expression were also considered. To appropriately assess causality, the aging paternal gamete was evaluated according to its origin from the male genital tract and its ability to contribute to viable pregnancies once utilized for ICSI.

Methods: FISH analysis for sperm aneuploidy, next generation sequencing technology on spermatozoal DNA and RNA was carried out. Chromatin integrity was assessed by TUNEL. Resulting embryo development and pregnancy characteristics were evaluated.

Results: FISH was carried out on 67 semen samples with concentration of 46.3±24x10/ml, motility of 52.8±19%, and normal morphology. The overall aneuploidy rate, whether for autosomal or gonosomal, progressively and consistently increased with advancing male age. A total of 113 ICSI cycles were assessed and grouped according to paternal age. Fertilization was 87.7% in men 20-30 years old and progressively decreased to 52% in the oldest group, while embryo cleavage and embryo morphology appeared unaffected. A clinical pregnancy of 60% in the 20-30 years old men was reported and progressively decreased in the 50 year olds. Accordingly, pregnancy loss steadily increased with the advancing male age to reach 50.0% in men >50 years old due to both gonosomal and autosomal defects (P<0.001). Paternal age increased chances of sperm chromatin fragmentation, with consequent effects on embryo implantation. This was confirmed by the decreasing expression of key DNA repair genes in older men.

Conclusion: As it may be expected but not undeniably documented, advancing paternal age affected spermatogenic meiosis almost exclusively through non-disjunction. While it is difficult to control for an eventual female factor, genomic errors occurring during the spermatogenesis of aging men adversely affect their ability to fertilize oocytes or achieve a successful embryo implantation. Male gamete apoptosis increases with age, therefore DNA repair genes are progressively less efficient in aging men, with consequence on embryo implantation. New molecular technologies may provide insight into the etiology of unexplained male infertility and guide toward the appropriate reproductive treatment.

SUNDAY, APRIL 23, 2017
10:15 a.m. - 10:45 a.m.

SYMPOSIUM I - New Insights into ART
AUTISM & OTHER DEVELOPMENTAL DISORDERS IN ART
Sven Sandin, PhD
Mount Sinai School of Medicine

Abstract not received by print date.

SUNDAY, APRIL 23, 2017
3:45 p.m. - 4:30 p.m.

EAA LECTURE:
THERAPEUTIC PROMISE OF SPERMATOGONIAL STEM CELLS
Stefan Schlatt, PhD
University of Muenster, Germany

Recent and fast progress in achieving excellent cure rates in childhood cancer patients encourages scientists to develop options for spermatogonial stem cell based strategies for fertility preservation in boys. Childhood cancer patients remain the major, but not the only group of pediatric patients which will benefit. Patients suffering from systemic diseases in need of gonadotoxic chemotherapy or patients undergoing gonadectomy, individuals with Turner or Kleinfelter's syndrome, and boys with cryptorchid testes may also belong to the target group.

Cryopreservation of sperm is the standardized fertility preservation method in adult patients facing gonadotoxic oncological therapy. However this strategy cannot be applied in prepubertal boys. Spermatogonial stem cells (SSCs) may provide novel strategies for male fertility preservation. These cells colonize the testes from birth to adulthood. Their high regenerative capacity to re-colonize the testicular stem cell niches and reconstitute spermatogenesis after germ cell depletion has been revealed in experimental studies. Germ cell transplantation is considered a promising strategy. While germ cell transplantation in rodents has become a widely used research tool, the transfer into a clinical application must still be regarded as experimental. However its application in non-human primates revealed a clinical perspective. Fragments from immature testes were shown to obtain full spermatogenic potential when grafted or cultured. The generation of sperm in xeno- or autografts as well as in vitro generation of sperm has recently evoked enormous scientific interest. However using isolated germ cells none of the studies has as yet resulted in an efficient process resulting in sufficient numbers of sperm. However, numerous studies have revealed worthy pieces of information, building up a body of information on conditions that are required to maintain and mature male germ cells in vitro. In recent years many novel approaches using 3D culture systems and organoids have revealed a promising outcome. Very recently the stepwise differentiation of ES cells and the aggregation with testicular cells has shown that the full process can be installed in vitro when complex scenarios are followed and when somatic and germ cells are combined. This talk aims to present an overview of the current state of knowledge in experimental strategies and an outlook into clinical scenarios, including clinical risks and limitations related to stem cell based approaches for male fertility preservation. Challenges and limitations are discussed and an attempt is made to judge the availability of such procedures in the near future.
Infertility impacts approximately 1 in 7 couples in the U.S. Nearly 50% of infertile couples will have a male factor to explain reproductive difficulties. Emerging data suggests a close relationship between a man’s reproductive and overall health. Obesity, diabetes, hypertension, higher Charlson Comorbidity Index have all been associated with impaired male fertility.

In addition to current health, male fertility may provide a window into future health. Danish investigators have linked impaired semen quality to a nearly 3-fold higher risk of testis cancer in men in the years following an infertility evaluation, a finding later confirmed in US studies. In addition to cancer, longitudinal studies suggest that men diagnosed with infertility had a higher incidence of diabetes, hyperlipidemia, and heart disease. Moreover, investigators have demonstrated higher overall mortality rates among infertile men with impaired semen parameters in both Europe and the US.

The etiology for the association between fertility and health is uncertain but convincing data exists supporting genetic, hormonal, environmental, lifestyle, and developmental factors.

Abstract not received by print date.
MONDAY, APRIL 24, 2017
10:30 a.m. - 11:15 a.m.

DIVERSITY LECTURE:
TRANSGENDER SURGERY: CROSSING DISCIPLINES AND CHANGING MINDS
Marci L. Bowers, MD
Trinidad Reproductive Health

Marci Bowers, M.D. of Burlingame, California, is acknowledged as a pioneer in the field of Genital Reassignment Surgery and is the first woman worldwide to hold a personal transgender history while performing transgender surgery. She is also the first US surgeon to learn the technique of functional clitoral restoration after Female Genital Mutilation (FGM).

Dr. Bowers is a pelvic and gynecologic surgeon with more than 26 years’ experience. She is a University of Minnesota Medical School graduate and former class and student body president. Her Ob/Gyn residency was at the University of Washington. She continued in Seattle as an Obstetrician/Gynecologist at the Polyclinic and Swedish Medical Center, then joined Dr. Stanley Biber in Trinidad, Colorado in 2003, redefining US transgender surgery. She gained expertise in FGM clitoral restoration from noted French surgeon, Pierre Foldes in 2007-2009. Dr. Bowers relocated her surgical practice to the San Francisco Bay Area in 2010.

As an international authority on clitoral reconstruction, Dr. Bowers is sought after as a speaker and worldwide surgical educator and has been featured in numerous documentaries and news features including the Guardian, BBC, Times of London, Esquire and many others. Dr. Bowers is a member of WPATH, and serves on the board of directors for both GLAAD and the Transgender Law Center. In 2016, she joined the faculty at Mt. Sinai-Beth Israel in New York to establish the first transgender surgical educational program in the US. Her transgender work has been highlighted by appearances on Oprah, CBS Sunday Morning and Discovery Health. Dr. Bowers was recently honored as one of the 100 most influential LGBT people on the Guardian’s World Pride Power List and also recognized as one of Huffington Post’s 50 Transgender Icons.

Dr. Bowers will highlight her surgical work with the backdrop of changing societal expectations.

MONDAY, APRIL 24, 2017
1:45 p.m. - 2:15 p.m

SYMPOSIUM III - Male Reproductive Tract
RELEVANCE OF CRISP PROTEINS FOR FERTILIZATION AND FERTILITY
Patricia S. Cuasnicu, PhD
Institute of Biology and Experimental Medicine (IBYME-CONICET), Buenos Aires, Argentina

Fertilization is a key process involving a series of coordinated interactions between the gametes. However, the mechanisms underlying this process still remain to be elucidated. Our laboratory has been dedicated to underpin the molecular mechanisms involved in both the acquisition of sperm fertilizing ability during maturation and fertilization using CRISP proteins as model molecules. Epididymal protein CRISP1, the first described member of the evolutionarily conserved CRISP (Cystein-Rich Secretory Protein) family, associates with the sperm surface during maturation. Whereas the loosely bound CRISP1 is released during capacitation having been proposed as a decapacitating factor, substantial evidence obtained using in vitro assays and knockout (KO) models shows that the strongly bound population still present in capacitated sperm participates in different stages of fertilization. These observations can be extended to human as our findings show that the human homologue of CRISP1 (hCRISP1) also associates with sperm during maturation and participates in fertilization. Recent observations revealed that CRISP1 is also expressed by the cumulus cells that surround the egg and participates in fertilization by modulating sperm orientation and hyperactivation through its ability to regulate Ca2+, a key sperm Ca2+ channel essential for male fertility. In spite of these important roles, KO mice for CRISP1 are fertile in the same way as mice lacking CRISP4, another epididymal CRISP protein involved in fertilization. Interestingly, recent evidence shows that, in addition to the lower fertilization rates observed in KO mice for each individual CRISP protein, the double CRISP1/CRISP4 KO males exhibited a significant decrease in fertility as well as severe defects at the epididymal level with abnormal presence of immune cells within the tissue. Together, these observations confirmed the relevance of CRISP proteins for fertility and revealed novel immunoregulatory roles for these proteins within the epididymis. We believe these results provide important information for a better mechanistic understanding of both epididymal maturation and fertilization and will contribute to future research on infertility and contraception.

MONDAY, APRIL 24, 2017
2:15 p.m. - 2:45 p.m

SYMPOSIUM III - Male Reproductive Tract
(DICER)-PERING EXTRACELLULAR MICRORNA COMMUNICATION IN THE EPIDIDYMIS
Clemence Belleannee, PhD
CRCHUQ-Laval University, Canada

The epididymis plays a key role in the control of male fertility, as it is the site in which spermatozoa acquire their motility and ability to interact with the oocyte. In that context, our goal is to decipher the role of extracellular factors such as microRNAs (miRNA) in the control of epididymal functions and post-testicular sperm maturation. Extracellular microRNAs secreted by the epididymal epithelium are conveyed throughout the epididymis by extracellular vesicles and participate to a complex system of intercellular communication for the control of ciliogenesis. Further deciphering this interplay will help identify molecular targets for the diagnosis and treatment of epididymal dysfunction and male infertility.
SPEAKER ABSTRACTS

MONDAY, APRIL 24, 2017
2:45 p.m. - 3:15 p.m.

SYMPOSIUM III - Male Reproductive Tract
NEW EMERGING ROLE FOR β-DEFENSINS: PLAYERS DURING EPIDIDYMAL DEVELOPMENT
Maria Christina W. Avellar, PhD
Department of Pharmacology, Universidade Federal de São Paulo, Escola Paulista de Medicina, São Paulo, Brazil.

The Wolffian duct (WD) undergoes a morphogenetic program induced by androgens to originate the epididymis, which is a highly convoluted and segmented tube that provides a unique luminal fluid microenvironment essential for sperm maturation and function. Androgen action in WD epithelium is indirect and involves paracrine factors of mesenchymal origin that operate by still poorly understood mechanisms. Recently, our research group has detected spatio-temporal changes in the expression of different β-defensins as the rat epididymis develops from prenatal to postnatal life. Through the lenses of molecular and cell biology studies, fluorescence imaging, in vivo studies and ex vivo organotypic culture of the WD, we have exploited Wistar rat WD morphogenesis (embryonic ages 17.5 through 20.5) to further learn about how different β-defensins are expressed and modulated by androgens, and about their potential function during prenatal development of the epididymis. We have found that androgen/AR signaling differentially modulates β-defensin expression throughout WD morphogenesis. We have also discovered that at least one of the β-defensins tested (recombinant hSPAG11C) delays ex vivo WD coiling/elongation progression, mainly by reducing WD epithelial cell proliferation. β-defensins are known as components of host defense with antimicrobial and pleiotropic immunomodulatory properties. Our current data broaden the view of their roles as novel potential regulators of WD morphogenesis and contribute to a better understanding of prenatal and postnatal events in the developing epididymis that may later affect male fertility in adulthood. Financial support: FAPESP (#2010/52711-0 and #2009/14649-3), CSF/CNPq (#401932/2013-3).

MONDAY, APRIL 24, 2017
3:30 p.m. - 4:15 p.m.

INTERNATIONAL LECTURE:
FERTILITY RESTORATION BY SPERMATOGONIAL STEM CELL TRANSPLANTATION
Takashi Shinohara, PhD
Horizontal Medical Research Organization, Japan

Spermatogonial stem cells (SSCs) provide the foundation for spermatogenesis. In 1994, spermatogonial transplantation technique was developed, which provided a unique opportunity to restore fertility in infertile recipient animals. However, the efficiency of spermatogonial transplantation was limited due to limited donor cell colonization in recipients. However, significant improvement was achieved when donor SSCs were transplanted into sexually immature animals. This is probably caused by the lack of blood-testis barrier and increased cytokine secretion in immature testes. Although this experimental system using immature recipients has long been used for fertility restoration by spermatogonial transplantation, the low efficiency of fertility restoration in adult recipients has remained to be resolved. We overcame this problem by using germline stem (GS) cells, cultured spermatogonia with enriched SSC activity. When GS cells were used for transplantation, 3 of 5 congenitally infertile Kit mutants and all of 7 busulfan-treated animals restored fertility. Approximately 40-80 SSCs were estimated to be required for fertility restoration. Using spermatogonial transplantation, we also recently discovered that germline transmission from SSCs occurs in non-random patterns: offspring were derived from a small number of specific SSCs within a limited time. Interestingly, the same SSC clones reappear later with an average functional life span of ~124.4 days. Although little is known about the germline transmission of SSCs, a combination of spermatogonial transplantation and GS cell culture is a powerful tool to understand candidate factors involved in spermatogenesis and male fertility, which will have important implication in clinical application of these techniques.

MONDAY, APRIL 24, 2017
4:15 p.m. - 5:00 p.m.

LECTURE III:
MOLECULAR GENETICS OF EXTERNAL GENITAL DEVELOPMENT
Martin J. Cohn, PhD
Department of Molecular Genetics & Microbiology, Department of Biology, and UF Genetics Institute, University of Florida, P.O. Box 103610, Gainesville, FL, 32610, USA

Congenital malformations of the external genitalia are among the most common birth defects in humans, with hypospadias, a failure of urethral tube closure, affecting ~1:250 live births. Affected children can have mislocalized, multiple, or oversized urethral openings, and males with severe hypospadias are born with ambiguous genitalia. Despite this, there is a relatively poor understanding of the cellular and molecular mechanisms that control development of external genitalia. At early stages, patterning of the genital tubercle is similar in males and females. Sexual differentiation of the genitalia occurs at later stages, when sex-specific hormonal cues masculinize or feminize the genital tubercle and sexual swellings. Prenatal exposures to environmental endocrine disrupting chemicals (EDCs) can disrupt genitourinary development in rodents and may play a causal role in the high incidence of genitourinary malformations in humans. To identify the developmental genetic mechanisms that pattern the genital tubercle and to understand how these circuits are affected by endogenous and environmental hormonal cues, we are integrating mouse developmental genetics, genomics, and environmental toxicology. For example, we have found that genetic disruption of fibroblast growth factor receptor 2 (Fgfr2) signaling in mice leads to hypospadias due to deficiencies in cell-cell and cell-matrix adhesion. This same pathway is susceptible to disruption by exposure to anti-androgenic EDCs, and exposed embryos develop genital defects similar to those of Fgfr2 mutants. Our findings raise the possibility that exposure to EDCs at critical developmental stages can “knock-down” transcription of developmental control genes and result in mutant phenotypes in the absence of mutations.
Male reproductive disorders are common and there is evidence for increasing incidence over recent decades. These disorders may present at birth (hypospadias and cryptorchidism) or in adulthood (infertility, testicular cancer) and can arise as a result of underlying genetic abnormalities or from environmental insults that occur during fetal or postnatal life. In addition, environmental exposures (e.g. pharmaceuticals) during postnatal life may also affect future reproductive function. Evidence for the effect of these perturbations on the testis is often based on the findings of animal studies, however reliable human experimental models that can validate these findings in order to indicate human and clinical relevance are limited.

We have validated a human testis xenograft system that can be utilised to investigate the development of the human testis during fetal and prepubertal life. This model system can recapitulate testicular development and function including seminiferous cord formation, germ cell differentiation and hormone (e.g. testosterone) production. Furthermore this model system can be used to investigate the long-term effects of genetic disruption and environmental exposures (e.g. industrial chemicals, pharmaceuticals and chemotherapeutics) on the testis. We have utilised this model to mimic in-utero exposure to analgesics on human fetal testis development and function and the effects of therapeutic analgesic exposures on testosterone and germ cell development will be described. The effect of knockdown, in the human fetal testis, of known and novel genes implicated in testicular dysgenesis and disorders of sex development will also be presented. The model system has also been adapted for the investigation of human prepubertal testis development as part of a fertility preservation program for boys treated for cancer and the utility of this system for developing options to preserve fertility in these patients will be described.

The cells of the walls of the seminiferous tubules in healthy adult men are inconspicuous, elongated smooth muscle-like cells. They are able to contract and thereby transport sperm. They also secrete the extracellular matrix components found in the walls of the tubules. In human samples from infertile men with deranged spermatogenesis, the tubular wall and peritubular cells are altered. Reduced cellular expression of contractility proteins and increased levels of extracellular matrix proteins imply that the balance between contractile and secretory abilities of peritubular cells is upset. Furthermore, mast cells and macrophages accumulate in the wall of seminiferous tubules in these patients, implying inflammatory changes. The human testis is not accessible for experimental studies. However, human testicular peritubular cells (HTPCs) can be studied in vitro. We isolate them from small testicular fragments of patients. During the last decade we have exploited this cellular model, and human testicular samples, to address the questions, whether and how peritubular cells may contribute to male (in)fertility. We found that HTPCs secrete a plethora of factors, e.g. glial cell line derived neurotrophic factor (GDNF), which is important for the renewal of spermatogonial stem cells (SSCs). Thus HTPCs may be a functional part of the SSC-niche. They also secrete pigment epithelium derived factor (PEDF), a potent anti-angiogenic factors, which may be responsible for the avascularity of seminiferous tubules. HTPCs can be differentiated to produce sex steroids and hence they may contain progenitors of Leydig cells. Recent data identified Toll like receptors (TLRs) of
The sperm-specific calcium channel, CatSper, transduces Ca2+ signals that mediate hyperactivated motility in the mouse spermatozoa. CatSper channels form a highly organized Ca2+ signaling nanodomains in the sperm principal piece. We report two genes that encode novel subunits of CatSper ion channel complex, CatSper epsilon and zeta. Targeted disruption of CatSperz reduces CatSper current and sperm rheotactic efficiency in mice, resulting in severe male subfertility. Normally distributed in linear quadrilateral nanodomains along the flagellum, the complex lacking CatSperz is disrupted along the flagellum. This disruption renders the proximal flagellum inflexible and alters the 3D flagellar envelope, thus preventing sperm from reorienting against fluid flow in vitro and efficiently migrating in vivo. Ejaculated CatSperz-null sperm cells retrieved from the mated female uterus partially rescue in vitro fertilization (IVF) that failed with epididymal spermatozoa alone. Human CatSpere is quadrilaterally arranged along the flagella, similar to the CatSper complex in mouse sperm. We speculate that the newly identified CatSperz subunit is a late evolutionary adaptation to maximize fertilization inside the mammalian female reproductive tract.

TUESDAY, APRIL 25, 2017
10:15 a.m. - 11:45 a.m.

SYMPOSIUM V - Sperm Function
LIPID REGULATION OF SPERM FUNCTION: FROM BASIC SCIENCE TO A CLINICAL TEST OF MALE FERTILITY
Alexander J. Travis, VMD, PhD
Cornell University, NY; Androvia LifeSciences, NJ

Introduction: Lipids play a key role in regulating sperm function, preventing premature acrosome exocytosis (AE), enabling sperm to fertilize through the process of capacitation and triggering AE. First we focus on lipid organization in the sperm head and how sterols and the ganglioside GM1 regulate transient Ca2+ flux through CaV2.3, enabling AE. We then show how changes in GM1 localization correlate with human sperm function clinically.

Methods: Cell biological, pharmacological, genetic, and electrophysiological approaches were used to investigate CaV2.3 regulation by GM1 in mouse sperm. Fluorescence microscopy was used to observe changes in GM1 localization in sperm from 42 men in response to stimuli for capacitation. Retrospective and prospective medical history data enabled study of the relationship between GM1 localization and clinical fertility. A comparison of GM1 localization patterns in sperm exposed to capacitating stimuli from cohorts of 76 men with known fertility and 122 men who were questioning their fertility was performed.

Results: Single sperm Ca2+ imaging demonstrated that GM1 stimulated Ca2+ transients through CaV2.3’s pore-forming 1E subunit. Mice lacking 1E had altered Ca2+ influx, reduced AE, and were subfertile. AE depended on spatiotemporal information encoded by flux through CaV2.3, not merely the presence/amplitude of Ca2+ waves. Interaction required GM1’s lipid and sugar components and CaV2.3’s 1E and 2Q subunits. Of the 42 men, 13 had ≥ 39.5% of their sperm show specific GM1 localization patterns consistent with response to capacitating stimuli. 12/13 (92.3%) achieved clinical pregnancy by natural conception or within ≤ 3 IUI cycles. Of the other 29 men, only 6 (20.7%) achieved clinical pregnancy by natural conception or within ≤ 3 IUI cycles. GM1 localization patterns associated with capacitation were distributed normally in fertile men but were significantly lower in men questioning their fertility (33.6% were below 1 StdDev below the mean versus 13.2% in fertile men).

Conclusion: GM1 regulated sperm Ca2+ flux and AE. GM1 localization patterns provided clinically-relevant insights into sperm function/male fertility. Funding: NIH, BioAccelerate NYC Prize, or Androvia LifeSciences.
TUESDAY, APRIL 25, 2017
11:15 a.m. - 12:15 p.m.

AUA LECTURE:
REGENERATIVE MEDICINE FOR GENITOURINARY ORGANS
Anthony Atala, MD
Wake Forest University School of Medicine
Director, Wake Forest Institute for Regenerative Medicine

Patients with injured or diseased organs may be treated with non-invasive or transplanted tissues. Regenerative medicine and tissue engineering apply the principles of cell transplantation, material sciences, and bioengineering to construct biological substitutes that may restore and maintain normal function in injured tissues. Stem cells may offer a potentially limitless source of cells for tissue engineering applications and are opening new options for therapy. Recent advances that have occurred in regenerative medicine will be reviewed and applications of these new technologies that may offer novel therapies for patients with tissue injury and organ failure will be described.
**ORAL ABSTRACTS**

**Sunday, April 23, 2017**  
2:00 p.m. – 3:00 p.m.  
**Concurrent Oral Session I**  
**Location: Symphony Ballroom III/IV**

1 **DIFFERENTIAL TOLEROGIC CAPACITY OF THE EPIDIDYMIS AND TESTIS IN MICE WITH CONDITIONAL DELETION OF TGFBR2 IN DENDRITIC CELLS.**  
Fernando Pierucci-Alves¹, Monica T. Midura-Kiela², Sherry D. Fleming³, Bruce D. Schultz¹ and Pawel R. Kiela¹  
¹Kansas State University, Dept of Anatomy & Physiology; ²University of Arizona, Dept of Pediatrics; ³Kansas State University, Division of Biology; ⁴University of Arizona, Depts of Pediatrics and Immunobiology  
(Presented By: Fernando Pierucci-Alves, D.V.M.)

Sperm are immunogenic and peripheral tolerance mechanisms are necessary for reproductive success. Initial data revealed prominent physiological signaling by transforming growth factor beta (TGFβ) in murine epididymis, where large networks of dendritic cells (DCs) and macrophages exist. This study’s overarching hypothesis is that TGFβ-signaling in epididymal DCs maintains immunotolerance to sperm in the epididymis and disruption of this signaling pathway breaks sperm tolerance through impaired or insufficient regulatory T cell (Treg) function. In male mice with DC-specific TGFβ receptor 2 deletion (Tgfbr2ΔDCFoxP3GFP-KI), we detected severe epididymal leukocytosis with sperm granulomas, antisperm antibodies but no apparent testicular pathology at the histological level. To further these observations, we quantified leukocytes (CD45+) and Tregs (FoxP3/GFP+) in epididymides, testes and kidneys from 4 Tgfbr2ΔDCFoxP3GFP-KI males and control littermates by flow cytometry. We used kidneys as a sperm-free organ of the genitourinary tract, and as an additional control. Compared to controls, the epididymidis of Tgfbr2ΔDCFoxP3GFP-KI mice had 3.4 times more infiltrating CD45+ leukocytes (P<0.05), while the Tgfbr2ΔDCFoxP3GFP-KI testis and kidney exhibited 1.2- and 1.5-fold increase in infiltrating leukocytes (P>0.05), respectively. Tregs were 5-6 times more abundant in epididymis and kidney of Tgfbr2ΔDCFoxP3GFP-KI mice, while the testis exhibited 53 times more Tregs – compared to controls. These data suggest the epididymis is most susceptible to inflammation when the DC/TGFβ-signaling axis is disrupted, and that the testis maintains alternative robust immunosuppressive mechanisms to fend off autoimmune responses. Additional studies are addressing how loss of TGFβ-signaling disrupts epididymal and testicular DC tolerogenic capacities and testing whether there is differential induction and function between epididymal and testicular Tregs. [Supported by P20GM103418 (K-INBRE); Johnson Cancer Research Center]

2 **HUMANIN TRANSGENIC MICE ARE PROTECTED FROM CYCLOPHOSPHAMIDE-INDUCED MALE GERM CELL APOPTOSIS.**  
YanHe Lue MD¹, Hemal Mehta MS², James Hoang BS¹, Kelvin Yen PhD³, Junxiang Wan PhD³, Ronald Swerdloff MD¹, Pinchas Cohen MD² and Christina Wang MD¹  
¹Division of Endocrinology, LABioMed at Harbor-UCLA; ²USC Leonard Davis School of Gerontology, University of Southern California, Los Angeles, CA  
(Presented By: YanHe Lue, MD)

Humanin (HN) is a cytoprotective peptide encoded by a mitochondrial gene. We have previously demonstrated that the pharmacological administration of HN or its analogue HNG protects male germ cells against cyclophosphamide (CP)-induced apoptosis in mice. To examine the role of endogenous HN in the cytoprotection of male germ cells from chemotherapy, we generated HN transgenic (HNt) mice expressing a CMV-promoter driven humanin transgene. After genotyping by PCR, 1) groups of 7 adult (5-10 month-old) HNt and age-matched wildtype (WT) mice were used for the characterization of male reproductive phenotype, and 2) groups of 6 adult HNt and age-matched WT mice were treated with a single-dose of CP injection (i.p. 200mg/kg) to examine male germ cell apoptosis (quantified as apoptotic index (AI): the number of apoptotic germ cells/100 Sertoli cells). The plasma testosterone (T) was measured by RIA. HNt mice were viable, fertile and smaller in size (BW:28.5±2.2g) with an average of 18% decrease in body weight (BW) as compared to WT (BW:34.9±10.3g) mice. The testis weight (TW:88±10.1mg, p=0.007) in HNt mice was significantly lower than WT (TW:105.2±9.3mg) mice. There was no difference in cauda epididymal sperm count between HNt (1.3±0.07 million/mg cauda) and WT (1.3±0.03 million/mg cauda) mice. Testis histological examination in HNt mice showed normal histology with the baseline germ cell apoptosis rates reminiscent of WT levels. HNt mice have similar plasma T levels (0.6±0.4ng/ml) as WT (0.7±0.5mg/ml) controls. Two days after CP treatment, there were no marked changes in body and testis weight, and plasma T levels. The germ cell apoptosis rate in WT mice was significantly (p<0.001) increased at spermatogenic stages I-III (AI:46.1±4.6), VII-VIII (AI:20.6±0.9) and XI-XII (AI:56.9±4.8) as compared to non-treated WT mice (stages I-III AI: 9.5±2.1; VII-VIII:2.5±0.6; XI-XII:17.5±1.8). In HNt mice, CP treatment significantly increased germ cell apoptosis at stages XI-XII (AI: 23.7±2.9; p=0.03), but not at stages I-III (AI:14.9±2.3) and VII-VIII (AI:4.8±1.1) as compared to baseline levels of HNt mice (stages I-III AI:8.3±1.8; VII-VIII:3.8±0.8; XI-XII:13.3±3.2), suggesting that male germ cells in HNt mice were partially resistant to CP-induced apoptosis. Thus, we conclude that HN 1) is cytoprotective hormone; and 2) mimics the effects of caloric-restriction on metabolism and chemotherapy-protection.
3 PATERNAL EXPOSURE TO ENVIRONMENTAL CONTAMINANTS ALTERS THE SPERM PROTEOME AND INDUCES NEGATIVE PREGNANCY OUTCOMES TRANSGENERATIONALLY

Janice Bailey PhD, Nancy Coté PhD, Clotilde Maurice PhD, Florence Roux-Dalvai MSc, Arnaud Droit PhD and Mathieu Dalvai PhD
Université Laval
(Presented By: Janice L. Bailey, PhD)

Background: The Arctic food chain is contaminated with persistent organic pollutants (POPs). As a consequence, there are major health discrepancies between Inuit and non-Aboriginal Canadians, including adverse pregnancy outcomes or disruption of the immune system. Although healthy pregnancies are multifactorial, it is possible that POPs exposure contributes to these adverse outcomes. Moreover, the paternal influence of contaminant exposure on his offspring has not been well-investigated. We hypothesized that early paternal exposure to Arctic POPs affects his sperm proteome and that of his offspring and future generations.

Methods: Sprague-Dawley females (F0) were gavaged with an environmentally-relevant concentration of an Arctic POPs mixture or corn oil (Control) and mated to untreated males. F1 fathers were mated to untreated females to generate F2 litters; F2 development was followed until PND 90. F3 and F4 generations were similarly produced. Isobaric Tags for Relative and Absolute Quantitation (iTRAQ) labelling, 2D–LC–MS/MS and immunoblotting analyses were used to identify differentially expressed sperm proteins from all generations.

Results: POPs-exposed F1 males had fewer motile sperm and decreased epididymal sperm counts (P=0.0001). F2 sons from the POPs lineage were subfertile (P=0.02) and their F3 POPs grandsons had fewer pups/litter (P<0.0001). For F1, F2 and F3 males, 7, 20 and 36 proteins were differentially expressed compared to the control lineage, some of which are implicated in motility, apoptosis or male infertility (SOD1, VDAC2, CS, SLCA3, IZUMO) and may explain the observed subfertility. Importantly, 3 differentially expressed sperm proteins were conserved between the F1 and F3 males and 6 between the F2 and F3 males, showing a transgenerational effect of POPs. Bioinformatics and GO analyses showed that 45-50% of these proteins are implicated in the respiratory chain. Surprisingly, a majority are also part of the same biological pathways as brain disorders. Finally, by converting the rat ID in human genes ID for human diseases identification, we observed a role of certain differentially expressed proteins in infection processes and reduced prostate cancer occurrence.

Conclusions: POPs exposure induces proteome changes in sperm that can be observed through three generations. The proteins and pathways identified have launched new hypotheses on POPs effects and in our understanding of the adverse health effects observed in Inuit populations.

4 DEVELOPMENT OF SPERM IN VITRO FROM SPERMATOGONIAL CELLS OF PREPUBERTAL CANCER PATIENTS

Mahmoud Huleihel PhD, Maram Abofoul-Azab PhD¹, Joseph Kapelushnik MD², Haim Pinkas MD³ and Eitan Lundenfeld MD⁴
¹The Center of Advanced Research and Education in Reproduction, The Shraga Segal Dep. of Microbiology, Immunology and Genetics, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel.; ²Dep. of Pediatric Oncology and Hematology, Soroka Medical Center, Beer-Sheva, Israel; ³Male Infertility & Sperm Bank, Helen Schneider Hospital for Women, Rabin Medical Center, Beilinson Hospital, Petach Tikva, Israel.; ⁴Fertility and IVF Unit, Dep. OB/GYN, Soroka Medical Center and The Center of Advanced Research and Education in Reproduction, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel.
(Presented By: Mahmoud Huleihel PhD)

Introduction: Childhood cancer estimated to affect 0.1% of prepubertal boys. About 80% will survive the disease due to the progress in anti-cancer treatments. Some of these cure patients will become azospermic. Prepubertal males do not produce spermatozoa; therefore, the only suggested option of their fertility preservation is testicular tissue/cells cryopreservation before aggressive anti-cancer treatments. None of the published in vitro methodology could induce differentiation of human spermatogonial stem cells (SCs) to sperm cell. Using three-dimensional (3D) culture systems we were able to induce proliferation and differentiation of isolated SSCs to meiotic and postmeiotic stages (mouse) and the generation of sperm (mouse).

Objectives: To examine the presence of spermatogonial cells (SCs) in chemotherapy-treated prepubertal cancer patient males and the possibility to induce those cells into complete spermatogenesis in vitro.

Methods: Testicular biopsies were obtained from eight prepubertal patients; seven from chemotherapy-treated cancer patient and one from a patient with β-thalassemia major. Testicular cells were enzymatically isolated and cultured in a methylcellulose culture system (MCS)-enriched with specific growth factors for a period of 5-15 weeks. The presence of premeiotic, meiotic and postmeiotic cells in MCS was examined by immunofluorescence staining (IF) and/or PCR analysis.

Results: We observed biologically active SCs in testicular biopsies from prepubertal cancer patient males who had already received substantial chemotherapy. Isolated testicular cells cultured in MCS developed into colonies which contained premeiotic (OCT4, PLZF, VASA, SALL4, GFR-a, CD9, a-6-INTEGRIN, c-KIT), meiotic (LDH, BOULE, CREM-1) and postmeiotic (PROTAMINE, ACROSIN) cells, as were confirmed with IF/PCR analyses. In addition, we were able to identify sperm-like cells in MCS.

Conclusion: We demonstrated for the first time, the presence of biologically active spermatogonial cells in testicular biopsies of chemotherapy-treated prepubertal cancer patient males, and the feasibility of their development in MCS to each stage of spermatogenesis including sperm. Should this system be further validated and improved for the production of fertilization competent gametes, then it may assist in future therapeutic strategies for infertility of cancer patient boys and non-obstructive azospermic patients where no sperm were found in their testicular biopsies.
5 REGULATION OF CYP26B1 EXPRESSION IN THE SPERMATOGONIAL STEM CELL NICHE
Parag Parekh PhD¹, Thomas Garcia PhD¹,², Reham Waheeb DVM, PhD³, Vivek Jain MS¹,², Gunopal Shetty PhD¹, Marvin Meistrich PhD¹, Marie-Claude Hofmann PhD¹ and Pooja Gandhi MS³
¹University of Texas MD Anderson Cancer Center; ²University of Houston Clear Lake; ³University of Alexandria, Damanhour
(Presented By: Parag Parekh, PhD)

Cytochrome P45026B1 (CYP26B1) regulates the concentration of all-trans-retinoic acid (RA) and plays a key role in germ cell differentiation by controlling local distribution of RA. Interestingly, little is known about the mechanisms of Cyp26b1 gene regulation. In Sertoli cells, it is maintained by SF1 and SOX9 during gonad development and throughout life but inhibitors that would balance its expression, possibly accounting for the pulses of RA in the adult seminiferous epithelium, are not known. Our previous data from Sertoli-cell specific NOTCH gain- and loss-of-function mouse models indicated that expression of Cyp26b1 is inversely correlated to NOTCH pathway activity. We hypothesized that 1) Spatiotemporal Cyp26b1 downregulation is directly dependent on canonical NOTCH signaling; and 2) A subset of premeiotic germ cells is responsible for Cyp26b1 downregulation through the NOTCH ligand JAG1. Germ cell-Sertoli cell co-cultures experiments demonstrated that JAG1, mainly expressed by Aundiff spermatogonia, activated NOTCH signaling in primary Sertoli cells and induced the transcriptional repressors and canonical NOTCH target genes Hes/Hey. Upregulation of Hes/Hey gene expression by JAG1 was associated with significant decreases in Cyp26b1 expression, while simultaneous downregulation of Hes/Hey by RNAi led to significant increases. Further, Luciferase and ChIP-PCR assays demonstrated that HES/HEY directly bind to the Cyp26b1 promoter to downregulate its expression. Investigation of stage-specific NOTCH activity using transgenic mice, together with qPCR analysis of Hes/Hey and Cyp26b1 expression, indicated lowest expression of Cyp26b1 at stages VI-VIII of the seminiferous epithelium, when NOTCH activity and RA production are highest. To elucidate which germ cells activate NOTCH signaling in Sertoli cells in vivo, we performed germ cell depletion experiments using moderate doses of busulfan. We found that elimination of undifferentiated spermatogonia will downregulate NOTCH signaling and upregulate Cyp26b1 expression in Sertoli cells. In conclusion, we believe that NOTCH signaling, induced by JAG1-expressing Aundiff in Sertoli cells, is a mediator of germ cell differentiation by controlling Cyp26b1 expression and possibly RA pulses.
Supported by NIH R01HD081244

6 HIGH-RESOLUTION PHENOTYPING OF SPERMATOCENIC DEFECTS USING SINGLE-CELL SEQUENCING
Min Jung, Jannette Rusch PhD, Abul Usmani PhD and Don Conrad PhD
Department of Genetics, Washington University in St. Louis
(Presented By: Min Jung)

Introduction: RNA sequencing of testis tissue provides great promise for improving the description of molecular defects in men with gonadal dysfunction. With thoughtful interpretation, gene expression data could be useful for classifying patients into a diagnostic hierarchy, defining i) disrupted cell types, ii) disrupted pathways, and, iii) in conjunction with genome sequencing data, disrupted gene(s) and causal genetic variants. However, the cellular diversity of testis severely limits the utility of expression measurements made on bulk tissue. Thus, the application of single-cell RNA-sequencing on male germ cells represents an amazing new set of scientific opportunities for research in male reproductive biology and translational medicine

Objectives: We aim to develop a single-cell framework that utilizes large-scale single-cell expression profiles from normal and disease models to elucidate the fundamentals of spermatogenesis and to phenotype spermatogenic defects.

Methods: Using Drop-seq, we generated single-cell expression measurements on over 30,000 cells from wild-type mice and over 20,000 cells from mouse mutants with infertility of mechanisms known (e.g. MLH3 deficiency) and unknown (spontaneous infertility after a transgene insertion). We constructed a pipeline for interpreting the single-cell data using publicly available single-cell computational tools such as RaceID2, Waterfall, and Monocle2, and an in-house cell-type assigner algorithm.

Results: We find that the increased resolution of single cell expression profiling reveals novel cell-type specific markers, 5 of which we have confirmed with immunofluorescence staining. As part of the framework, we developed a cell-type identifier that provides automated assignments of cells to 4 stages of germ cells and 3 types of somatic cells. Our cell-type assigner algorithm has 96% accuracy when benchmarked with data from flow-sorted germ cells. Finally, unsupervised ordering of male germs on a developmental timescale depicts the genetic landscape of both normal and infertile mice, inferring the cell-types and pathways that are dysregulated in the germ cell development of disease models.

Conclusions: Our single-cell framework has great potential for expanding our ability to dissect pathophysiology in tissues with extensive cellular heterogeneity and decrypt the spermatogenic failure in more patients.
7

ISOTRETINOIN IMPROVES TOTAL MOTILE SPERM COUNT IN SOME MEN WITH IDIOPATHIC OLIGOASTHENOZOOSPERMIA

John Amory, Kevin Ostrowski MD, John Gannon MD, Kathryn Berkseth MD, Faith Stevison MS, Nina Isoherranen PhD, Charles Muller PhD and Thomas Walsh MD, MSE

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Introduction: There is no effective medical therapy for men with infertility due to idiopathic oligoasthenozoospermia (IOA). As men with IOA have lower intratesticular concentrations of 13-cis-retinoic acid, we hypothesized that men with IOA may exhibit improved sperm counts during treatment with 13-cis-retinoic acid (isotretinoin).

Methods: We conducted a single-arm, pilot study to determine impact of therapy with isotretinoin on sperm indices in 20 infertile men with IOA. Men were between 21 and 60 years of age without identifiable hormonal or genetic abnormalities and with total motile sperm counts of less than 10 Million on two occasions. All men received isotretinoin 20 mg by mouth twice daily for 20 weeks and had semen analyses, routine blood counts, chemistries and examinations every four weeks during treatment.

Results: Twenty men enrolled in the study and 16 completed all study procedures. All men experienced dry facial skin and chapped lips during treatment, which resolved after Isotretinoin discontinuation. There were no significant laboratory abnormalities noted in any subject, and no subject experienced worsening mood. Mean (SD) total motile sperm count increased from 3.2 (3.1) Million at baseline to 8.5 (13) Million after twenty weeks of therapy (p=0.005 c.f. baseline). Eight of sixteen men (50%) men achieved a total motile sperm concentration of greater than 10 million, and nine men (56%) had a greater than a five-fold increase in total motile sperm count by the end of treatment. The remaining seven men had either minimal or no apparent response to therapy. No significant improvement in sperm motility was observed. Six clinical pregnancies (three spontaneous, 3 via ART) occurred, four of which, including all three of the spontaneous pregnancies, were observed in men with improvements in sperm counts on therapy.

Summary: Approximately 50% of men with idiopathic IOA experienced an increase in total, motile sperm count with isotretinoin therapy. Treatment was generally well tolerated.

Conclusion: Isotretinoin therapy of men with IOA is feasible and is associated with significant improvements in sperm production in a subset of men. Randomized, placebo-controlled studies of isotretinoin therapy for infertile men with IOA are warranted, using live birth as the outcome measure.

Funding: The Eunice Kennedy Shriver National Institute of Child Health and Human Development supported this work through grant K24 HD082231 to J. Amory.

8

GNRH-ANTAGONIST TREATMENT BEFORE ALLOGENEIC SPERMATOGONIAL STEM CELL TRANSPLANTATION ENHANCES SPERMATOGENIC RECOVERY IN RHESUS MONKEYS

Gunapala Shetty PhD1, Jennifer Mitchell VMD1, Zhuang Wu MD1, Truong Lam BS1, Lorraine Hill DVM1, Ramesh Tailor PhD1, Karen Peters BS2, Kyle Orwig PhD2 and Marvin Meistrich PhD1

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(Presented By: Gunapala Shetty, PhD)

Cancer treatment regimens can completely kill the stem spermatogonia in children and young patients in which case cryopreservation of spermatogonia before therapy and subsequent autologous transplantation may be the only option for restoring male fertility. Previous studies suggested that cancer treatment regimen can cause functional damage in the somatic environment of the testis, which can at least partially be alleviated by hormone suppression treatments.

To optimize conditions for the restoration of spermatogenesis by spermatogonial stem cell (SSC) transplantation, we combined transplantation with the hormone suppression during different times relative to transplantation. We irradiated the testes of 16 pubertal rhesus monkeys with 7 Gy and 4 months later transplanted cryopreserved testicular cells containing SSCs, allogeneically to one of the testes. Six of these irradiated monkeys were treated with GnRH-antagonist (GnRH-ant) starting 2 months after irradiation until the time of transplantation (GnRH-pre group). Five of the monkeys received GnRH-ant treatment starting 3 months after irradiation and lasting until 1 month after transplantation (pre+post group). This GnRH-ant treatment suppressed serum testosterone levels to an about 25% of the pre-treatment values of about 2.5 ng/ml. Five of the monkeys received sham-injections instead of GnRH-ant.

At 9 months after transplantation the transplanted testes in control group showed average weights that were 5% greater than those of the sham-transplanted testes. However in the pre-GnRH-ant group the increase was consistently around 10%, whereas there was no difference in the pre+post GnRH-ant group. Similarly the average numbers of cauda epididymal sperm derived from the transplanted testes in the control group were 2.6-fold higher than those from the sham-transplanted testes. However in the pre-GnRH-ant group the ratio of sperm in the transplanted to untransplanted side was 4.0, whereas in the pre+post-GnRH-ant group the ratio was only 1.4-fold. The results suggested that the hormone suppression prior to transplantation has a beneficial effect on the recovery of sperm from the transplanted SSCs, but hormone suppression after transplantation does not augment the recovery, and rather could be detrimental instead. The tubule differentiation indices indicating the testicular spermatogenic potential in the testes will be discussed. This work was supported by the grant 1P01HD075795-01 from NIH/NICHD.
SPERM MITOCHONDRIAL COPY NUMBER AND DELETIONS: ASSOCIATIONS WITH URINARY-ISOPROSTANE AND PHTHALATE METABOLITES IN MALE PARTNERS UNDERGOING ASSISTED REPRODUCTIVE TECHNOLOGIES (ART)

Alexandra Olmsted¹, Haotian Wu MS¹, Rahul Tayyab PhD², Cynthia Sites MD³ and J. Richard Pilsner MPH, PhD⁴
¹University of Massachusetts Amherst, Department of Environmental Health; ²Baystate Medical Center, Department of Obstetrics and Gynecology
(Presented By: Alexandra Olmsted)

Introduction: Phthalates, a chemical class of plasticizers, are ubiquitous in the environment and recognized as endocrine disrupting compounds (EDCs). Recent data suggest that oxidative stress is a potential mediator for the associations between phthalate exposure and poor male reproductive health. Mitochondria are implicated in the production of excess oxidative stress and sperm mitochondrial copy number (MtCopy) and deletions (MtDeletions) have been linked with male infertility. However, little is known about the relationship of these mitochondrial biomarkers in sperm with phthalate exposure and oxidative stress.

Objectives: To examine associations of MtCopy and MtDeletions with concentrations of urinary phthalate metabolites and isoprostane in male partners undergoing ART.

Methods: A total of (n=96) sperm samples were collected from male partners undergoing ART at Baystate Medical Center, in Springfield, MA from 2014 to 2016 as part of the Sperm Environmental Epigenetics and Development Study (SEEDS). Seventeen urinary phthalate metabolites (n=50) were analyzed by the Centers for Disease Control using tandem mass spectrometry. 15F2t-Isoprostane (n=90) was measured using a competitive enzyme-linked immunosorbent assay. A triplex Taqman qPCR method was developed for relative quantification of genomic DNA, MtCopy and MtDeletions. Multivariable linear or logistic regression was employed to examine associations controlling for age, BMI, batch and male infertility status, as defined by abnormal semen quality parameters.

Results: Quartiles of MtCopy and MtDeletions were positively associated with the odds of male infertility (p for trend <.0001 and 0.007, respectively). Urinary metabolites of DiBP, MiBP, and MHIBP displayed an inverse borderline association with MtCopy (β=−0.86; p =0.07 and β=−0.99; p = 0.06, respectively); whereas, urinary MEHP concentrations were positively associated with MtDeletions (β =0.06; p = 0.004). Urinary isoprostane levels were inversely associated with MtCopy but did not reach statistical significance (β =−0.13; p = 0.07).

Conclusion: These results suggest that certain phthalate metabolites and a known biomarker of oxidative stress may be associated with MtCopy and MtDeletions. Current research is investigating these relationships in a larger sample size.
ORAL ABSTRACTS

11 IMPLICATIONS OF ANDROGEN RECEPTOR ACTIVATION ON THYROID CANCER PHENOTYPE
Anvita Gupta BE¹, Melanie Jones PhD², Timmy O’Connell MS³, Monica Schwarze MD¹, Dorota Halicka MD, PhD¹, Jiangwei Li PhD¹, Zbigniew Darzyznkiewicz MD, PhD¹, JK Rasamny MD¹, Codrin Iacob MD³, Nina Suslina MD¹, Edward Shin MD¹, Augustine Moscabello MD¹, Raj Tiwari PhD¹ and Jan Geliebert PhD¹
¹New York Medical College; ²United States Military Academy Preparatory School, West Point, NY; ³New York Eye and Ear Infirmary
(Presented By: Anvita Gupta, BE)

Introduction: Papillary Thyroid Cancer (PTC) comprises more than 90% of neoplasms in the endocrine system, with a three-fold higher incidence in women than in men. With an overall five-year survival rate of 98.1%, early stage PTC has a favorable prognosis. However, PTC exhibits increased aggressiveness with poor prognosis in men diagnosed with the disease. These striking observations led us to explore the role of androgen and androgen receptor (AR) in this disease.

Methods: Development of our model system consisted of (1) Determining levels of AR expression in PTC patient tissue samples, (2) Determining AR expression in thyroid cancer cell lines, (3) Stable transfection of 8505c PTC/anaplastic thyroid cancer cell line with AR (clone 84e7), (4) Transcriptional profiling using RNAseq on 48 hour 5α-dihydrotestosterone (DHT) treated 84E7 cells, (5) Continually activating AR in 84e7 cells with DHT for 3-6 days, followed by beta-galactosidase (SA-βGal) assays, flow cytometry, western blots and immunocytochemistry to investigate development of senescence, (6) Cytokine profiling of the senescence-associated secretory phenotype (SASP) to define the pro-tumorigenic or tumor-suppressive potential of androgen-induced senescent thyrocytes.

Results: We found a 70% decrease in median AR expression (p<0.0001) in 24 PTC patient tissue samples, compared to matched, normal thyroid tissue. Preliminary data from our lab indicate that androgen receptor (AR) acts as a negative regulator of growth as evidenced by a statistically significant 48% decrease in proliferation over 72 hours upon DHT addition to 84E7 cells. RNAseq revealed significant changes in gene expression associated with proliferation (474 genes, p=2.4E-24) and cell cycle progression (129 genes, p= 6.54E-6). AR stimulation induced senescence, evidenced by a flattened, vacuolized and granular cell morphology, and expression of SA-βGal, leading to a permanent growth arrest, without apparent cell death. Senescence was accompanied by an increase in total RNA and protein content, Reactive Oxygen Species, and markers such as p21, p27, p16, γ-H2AX, HP1- γ, and H3K9 methylation. Profiling of SASP revealed a primarily anti-inflammatory microenvironment initiated and sustained by the senescent cells.

Conclusion: Our study elucidates the induction of senescence as a novel function of AR activation in thyrocytes and may indicate a protective role of AR activation in the decreased incidence of thyroid cancer in men.

12 TARGETED DEGRADATION OF ANDROGEN RECEPTOR (AR) AND ITS SPLICED VARIANT AR-V7 BY THE PHYTOCHEMICAL SULFORAPHANE: NEW THERAPEUTIC OPPORTUNITY FOR CASTRATION RESISTANT PROSTATE CANCER (CRPC)
Namrata Khurana M TECH¹, Hogyoung Kim PhD², Partha K. Chandra PhD³, Sudha Talwar PhD², Pankaj Sharma PhD³, Asim B. Abdel-Mageed PhD³, Debasis Mondal PhD⁴ and Suresh C. Sikka PhD³
¹PhD Student; ²Post Doc, Dept. of Urology, Tulane University School of Medicine; ³Post Doc, Dept. of Pharmacology, Tulane University School of Medicine; ⁴Professor, Amity Institute of Biotechnology, Amity University, Noida, U.P., India.; ⁵Professor, Dept. of Urology, Tulane University School of Medicine; ⁶Research Associate Professor, Dept. of Pharmacology, Tulane University School of Medicine
(Presented By: Namrata Khurana, M.TECH)

Introduction: Androgen deprivation therapy (ADT) suppresses the growth of prostate cancer (PC) expressing full length androgen receptor (AR-fl). However, castration resistant prostate cancer (CRPC) recurs due to the induction of ligand-independent AR splice variants, particularly AR-V7. Strategies to suppress both AR-fl and AR-V7 levels are critically needed for treating CRPC.

Our previous study demonstrated that sulforaphane (SFN), an isothiocyanate phytochemical, enhances the rate of degradation of AR-fl in several PC cell lines, e.g. LNCaP and C4-2B. SFN has been shown to inhibit the chaperone activity of heat-shock protein 90 (HSP90) and induce the potent antioxidant transcription factor, nuclear factor erythroid-2-like 2 (Nrf-2). We hypothesize that the combined exposure of SFN with clinically approved drugs that inhibit HSP90 (e.g. Ganetespiib) (G) and activate Nrf-2 (e.g. Bardoxolone-methyl) (BM) would suppress AR-fl and AR-V7 for treating CRPC.

Methods: The current study was conducted in AR-V7- expressing CRPC cell line, CWR22RV1 (22RV1). Effect of drug(s) on cell viability and migration were monitored by MTT and migration assays, respectively. AR protein expression and its subcellular localization were measured by immunoblot analysis (IB) and immunofluorescence microscopy (IFM), respectively. Proteasomal activity was monitored by proteasomal assay.

Results: 22RV1 cells were significantly (p<0.05) more resistant to the potent anti-androgen, enzalutamide (ENZ) compared to LNCaP and C4-2B cells. Co-exposure to SFN (5-25 μM) significantly (p<0.01) enhanced the efficacy of ENZ. The immunoblot studies showed that SFN decreases the half-life of both AR-fl and AR-V7 proteins (p<0.01), possibly by increased protein ubiquitination and proteasomal activity. The IFM analysis showed that SFN treatment down-regulated both cytosolic and nuclear AR levels. Co-exposure of SFN with physiologic doses (<1 μM) of G and BM caused rapid degradation of both AR-fl and AR-V7, decreased cell viability and further augmented the efficacy of ENZ in 22RV1 cells.

Conclusion: Our findings suggest that the multimodal actions of SFN can cause rapid decrease in both AR-fl and AR-V7 protein levels and further implicate that its combination with G and BM is an effective adjunct to current ADT in CRPC patients, especially those expressing AR-V7.
POSTER SESSION I

Sunday, April 23, 2017
*Poster Session I
11:00 a.m. – 12:30 p.m.
Location: Symphony Ballroom I/II
*Not CME Accredited

Poster #1
DIFFERENTIAL TOLEROGENIC CAPACITY OF THE EPIDIDYMIS AND TESTIS IN MICE WITH CONDITIONAL DELETION OF TGFBR2 IN DENDRITIC CELLS.
Fernando Pierucci-Alves¹, Monica T. Midura-Kiela², Sherry D. Fleming³, Bruce D. Schultz¹ and Pawel R. Kiela⁴
¹Kansas State University, Dept of Anatomy & Physiology; ²University of Arizona, Dept of Pediatrics; ³Kansas State University, Division of Biology; ⁴University of Arizona, Depts of Pediatrics and Immunobiology
(Presented By: Fernando Pierucci-Alves, DVM)

Poster #2
HUMANIN TRANSGENIC MICE ARE PROTECTED FROM CYCLOPHOSPHAMIDE-INDUCED MALE GERM CELL APOPTOSIS
YanHe Lue MD¹, Hemal Mehta MS², James Hoang BS¹, Kelvin Yen PhD², Junxiang Wan PhD², Ronald Swerdloff MD¹, Pinchas Cohen MD² and Christina Wang MD¹
¹Division of Endocrinology, LABioMed at Harbor-UCLA; ²USC Leonard Davis School of Gerontology, University of Southern California, Los Angeles, CA
(Presented By: YanHe Lue, MD)

Poster #3
PATERNAL EXPOSURE TO ENVIRONMENTAL CONTAMINANTS ALTERS THE SPERM PROTEOME AND INDUCES NEGATIVE PREGNANCY OUTCOMES TRANSGENERATIONALLY
Janice Bailey PhD, Nancy Coté PhD, Clotilde Maurice PhD, Florence Roux-Dalvai MSc, Arnaud Droit PhD and Mathieu Dalvai PhD Université Laval
(Presented By: Janice L. Bailey, PhD)

Poster #4
DEVELOPMENT OF SPERM IN VITRO FROM SPERMATOGONIAL CELLS OF PREPUBERTAL CANCER PATIENTS
Mahmoud Huleihel PhD, Maram Abofoul-Azab PhD¹, Joseph Kapelushnik MD², Haim Pinkas MD² and Eitan Lunenfeld MD⁴
¹The Center of Advanced Research and Education in Reproduction, The Shraga Segal Dep. of Microbiology, Immunology and Genetics, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel.; ²Dep. of Pediatric Oncology and Hematology, Soroka Medical Center, Beer-Sheva, Israel; ³Male Infertility & Sperm Bank, Helen Schneider Hospital for Women, Rabin Medical Center, Beilinson Hospital, PetaTikva, Israel.; ⁴Fertility and IVF Unit, Dep. OB/GYN, Soroka Medical Center and The Center of Advanced Research and Education in Reproduction, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel.
(Presented By: Mahmoud Huleihel PhD)

Poster #5
REGULATION OF CYP26B1 EXPRESSION IN THE SPERMATOGONIAL STEM CELL NICHE
Parag Parekh PHD¹, Thomas Garcia PHD¹, Reham Waheeb DVM, PHD³, Vivek Jain MS¹,², Gunapal Shetty PHD¹, Marvin Meistrich PHD¹, Marie-Claude Hofmann PHD¹ and Pooja Gandhi MS¹
¹University of Texas MD Anderson Cancer Center; ²University of Houston Clear Lake; ³University of Alexandria, Damanhour
(Presented By: Parag Parekh, PhD)

Poster #6
HIGH-RESOLUTION PHENOTYPING OF SPERMATOGONIAL DEFECTS USING SINGLE-CELL SEQUENCING
Min Jung, Janeette Rusch PhD, Abul Usmani PhD and Don Conrad PhD
Department of Genetics, Washington University in St. Louis
(Presented By: Min Jung)
Poster #7
ISOTRETINOIN IMPROVES TOTAL MOTILE SPERM COUNT IN SOME MEN WITH IDIOPATHIC OLIGOASTHENOZOOSPERMIA
John Amory, Kevin Ostrowski MD¹, John Gannon MD², Kathryn Berkseth MD¹, Faith Stevison MS¹, Nina Isoherranen PhD¹, Charles Muller PhD¹ and Thomas Walsh MD, MSE¹
¹UW; ²Intermountain Health
(Presented By: John K. Amory, MD, MPH)

Poster #8
GNRH-ANTAGONIST TREATMENT BEFORE ALLOGENEIC SPERMATOGONIAL STEM CELL TRANSPLANTATION ENHANCES SPERMATOGENIC RECOVERY IN RHESUS MONKEYS
Gunapala Shetty PhD¹, Jennifer Mitchell VMD¹, Zhuang Wu MD¹, Truong Lam BS¹, Lorraine Hill DVM¹, Ramesh Tailor PhD¹, Karen Peters BS², Kyle Orwig PhD² and Marvin Meistrich PhD¹
¹University of Texas M.D. Anderson Cancer center; ²Magee-Womans Research Institute, University of Pittsburgh School of Medicine
(Presented By: Gunapala Shetty, PhD)

Poster #9
SPERM MITOCHONDRIAL COPY NUMBER AND DELETIONS: ASSOCIATIONS WITH URINARY-ISOPROSTANE AND PHTHALATE METABOLITES IN MALE PARTNERS UNDERGOING ASSISTED REPRODUCTIVE TECHNOLOGIES (ART)
Alexandra Olmsted¹, Haotian Wu MS¹, Rahil Tayyab PhD², Cynthia Sites MD² and J.Richard Pilsner MPH, PhD³
¹University of Massachusetts Amherst, Department of Environmental Health; ²Baystate Medical Center, Department of Obstetrics and Gynecology
(Presented By: Alexandra Olmsted)

Poster #10
EFFECTS OF LONG-TERM TESTOSTERONE THERAPY (TTH) WITH TESTOSTERONE UNDECAANOATE INJECTIONS (TU) ON ANTHROPOMETRIC AND METABOLIC PARAMETERS IN HYPOGONADAL MEN AND AN UNTREATED CONTROL GROUP: REAL-LIFE REGISTRY DATA FROM A UROLOGY/ANDROLOGY OFFICE
Farid Saad DVM, PhD¹,²,³, Aksam Yassin MD, PhD⁴, Gheorghe Doros PhD⁵ and Abdulmaged Traish PhD⁶
¹Bayer AG, Berlin, Germany; ²Dresden International University, Berlin, Germany; ³Gulf Medical University, Ajman, UAE; ⁴Institute of Urology and Andrology; ⁵Boston University School of Public Health; ⁶Boston University School of Medicine
(Presented By: Farid Saad, DVM, PhD)

Poster #11
IMPLICATIONS OF ANDROGEN RECEPTOR ACTIVATION ON THYROID CANCER PHENOTYPE
Anvita Gupta BE¹, Melanie Jones PhD², Timmy O'Connell MS¹, Monica Schwarcz MD¹, Dorota Halicka MD, PhD¹, Jiangwei Li PhD¹, Zbigniew Darzynkiewicz MD, PhD¹, JK Rasamny MD¹, Codrin Iacob MD³, Nina Suslina MD¹, Edward Shin MD¹, Augustine Moscatello MD¹, Raj Tiwari PhD¹ and Jan Geliebter PhD¹
¹New York Medical College; ²United States Military Academy Preparatory School, West Point, NY; ³New York Eye and Ear Infirmary
(Presented By: Anvita Gupta, BE)

Poster #12
TARGETED DEGRADATION OF ANDROGEN RECEPTOR (AR) AND ITS SPLICED VARIANT AR-V7 BY THE PHYTOCHEMICAL SULFORAPHANE: NEW THERAPEUTIC OPPORTUNITY FOR CASTRATION RESISTANT PROSTATE CANCER (CRPC)
Namrata Khurana M TECH¹, Hogyoun Kim PhD², Partha K. Chandra PhD³, Sudha Talwar PhD³, Pankaj Sharma PhD⁴, Asim B. Abdel-Mageed PhD³, Debasis Mondal PhD⁵ and Suresh C. Sikka PhD⁶
¹PhD Student; ²Post Doc, Dept. of Urology, Tulane University School of Medicine; ³Post Doc, Dept. of Pharmacology, Tulane University School of Medicine; ⁴Professor, Amity Institute of Biotechnology, Amity University, Noida, U.P., India.; ⁵Professor, Dept. of Urology, Tulane University School of Medicine; ⁶Research Associate Professor, Dept. of Pharmacology, Tulane University School of Medicine
(Presented By: Namrata Khurana, M.TECH)
POSTER SESSION I

Poster #13
EFFECTS OF TESTOSTERONE REPLACEMENT THERAPY ON METABOLIC DISORDERS IN PATIENT WITH TYPE 2 DIABETES MELLITUS AND ANDROGEN DEFICIENCY.
Shota Janjgava MD, PhD¹, Elene Giorgadze MD, PhD² and Lasha Uchava MD, PhD²
¹National Institute of Endocrinology; ²National Institute of Endocrinology
(Presented By: Shota Janjgava, PhD)

Poster #14
GASTRIC DISORDERS, HIGHER STRESS AND IRRITABILITY ARE ASSOCIATED WITH MALE INFERTILITY
Dayane Reis BSc student¹,²,³, Juliana R Pariz MSc, PhD student¹,²,³,⁴,⁵, Victória Coutinho BSc student¹,²,³,⁴, Rosa Alice C Monteiro BSc¹, and Jorge Hallak MD; PhD¹,³,⁴,⁵
¹Androscience – High Complexity Clinical and Research Andrology Laboratory, Brazil; ²Methodist University of Sao Paulo, Brazil; ³Dept. of Urology, FMUSP, Brazil; ⁴Reproductive Toxicology Unit, Dept. of Pathology, FMUSP, Brazil; ⁵Oswaldo Cruz German, Brazil
(Presented By: Dayane Guerino Reis, BSc)

Poster #15
THE INFLUENCE OF WINE CONSUMPTION IN MALE FERTILITY POTENTIAL: INITIAL REPORT
Victória Coutinho BSc student¹,²,³, Juliana Pariz PhD student¹,²,³,⁴, Dayane Reis BSc student¹,²,³,⁴, Rosa Monteiro BSc¹,⁶ and Jorge Hallak MD;PhD¹,³,⁵,⁶
¹Androscience – High Complexity Clinical and Research Andrology Laboratory, Brazil; ²Methodist University of Sao Paulo, Brazil; ³Department of Urology, FMUSP, Brazil; ⁴Reproductive Toxicology Unit, Department of Pathology, FMUSP, Brazil; ⁵Oswaldo Cruz German, Brazil
(Presented By: Victória Santos Coutinho)

Poster #16
ARE RESPIRATORY ALLERGIES RELATED TO MALE FERTILITY?
Dayane Reis BSc student¹,²,³, Juliana Pariz PhD student¹,²,³,⁴, Victória Coutinho BSc student¹,²,³,⁴, Rosa Alice Monteiro BSc¹, and Jorge Hallak MD;PhD¹,³,⁴,⁵
¹Androscience – High Complexity Clinical and Research Andrology Laboratory, Brazil; ²Methodist University of Sao Paulo, Brazil; ³Dept. of Urology, FMUSP, Brazil; ⁴Reproductive Toxicology Unit, Dept. of Pathology, FMUSP, Brazil; ⁵Oswaldo Cruz German, Brazil
(Presented By: Dayane Guerino Reis, BSc)

Poster #17
NEW INSIGHTS INTO THE PANDEMIC OF LOW VITAMIN “D” LEVELS AND ITS ASSOCIATION WITH SEMEN QUALITY AND HORMONAL LEVELS IN FERTILE AND INFERTILE MALE SUBJECTS
Inari Ciccone BSc; MSc student¹,²,³, Juliana R Pariz MSc; PHD Student¹,²,³,⁴, Elaine Costa MD; PHD¹,²,³,⁴,⁵ and Jorge Hallak MD, PHD¹,²,³,⁴,⁵
¹Androscience – High Complexity Clinical and Research Andrology Laboratory, Brazil; ²Methodist University of Sao Paulo, Brazil; ³Dept. of Urology, USP, Brazil; ⁴Reproductive Toxicology Unit, Dept. of Pathology, USP, Brazil; ⁵Oswaldo Cruz German Hospital, Brazil
(Presented By: Inari Ciccone, Msc Student)

Poster #18
HEAT SHOCK PROTEINS 70 AND 90 ALPHA ARE INCREASED IN SEMEN OF SMOKERS
Mariana Antoniassi BSc, MSc, Larissa Belardin BSc, MSc, Rhayza Andretta BSc, MSc, Jheysson Moura BSc and Ricardo Bertolla DVM, PhD
Department of Surgery, Division of Urology, Human Reproduction Section, Sao Paulo Federal University
(Presented By: Mariana Pereira Antoniassi, BSc, MSc)

Poster #19
SPERM DNA INTEGRITY IN ADULT SURVIVORS OF PAEDIATRIC LEUKEMIA AND LYMPHOMA
Hermance Beaud MSc¹, Oceane Albert PhD², Bernard Robaire PhD³, Marie Claude Rousseau PhD¹, Peter Chan MD, CM, MSc⁴ and Geraldine Delbes PhD¹
¹INRS-Institut Armand-Frappier, Laval, Canada; ²Department of Pharmacology and Therapeutics, McGill University, Montreal, (Quebec) Canada; ³Department of Pharmacology and Therapeutics, McGill University, Montreal, (Quebec) Canada. Department of Obstetrics & Gynecology, McGill University, Montreal, QC, H4A 3J1, Canada.; ⁴Division of Urology, McGill University Health Center, Montreal, (Quebec) Canada.
(Presented By: Hermance Beaud MSc)
POSTER SESSION I

Poster #20
ASSOCIATIONS OF PHENOLS AND PARABENS WITH SPERM GENOME-WIDE DNA METHYLATION
Haotian Wu¹, Molly Estill², Stephen A. Krawetz², Cynthia Sites³, Tayyab Rahil³ and J. Richard Pilsner¹
¹UMass Amherst; ²Wayne State University School of Medicine; ³Baystate Medical Center
(Presented By: Haotian Wu)

Poster #21
EFFECTS OF PRENATAL EXPOSURE TO DI-N-BUTYL PHTHALATE ON THE DEVELOPMENT OF ADULT LEYDIG CELLS IN RAT DURING PUBERTY
Linxi Li PhD¹, Guoxin Hu PhD², Xiaomin Chen PhD¹, Huitao Li Master¹ and Ren-Shan Ge MD¹
¹The Second Affiliated Hospital and Yuying Children’s Hospital of Wenzhou Medical University; ²School of Pharmaceutical Sciences of Wenzhou Medical University
(Presented By: Linxi Li, PhD)

Poster #22
AMELIORATIVE EFFECTS OF VITAMIN C ON THE HEMATOLOGY, SEMEN QUALITY AND HORMONAL PROFILE OF TEDDY GOAT BUCKS IN ARSENIC TOXICITY
Muhammad Zubair, PhD
University of Poonch rwawalakot Azad Kashmir
(Presented By: Muhammad Zubair, Lecturer)

Poster #23
IS IT POSSIBLE FOR SMOKING-ABSTINENCE TO REVERSE THE NICOTINE-INDUCED ALTERATIONS IN THE EPIDIDYMIS?
Panagiota Tsounapi PhD¹, Masashi Honda PhD², Fotios Dimitriadiis PhD³, Katsuya Hikita PhD², Nikolaos Sofikitis PhD, DMSci⁴ and Atsushi Takenaka PhD²
¹Division of Urology Tottori University Faculty of Medicine; ²Division of Urology Tottori University Faculty of Medicine; ³Department of Urology Aristotle University; ⁴Department of Urology University of Ioannina School of Medicine
(Presented By: Panagiota Tsounapi, PhD)

Poster #24
PURINERGIC MODULATION OF V-ATPASE-DEPENDENT PROTON SECRETION IN EPIDIDYMAL CLEAR CELLS
Maria Agustina Battistone PhD¹, Flavia Gombar Master², Maria Alejandra Peralta Bachelor¹, Nicolas DaSilva PhD¹, Dennis Brown PhD and Sylvie Breton PhD¹
¹Program in Membrane Biology/Division of Nephrology. Massachusetts General Hospital. Harvard Medical School; ²Laboratory of Morphometry, Metabolism & Cardiovascular disease Department of Anatomy - IBRAg - UERJ
(Presented By: Maria Agustina Battistone, PhD)

Poster #25
MAZ HAPLOINSUFFICIENCY ALTERS BACULUM MORPHOGENESIS IN MICE
Marisol O'Neill MS, Gene Huang MD, Meade Haller PhD and Dolores J. Lamb PhD
Baylor College of Medicine
(Presented By: Marisol Ann O'Neill, M.S.)

Poster #26
CRITICAL ROLE OF REGULATORY SPERMATOZOAL TRANSCRIPTS IN EARLY EMBRYONIC DEVELOPMENT
VIDHU DHAWAN MD, MANOJ KUMAR MSc PhD, DIPIKA DEKA MD, NEENA MALHOTRA MD, NEETA SINGH MD, VATSLA DADHWAL MD and RIMA DADA MD
AIIMS, NEW DELHI, INDIA
(Presented By: Vidhu Dhawan, MBBS, MD)

Poster #27
RETROSPECTIVE STUDY ON 1578 CASES OF PATIENTS WITH AZOOSPERMIA WHO HAVE TAKEN PRIOR DIAGNOSTIC TESTICULAR BIOPSY.
Xunbin Huang, wenjing Li BS, na Fang Bs and congcong Cao Bs
Family Planning Research Institute, Tongji Medical College, Huazhong University of Science and Technology
(Presented By: Xunbin Huang, MD)
POSTER SESSION I

Poster #28
ANALYSIS OF THE CELLULAR AND NUCLEAR INTEGRITY OF SPERM FROM PATIENTS WITH VARICOCELE
Viviane Paiva Santana MSc, Cristiana Libardi Miranda-Furtado PhD, Daiana Cristina Chieli Pedroso MSc, Matheus Credendio Eiras, Marilda Hatsumi Yamada Fantas and Rosana Maria Reis MD, PhD
Department of Gynecology and Obstetrics, Ribeirao Preto Medical School, University of Sao Paulo, Ribeirao Preto, Brazil
(Presented By: Viviane Paiva Santana, MSc.)

Poster #29
IMPACT OF INCREASED SEMINAL 8-HYDROXY-2’-DEOXYGUANOSINE LEVELS ON INCREASED RISK OF CHILDHOOD CANCER RETINOBLASTOMA
Shilpa Bisht MSc, Bhavna Chawla MS, Manoj Kumar MSc, PhD and Rima Dada MD, PhD
All India Institute of Medical Sciences, New Delhi, India
(Presented By: Shilpa Bisht, MSc)

Poster #30
SIMPLE AND HIGHLY EFFICIENT POLYETHYLENIMINE TRANSFECTION PROTOCOL FOR TRANSIENT TRANSFECTION IN MOUSE SPERMATOGENIAL STEM CELLS
Chatchanan Doungkamchan MD¹, Yi Sheng MD², Meena Sukhwani PhD³, and Kyle E. Orwig PhD¹,²
¹Molecular Genetics and Developmental Biology Graduate Program, Magee-Womens Research Institute, University of Pittsburgh School of Medicine; ²Magee-Womens Research Institute, Pittsburgh; ³Department of Obstetrics, Gynecology and Reproductive Sciences, Magee-Womens Research Institute, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213
(Presented By: Chatchanan Doungkamchan, MD)

Poster #31
SPERM DNA METHYLATION ALTERATIONS AND EPIGENETIC VARIABILITY IN TOBACCO SMOKERS
Emma James BS¹, Timothy Jenkins PhD², David Alonso BS³, James Hotaling MD, MS⁴, Douglas Carrell PhD and Kenneth Aston PhD²
¹Andrology and IVF Laboratories, Department of Surgery, University of Utah School of Medicine, Salt Lake City, Utah, USA; ²Andrology and IVF Laboratories, University of Utah Department of Surgery, Salt Lake City, Utah, USA; ³Department of Obstetrics, Gynecology and Reproductive Sciences, Magee-Womens Research Institute, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213
(Presented By: Emma Rae James, BS)

Poster #32
IN VITRO CULTURE OF KLINEFELTER MOUSE SPERMATOGONIAL STEM CELLS
Guillermo Galdon MD¹, Nima Pourhabibi Zarandi MD², YanHe Lue MD, PhD², Ronald Swerdloff MD³, Stanley Kogan MD, FACS⁴,⁵, Hooman Sadri-Ardekani MD, PhD¹,² and Anthony Atala MD¹,²,⁴,⁵
¹Wake Forest Institute for Regenerative Medicine; ²Wake Forest Institute for Regenerative Medicine; ³Division of Endocrinology, Department of Medicine, Harbor-UCLA Medical Center and Los Angeles Biomedical Research Institute; ⁴Department of Urology; ⁵Wake Forest School of Medicine
(Presented By: Guillermo Galdon MD)

Poster #33
PRENATAL AND POSTNATAL GENETIC DIAGNOSIS OF 45,X/46,XY MOSAICISM AND ITS CLINICAL IMPLICATIONS: A 20-YEAR STUDY
Mahmoud Aarabi MD PhD¹, Urvashi Surti PhD², Selma F. Witchel MD³, Francis Schneck MD², Aleksandar Rajkovic MD PhD² and Svetlana Yatsenko MD²
¹Medical Genetics & Genomics Laboratories, Magee-Womens Hospital of UPMC and Department of Obstetrics, Gynecology and Reproductive Sciences, University of Pittsburgh School of Medicine, Pittsburgh, PA; ²Medical Genetics & Genomics Laboratories, Magee-Womens Hospital of UPMC and Departments of Obstetrics, Gynecology and Reproductive Sciences, Pathology, Human Genetics, University of Pittsburgh, Pittsburgh, PA; ³Pediatric Endocrinology, Children’s Hospital of Pittsburgh of UPMC, Pittsburgh, PA; ⁴Pediatric Urology, Children’s Hospital of Pittsburgh of UPMC, Pittsburgh, PA; ⁵Medical Genetics & Genomics Laboratories, Magee-Womens Hospital of UPMC and Departments of Obstetrics, Gynecology and Reproductive Sciences, Pathology, Human Genetics, University of Pittsburgh, and Magee-Womens Research Institute, Pittsburgh, PA
(Presented By: Mahmoud Aarabi, MD PhD)
Poster #34
WHOLE EXOME SEQUENCING IDENTIFIES GENES AND PATHWAYS WITH POTENTIAL INVOLVEMENT IN PEYRONIE’S AND DUPUYTREN’S DISEASES
Alexander W. Pastuszak MD, PhD, Yofre Cabeza-Arvelaiz PhD, Suman Maity PhD, Cristian Coarfa PhD, Larry I. Lipshultz MD and Dolores J. Lamb PhD
Baylor College of Medicine
(Presented By: Alexander W. Pastuszak, MD, PhD)

Poster #35
CHARACTERIZATION OF THE PARTIAL AZFc Y-CHROMOSOME MICRODELETIONS IN SUBFERTILE AND INFERTILE MEN
Phil Bach MD¹, Anna Mielnik MS², Alexander Bolyakov MS³, Ryan Flannigan MD², Peter Schlegel MD² and Darius Paduch MD, PhD²
¹Weill Cornell Medicine; ²Department of Urology, Weill Cornell Medicine
(Presented By: Phil V. Bach, MD)

Poster #36
LOSS OF TRANSLATIONAL SUPPRESSION OF PRM1/2 VIA YBX2 IS A CULPRIT OF EARLY AND LATE MATURATION ARREST IN HUMANS.
Ryan Flannigan MD¹, Anna Mielnik MSc¹, Alex Bolyakov MSc¹, Phil Bach MD¹, Peter Schlegel MD¹, Jen Grenier PhD², Andrew Grimson PhD² and Darius Paduch MD PhD¹
¹Weill Cornell Medical College; ²Cornell University
(Presented By: Ryan Kendrick Flannigan, BSc (Hon), MD)

Poster #37
TESTICULAR PATHOLOGY IS NOT ALTERED IN OBESE INFERTILE MEN WHO PRESENT SEMEN ANALYSES, SPERM FUNCTIONAL TESTS, ELECTRON MICROSCOPY AND TESTIS HISTOLOGY IN OBESE INFERTILE PATIENTS
Caroline Ranéa BSc¹,²,³, Juliana Risso Pariz MSc, PhD student¹,²,³,4,5, Rosa Alice Casemiro Monteiro BSc¹,², Inari Ciccone BSc, MSc student¹,²,³,4, Elaine Maria Frade Costa MD, PhD¹,³,4,5, Hector E Chemes MD, PhD¹ and Jorge Hallak MD, PhD¹,²,³,4,5
¹Androscience – High Complexity Clinical and Research Andrology Laboratory, Brazil; ²Dept. of Urology, FMUSP, Brazil; ³Reproductive Toxicology Unit, Dept. of Pathology, FMUSP, Brazil; ⁴Methodist University of Sao Paulo, Brazil; ⁵Oswaldo Cruz German Hospital, Brazil
(Presented By: Caroline Ranea)

Poster #38
IMPROVING POST-THAW SPERM CRYOSURVIVAL RATES IN THE ANDROLOGY LAB: CHOOSING THE BEST PROCESSING TECHNIQUE PREVIOUS TO THE CRYOPRESERVATION PROCESS IS CRUCIAL
Beatriz de Campos BSc student¹,², Julia Pariz PhD student¹,²,³,4,5, Rosa Monteiro BSc¹,² and Jorge Hallak MD; PhD¹,²,³,4,5
¹Androscience – High Complexity Clinical and Research Andrology Laboratory, Brazil; ²Dept. of Urology, FMUSP, Brazil; ³Reproductive Toxicology Unit, Dept. of Pathology, Universidade de São Paulo, Brazil; ⁴Oswaldo Cruz German Hospital, Brazil
(Presented By: Beatriz Crossiol Vicente De Campos)

Poster #39 - WITHDRAWN

Poster #40
POSITIVE EFFECT OF MELATONIN AND CAFFEINE SUPPLEMENTATION IN STRUCTURAL AND FUNCTIONAL CHARACTERISTICS IN PRE-FREEZE AND POST-THAW SEMEN SAMPLES
Juliana R Pariz MSc, PhD student¹,²,³, Priscilla R Costa PhD¹, Dayane G Reis BSc student¹,²,³, Victória S Coutinho BSc student¹,²,³, Donald P Evenson PhD and Jorge Hallak MD, PhD¹,²,³,4
¹Androscience – High Complexity Clinical and Research Andrology Laboratory, Brazil; ²Dept. of Urology, USP, Brazil; ³Reproductive Toxicology Unit, Dept. of Pathology, USP, Brazil; ⁴Oswaldo Cruz German Hospital, Brazil; ⁵Department of Immunology, Universidade de São Paulo, Brazil; ⁶SCSA Diagnostics, United States of America
(Presented By: Juliana Risso Pariz, BSc, MSc)
POSTER SESSION I

Poster #41
VITAMIN E REDUCES INTRACELLULAR SUPEROXIDE ANION ACTIVITY IN CRYOPRESERVED HUMAN SEMEN
Bruna Lima BSc, Luana Adami BSc, Larissa Belardin MSc, Fátima Okada PhD, Ricardo Bertolla DVM, PhD and Deborah Spaine PhD
Universidade Federal de São Paulo
(Presented By: Larissa Belardin, MSc)

Poster #42
SEmen CRISP3 LEVELS IN THE ADULT VARICOCELE.
Larissa Belardin MSc, Mariana Camargo PhD, Paula Intasqui MSc, Paula Del Giudice PhD, Mariana Antoniassi MSc, Renato Fraietta MD; PhD and Ricardo Bertolla DVM; PhD
Universidade Federal de São Paulo - UNIFESP
(Presented By: Larissa Belardin, MSc)

Poster #43
THE EFFECT OF TESTICULAR GERM CELL TUMORS ON FUNCTIONAL ASPECTS OF SPERM AND OXIDATIVE STRESS OF SEMINAL PLASMA
Maria Beatriz Ribeiro de Andrade MSc, Paula Intasqui MSc, Larissa Belardin MSc, Danielle Tibaldi MSc, Ricardo Pimenta Bertolla DVM; PhD and Deborah Montagnini Spaine PhD
Sao Paulo Federal University
(Presented By: Maria Beatriz Ribeiro De Andrade, BSc, MSc)

Poster #44
TRANSGENDER SPERM CRYOPRESERVATION: TRENDS AND FINDINGS IN THE PAST DECADE
Kai Li MD¹, Dayron Rodriguez MD¹, Scott Gabrielsen MD, PhD¹, Amy Blanchard², Grace Centola PhD² and Cigdem Tanrikut MD¹
¹Massachusetts General Hospital; ²New England Cryogenic Center
(Presented By: Kai Li, MD)

Poster #45
NORMAL PREOPERATIVE FOLLICLE-STIMULATING HORMONE LEVEL IS ASSOCIATED WITH IMPROVEMENT IN SEMEN PARAMETERS FOLLOWING MICROSCOPIC VARICOCELECTOMY
Lunan Ji MD, Samuel Shabtaie, Nachiketh Soodana Prakash MD and Ranjith Ramasamy MD
University of Miami
(Presented By: Lunan Ji, MD)

Poster #46
EFFECT OF SPERM MORPHOLOGY ON INTRAUTERINE INSEMINATION PREGNANCY SUCCESS: A SYSTEMATIC REVIEW AND META-ANALYSIS
Taylor P. Kohn MPhil¹, Jaden R. Kohn BS¹, Nancy Brackett PhD², Charles Lynne MD² and Ranjith Ramasamy MD²
¹Baylor College of Medicine, Houston, TX; ²Department of Urology, University of Miami Miller School of Medicine, Miami, FL
(Presented By: Taylor P. Kohn, MPhil)

Poster #47
A SYSTEMATIC REVIEW OF THE EFFICACY AND SAFETY OF TRANSURETHRAL SURGERY FOR EJACULATORY DUCT OBSTRUCTION-RELATED INFERTILITY
Clark Judge BA and Peter Stahl MD
Columbia University
(Presented By: Clark Judge, BA)

Poster #49 - WITHDRAWN

Poster #50
POLICY ON POSTHUMOUS SPERM RETRIEVAL: SURVEY OF 75 MAJOR ACADEMIC MEDICAL CENTERS
Nicholas Waler¹ and Ranjith Ramasamy MD²
¹University of Miami Miller School of Medicine; ²Department of Urology, University of Miami, Miami, FL
(Presented By: Nicholas Waler)
POSTER SESSION I

Poster #51
SERUM METABOLIC PROFILING IDENTIFIES CHARACTERIZATION OF NON-OBSTRUCTIVE AZOOSPERMIC MEN
Zhe Zhang MD, Yuzhuo Yang MD and Hui Jiang MD
Peking University Third Hospital
(Presented By: Zhe Zhang, MD)

Poster #52
PENILE PROSTHESIS COMPLICATIONS: A DESCRIPTIVE STUDY OF THE DETROIT AFRICAN AMERICAN PATIENT POPULATION.
Mohammed Zaher DO¹, William Ducomb Medical Student², Maha Husainat Research Assistant¹, Ibraheem Malik Research Assistant¹ and Mazen Abdelhady MD¹
¹Detroit Medical Center; ²Michigan State University
(Presented By: Mohammed T. Zaher, DO)

Poster #53
SOCIOECONOMIC DISPARITIES IN THE TREATMENT OF ERECTILE DYSFUNCTION: A SYSTEMATIC REVIEW
Denise Asafu-Adjei MD, MPH¹, Mofan Gu MPH¹, Matthew Pagano MD¹, Ifeanyi Onyeji MD¹ and Peter Stahl MD¹
¹Columbia University Medical Center; ²Columbia University Mailman School of Public Health
(Presented By: Denise A. Asafu-Adjei, MD)

Poster #54
TESTICULAR SPERM RETRIEVAL IN LATE ADOLESCENTS (AGED 15-19 YEARS) WITH NON-MOSAIC KLINEFELTER SYNDROME AND AZOOSPERMIA
Han-Yu Weng, Yung-Ming Lin PhD and Yu-Sheng Cheng
National Cheng Kung University Hospital
(Presented By: Han-Yu Weng, MD)

Poster #55
ANXA7 AND PSMA5 ARE SEMINAL BIOMARKERS OF SPERM ACROSOME INTEGRITY.
Paula Intasqui MSc, Larissa Belardin MSc, Mariana Antoniassi MSc, Mariana Camargo PhD, Daniel S. Zylbersztejn PhD and Ricardo P. Bertolla PhD
Department of Surgery, Division of Urology, Sao Paulo Federal University
(Presented By: Paula Intasqui Lopes, MSc, BSc)

Poster #56
EFFECTS OF VARICOCELE ON SPERM CAPACITATION
Rhayza Andretta PhD candidate¹, Larissa Belardin MSc¹, Leticia Castro DVM, MSc², Jheysson Moura BSc¹, Renato Fraietta DM, PhD¹, Fatima Okada PhD¹ and Ricardo Bertolla DVM, PhD¹
¹Federal University of Sao Paulo; ²University of Sao Paulo (USP)
(Presented By: Rhayza Andretta PhD candidate)

Poster #57
PROTECTIVE ROLE OF LYCOPODIUM CLAVATUM ON AGEING INDUCED CHANGES IN SPERM CHARACTERISTICS AND TESTICULAR OXIDATIVE DAMAGE: A DOSE-DEPENDENT STUDY IN WISTAR ALBINO RATS
Ganesh Lakshmanan BHMS, MSc¹ and Prakash seppan PhD²
¹University of Madras; ²Department of Anatomy, University of Madras.
(Presented By: Ganesh Lakshmanan, BHMS, MSc)

Poster #58
OXIDATIVE STRESS EVALUATION IN LEUKOCYTOSPERMIC INFERTILE MEN: ROLE OF SEMINAL OXIDATION-REDUCTION POTENTIAL (ORP), 8-ISO-PGF2? AND PROTEIN CARBONYL CONTENT
Ahmet Ayaz PhD, Wayne J. Hellstrom MD, FACS and Suresh C. Sikka PhD, HCLD/CC
Tulane Medical Center, Department of Urology
(Presented By: Ahmet Ayaz PhD)
**POSTER SESSION I**

**Poster #59**
**POPULATION-BASED SEMEN ANALYSIS RESULTS AMONG PATIENTS WITH INFLAMMATORY BOWEL DISEASE**
Luke Martin MD¹, William Peche MD¹, Kathryn Peterson MD², Stephanie Chan MD², Ryan Morton MD², Yuan Wan MSCE³, Benjamin Emery PhD¹, Kenneth Aston PhD¹, Timothy Jenkins PhD⁴, Angela Presson PhD⁵, Chong Zhang MS⁵, Douglas Carrell PhD⁴ and James Hotaling MD MS⁶
¹University of Utah, Division of General Surgery; ²University of Utah, Division of Gastroenterology; ³University of Utah, Utah Population Database; ⁴University of Utah, Division of Andrology; ⁵University of Utah, Division of Epidemiology; ⁶University of Utah, Division of Urology
(Presented By: Luke Martin, MD)

**Poster #60**
**META-ANALYSIS: EFFECT OF SPERM DNA DAMAGE ON PREGNANCY OUTCOME AFTER ART**
Luke Simon PhD¹, Armand Zini MD² and Douglas Carrell PhD³
¹University of Utah; ²Division of Urology, Department of Surgery, St Mary’s Hospital Center, Mary’s Hospital, 3830 Lacombe Avenue, Montreal, Quebec, Canada H3T 1M5; ³Department of Surgery, University of Utah School of Medicine, Salt Lake City, UT, USA
(Presented By: Luke Simon PhD)

**Poster #61**
**COMPUTATIONAL FLOW CYTOMETRY REVEALS THAT CRYOPRESERVATION INDUCES SPERMPTOSIS BUT SUBPOPULATIONS OF SPERMATOZOA MAY EXPERIENCE CAPACITATION LIKE CHANGES**
Fernando Pena PhD¹, Cristina Ortega Ferrusola PhD², Patricia Martin DVM¹ and Jose Manuel Ortiz DVM³
¹University of Extremadura; ²University of Leon; ³UNIVERSITY OF EXTREMADURA
(Presented By: Fernando Juan Pena Vega, PhD)

**Poster #62 - WITHDRAWN**

**Poster #63**
**EFFECT OF GHRELIN ON MOUSE REPRODUCTIVE PERFORMANCE AND SPERMATOGENESIS**
Enrica Bianchi PhD¹, Kim Boekelheide MD, PhD², Mark Sigman MD¹, Susan Hall BS² and Kathleen Hwang MD¹
¹Division of Urology/Surgery; ²Department of Pathology and Laboratory Medicine
(Presented By: Enrica Bianchi, PhD)

**Poster #64**
**DYNAMIC SUBCELLULAR LIPID ORGANIZATION IN HORMONE INDUCED MA-10 MOUSE TUMOR LEYDIG CELLS.**
Sathvika Venugopal PhD¹, Rachel Chan BS², Esha Sanyal BS², Lorne Taylor MSc¹ and Vassilios Papadopoulos DPharm, PhD, DSc ³
¹Research Institute of the McGill University Health Centre and Department of Medicine, McGill University; ²McGill University; ³Research Institute of the McGill University Health Centre and Department of Medicine, McGill University and Department of Pharmacology & Pharmaceutical Sciences, School of Pharmacy, University of Southern California
(Presented By: Sathvika Venugopal PhD)

**Poster #65**
**GONADOTROPIN INDEPENDENT ANDROGEN SYNTHESIS IN THE HUMAN PREPUBERTAL TESTIS: BREAKING THE DOGMA**
Paula Aliberti¹, Maria Sonia Baquedano PhD², Nora Isabel Saraco PhD², Roxana Marino², Marco Aurelio Rivarola MD, PhD², Esperanza Beatriz Berenzstein PhD² and Alicia Belgorosky MD, PhD²
¹Endocrinology Service, Hospital de Pediatria Garrahan, Buenos Aires, Argentina sonybaquedano@yahoo.com.ar; ²Endocrinology Service, Hospital de Pediatria Garrahan, Buenos Aires, Argentina
(Presented By: Paula Aliberti)

**Poster #66**
**THE ROLE OF HMGN5 IN SPERMATOGENESIS**
Boryana Zhelyazkova, Carolina Jorgez PhD¹ and Dolores J. Lamb PhD²
¹Scott Department of Urology, Baylor College of Medicine, Houston, Texas; ²Center for Reproductive Medicine, Department of Molecular and Cellular Biology, Scott Department of Urology, Baylor College of Medicine, Houston, Texas
(Presented By: Boryana Zhelyazkova)
POSTER SESSION I

Poster #67
MULTIPLE NUCLEAR RECEPTORS AND SIGNALLING PATHWAYS ARE AFFECTED BY INHIBITION OF SERTOLI CELL SUMOYLATION
KeumSil Hwang MA¹, Keisuke Okada MD, PhD¹ and Patricia L Morris MS, PhD²
¹Population Council; ²Population Council, The Rockefeller University
(Presented By: Keumsil Hwang, BS, MS)

Poster #68
DEFECTS OF USP42 CAUSE MALE INFERTILITY AND ARE ASSOCIATED WITH NONOBSTRUCTIVE AZOOSPERMIA IN MEN
Bo Zheng PhD and Mingxi Liu PhD
State Key Laboratory of Reproductive Medicine, Department of Histology and Embryology, Nanjing Medical University
(Presented By: Bo Zheng, Jr., PhD)

Poster #69
3 DIMENSIONAL HUMAN TESTIS ORGANOID SYSTEM CREATED FROM IMMATURE TESTICULAR CELLS
Nima Pourhabibi Zarandi MD¹, Guillermo Galdon MD¹, Hooman Sadri-Ardekani MD, PhD² and Anthony Atala MD²
¹Wake Forest Institute for Regenerative Medicine, Wake Forest School of Medicine; ²Wake Forest Institute for Regenerative Medicine, and Department of Urology, Wake Forest School of Medicine
(Presented By: Nima Pourhabibi Zarandi, MD)

Poster #70
CLONAL DEVELOPMENT OF SPERMATOGONIA IN RHESUS TESTES
Adetunji Fayomi DVM, MVSc, Karen Peters BS¹ and Kyle Orwig PhD²
¹Magee Womens Research Institute; ²Magee Womens Research Institute, University of Pittsburgh School of Medicine
(Presented By: Adetunji Fayomi, DVM)

Poster #71
VITAMIN A DEFICIENT LECITHIN RETINOL ACYLTRANSFERASE (LRAT) MICE SERVE AS AN INDUCIBLE MODEL OF SERTOLI CELL ONLY SYNDROME
Ryan Flannigan MD¹, Anna Mielnik MSc¹, Alex Bolyakov MSc¹, Jen Grenier PhD², William Wright PhD³, Lorraine Gudas PhD¹, Peter Schlegel MD¹ and Darius Paduch MD PhD¹
¹Weill Cornell Medical College; ²Cornell University; ³John Hopkins University
(Presented By: Ryan Kendrick Flannigan, BSc (Hon), MD)

Poster #72
KNOCKDOWN OF IFT140 MAY DISRUPT SPERMATOGENESIS BY DYSREGULATING THE NFKB SIGNALING PATHWAY
Amin Herati MD¹, Peter Bulter BA¹ and Dolores Lamb PhD²
¹Baylor College of Medicine, Scott Department of Urology, Center for Reproductive Medicine; ²Baylor College of Medicine, Scott Department of Urology, Center for Reproductive Medicine, Department of Molecular and Cellular Biology
(Presented By: Amin S. Herati, MD)

Poster #73
MUTATION OF A SINGLE AMINO ACID OF MEIOSIS-EXPRESSED GENE 1 BY CRISPR/CAS9 SYSTEM RESULTS IN IMPAIRED SPERMIOGENESIS AND MALE INFERTILITY IN MICE
Shiyang Zhang, Wei Li MD¹, Hong Liu MD², Ling Zhang MD, PhD¹, Yuhong Li MD, PhD², Rex Hess PhD³ and Zhibing Zhang MD, PhD¹
¹Virginia Commonwealth University; ²Virginia Commonwealth University/Wuhan University of Science and Technology; ³Wuhan University of Science and Technology; ⁴University of Illinois
(Presented By: Shiyang Zhang, Master)
**Poster #74**

RESTORATION OF AGING LEYDIG CELL STEROIDOGENIC FUNCTION IN VITRO: INVOLVEMENT OF EXTRINSIC FACTORS IN LEYDIG CELL AGING

Yiyan Wang MD¹,², Leping Ye PhD¹, June Liu BS², Renshan Ge PhD¹, Barry Zirkin PhD² and Haolin Chen PhD¹,²

¹The Second Affiliated Hospital and Yuying Children’s Hospital of Wenzhou Medical University, Wenzhou, Zhejiang, China; ²Department of Biochemistry and Molecular Biology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland

(Presented By: Yiyan Wang)

**Poster #75**

TSEP7, A SMALL PROTEIN ENCODED BY A PUTATIVE LONG NONCODING RNA, NEGATIVELY REGULATES PROLIFERATION OF UNDIFFERENTIATED SPERMATOGENIA BY AFFECTING CHROMATIN STRUCTURE

Mingxi Liu PhD
Nanjing Medical University

(Presented By: Mingxi Liu, PhD)

**Poster #97**

WHOLE EXOME SEQUENCING OF A CONSANGUINEOUS TURKISH FAMILY IDENTIFIES A MUTATION IN GTF2H3 IN BROTHERS WITH MALE FACTOR INFERTILITY

Raul Clavijo MD¹, Samuel Cohen¹, Anthony Griswold PhD², Emre Bakircioglu MD³ and Ranjith Ramasamy MD¹

¹University of Miami Miller School of Medicine; ²John P. Hussman Institute for Human Genomics, Miami, FL; ³Urology and Andrology, Istanbul, Turkey

(Presented By: Raul Clavijo, MD)
POSTER SESSION II

Monday, April 24, 2017
*Poster Session II
11:15 a.m. – 12:30 p.m.
Location: Symphony Ballroom II
*Not CME Accredited

Poster #48
WHOLE EXOME SEQUENCING IDENTIFIES X-LINKED FHL1 MUTATION IN CONSANGUINEOUS TURKISH FAMILY WITH NON OBSTRUCTIVE AZOOSPERMIA AND CHEST WALL DEFORMITIES.
Samuel Cohen BS1, Raul Clavijo MD2, Anthony Griswold PhD3, Emre Bakircioglu MD4 and Ranjith Ramasamy MD2
1University of Miami Miller School of Medicine; 2Department of Urology, University of Miami, Miami FL; 3John P. Hussman Institute for Human Genomics, Miami, FL; 4Urology and Andrology, Istanbul, Turkey
(Presented By: Samuel Michael Cohen)

Poster #76 - WITHDRAWN

Poster #77
FGF21 PROMOTES DIFFERENTIATION OF RAT STEM LEYDIG CELLS WITHOUT AFFECTING THE PROLIFERATION
Ren-Shan Ge MD, Yiyan Wang MD, Chunyan Jin PhD, Lanlan Chen MD, Tiantian Song MD, Jingjing Guo MD and Xingwang Li MD
The Second Affiliated Hospital and Yuying Children’s Hospital of Wenzhou Medical University
(Presented By: Ren-Shan Ge, MD)

Poster #78
FGF1 INCREASES THE PROLIFERATION OF RAT STEM LEYDIG CELL BUT INHIBITS ITS DIFFERENTIATION
Xiaoheng Li PhD, Jingjing Guo PhD, Xiaoling Guo PhD and Ren-Shan Ge MD
The Second Affiliated Hospital and Yuying Children’s Hospital of Wenzhou Medical University, Wenzhou, Zhejiang 325027, China
(Presented By: Xiao-Heng Li, MS)

Poster #79
METABOLIC AND HORMONAL PROFILE IN MALE INFERTILITY: THE ROLE OF INSULIN, HIGH DENSITY LIPOPROTEINS, FSH ON TESTOSTERONE LEVELS AND SPERM PARAMETERS
Elaine MF Costa MD; PhD1, 2, 3, 4, Juliana R Pariz MSc, PhD student1, 2, 3, 4 and Jorge Hallak MD, PhD1, 2, 3, 4
1Androscience – High Complexity Clinical and Research Andrology Laboratory, Brazil; 2Reproductive Toxicology Unit, Dept. of Pathology, USP, Brazil; 3Dept. of Endocrinology, USP, Brazil; 4Oswaldo Cruz German Hospital, Brazil; 5Dept. of Urology, USP, Brazil
(Presented By: Elaine Costa, MD, PhD)

Poster #80
THE UV-FILTER BENZOPHENONE-1 INHIBITS HUMAN TESTIS RETINALDEHYDE DEHYDROGENASE 1 MEMBER A1 AS A POTENTIAL ENDOCRINE DISRUPTING CHEMICAL
Hongqin Zhang MD1, Xiaoheng Li MSc2, Ren-shan Ge MD2, Ying Zhong MD1 and Siyao Liu MD1
1Jinjiang Maternity and Child Health Hospital; 2The Second Affiliated Hospital and Yuying Children’s Hospital of Wenzhou Medical University
(Presented By: Hongqin Zhang, MD)

Poster #81
KNOCKDOWN OF IFT140 DECREASES TESTOSTERONE PRODUCTION IN MLTC-1 CELLS
Amin Herati MD1, Peter Bulter BA1 and Dolores Lamb PhD2
1Baylor College of Medicine, Scott Department of Urology, Center for Reproductive Medicine; 2Baylor College of Medicine, Scott Department of Urology, Center for Reproductive Medicine, Department of Molecular and Cellular Biology
(Presented By: Amin S. Herati, MD)
POSTER SESSION II

Poster #82
BREAKING PARADIGMS: MARIJUANA IS NOT A HARMLESS RECREATIONAL DRUG AND IS WORSE THAN TOBACCO ON SPERM AND TESTICULAR FUNCTION
Jorge Hallak MD, PhD¹,²,³,⁴, Juliana R Pariz MSc, PhD student¹,²,³,⁴, Elaine MF Costa MD, PhD¹,²,³,⁴,⁵ and Paulo HN Saldiva MD, PhD³
¹Androscience – High Complexity Clinical and Research Andrology Laboratory, Brazil; ²Dept. of Urology, USP, Brazil; ³Reproductive Toxicology Unit, Dept. of Pathology, USP, Brazil; ⁴Oswaldo Cruz German Hospital, Brazil; ⁵Dept. of Endocrinology, Laboratory of Hormones and Molecular Genetics, USP, Brazil
(Presented By: Jorge Hallak, MD, PhD)

Poster #83
ZIRAM COMPETITIVELY INHIBITS HUMAN TESTIS RETINALDEHYDE DEHYDROGENASE 1A1
Ling Wang MD¹, Xiaoheng Li MS², Ren-Shan Ge MD² and Ying Zhong MD¹
¹Jinjiang Maternity and Child Health Hospital; ²The Second Affiliated Hospital and Yuying Children’s Hospital of Wenzhou Medical University
(Presented By: Li Wang, MD)

Poster #84
GINSENOSIDE RG3-ENRICHED KOREAN RED GINSENG EXTRACT ALLEVIATES DOXORUBICIN-INDUCED TESTICULAR DAMAGE IN RATS BY MODULATING INFLAMMATION AND AUTOPHAGY - AN EXPERIMENTAL STUDY
Jae Yup Hong, Kyu-Min Cha¹, Seung-Hun Song¹, Kyung Hwa Choi¹ and Si-Kwan Kim¹
¹Department of Life Science, College of Biomedical & Health Science, Konkuk University; ²Department of Urology, Fertility Center, CHA Gangnam Medical Center; ³Department Urology, CHA Bundang medical center, CHA University, Seongnam
(Presented By: Jae Yup Hong, M.D., PhD)

Poster #85
PERINATAL EXPOSURE TO 2,2′,4′,4′-TETRABROMODIPHENYL ETHER IMPAIRS MALE REPRODUCTIVE HEALTH AND SPERM EPIGENOME IN ADULT RATS
Ahmed Khalil PhD¹, Michael Parker PhD¹, Jake Jensen BS¹, Daneal Portman BS¹, Oleg Sergeyev MD, PhD², J. Richard Pilsner PhD¹, Haotian Wu MS¹, Alexander Shershebnev MS¹, Gregory Teicher BS¹ and Alexander Suvorov PhD¹
¹University of Massachusetts; ²Vavilov Institute of General Genetics and Chapaevsk Medical Association
(Presented By: Alexander Suvorov, PhD)

Poster #86
ENVIRONMENTAL TEMPERATURE AND PARTICULATE MATTER ARE CORRELATED WITH SEMEN PARAMETERS: A BIG-DATA APPROACH
Daniele Santi MD¹, Elisa Magnani MD¹, Antonio Granata MD, PhD¹, Laura Roli PhD², Maria Cristina De Santis PhD², Enrica Baraldi PhD², Tommaso Trenti PhD², Monica Setti PhD² and Manuela Simoni
¹University of Modena, Italy; ²Azienda Universitaria-Ospedaliera of modena, Italy
(Presented By: Manuela Simoni, MD, PhD)

Poster #87
PHTHALATE EXPOSURE DURING SPERMATOGENESIS IN ADULT MICE AND SPERM EPIGENETIC DYSREGULATION.
J. Richard Pilsner, PhD¹, Alex Shershebnev MS¹, Haotian Wu MS², Chelsea Marcho MS², Alexander Suvorov PhD² and Jesse Mager PhD²
¹UMASS Amherst, Department of Environmental Health Sciences; ²UMASS Amherst
(Presented By: J. Richard Pilsner, PhD)
Poster #88
PERIPUBERTAL DIOXIN CONCENTRATIONS AND SUBSEQUENT SPERM METHYLOME PROFILES OF RUSSIAN YOUNG ADULTS
Alex Shershebnev MS¹, Yulia Medvedeva PhD², Alexander Suvorov PhD³, Andrey Goltsov³, Evgeny Loukianov⁴, Tatiana Andreeva⁴, Fedor Gusev⁴, Andrey Manakhov⁴, Luidmila Smigulina⁴, Rogaev Evgeny⁴, Russ Hauser MD, MPH, ScD⁵, Oleg Sergeyev MD, PhD⁶ and J. Richard Pilsner PhD, MPH¹
¹UMASS Amherst, Department of Environmental Health Sciences; ²Institute of Bioengineering, Research Center of Biotechnology, Russian Academy of Sciences, Moscow, Russia; ³Research Center for Obstetrics, Gynecology and Perinatology, Moscow, Russia; ⁴Vavilov Institute of General Genetics, Russian Academy of Sciences, Moscow, Russia; ⁵Chapaevsk Medical Association, Samara region, Russia; ⁶Harvard T.H. Chan School of Public Health, Department of Environmental Health
(Presented By: Aleksandr Shershebnev, Master's)

Poster #89
MALE REPRODUCTIVE HEALTH OF AN INSECTICIDE EXPOSED POPULATION IN A MALARIA AREA IN SOUTH AFRICA (2003-2016).
Christiaan de Jager PhD¹,², Natalie Aneck-Hahn D'Tech¹,², Sean Patrick PhD¹,², Paulina Farias PhD³ and Riana Bornman DSc¹,²
¹School of Health Systems and Public Health; ²UP Institute for Sustainable Malaria Control, University of Pretoria, Pretoria, South Africa; ³National Institute of Public Health, Cuernavaca, Mexico
(Presented By: Christiaan de Jager, BSc, MSc, PhD)

Poster #90
TESTICULAR AND METABOLIC EFFECTS OF PRENATAL EXPOSURE TO 1,2-CYCLOHEXANE DICARBOXYLIC ACID DIsononyl ESTER (DINCh) IN YOUNG AND OLD SPRAGUE DAWLEY MALE RATS
Enrico Campioli PharmD, PhD¹, Matthew Lau², Sunghoon Lee MSc³, Lucas Marques³ and Vassilios Papadopoulos DPharm, PhD⁴
¹Research Institute of the McGill University Health Centre and Department of Medicine, McGill University; ²Research Institute of the McGill University Health Centre and Department of Pharmacology and Therapeutics, McGill University; ³Research Institute of the McGill University Health Centre and Department of Biochemistry, McGill University; ⁴Research Institute of the McGill University Health Centre and Department of Medicine, McGill University and Department of Pharmacology & Pharmaceutical Sciences, School of Pharmacy, University of Southern California
(Presented By: Enrico Campioli, PharmD, PhD)

Poster #91
FETAL EXPOSURE TO GENISTEIN (GEN) AND DI-(2-ETHYLHEXYL) PHTHALATE (DEHP) ALTERS JAK/STAT SIGNALING IN RAT TESTIS
Shahrzad Ghazisaeidi PhD student¹, Gurpreet Manku PhD¹, Annie Boisvert Research Assistant¹ and Martine Culty PhD²
¹McGill University; ²University of Southern California
(Presented By: Martine Culty, PhD)

Poster #92
CHARACTERIZATION OF PRIMARY CILIA OF THE EPIDIDYMIS DURING POSTNATAL DEVELOPMENT
Agathe Bernet master student, Olivia Jerczynski master student¹, Cynthia Locours master student¹, Alexandre Bastien Research Assistant², Marie-Ève Tremblay Researcher¹, Denis Soulet Researcher¹, Claude Robert Researcher², Janice Bailey Researcher¹ and Clémence Belleannée Researcher¹
¹chul; ²inaf; ³ulaval
(Presented By: Agathe Bernet)

Poster #93
NEW INSIGHTS ON THE CELLULAR DISTRIBUTION OF BETAl-DEFENSINS DURING EPIDIDYMAL MORPHOGENESIS
Lucas G.A. Ferreira, MSc Student¹, Camilla M. Ribeiro, PhD², Barry T. Hinton, PhD², and Maria Christina W. Avellar, PhD³
¹Section of Experimental Endocrinology, Department of Pharmacology, Universidade Federal de São Paulo, Escola Paulista de Medicina, São Paulo, Brazil. ²Department of Cell Biology, University of Virginia School of Medicine, Charlottesville, Virginia, USA.
(Presented By: Lucas G.A. Ferreira, MSc Student)
POSTER SESSION II

Poster #94
TRANSPLANTATION OF SPERMATOGONIAL STEM CELL (SCC) IN STALLIONS
Minjung Yoon PhD and Heejun Jung MS
Kyungpook National University
(Presented By: Minjung Yoon, Ph.D)

Poster #95
IMPACT OF THE GENETIC BACKGROUND ON THE REPRODUCTIVE PHENOTYPE OF CRISP1 AND CRISP4 KNOCKOUT MICE
Mariana Weigel Muñoz PhD, Guillermo Carvajal BSc, Nicolas Gaston Brukman BSc, Maria Agustina Battistone PhD, Omar Pignataro PhD, Vanina G. Da Ros PhD and Patricia S. Cuasnicu PhD
IBYME
(Presented By: Mariana Weigel Munoz)

Poster #96
EXPOSURE TO TERTIARY-BUTYL HYDROPEROXIDE (TBHP) - DOWN REGULATES THE EXPRESSION OF USP9Y IN MATURE MICE TESTIS
Pegah Mokhtari Msc, Anahita Mohseni Meybodi Assistant Professor and Hamid Gourabi Associate Professor
Department of Genetics, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran.
(Presented By: Pegah Mokhtari, MA)

Poster #99
NOVEL COMPOUND HETEROZYGOUS DNAAF2 MUTATION CAUSE PRIMARY CILIARY DYSKINESIA IN A HAN CHINESE FAMILY
Minghan Sun MD, PhD, Yngxin Ma PhD, Wei Xiong MD, PhD, Qun Lv MD, Ke Dou MD, Jiyun Yang MD, PhD and Xiaojie Li MD
Sichuan Provincial Hospital
(Presented By: Minghan Sun, MD, PHD)

Poster #100
A MULTIDISCIPLINARY MODEL OF EARLY FERTILITY PRESERVATION IN KLINEFELTER PATIENTS: DESCRIPTION AND UPDATE OF A PROGRAM
Stanley Kogan MD¹, Guillermo Galdon MD², Nima Pourhabibi Zarandi MD², David Crudo MD³, Mark Pettenati PhD⁴, Shadi Quasem MD⁵, Yimin Shu MD, PhD⁶, David Childs MD⁷, Daniel Rukstalis MD⁸, Stuart Howards MD⁹, Hooman Sadri-Ardekani MD, PhD¹ and Anthony Atala MD¹
¹Wake Forest Institute for Regenerative Medicine. Department of Urology; ²Wake Forest Institute for Regenerative Medicine; ³Section of Pediatric Endocrinology; ⁴Section of Medical Genetics; ⁵Department of Pathology; ⁶Center for Reproductive Medicine; ⁷Department of Radiology; ⁸Department of Urology
(Presented By: Stanley Jay Kogan, MD)

Poster #101
YOGA AND MEDITATION PROMOTES QUALITY OF LIFE BY DECREASING DEPRESSION SEVERITY AND CELLULAR AGING IN MALE INFERTILITY: RANDOMIZED CONTROLLED TRIAL
Madhuri Tolahunase MSc¹, Rajesh Sagar MD², Rajeev Kumar MS³, Neena Malhotra MD⁴, Neeta Singh MD⁴ and Rima Dada MD, PhD⁴
¹Lab for Molecular Reproduction and Genetics, Department of Anatomy, All India Institute of Medical Sciences, New Delhi, India; ²Department of Psychiatry, All India Institute of Medical Sciences, New Delhi, India; ³Department of Urology, All India Institute of Medical Sciences, New Delhi, India; ⁴Department of Obstetrics and Gynaecology, All India Institute of Medical Sciences, New Delhi, India
(Presented By: Madhuri Rajaneesh Tolahunase, BAMS, MSc(Med))

Poster #103
A FRESH PERSPECTIVE ON AN OLD MODEL: SEGMENTALLY ORGANIZED HAIRPIN-LOOP CHROMOSOME CONFIGURATIONS WITHIN THE 3D SPERM NUCLEUS
Helen Tempest PhD and Dimitrios Ioannou PhD
Florida International University
(Presented By: Helen Ghislaine Tempest, PhD)
POSTER SESSION II

Poster #104
CHANGES IN SPERM BANKING RATES WITHIN THE FIRST SEVEN MONTHS OF A FORMAL MALE ONCOFERTILITY PROGRAM
Diana M Lopategui MD, Emad Ibrahim MD, Raphael Yechieli MD, Nancy Brackett MD and Ranjith Ramasamy MD
University of Miami
(Presented By: Diana Maria Lopategui, MD)

Poster #105
12 YEARS EXPERIENCE TRANSURETHRAL CATHETERIZATION OF THE EJACULATORY DUCTS FOR TREATMENT OF PROSTATIC OBSTRUCTIVE AZOOSPERMIA.
Oleksandr Knigavko MD, PhD, Volodymyr Lesovoy MD,PhD,DS, Andriy Arkatov MD,PhD and Mykola Panasovskyi MD,PhD
Kharkiv National Medical University
(Presented By: Oleksandr Volodymyrovych Knigavko, MD,PhD)

Poster #106
OPEN EPIDIDYMAL SPERM ASPIRATION (OESA): RESULTS OF A TWELVE-YEAR EXPERIENCE
JM Blok MD, J Van Roekel MD, RJA Oude Ophuis MD and MTWT Lock MD, FEBU
UMC Utrecht
(Presented By: Tycho M.T.W. Lock, MD, PhD, FEBU)

Poster #107
INFLUENCE OF 5A-REDUCTASE INHIBITOR (5-ARI) USAGE ON REPRODUCTIVE FUNCTION IN MEN OF MARRIED COUPLES
Seung-Hun Song MD, Dong Suk Kim MD, Sung Han Shim PhD and Jae Yup Hong MD
CHA Gangnam Medical Center
(Presented By: Seung-Hun Song, MD)

Poster #108
TESTICULAR DAMAGE AND ALTERATION IN SEMINAL QUALITY BY CHANGES IN TESTICULAR MICROCIRCULATION IN SPONTANEOUSLY HYPERTENSIVE RATS.
Lucas Giglio Colli BSc; PhD candidate¹, Larissa Belardin MSc², Stephen Fernandes de Paula Rodrigues PhD¹, Mariana Antoniassi MSc², Rhayza Andretta MSc², Ricardo Bertolla DVM; PhD² and Maria Helena Catelli de Carvalho PhD¹
¹Universidade de São Paulo - USP; ²Universidade Federal de São Paulo - UNIFESP
(Presented By: Larissa Belardin, MSc)

Poster #109
THE MALE CONTRACEPTION INITIATIVE'S STRATEGY FOR MALE CONTRACEPTIVE RESEARCH AND DEVELOPMENT
David Sokal MD, Edward Eddy MS, PhD, Carol Sloan MS and Aaron Hamlin
Male Contraception Initiative
(Presented By: Aaron Hamlin)

Poster #110
SEARCH FOR NEW PREDICTIVE PARAMETERS OF ASSISTED REPRODUCTION OUTCOMES THROUGH ANALYSIS OF MALE GAMETE
Lara Tamburrino PhD¹, Sara Marchiani PhD¹, Rosanna Dolce biologist, Fanfani Laura biologist², Benini Francesca biologist², Pellegrini Sandra MD², Maggi Mario MD, PhD² and Baldi Elisabetta PhD¹
¹Department of Experimental and Clinical Biomedical Sciences; ²center procreazione assistita Demetra; ³Department of Experimental and Clinical Biomedical Sciences
(Presented By: Lara Tamburrino, PhD)

Poster #111
STAT III STAIN CAN BE A COST EFFECTIVE ALTERNATIVE TO DIFF-QUIK ANDROLOGY STAIN
Danielle Stawkey BSc, Dorina Dulaj MSc, Sule Dogan PhD, Kamran Ullah MD, Michael Fakih MD, Nicholas Shamma MD, Ahmad Hammoud MD, Jonathan Ayers MD and Iqbal Khan MD
IVF Michigan Fertility Center
(Presented By: Danielle Stawkey, BSc)
POSTER SESSION II

Poster #112
VALIDATION OF TESTIS EXPRESSED 101 (TEX101) PROTEIN AS A POTENTIAL CAPTURE ANTIGEN IN LIVE SPERMATOZOA SORTING.

junyan zhang MSc¹, Christina Schiza MSc², Andrei Drabovich PhD², Kirk Lo MD³, Andrée Fisher PhD⁴, Sergey Moskovtsev MD PhD⁴, Clifford Librach MD⁴, Keith Jarvi MD² and Eleftherios Diamandis MD PhD²

¹CReATe Fertility Centre; ²Department of Lab Medicine & Pathobiology, University of Toronto; ³Murray Koffler Urologic Wellness Centre, Mount Sinai Hospital, Toronto; ⁴CReATe Fertility Centre, Toronto

(Presented By: Junyan Zhang, MSc.)

Poster #113
FERTILITY ATTITUDES AMONG MEN WITH KLINEFELTER SYNDROME

Sergio Lizama MD¹, Swaytha Yalamanchi MD² and Adrian Dobs MD, MHS²

¹Department of Internal Medicine, St. Agnes Hospital; ²Division of Endocrinology, Diabetes, and Metabolism, Johns Hopkins University School of Medicine

(Presented By: Sergio A. Lizama, MD)

Poster #114 - WITHDRAWN

Poster #115
SEMINAL PLASMA PROTEOMIC MECHANISMS – ONE YEAR FOLLOW-UP AFTER VARICOCELECTOMY

Mariana Camargo PhD¹, Larissa Belardin MSc¹, Paula Intasqui MSc¹, Valdemir Carvalho PhD², Karina Cardozo PhD² and Ricardo Bertolla PhD¹

¹Sao Paulo Federal University; ²Fleury Group

(Presented By: Mariana Camargo, MSc, BSc)

Poster #116
ERYTHROPOIETIN AND A FEEDER CELL-FREE HYDROGEL-LAMININ SCAFFOLD PROMOTE THE EXPANSION AND MAINTENANCE OF HUMAN SPERMATOGONIAL STEM CELLS IN CULTURE

Sarayu Ratnam¹, Robert Brannigan² and Christopher Payne²

¹Ann & Robert H. Lurie Children’s Hospital of Chicago; ²Northwestern University Feinberg School of Medicine

(Presented By: Christopher Payne, PhD)

Poster #117
EVALUATION OF DYNAMIC FCR EXPRESSION PATTERNS ON HUMAN SPERMATOZOA: A POTENTIAL NOVEL DIAGNOSTIC TEST AND METHOD FOR DETERMINING OPTIMAL TIMING FOR INTRAUTERINE INSEMINATION (IUI).

Annie Qu BSc¹,², Sergey I. Moskovtsev MD, PhD¹,³, Junyan Y. Zhang MSc¹, Andrew Lee BSc¹, Barb A. Cohen PhD¹, Ronald A. Parkinson BSc¹ and Clifford L. Librach MD¹,⁵,⁶

¹CReATe Fertility Centre; ²Department of Medicine, University of Toronto; ³Department of Obstetrics & Gynaecology, University of Toronto; ⁴Arex Life Sciences LLC, Watertown, MA; ⁵Department of Obstetrics and Gynaecology, University of Toronto; ⁶Department of Gynaecology, Women’s College Hospital, Toronto, Canada

(Presented By: Sergey I. Moskovtsev, MD, PhD)

Poster #118
VARICOCELE REPAIR IN THE INFERTILE COUPLE, DOES THIS AFFECT IN VITRO FERTILIZATION SUCCESS RATES? A COST-EFFECTIVENESS ANALYSIS

James Craig MD, Jeremy Myers MD, Sara Lenherr MD, Will Brant MD and Jim Hotaling MD

University of Utah

(Presented By: James Craig, MD)

Poster #119 - WITHDRAWN
POSTER SESSION II

Poster #120
SUSTAINED IMPROVEMENT OF ERECTILE AND VOIDING FUNCTION IN OBESE HYPOGONADAL MEN TREATED UP TO 8 YEARS WITH TESTOSTERONE THERAPY (TTH) WITH TESTOSTERONE UNDECANOATE INJECTIONS (TU) IN COMPARISON TO AN UNTREATED CONTROL GROUP
Farid Saad DVM, PhD¹,²,³, Ahmad Haider MD, PhD⁴, Karim Haider⁵, Gheorghe Doros PhD⁶ and Abdulmaged Traish PhD⁷
¹Bayer AG, Berlin, Germany; ²Dresden International University, Berlin, Germany; ³Gulf Medical University, Ajman, UAE; ⁴Private Urological Practice; ⁵medical student; ⁶Boston University School of Public Health; ⁷Boston University School of Medicine
(Presented By: Farid Saad, DVM, PhD)

Poster #121
SEXUAL ACTIVITY IN MEN IN NORTHERN REMOTE NON-INDUSTRIALIZED BRAZILIAN AMAZON IS HIGHLY MAINTAINED THROUGHOUT LIFESPAN EMPHASIZING THE ROLE OF GOOD HABITS, NATURAL NUTRITION AND AN UNPOLLED ENVIRONMENT IN SEXUAL HEALTH
Thiago ACC Teixeira MD, MSc¹,², Maira TST Nazima MD, PhD³ and Jorge Hallak MD, PhD²,⁴
¹Universidade Federal do Amapá, Brazil; ²Reproductive Toxicology Unit, Dept. of Pathology, USP, Brazil; ³Universidade Federal do Amapá; ⁴Androscience – High Complexity Clinical and Research Andrology Laboratory, Brazil
(Presented By: Thiago Teixeira, MD, MSc)

Poster #122
10 YEARS USING MICRO SURGICAL PENILE DENERVATION FOR TREATMENT SEVERE PREMATURE EJACULATION
Oleksandr Knigavko MD, PhD
Kharkiv National Medical University
(Presented By: Oleksandr Volodymyrovych Knigavko, MD,PhD)

Poster #123
MINIMALLY INVASIVE SURGICAL TREATMENT OF VENO-OCCULSIVE FORM OF ERECTILE DYSFUNCTION.
Said Kaziiev PhD student¹ and Oleksandr Knigavko PhD, A professor²
¹Kharkiv National Medical University, Department of Urology, Nephrology and Andrology; ²Kharkiv National Medical University
(Presented By: Said Kaziiev, PhD student)

Poster #124
INVESTIGATING THE ROLE OF THE CAENORHABDITIS ELEGANS GENE M05D6.2, AN ORTHOLOG OF HUMAN T-COMPLEX PROTEIN 11 (TCP11), IN SPERM FUNCTION AND FERTILITY
Emily Lopes and Matthew Marcello PhD
Pace University
(Presented By: Emily Lopes)

Poster #125
COMPREHENSIVE PELVIC FLOOR PHYSICAL THERAPY FOR MEN WITH IDIOPATHIC CHRONIC PELVIC PAIN SYNDROME: A PROSPECTIVE STUDY
Thomas Masterson MD¹ and Ranjith Ramasamy MD²
¹University of Miami; ²University of Miami Miller School of Medicine
(Presented By: Thomas Masterson, III, MD)

Poster #126
THE BENEFICIAL ROLE OF COQ10 SUPPLEMENTATION IN MALE INFERTILITY: FACT OR FICTION?
Parviz Gharagozloo PhD and Aron Moazamian BSc
CellOxess LLC
(Presented By: Parviz Gharagozloo, PhD)
POSTER SESSION II

Poster #127
PATHOLOGICAL THRESHOLD OF HUMAN SPERM DNA OXIDATION: OPTIMIZATION OF A DIAGNOSTIC ASSAY FOR CLINICAL USE.
S. Vorilhon¹, F. Brugnon², A. Kocer¹, S. Dollet¹, C. Bourgne³, M. Berger³, L. Janny², B. Pereira⁴, RJ Aitken⁵, A. Moazamian⁶, P. Gharagozloo⁶, J. Drevet¹ and H. Pons-Rejraji²
¹Université Clermont Auvergne, CNRS, Inserm, GReD; ²CHU Clermont Ferrand, Hôpital Estaing, Laboratoire de Biologie du Développement et de la Reproduction; ³CHU Clermont Ferrand, Hôpital Estaing, Laboratoire d’Hématologie Biologique; ⁴CHU Clermont-Ferrand, DRCI, ‘Délegation Recherche Clinique et Innovation; ⁵University of Newcastle, Callaghan, NSW Australia; ⁶CellOxess LLC
(Presented By: Aron Moazamian)

Poster #128
THE ROLE OF SUBCLINICAL GENITOURINARY INFECTIONS IN MALE INFERTILITY
Juliana R Pariz BSc, MSc, PhD student¹,²,³,⁴, Rosa Alice C Monteiro BSc¹,⁴ and Jorge Hallak MD, PhD¹,²,³,⁴
¹Androscience – High Complexity Clinical and Research Andrology Laboratory, Brazil; ²Dept. of Urology, USP, Brazil; ³Reproductive Toxicology Unit, Dept. of Pathology, USP, Brazil; ⁴Oswaldo Cruz German Hospital, Brazil
(Presented By: Juliana Risso Pariz, BSc, MSc)

Poster #129
CASE REPORT AND REVIEW OF THE LITERATURE: BILATERAL TESTICULAR DIFFUSE LARGE B-CELL LYMPHOMA
Janeske Vonkeman BSc ¹ and Gavin Langille MD FRCSC²
¹MD Candidate, Dalhousie University; ²Assistant professor, Dalhousie University, Dept. of Urology
(Presented By: Janeske Vonkeman BSc)

Poster #130
EFFECT OF MUCUNA PRURIENS (LINN.) ON SPERM DAMAGE INDUCED BY HYPERCHOLESTEROLEMIA: AN EXPERIMENTAL STUDY USING WISTAR ALBINO RAT
Prakash Seppan PhD¹, Anuradha Murgesh PhD¹, Ibrahim Muhammed PhD¹, Karthik Ganesh Mohanraj PhD², Ganesh Lakshmanan MSc¹, Dinesh Premavathy MSc¹, Sakti Jothi Muthu MSc¹ and Khayinmi Wungpam MSc¹
¹University of Madras; ²Saveetha University
(Presented By: Seppan Prakash, MSc, PhD)

Poster #131
THE EFFECT OF SEMINAL PLASMA AND POTENTIATORS OF DNA DAMAGE ON STALLION EPIDIDYMAL SPERM
Rosanna Serafini DVM, PhD, Dickson Varner, Terry Blanchard, Sheila Teague and Charles Love
Department of Large Animal Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, Texas, USA
(Presented By: Rosanna Serafini, DVM)

Poster #132
HOW CAN PHYSOSOCIAL STRESS IMPACT ON NATURAL MALE FERTILITY? UN HYPOTHESIS EMERGED FROM OUR CLINICAL PRACTISE
Julia Irene Ariagno Bioq¹, Gabriela Ruth Mendeluk PhD¹, Herberto Repetto Biochemist, Specialist in Andrology¹, Dario Jacobsen Biochemist, Specialist in Endocrinology², Diego Gonzalez Biochemist, Specialist in Endocrinology², Martin Repetto PhD², Gabriela Berg PhD² and Bibiana Fabre PhD²
¹Laboratory of Male Fertility, Hospital de Clinicas “José de San Martin”, Faculty of Pharmacia and Biochemistry, University of Buenos Aires, Bs. As., Argentina.; ²Clinical Biochemistry Department, INFIBIOC, Faculty of Pharmacia and Biochemistry, University of Buenos Aires, Bs. As., Argentina.
(Presented By: Julia Irene Irene Ariagno, Sr., Professor)

Poster #133
DNA FRAGMENTATION, A NUCLEAR EVALUATION FOR SPERM PRODUCTION DROUGHT DURING LIFE YEARS.
Héctor Salvador Godoy Morales MD¹, Karina Cázarez Pérez MD¹, José Alfonso Gutiérrez Frusch MD², Paola Berenice Merchand Álvarez MD², Ricardo Mera Mejía Biology² and José Manuel Lozano Sánchez MD²
¹ART reproduccion; ²ART reproducción
(Presented By: Karina Cazarez Perez, MD)
Poster #134
EFFECTS OF A MICRONUTRIENT SUPPLEMENTATION COMBINED WITH A PHOSPHODIESTERASE TYPE 5 INHIBITOR ON SPERM QUANTITATIVE, QUALITATIVE, AND FUNCTIONAL PARAMETERS: A RANDOMIZED, CONTROLLED TRIAL
Fotios Dimitriadis Ast Professor¹, Panagiota Tsounapi Ast Professor², Masashi Honda Ast Professor³, Athanasios Zachariou MD³, Sotirios Skouros MD³, Katsuya Hikita MD², Irene Matthaiou MD³, Gergji Semini MD³, Charalampos Mamoulakis Ast Professor⁴, Apostolos Kaponis Ast Professor⁵, Georgios Antonakis Ass Professor³ and Nikolaos Sofikitis Professor³ and Atsushi Takenaka Professor²
¹Aristotle University, Thessaloniki, Greece; ²Tottori University; ³Ioannina University; ⁴University of Crete; ⁵Patras University
(Presented By: Fotios Dimitriadis, Ast. Professor)

Poster #135
EVALUATION OF AN IN-HOME SEMEN TESTING SYSTEM BY COUPLES PARTICIPATING IN AN INTERNET-BASED PRECONCEPTION STUDY
Greg Sommer PhD¹, Tiffany Trinidad BS¹, Ulrich Schaff PhD¹, Michael Eisenberg MD², Amelia Wesselink MPH³, Elizabeth Hatch PhD³ and Lauren Wise ScD¹
¹Sandstone Diagnostics; ²Stanford University School of Medicine; ³Boston University School of Public Health
(Presented By: Greg Sommer, PhD)

Poster #136
LOCALIZATION PATTERNS OF THE GANGLIOSIDE GM1 IDENTIFY SPERM CAPABLE OF UNDERGOING CAPACITATION AND ACROSOME EXOCYTOSIS
Alexander J. Travis VMD, PhD¹,², Cristina Cardona PhD², Melissa A. Moody MS², Alana J. Simpson BS², Romeo Mendoza BS² and Charles G. Ostermeier PhD²
¹Cornell University, NY; ²Androvia LifeSciences, NJ
(Presented By: Alexander J. Travis, VMD, PhD)

Poster #137
STRUCTURAL ORGANIZATION OF THE ACTIN CYTOSKELETON OF THE MOUSE SPERM FLAGELLUM
Maria Gracia Gervasi, PhD¹, Xinran Xu, PhD², Blanca Carbajal-Gonzalez, PhD³, Mariano Buffone, PhD⁴, Diego Krapf, PhD² and Pablo E. Visconti, PhD¹
¹University of Massachusetts; ²University of Colorado; ³Mount Holyoke College; ⁴IBYME, CONICET, Argentina
(Presented By: Pablo E. Visconti, PhD)

Poster #138
IMPROVEMENT OF SEMEN ANALYSIS QUALITY - SLOWLY MOVING FORWARD?
Lars Björndahl MD PhD, Rebecka Holmberg PhD, Biomedical Scientist, Ulrik Kvist MD, PhD, John Flanagan PhD and Stefan Arver MD, PhD
ANOVA, Karolinska University Hospital and Karolinska Institutet
(Presented By: Lars Björndahl, MD, PhD)

Poster #139
PRSS50: A SERINE PROTEASE REQUIRED FOR PROPER SPERM FLAGELLUM ASSEMBLY
Carolina Jorgez PhD
Baylor College of Medicine
(Presented By: Carolina Jorgez, PhD)

Poster #140
SLO3 K+ CHANNEL PH AND CA2+ SENSITIVITY ALTERED IN A NATURAL VARIANT
Yanyan Gang PhD¹, Juan Ferreira BS², Victor Dzikunu BS³, Alice Butler MS⁴, Pascale Lybaert PhD³, Pen Yuan PhD⁵, Karl Magleby PhD², Lawrence Salkoff PhD⁴ and Celia Santi MD PhD⁹
¹University of Miami. Dept. of Physiology & Biophysics; ²Washington University. Dept. of Obstetrics and Gynecology; ³Washington University. Dept of Neurosciences; ⁴Washington University School of Medicine. Dept of Obstetrics and Gynecology; ⁵Washington University. Dept. of Cell Biology; ⁶University of Miami. Dept of Physiology and Biophysics; ⁷Washington University. Dept of Obstetrics & Gynecology
(Presented By: Celia Santi, MD, PhD)
POSTER SESSION II

Poster #141
CLAUDIN FAMILY EXPRESSION IN TESTIS; A DYNAMIC MEMBRANE BEHAVIOR FOR SPERM FORMATION IN PATIENTS WITH INFERTILITY
Héctor Salvador Godoy Morales MD¹, José Manuel Lozano Sánchez MD², Alejandro Sandoval Travesí MD³, Paola Berenice Merchand Álvarez MD⁴, Catalina Romo Aguirre MD⁴, Ricardo Mera Mejia Biology³, Priscila Judith Torres Granados PhD⁴, Luis Felipe Montaño Estrada PhD⁴ and Erika Patricia Rendon Huerta PhD⁴
¹ART reproduccion; ²ART reproducción; ³Hospital Ángeles Pedregal; ⁴Universidad Nacional Autónoma de México
(Presented By: Alejandro Sandoval Travesí, MD)

Poster #142
GONADOTROPIN REGULATION OF RETINOIC ACID ACTIVITY IN THE TESTIS
Seyedmehdi Nourashrafeddin, Batool Hosseini Rashidi and Tony M. Plant
(Presented By: SeyedMehdi Nourashrafeddin)

Poster #143
SUMOYLATION MAY REGULATE TRANSCRIPTION AND PHOSPHORYLATION EVENTS IN MOUSE SPERMATOCYTES, AND IS REQUIRED FOR G2/M MEIOSIS TRANSITION IN VITRO.
Margarita Vigodner PhD¹, Benjamin Lucas PhD² and Elana Molcho BSc²
¹Yeshiva University and AECOM; ²Yeshiva University
(Presented By: Margarita Vigodner, PhD)

Poster #144
CRISPR/CAS9-MEDIATED TSPO GENE MUTATIONS LEAD TO REDUCED MITOCHONDRIAL MEMBRANE POTENTIAL (?M) AND STEROID FORMATION IN MA-10 MOUSE LEYDIG TUMOR CELLS
Jinjiang Fan PhD¹ and Vassilios Papadopoulos DPharm, PhD²
¹Research Institute of the McGill University Health Centre and Department of Medicine, McGill University; ²Research Institute of the McGill University Health Centre and Department of Medicine, McGill University and Department of Pharmacology & Pharmaceutical Sciences, School of Pharmacy, University of Southern California
(Presented By: Vassilios Papadopoulos, DPharm, PhD)

Poster #146
CHARACTERIZATION OF THE COOPERATION BETWEEN THE NUCLEAR RECEPTORS COUP-TFII AND SF1 IN LEYDIG CELL GENE EXPRESSION
Nicholas Robert M Sc, Mickaël Di-Luoffo PhD and Jacques J Tremblay PhD
CHU de Quebec Research Centre - Laval University
(Presented By: Nicholas Robert)

Poster #147
EFFECT OF EARLY TYPE 2 DIABETES ON MALE FERTILITY.
Jannette Dufour PhD¹, Robbin Hannah Greer¹, Gurvinder Kaur PhD¹, Kandis Wright BS¹, Michael D. Tomison BS¹, Latha Ramalingam PhD², Eunhee Chung PhD¹, Naima Moustaid-Moussa PhD² and Chwan-Li Shen PhD¹
¹Texas Tech University Health Sciences Center; ²Texas Tech University; ³University of Texas San Antonio
(Presented By: Jannette Dufour, PhD)

Poster #148
THE TESTICULAR EXPLANT SYSTEM PROVIDES AN ALTERNATIVE PLATFORM TO ASSESS THE IMPACT OF GERM CELL TOXICANTS AND PATHOGENS.
Prabagaran Esakky PhD, Deborah Hansen PhD, Andrea Drury BS, Paul Felder, Andrew Cusumano BS and Kelle Moley MD
Washington University School of Medicine in St Louis, St Louis, MO, USA 63110
(Presented By: Prabagaran Esakky, PhD)
POSTER SESSION II

Poster #149
THYROID HORMONES AND CELL SERTOLI PROLIFERATION AND DIFFERENTIATION IN PROGENIES FROM CARBAMAZEPINE-TREATED RAT DAMS DURING PREGNANCY AND LACTATION
Rhayza Andretta PhD candidate, Renato Tesser PhD, Camila Paccola PhD, Taiza Stumpp PhD, Samara de Oliva PhD and Sandra Miraglia PhD
Federal University of Sao Paulo
(Presented By: Rhayza Andretta PhD candidate)

Poster #150
TESTIS HISTOLOGY IN MEN SUBMITTED TO MICROSURGICAL CORRECTION OF SUBCLINICAL VARICOCELE WITH LONG REFLUX AS A VARIABLE TO UNDERSTAND IMPROVEMENT IN SPERM QUALITY POST-TREATMENT
Jorge Hallak MD, PhD¹,²,³,⁴, Robertson T Dutra BSc, MSc¹,²,³,⁴, Juliana R Pariz MSc, PhD student¹,²,³,⁴, and Elaine MF Costa MD, PhD¹,²,³
¹Androscience – High Complexity Clinical and Research Andrology Laboratory, Brazil; ²Dept. of Urology, USP, Brazil; ³Reproductive Toxicology Unit, Dept. of Pathology, USP, Brazil; ⁴Oswaldo Cruz German Hospital, Brazil
(Presented By: Jorge Hallak, MD, PhD)

Poster #151
THE FUNCTION OF EPIDIDYMAL CYSTEINE-RICH SECRETORY PROTEINS (CRISPS)
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(Presented By: Jinghua Hu, MSc)
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ABSTRACTS

1 (Oral/Poster)
DIFFERENTIAL TOLEROGEOgenic CAPACITY OF THE EPIDIDYMIS AND TESTIS IN MICE WITH CONDITIONAL DELETION OF TGFBR2 IN DENDRITIC CELLS
Fernando Pierucci-Alves¹, Monica T. Midura-Kiela², Sherry D. Fleming⁴, Bruce D. Schultz¹ and Pawel R. Kiela³
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(Presented By: Fernando Pierucci-Alves, DVM)

Sperm are immunogenic and peripheral tolerance mechanisms are necessary for reproductive success. Initial data revealed prominent physiological signaling by transforming growth factor beta (TGFβ) in murine epididymis, where large networks of dendritic cells (DCs) and macrophages exist. This study’s overarching hypothesis is that TGFβ-signaling in epididymal DCs maintains immunotolerance to sperm in the epididymis and disruption of this signaling pathway breaks sperm tolerance through impaired or insufficient regulatory T cell (Treg) function. In male mice with DC-specific TGFβ receptor 2 deletion (Tgfbr2ΔDCFoxP3GFP-KI), we detected severe epididymal leukocytosis with sperm granulomas, antisperm antibodies but no apparent testicular pathology at the histological level. To further these observations, we quantified leukocytes (CD45+) and Tregs (FoxP3/GFP+) in epididymides, testes and kidneys from 4 Tgfbr2ΔDCFoxP3GFP-KI males and control littermates by flow cytometry. We used kidneys as a sperm-free organ of the genitourinary tract, and as an additional control. Compared to controls, the epididymis of Tgfbr2ΔDCFoxP3GFP-KI mice had 3.4 times more infiltrating CD45+ leukocytes (P<0.05), while the Tgfbr2ΔDCFoxP3GFP-KI testis and kidney exhibited 1.2- and 1.5-fold increase in infiltrating leukocytes (P<0.05), respectively. Tregs were 5-6 times more abundant in epididymis and kidney of Tgfbr2ΔDCFoxP3GFP-KI mice, while the testis exhibited 53 times more Tregs – compared to controls. These data suggest the epididymis is most susceptible to inflammation when the DC/TGFβ-signaling axis is disrupted, and that the testis maintains alternative robust immunosuppressive mechanisms to fend off autoimmune responses. Additional studies are addressing how loss of TGFβ-signaling disrupts epididymal and testicular DC tolerogenic capacities and testing whether there is differential induction and function between epididymal and testicular Tregs. Supported by P20GM103418 (K-1NBR); Johnson Cancer Research Center

2 (Oral/Poster)
HUMANIN TRANSGENIC MICE ARE PROTECTED FROM CYCLOPHOSPHAMIDE-INDUCED MALE GERM CELL APOPTOSIS
YanHe Lue MD¹, Hemal Mehta MS², James Hoang BS¹, Kelvin Yen PhD³, Junxiang Wan PhD³, Ronald Swerdlaff MD¹, Pinchas Cohen MD² and Christina Wang MD¹
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(Presented By: YanHe Lue, MD)

Humanin (HN) is a cytoprotective peptide encoded by a mitochondrial gene. We have previously demonstrated that the pharmacological administration of HN or its analogue HNG protects male germ cells against cyclophosphamide (CP)-induced apoptosis in mice. To examine the role of endogenous HN in the cytoprotection of male germ cells from chemotherapy, we generated HN transgenic (HNt) mice expressing a CMV-promoter driven humanin transgene. After genotyping by PCR, 1) groups of 7 adult (5-10 month-old) HNt and age-matched wildtype (WT) mice were used for the characterization of male reproductive phenotype, and 2) groups of 6 adult HNt and age-matched WT mice were treated with a single-dose of CP injection (i.p. 200mg/kg) to examine male germ cell apoptosis (quantified as apoptotic index (AI): the number of apoptotic germ cells/100 Sertoli cells). The plasma testosterone (T) was measured by RIA. HNt mice were viable, fertile and smaller in size (BW:28.5±2.2g) with an average of 18% decrease in body weight (BW) as compared to WT (BW:34.9±10.3g) mice. The testis weight (TW:88±10.1mg, p=0.007) in HNt mice was significantly lower than WT (TW:105.2±9.3mg) mice. There was no difference in cauda epididymal sperm count between HNt (1.3±0.07 million/mg cauda) and WT (1.3±0.03 million/mg cauda) mice. Testis histological examination in HNt mice showed normal histology with the baseline germ cell apoptosis rates reminiscent of WT levels. HNt mice have similar plasma T levels (0.6±0.4ng/ml) as WT (0.7±0.5ng/ml) controls. Two days after CP treatment, there were no marked changes in body and testis weight, and plasma T levels. The germ cell apoptosis rate in WT mice was significantly (p<0.001) increased at spermatogenic stages I-III (AI:46.1±4.6), VII-VIII (AI:20.6±0.9) and XI-XII (AI:56.9±4.8) as compared to non-treated WT mice (stages I-III AI: 9.5±2.1; VII-VIII:2.5±0.6; XI-XII:17.5±1.8). In HNt mice, CP treatment significantly increased germ cell apoptosis at stages XI-XII (AI: 23.7±2.9; p=0.03), but not at stages I-III (AI:14.9±2.3) and VII-VIII (AI:4.8±1.1) as compared to baseline levels of HNt mice (stages I-III AI:8.3±1.8; VII-VIII:3.8±0.8; XI-XII:13.3±3.2), suggesting that male germ cells in HNt mice were partially resistant to CP-induced apoptosis. Thus, we conclude that HN 1) is cytoprotective hormone; and 2) mimics the effects of caloric-restriction on metabolism and chemotherapy-protection.
3 (Oral/Poster)

PATERNAL EXPOSURE TO ENVIRONMENTAL CONTAMINANTS ALTERS THE SPERM PROTEOME AND INDUCES NEGATIVE PREGNANCY OUTCOMES TRANSGENERATIONALLY

Janice Bailey PhD, Nancy Coté PhD, Clotilde Maurice PhD, Florence Roux-Dalvai MSc, Arnaud Droit PhD and Mathieu Dalvai PhD
Université Laval
(Presented By: Janice L. Bailey, PhD)

Background: The Arctic food chain is contaminated with persistent organic pollutants (POPs). As a consequence, there are major health discrepancies between Inuit and non-Aboriginal Canadians, including adverse pregnancy outcomes or disruption of the immune system. Although healthy pregnancies are multifactorial, it is possible that POPs exposure contributes to these adverse outcomes. Moreover, the paternal influence of contaminant exposure on his offspring has not been well-investigated. We hypothesized that early paternal exposure to Arctic POPs affects his sperm proteome and that of his offspring and future generations.

Methods: Sprague-Dawley females (F0) were gavaged with an environmentally-relevant concentration of an Arctic POP mixture or corn oil (Control) and mated to untreated males. F1 fathers were mated to untreated females to generate F2 litters; F2 development was followed until PND 90. F3 and F4 generations were similarly produced. Isobaric Tags for Relative and Absolute Quantitation (iTRAQ) labelling, 2D−LC−MS/MS and immunoblotting analyses were used to identify differentially expressed sperm proteins from all generations.

Results: POPs-exposed F1 males had fewer motile sperm and decreased epididymal sperm counts (P=0.0001). F2 sons from the POPs lineage were subfertile (P=0.02) and their F3 POPs grandsons had fewer pups/litter (P≤0.0001). For F1, F2 and F3 males, 7, 20 and 36 proteins were differentially expressed compared to the control lineage, some of which are implicated in motility, apoptosis or male infertility (SOD1, VDAC2, CS, SLCA3, IZUMO) and may explain the observed subfertility. Importantly, 3 differentially expressed sperm proteins were conserved between the F1 and F3 males and 6 between the F2 and F3 generations.

Conclusion: POPs exposure induces proteome changes in sperm that can be observed through three generations. The proteins and pathways identified have launched new hypotheses on POPs effects and in our understanding of the adverse health effects observed in Inuit populations.
ABSTRACTS

non-obstructive azoospermic patients where no sperms were found in their testicular biopsies.

5 (Oral/Poster)
REGULATION OF CYP26B1 EXPRESSION IN THE SPERMATOGONIAL STEM CELL NICHE
Parag Parekh PhD¹, Thomas Garcia PhD¹,², Reham Waheed DVM, PhD¹, Vivek Jain MS¹,², Gunapal Shetty PhD¹, Marvin Meistrich PhD¹, Marie-Claude Hofmann PhD¹ and Pooja Gandhi MS²
¹University of Texas MD Anderson Cancer Center; ²University of Houston Clear Lake; ³University of Alexandria, Damanhour
(Presented By: Parag Parekh, PhD)

Cytochrome P45026B1 (CYP26B1) regulates the concentration of all-trans-retinoic acid (RA) and plays a key role in germ cell differentiation by controlling local distribution of RA. Interestingly, little is known about the mechanisms of Cyp26b1 gene regulation. In Sertoli cells, it is maintained by SF1 and SOX9 during gonad development and throughout life but inhibitors that would balance its expression, possibly accounting for the pulses of RA in the adult seminiferous epithelium, are not known. Our previous data from Sertoli-cell specific NOTCH gain- and loss-of-function mouse models indicated that expression of Cyp26b1 is inversely correlated to NOTCH pathway activity. We hypothesized that 1) Spatiotemporal Cyp26b1 downregulation is directly dependent on canonical NOTCH signaling; and 2) A subset of premeiotic germ cells is responsible for Cyp26b1 downregulation through the NOTCH ligand JAG1. Germ cell-Sertoli cell co-cultures experiments demonstrated that JAG1, mainly expressed by Aundiff spermatogonia, activated NOTCH signaling in primary Sertoli cells and induced the transcriptional repressors and canonical NOTCH target genes Hes/Hey. Upregulation of Hes/Hey gene expression by JAG1 was associated with significant decreases in Cyp26b1 expression, while simultaneous downregulation of Hes/Hey by RNAi led to significant increases. Further, Luciferase and ChIP-PCR assays demonstrated that HES/HEY directly bind to the Cyp26b1 promoter to downregulate its expression. Investigation of stage-specific NOTCH activity using transgenic mice, together with qPCR analysis of Hes/Hey and Cyp26b1 expression, indicated lowest expression of Cyp26b1 at stages VI-VIII of the seminiferous epithelium, when NOTCH activity and RA production are highest. To elucidate which germ cells activate NOTCH signaling in Sertoli cells in vivo, we performed germ cell depletion experiments using moderate doses of busulfan. We found that elimination of undifferentiated spermatogonia will downregulate NOTCH signaling and upregulate Cyp26b1 expression in Sertoli cells. In conclusion, we believe that NOTCH signaling, induced by JAG1-expressing Aundiff in Sertoli cells, is a mediator of germ cell differentiation by controlling Cyp26b1 expression and possibly RA pulses.
Supported by NIH R01HD081244

6 (Oral/Poster)
HIGH-RESOLUTION PHENOTYPING OF SPERMATOGENIC DEFECTS USING SINGLE-CELL SEQUENCING
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Department of Genetics, Washington University in St. Louis
(Presented By: Min Jung)

Introduction: RNA sequencing of testis tissue provides great promise for improving the description of molecular defects in men with gonadal dysfunction. With thoughtful interpretation, gene expression data could be useful for classifying patients into a diagnostic hierarchy, defining i) disrupted cell types, ii) disrupted pathways, and, iii) in conjunction with genome sequencing data, disrupted gene(s) and causal genetic variants. However, the cellular diversity of testis severely limits the utility of expression measurements made on bulk tissue. Thus, the application of single-cell RNA-sequencing on male germ cells represents an amazing new set of scientific opportunities for research in male reproductive biology and translational medicine

Objectives: We aim to develop a single-cell framework that utilizes large-scale single-cell expression profiles from normal and disease models to elucidate the fundamentals of spermatogenesis and to phenotype spermatogenic defects.

Methods: Using Drop-seq, we generated single-cell expression measurements on over 30,000 cells from wild-type mice and over 20,000 cells from mouse mutants with infertility of mechanisms known (e.g. MLH3 deficiency) and unknown (spontaneous infertility after a transgene insertion). We constructed a pipeline for interpreting the single-cell data using publicly available single-cell computational tools such as RaceID2, Waterfall, and Monocle2, and an in-house cell-type assigner algorithm.

Results: We find that the increased resolution of single cell expression profiling reveals novel cell-type specific markers, 5 of which we have confirmed with immunofluorescence staining. As part of the framework, we developed a cell-type identifier that provides automated assignments of cells to 4 stages of germ cells and 3 types of somatic cells. Our cell-type assigner algorithm has 96% accuracy when benchmarked with data from flow-sorted germ cells. Finally, unsupervised ordering of male germons on a developmental timescale depicts the genetic landscape of both normal and infertile mice, inferring the cell-types and pathways that are dysregulated in the germ cell development of disease models.

Conclusions: Our single-cell framework has great potential for expanding our ability to dissect pathophysiology in tissues with extensive cellular heterogeneity and decrypt the spermatogenic failure in more patients.
ABSTRACTS

7 (Oral/Poster)
ISOTRETINOIN IMPROVES TOTAL MOTILE SPERM COUNT IN SOME MEN WITH IDIOPATHIC OLIGOAOSTHENOZOOSPERMIA
John Amory, Kevin Ostrowski MD¹, John Gannon MD², Kathryn Berkseth MD¹, Faith Stevison MS¹, Nina Isoherranen PhD¹, Charles Muller PhD¹ and Thomas Walsh MD, MSE¹
¹UW; ²Intermountain Health
(Presented By: John K. Amory, MD, MPH)

Introduction: There is no effective medical therapy for men with infertility due to idiopathic oligoasthenozoospermia (IOA). As men with IOA have lower intratesticular concentrations of 13-cis-retinoic acid, we hypothesized that men with IOA may exhibit improved sperm counts during treatment with 13-cis-retinoic acid (isotretinoin).

Methods: We conducted a single-arm, pilot study to determine impact of therapy with isotretinoin on sperm indices in 20 infertile men with IOA. Men were between 21 and 60 years of age without identifiable hormonal or genetic abnormalities and with total motile sperm counts of less than 10 Million on two occasions. All men received isotretinoin 20 mg by mouth twice daily for 20 weeks and had semen analyses, routine blood counts, chemistries and examinations every four weeks during treatment.

Results: Twenty men enrolled in the study and 16 completed all study procedures. All men experienced dry facial skin and chapped lips during treatment, which resolved after Isotretinoin discontinuation. There were no significant laboratory abnormalities noted in any subject, and no subject experienced worsening mood. Mean (SD) total motile sperm count increased from 3.2 (3.1) Million at baseline to 8.5 (13) Million after twenty weeks of therapy (p=0.005 c.f. baseline). Eight of sixteen men (50%) men achieved a total motile sperm concentration of greater than 10 million, and nine men (56%) had a greater than a five-fold increase in total motile sperm count by the end of treatment. The remaining seven men had either minimal or no apparent response to therapy. No significant improvement in sperm motility was observed. Six clinical pregnancies (three spontaneous, 3 via ART) occurred, four of which, including all three of the spontaneous pregnancies, were observed in men with improvements in sperm counts on therapy.

Summary: Approximately 50% of men with idiopathic IOA experienced an increase in total, motile sperm count with isotretinoin therapy. Treatment was generally well tolerated.

Conclusions: Isotretinoin therapy of men with IOA is feasible and is associated with significant improvements in sperm production in a subset of men. Randomized, placebo-controlled studies of isotretinoin therapy for infertile men with IOA are warranted, using live birth as the outcome measure.

Funding: The Eunice Kennedy Shriver National Institute of Child Health and Human Development supported this work through grant K24 HD082231 to J. Amory.

8 (Oral/Poster)
GNRH-ANTAGONIST TREATMENT BEFORE ALLOGENEIC SPERMATOGENONAL STEM CELL TRANSPLANTATION ENHANCES SPERMATOGENE RECOVERY IN RHESUS MONKEYS
Gunapala Shetty PhD¹, Jennifer Mitchell VMD², Zhuang Wu MD¹, Truong Lam BS¹, Lorraine Hill DVM¹, Ramesh Tailor PhD¹, Karen Peters BS², Kyle Orwig PhD² and Marvin Meistrich PhD¹
¹University of Texas M.D. Anderson Cancer center; ²Magee-Womans Research Institute, University of Pittsburgh School of Medicine
(Presented By: Gunapala Shetty, PhD)

Cancer treatment regimens can completely kill the stem spermatogonia in children and young patients in which case cryopreservation of spermatogonia before therapy and subsequent autologous transplantation may be the only option for restoring male fertility. Previous studies suggested that cancer treatment regimen can cause functional damage in the somatic environment of the testis, which can at least partially be alleviated by hormone suppression treatments.

To optimize conditions for the restoration of spermatogenesis by spermatogonial stem cell (SSC) transplantation, we combined transplantation with the hormone suppression during different times relative to transplantation. We irradiated the testes of 16 pubertal rhesus monkeys with 7 Gy and 4 months later transplanted cryopreserved testicular cells containing SSCs, allogeneically to one of the testes. Six of these irradiated monkeys were treated with GnRH-antagonist (GnRH-ant) starting 2 months after irradiation until the time of transplantation (GnRH-pre group). Five of the monkeys received GnRH-ant treatment starting 3 months after irradiation and lasting until 1 month after transplantation (pre+post group). This GnRH-ant treatment suppressed serum testosterone levels to an about 25% of the pretreatment values of about 2.5 ng/ml. Five of the monkeys received sham-injections instead of GnRH-ant.

At 9 months after transplantation the transplanted testes in control group showed average weights that were 5% greater than those of the sham-transplanted testes. However in the pre-GnRH-ant group the increase was consistently around 10%, whereas there was no difference in the pre+post GnRH-ant group. Similarly the average numbers of cauda epididymal sperm derived from the transplanted testes in the control group were 2.6-fold higher than those from the sham-transplanted testes. However in the pre-GnRH-ant group the ratio of sperm in the transplanted to untransplanted side was 4.0, whereas in the pre+post-GnRH-ant group the ratio was only 1.4-fold. The results suggested that the hormone suppression prior to transplantation has a beneficial effect on the recovery of sperm from the transplanted SSCs, but hormone suppression after transplantation does not augment the recovery, and rather could be detrimental instead. The tubule differentiation indices indicating the testicular spermatogenic potential in the testes will be discussed.

Funding: This work was supported by the grant 1P01HD075795-01 from NIH/NICHD.
ABSTRACTS

9 (Oral/Poster)
SPERM MITOCHONDRIAL COPY NUMBER AND DELETIONS: ASSOCIATIONS WITH URINARY-ISOPROSTANE AND PHTHALATE METABOLITES IN MALE PARTNERS UNDERGOING ASSISTED REPRODUCTIVE TECHNOLOGIES (ART)
Alexandra Olmsted¹, Haotian Wu MS¹, Rahil Tayyab PhD², Cynthia Sites MD² and J.Richard Pilsner MPH, PhD¹
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(Presented By: Alexandra Olmsted)

Introduction: Phthalates, a chemical class of plasticizers, are ubiquitous in the environment and recognized as endocrine disrupting compounds (EDCs). Recent data suggest that oxidative stress is a potential mediator for the associations between phthalate exposure and poor male reproductive health. Mitochondria are implicated in the production of excess oxidative stress and sperm mitochondrial copy number (MtCopy) and deletions (MtDeletions) have been linked with male infertility. However, little is known about the relationship of these mitochondrial biomarkers in sperm with phthalate exposure and oxidative stress.

Objectives: To examine associations of MtCopy and MtDeletions with concentrations of urinary phthalate metabolites and isoprostane in male partners undergoing ART.

Methods: A total of (n=96) sperm samples were collected from male partners undergoing ART at Baystate Medical Center, in Springfield, MA from 2014 to 2016 as part of the Sperm Environmental Epigenetics and Development Study (SEEDS). Seventeen urinary phthalate metabolites (n=50) were analyzed by the Centers for Disease Control using tandem mass spectrometry. 15F2t-Isoprostane (n=90) was measured using a competitive enzyme-linked immnosorbent assay. A triplex Taqman qPCR method was developed for relative quantification of genomic DNA, MtCopy and MtDeletions. Multivariable linear or logistic regression was employed to examine associations controlling for age, BMI, batch and male infertility status, as defined by abnormal semen quality parameters.

Results: Quartiles of MtCopy and MtDeletions were positively associated with the odds of male infertility (p for trend < .0001 and 0.007, respectively). Urinary metabolites of DiBP, MiBP, and MHiBP displayed an inverse borderline association with MtCopy (β=-0.86; p =0.07 and β=-0.99; p = 0.06, respectively); whereas, urinary MEHP concentrations were positively associated with MtDeletions (β = 0.06; p = 0.004). Urinary isoprostane levels were inversely associated with MtCopy but did not reach statistical significance (β = -0.13; p = 0.07).

Conclusion: These results suggest that certain phthalate metabolites and a known biomarker of oxidative stress may be associated with MtCopy and MtDeletions. Current research is investigating these relationships in a larger sample size.

10 (Oral/Poster)
EFFECTS OF LONG-TERM TESTOSTERONE THERAPY (TTH) WITH TESTOSTERONE UNDECANOATE INJECTIONS (TU) ON ANTHROPOMETRIC AND METABOLIC PARAMETERS IN HYPOGONADAL MEN AND AN UNTREATED CONTROL GROUP: REAL-LIFE REGISTRY DATA FROM A UROLOGY/ANDROLOGY OFFICE
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(Presented By: Farid Saad, DVM, PhD)

Introduction and Objectives: Although TTh is considered lifelong treatment, very few groups have reported long-term data. The present ongoing registry has been established in long-term to monitor effectiveness and safety of TU.

Methods: Of 505 hypogonadal men (mean age 59.0±9.5 years) with total testosterone ≤12 nmol/L and symptoms, 321 received TU 1000 mg every 12 weeks following an initial 6-week interval for a maximum of 12 years (T-group). 184 men had opted against TTh and served as controls (CTRL). Mean follow-up was 8.3±3.5 years in the T-group and 5.5±1.6 years in CTRL.

Results: In the T-group, weight decreased from 99.4±13.4 to 87.5±5.9 kg at 12 years. In CTRL, weight increased from 91.4±10.5 to 96.5±12.4 kg at 8 years (p=0.0001 for both). In the T-group, waist circumference decreased from 107.2±9.6 to 93.6±3.1 cm at 12 years. In CTRL, waist circumference increased from 99.8±9.1 to 104.7±8.3 cm at 8 years (p=0.0001 for both). BMI decreased from 31.5±4.3 to 27.6±2.1 kg/m2 at 12 years in the T-group and increased from 29.2±3.2 to 30.7±4.0 kg/m2 at 8 years in CTRL (p=0.0001 for both).

In the T-group (29.3% had type 2 diabetes), HbA1c decreased from 6.5±1.2 to 5.5±0.4% at 12 years. In CTRL (28.4% with T2DM), HbA1c increased from 6.0±0.7 to 6.2±0.8% at 8 years. All lipids (mmol/L) improved in the T-group at 12 years: total cholesterol from 6.7±1.3 to 5.1±0.7; HDL from 1.1±0.3 to 1.5±0.3; LDL from 4.0±0.8 to 2.8±0.7; triglycerides from 2.9±1.0 to 2.0±0.4; Non-HDL cholesterol from 5.6±1.4 to 3.6±0.9. In CTRL, lipids worsened at 8 years: total cholesterol from 6.4±1.5 to 6.8±1.4; HDL from 1.4±0.4 to 1.2±0.3; LDL from 3.3±0.9 to 4.0±0.6; triglycerides from 2.2±1.0 to 2.8±0.7; Non-HDL cholesterol from 5.0±1.6 to 5.6±1.4.

Blood pressure (BP; mmHg) improved in the T-group at 12 years: systolic BP from 136.4±13.2 to 118.3±4.1; diastolic BP from 81.4±8.8 to 72.9±3.9. In CTRL, BP increased at 8 years: systolic BP from 128.7±11.2 to 132.1±9.5; diastolic BP from 81.4±8.8 to 87.3±5.7.

Adherence to testosterone was 100% as all injections were administered in the office and documented. There were 24 deaths (7.5%) in the T-group and 27 deaths (14.7%) in CTRL.

Conclusions: Very long-term TTh with TU resulted in sustained improvements in anthropometric and metabolic parameters. All components of the metabolic syndrome improved, thus potentially reducing cardiometabolic risk. These effects may have contributed to the observed reduced incident all-cause mortality.

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11 (Oral/Poster)
IMPLICATIONS OF ANDROGEN RECEPTOR ACTIVATION ON THYROID CANCER PHENOTYPE
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¹New York Medical College; ²United States Military Academy Preparatory School, West Point, NY; ³New York Eye and Ear Infirmary

Introduction: Papillary Thyroid Cancer (PTC) comprises more than 90% of neoplasms in the endocrine system, with a three-fold higher incidence in women than in men. With an overall five-year survival rate of 98.1%, early stage PTC has a favorable prognosis. However, PTC exhibits increased aggressiveness with poor prognosis in men diagnosed with the disease. These striking observations led us to explore the role of androgen and androgen receptor (AR) in this disease.

Methods: Development of our model system consisted of (1) Determining levels of AR expression in PTC patient tissue samples, (2) Determining AR expression in thyroid cancer cell lines, (3) Stable transfection of 8505c PTC/anaplastic thyroid cancer cell line with AR (clone 84e7), (4) Transcriptional profiling using RNAseq on 48 hour 5α-dihydrotestosterone (DHT) treated 84E7 cells, (5) Continuously activating AR in 84e7 cells with DHT for 3-6 days, followed by beta-galactosidase (SA-βGal) assays, flow cytometry, western blots and immunocytochemistry to investigate development of senescence, (6) Cytokine profiling of the senescence-associated secretory phenotype (SASP) to define the pro-tumorigenic or tumor-suppressive potential of androgen-induced senescent thyrocytes.

Results: We found a 70% decrease in median AR expression (p<0.0001) in 24 PTC patient tissue samples, compared to matched, normal thyroid tissue. Preliminary data from our lab indicate that androgen receptor (AR) acts as a negative regulator of growth as evidenced by a statistically significant 48% decrease in proliferation over 72 hours upon DHT addition to 84E7 cells. RNAseq revealed significant changes in gene expression associated with proliferation (474 genes, p=2.4E-24) and cell cycle progression (129 genes, p=6.54E-6). AR stimulation induced senescence, evidenced by a flattened, vacuolized and granular cell morphology, and expression of SA-βGal, leading to a permanent growth arrest, without apparent cell death. Senescence was accompanied by an increase in total RNA and protein content, Reactive Oxygen Species, and markers such as p21, p27, p16, γ-H2AX, HP1- γ, and H3K9 methylation. Profiling of SASP revealed a primarily anti-inflammatory microenvironment initiated and sustained by the senescent cells.

Conclusion: Our study elucidates the induction of senescence as a novel function of AR activation in thyrocytes and may indicate a protective role of AR activation in the decreased incidence of thyroid cancer in men.

12 (Oral/Poster)
TARGETED DEGRADATION OF ANDROGEN RECEPTOR (AR) AND ITS SPLICED VARIANT AR-V7 BY THE PHYTOCHEMICAL SULFORAPHANE: NEW THERAPEUTIC OPPORTUNITY FOR CASTRATION RESISTANT PROSTATE CANCER (CRPC)
Namrata Khurana M TECH¹, Hogyoung Kim PhD², Partha K. Chandra PhD², Sudha Talwar PhD², Pankaj Sharma PhD², Asim B. Abdel-Mageed PhD³, Debasish Mondal PhD⁴ and Suresh C. Sikka PhD⁵
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Introduction: Androgen deprivation therapy (ADT) suppresses the growth of prostate cancer (PC) expressing full length androgen receptor (AR-fl). However, castration resistant prostate cancer (CRPC) recurs due to the induction of ligand-independent AR splice variants, particularly AR-V7. Strategies to suppress both AR-fl and AR-V7 levels are critically needed for treating CRPC. Our previous study demonstrated that sulforaphane (SFN), an isothiocyanate phytochemical, enhances the rate of degradation of AR-fl in several PC cell lines, e.g. LNCaP and C4-2B. SFN has been shown to inhibit the chaperone activity of heat-shock protein 90 (HSP90) and induce the potent antioxidant transcription factor, nuclear factor erythroid-2-like 2 (Nrf-2). We hypothesize that the combined exposure of SFN with clinically approved drugs that inhibit HSP90 (e.g. Ganetespib) (G) and activate Nrf-2 (e.g. Bardoxolone-methyl) (BM) would suppress AR-fl and AR-V7 for treating CRPC.

Methods: The current study was conducted in AR-V7-expressing CRPC cell line, CWR22RV1 (22RV1). Effect of drug(s) on cell viability and migration were monitored by MTT and migration assays, respectively. AR protein expression and its subcellular localization were measured by immunoblot analysis (IB) and immunofluorescence microscopy (IFM), respectively. Proteasomal activity was monitored by proteasomal assay.

Results: 22RV1 cells were significantly (p<0.05) more resistant to the potent anti-androgen, enzalutamide (ENZ) compared to LNCaP and C4-2B cells. Co-exposure to SFN (5-25 μM) significantly (p<0.01) enhanced the efficacy of ENZ. The immunoblot studies showed that SFN decreases the half-life of both AR-fl and AR-V7 proteins (p<0.01), possibly by increased protein ubiquitination and proteasomal activity. The IFM analysis showed that SFN treatment down-regulated both cytosolic and nuclear AR levels. Co-exposure of SFN with physiologic doses (<1 uM) of G and BM caused rapid degradation of both AR-fl and AR-V7, decreased cell viability and further augmented the efficacy of ENZ in 22RV1 cells.

Conclusion: Our findings suggest that the multimodal actions of SFN can cause rapid decrease in both AR-fl and AR-V7 protein levels and further implication that its combination with G and BM is an effective adjunct to current ADT in CRPC patients, especially those expressing AR-V7.
13 EFFECTS OF TESTOSTERONE REPLACEMENT THERAPY ON METABOLIC DISORDERS IN PATIENT WITH TYPE 2 DIABETES MELLITUS AND ANDROGEN DEFICIENCY.

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(Presented By: Shota Janjgava, PhD)

Over the past few decades, obesity and Diabetes mellitus has become a global health challenge. Multiple epidemiological studies have shown that low testosterone levels are associated with and predict the future development of T2D and the metabolic syndrome.

Objective: The aim of study was to show the influence of testosterone replacement therapy on obesity, HbA1c level, arterial hypertension and dyslipidemia with patient diabetes mellitus and Androgen deficiency.

Methods: 125 male patient with diabetes mellitus was screened, 85 subjects with 41-65 years and BMI 27.0 – 48.0 kg/m2 were randomized In placebo-controlled study, who underwent a routine physical examination and choose free testosterone examination. According to the laboratory and clinical condition we divided patients into two groups. 1) First group treatment group 2) Second group placebo group. In the first group we used diet, physical activity (Lifestyle intervention implies reduced calorie diet (The reduction of daily calorie intake in 800-1200 calorie, it was selected individually), patient’s antidiabetic therapy and testosterone replacement therapy (TRT), (testosterone undecanoate 250 mgr/ml intra- muscular 3 months 1 time). In second group we used diet, physical activity (Lifestyle intervention implies reduced calorie diet (The reduction of daily calorie intake in 800-1200 calorie, it was selected individually), patient’s antidiabetic therapy and placebo.

Results: After six months of treatment we repeated the diagnostic assessments: We had some positive results cholesterol, triglyceride and LDL levels decreased, and HDL increased both of group but better results was in first group which was clinically significant. Free testosterone level increased in all groups but the best results was in I group which was clinically significant where was used of testosterone undecanote. HbA1c decreased in both group but in I group we had the best result. BMI decreased in both groups but more reduction was in I group. leptin level after treatment was approximately same in both groups, but compared best results was achieved in I group, also blood pressure were reduced in both group, where we found alike results .

Conclusion: Our study demonstrated that it is possible to break into this vicious circle by raising testosterone levels in diabetic men and low testosterone level. In addition to traditional CV risk factors, novel risk factors are also inversely related to testosterone levels.
15
THE INFLUENCE OF WINE CONSUMPTION IN MALE FERTILITY POTENTIAL: INITIAL REPORT

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¹Androscience – High Complexity Clinical and Research Andrology Laboratory, Brazil; ²Methodist University of Sao Paulo, Brazil; ³Department of Urology, FMUSP, Brazil; ⁴Reproductive Toxicology Unit, Department of Pathology, FMUSP, Brazil; ⁵Reproductive Toxicology Unit, Department of Pathology, FMUSP, Brazil; ⁶Oswaldo Cruz German Hospital, Brazil.

(Presented By: Victória Santos Coutinho)

Introduction: Male fertile potential is determined by the homeostasis of a complex system involving hormonal balance, sperm production, environmental factors and lifestyle habits. High alcohol consumption has been associated with a variety of diseases, including male infertility, which occurs due to adverse effects in hypothalamic-pituitary-gonadal axis, influencing the activity of Sertoli and Leydig cells and consequently on spermatogenesis.

Objectives: To correlate wine consumption with hormonal, semen and sperm functional parameters in an infertile population.

Methods: Medical records of 432 patients (22 to 69 y.o.), between 2000 and 2016, in which anamnesis contained clinical data on self-reported wine consumption (time in years and quantity in glasses mL/week; n=52), semen analysis, sperm function tests (ROS and DNA fragmentation by SCSA) and sex hormone profile. Azospermic patients were excluded. The Pearson's correlation coefficient test (p <0.05) was used to evaluate the correlations between the study data.

Results: We observed a mean of 3.02 wine doses per week and mean of 10.35 years of consumption in the study group and a negative correlation with progressive spermatozoa (-2.34; p = 0.043). We found a positive correlation between time of consumption (years) with higher LH (0.962, p = 0.038) and androstenedione levels (0.845, p = 0.008).

Conclusion: Moderate wine consumption for a long period of time, was associated with changes in semen parameters that may influence male fertility potential and should be critically investigated in the anamnesis of the infertile male.

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Ethics Committee Approval: FMUSP n°859215/2014

16
ARE RESPIRATORY ALLERGIES RELATED TO MALE FERTILITY?

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(Presented By: Dayane Guerino Reis, BSc)

Introduction: Respiratory allergies are achieving epidemic proportions, affecting approximately 30% of the population in urban areas of industrialized countries. Respiratory allergies, rhinitis and sinusitis have been frequently reported by men in the fertility evaluation. Studies have already described ultra-structural changes in nasal tissue, but the association between these allergies and male fertility is still unknown.

Objective: To evaluate the effect of respiratory allergies, rhinitis and sinusitis on sperm quality, sperm functional parameters and hormonal profile.

Methods: 432 patients (22 to 69 y.o.), between 2000-2016, in which anamnesis revealed clinical data and self-report of respiratory allergies, sinusitis and rhinitis, were correlated with semen analyzes, sperm functional tests and sex hormones profile. The Pearson's correlation coefficient test (p <0.05) was used.

Results: We observed a negative correlation between respiratory allergies and progressive motility (-0.124, p=0.010), total motility (-0.147, p=0.002), grade A motility (-0.129, p=0.008), sperm vitality (-0.956; p<0.001) and LH (-0.475; p=0.046); and positive correlation with immotile spermatozoa (0.136, p=0.005) and T4 (-0.576, p=0.005). When evaluating sinusitis, there was a negative correlation with normal morphology sperm (-0.106, p=0.033), sperm vitality (-0.956, p<0.001), sperm creatine kinase activity (-1,000, p=0.019), LH (-0.455, p=0.058) and TSH (-0.733, p=0.025); and positive correlation with spermatozoa with abnormal sperm morphology (0.100; p=0.033). In addition, rhinitis presented a positive correlation with seminal ROS (0.937, p<0.001), estradiol (0.307, p=0.015), prolactin (0.325, p=0.011), and IGFBP-3 (1,000; p=0.001).

Conclusion: Our results indicate that respiratory allergies, rhinitis and sinusitis are related to changes in parameters that determine the male fertile pattern. This initial study allows us to suggest two mechanisms of influence of respiratory allergies in male fertility: (I) ultrastructural modifications in microtubules, dinein sheaths and ciliary membrane observed in patients with chronic respiratory disorders are similar to those observed in spermatozoa of asthenozoospermia and teratozoospermia of infertile patients; (II) hormonal and sperm function changes may be related to medications often used for patients with chronic respiratory allergies.

Financial support: Androscience/FAPESP

Ethics Committee Approval: FMUSP n°859215/2014

17
NEW INSIGHTS INTO THE PANDEMIC OF LOW VITAMIN “D” LEVELS AND ITS ASSOCIATION WITH SEMEN QUALITY AND HORMONAL LEVELS IN FERTILE AND INFERTILE MALE SUBJECTS

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¹Androscience – High Complexity Clinical and Research Andrology Laboratory, Brazil; ²Dept. of Urology, USP, Brazil; ³Reproductive Toxicology Unit, Dept. of Pathology, USP, Brazil; ⁴Oswaldo Cruz German Hospital, Brazil; ⁵Reproductive Toxicology Unit, Dept. of Endocrinology, USP, Brazil

(Presented By: Inari Ciccone, Msc Student)
Background: Vitamin D is a versatile signaling molecule, that targets also male reproductive organs, in addition to the classic effects on bone, calcium and phosphate homeostasis. Accumulating evidence from animal and human studies suggests that it is involved in many functions in both genders. Objective: To evaluate the influence of vitamin D status on semen quality and hormonal profile in male fertility and infertility.

Methods: We evaluated 100 men (aged 18 to 50 y.o.) from a private andrology reference medical clinic. Infertility (n=70) and fertility (n=30) groups. According to vitamin D level status of all of them were classified in sufficient (group 1 - 25OHDvitaminD ≥ 30ng/ml), insufficient (group 2 - 25OHDvitaminD from 21 to 29ng/ml) and deficient (group 3 - 25OHDvitaminD ≤ 20ng/ml). Blood samples were collected to analyze serum vitamin D, LH, FSH, estradiol, total and free testosterone, prolactin and SHBG levels. Semen was analyzed according to WHO guidelines, strict criteria and sperm functional tests were performed (ROS, CK, beads). In addition, karyotype, frequency of varicocele, smoking, alcohol ingestion, and body composition were considered. Statistical analysis was performed by SPSS program version 19.0 (SPSS Inc., Chicago, IL). T-test was used for unpaired samples and Spearman test for correlation analysis. Statistical significance was considered with P value < 0.05.

Results: According to vitamin D status, patient distribution was: Infertile: group 1 - 26% (20/70), group 2 - 43% (30/70) and group 3 - 28.5% (20/70). Fertile: group 1 - 34% (10/30), group 2 - 40% (12/30) and group 3 - 26% (8/30). Sperm motility was significantly lower in group 3 in comparison to group 1 in infertile patients. Regarding fertile men, we found higher sperm volume in group 3 than the group 1, a significant reduction of sperm concentration and worse morphology by strict criteria in group 3 in comparison to group 1. Hormonal levels were similar in all vitamin D groups.

Conclusion: Our results demonstrated that sufficient vitamin D levels has a positive influence on spermatogenesis and semen quality, suggesting that vitamin D replacement should highly be concerned on male fertility treatment and that low vitamin D have reached epidemic proportions in industrialized cities, even in Brazil.

18 HEAT SHOCK PROTEINS 70 AND 90 ALPHA ARE INCREASED IN SEMEN OF SMOKERS
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Department of Surgery, Division of Urology, Human Reproduction Section, Sao Paulo Federal University
(Presented By: Mariana Pereira Antoniassi, BSc, MSc)

Introduction: Heat shock proteins (HSPs) are a family of proteins that function as molecular chaperones by stabilizing new proteins to ensure correct folding or by helping to refold proteins that were damaged by cellular stress. Production of high levels of heat shock proteins can also be triggered by exposure to different kinds of environmental stress conditions, such as infection, inflammation, and exposure to toxins (smoking, metals). In this study we wished to verify if smoking alters seminal HSP expression levels, and if this is potentiated by the presence of varicocele.

Methods: To verify the levels of HSP, we recruited 15 controls (healthy adult men without varicocele, non-smokers), 17 smokers without varicocele, and 15 smokers with varicocele. Semen was collected and an aliquot was submitted to standard semen analysis, as per the World Health Organization (2010). The remaining volume was centrifuged at 800 g for 30 minutes to separate the supernatant seminal plasma, which was frozen without cryoprotectants and kept at -20 C. At the time of analysis, the seminal plasma was thawed and centrifuged at 16,100 x g for 1 hour at 4 C to remove cellular debris. The total amount of proteins in each sample was quantified using a BCA protein assay. Quantification was performed by measuring absorbance at 540 nm wavelength, using a microplate reader. An aliquot of each sample was diluted in Milli Q water (1:250) and a volume corresponding to 4 ug/mL of protein was used for the analysis. The HSP Magnetic Bead Kit was used to detect changes in HSP27 (Total), HSP27 (pS78/pS82), HSP60, HSP70 (HSP72), and HSP90 alpha in human seminal plasma using the Luminex® system. Univariate statistics were performed using a Kruskal-Wallis test followed by Games-Howell post-hoc test (p<0.05).

Results: Seminal plasma results are presented in table 1. The levels of HSP 70 and HSP 90 alpha were increased in smokers and decreased in control and smokers with varicocele.

Conclusion: The semen of smokers seems to have an inflammatory state characterized by increased levels of HSP 70 and HSP 90 alpha. These proteins works as molecular chaperones, providing sperm protection against stress, such as cytokines and other inflammation molecules.

Table 1: Seminal plasma levels of HSP70, HSP 90 alpha, HSP 27 (total), HSP27 (pS78/pS82) and HSP 60. Groups were compared by Kruskal-Wallis test followed by Games-Howell post-hoc test (values presented as median, interquartile range).

<table>
<thead>
<tr>
<th></th>
<th>Control (n=15)</th>
<th>Smoker (n=17)</th>
<th>Varicocele smoker (n=15)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSP 70</td>
<td>6.5; 4.00</td>
<td>7.5; 11.00</td>
<td>3.5; 4.50</td>
<td>0.002*</td>
</tr>
<tr>
<td>HSP 90 alpha</td>
<td>9.5; 9.00 *</td>
<td>15.3; 21.00 a</td>
<td>7.5; 10.00 b</td>
<td>0.025*</td>
</tr>
<tr>
<td>HSP 27 (total)</td>
<td>76.7; 59.00</td>
<td>136.7; 111.00</td>
<td>51.7; 61.00</td>
<td>0.007*</td>
</tr>
<tr>
<td>HSP 27 (pS78/pS82)</td>
<td>0.0; 2.00</td>
<td>0.0; 0.00</td>
<td>0.0; 0.009</td>
<td>1.00</td>
</tr>
<tr>
<td>HSP 60</td>
<td>2.7; 2.00</td>
<td>1.7; 5.00</td>
<td>0.0; 3.00</td>
<td>0.070</td>
</tr>
</tbody>
</table>

Different superscript letters in a same row indicate a significant difference in the post-hoc test.
Quality of life of young cancer survivors is an important healthcare issue. Chemotherapeutic drugs are well-known toxicants to the male gonad. Prospective studies on adult cancer survivors show that although sperm production may recover, DNA damage and chromatin abnormalities can persist years post-chemotherapy. Such biomarkers of sperm damage have been correlated to male infertility and poor embryo development. In the case of childhood cancer, it has been shown that survivors are more likely than siblings to report low sperm count and to use assisted reproductive technologies. However, it is still unclear if the sperm produced many years after remission of cancer are damaged. To address this issue, we investigated the long-term impact of the chemotherapeutic treatment of childhood acute lymphoblastic leukemia and lymphoma, two malignancies with highest incidence in children, on male reproductive health and sperm quality. Men 19-40 years were recruited into 3 groups: diagnosed before (ages 4-13, n=7) or after puberty (ages 14-18, n=6), or without history of cancer (control, n=12). All cancer subjects had been in remission for at least 3 years and had no comorbidity related to fertility. Interestingly, we observed that survivors were significantly overweight compared to controls and that this difference was particularly significant in the group of men diagnosed after puberty. Average levels of circulating hormones (LH, FSH, testosterone, estradiol), sperm concentrations, and progressive motility showed no difference among groups. However, 5 survivors of lymphoma (38.5%) were azoo/oligospermic, including 3 diagnosed pre-puberty and 2 after puberty. For non-azoospermic participants, the DNA fragmentation index (DFI) and the high DNA stainability were obtained using the HT-COMET assay. Interestingly, the %DFI correlated significantly with the % tail DNA (r=0.73; p=0.0002). Nevertheless, none of these parameters were different among groups, suggesting that sperm quality is not impaired in cancer survivors after protracted time periods. Although limited by the small number of subjects, these data suggest that survivors of childhood cancer, independently of the age of diagnosis, have a higher risk of infertility due to no or low sperm count and that when sperm are present, chances of DNA and chromatin abnormalities appear similar to those seen in the general population.

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20 ASSOCIATIONS OF PHENOLS AND PARABENS WITH SPERM GENOME-WIDE DNA METHYLATION
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(Presented By: Haotian Wu)

Background: Phenols and parabens are diverse and ubiquitous families of endocrine disruptors with widespread human exposure around the world. Previous epidemiologic studies report that select compounds within these chemical families may be associated with adverse male reproductive endpoints. Given the emerging evidence that the sperm epigenome during spermatogenesis is responsive to environmental conditions and can affect offspring health and development, we examined the associations between eleven urinary phenols and parabens and sperm DNA methylation.

Methods: A total of 48 male participants were recruited from the Baystate Medical Center’s IVF clinic from 2014 to 2015 as part of the Sperm Environmental Epigenetics and Development Study (SEEDS). Seven phenols and four parabens were measured from spot urine samples by the CDC. Sperm DNA methylation was assessed with the HumanMethylation 450K array. We used the minfi package to correct for technical variation in background signals, remove probes below the background fluorescence level, and adjust for differences in Type I and Type II probes. Batch effects were corrected via ComBat and sex chromosomes were removed by DMRcate. The resulting beta-values were analyzed using Aclust and CpGassoc, corrected for false-discovery rate.

Results: After pre-processing, 6479 clusters were constructed with a mean of 3.5 CpG sites per cluster. Adjusting for male age, BMI, infertility diagnosis, and current smoking, urinary concentrations of bisphenol-A, propyl paraben and 5-dichlorophenol were associated with one differentially methylated region(s) (DMR) each, butyl paraben and triclocarban were associated with 2 DMRs and methyl paraben were associated with 3 DMRs. Of the nine unique clusters (one cluster was identified by both Methyl- and Propyl- Parabens), six are entirely within genes or span the transcription start site. These affected genes are all protein-coding and have known functions related to DNA double strand repair, internal cell motility, brain development, and vasoconstriction in vas deferens.

Discussion: To our knowledge, this is the first study to associate paternal phenol and paraben exposures with sperm DNA methylation in humans. Future analyses will further investigate biological pathways of the identified regions using ontological analyses and whether these sperm DNA methylation patterns are linked to early life development.

21 EFFECTS OF PRENATAL EXPOSURE TO DI-N-BUTYL PHTHALATE ON THE DEVELOPMENT OF ADULT LEYDIG CELLS IN RAT DURING PUBERTY
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(Presented By: Linxi Li, PhD)

Introduction: Fetal exposure to di-n-butyl phthalate (DBP) causes the adult disease such as lower testosterone production and infertility. However, the mechanism is still unknown. The objective of the present study is to determine how DBP affects the involution of fetal Leydig cells during neonatal period and how this event causes the delayed development of the adult Leydig cells during puberty.

Methods: The pregnant Sprague-Dawley dams were randomly divided into 3 groups and were gavaged with 0 (corn oil, the
vehicle control), 100 or 500 mg/kg DBP from gestational day 12 to 21. The blood and testes were collected from male pups at postnatal day 4, 7, 14, 21, 28, and 56. Serum testosterone concentrations were assessed and the mRNA levels of Leydig cell- or gonadotroph cell-specific genes were measured.

**Results:** Prenatal exposure to DBP caused the aggregation of fetal Leydig cells, which slowly disappeared when compared to the control. This effect was associated with the reduction of testicular testosterone secretion and down-regulation of the mRNA levels of Leydig cell biomarkers including Scarb1, Star, Cyp11a1, Hsd3b1, Hsd11b, and Hsd17b3.

**Conclusion:** We demonstrated that the increasing aggregation of fetal Leydig cells with the increasing doses of DBP delayed their involution, thus leading to the delayed development of the adult Leydig cells.

### 22 AMELIORATIVE EFFECTS OF VITAMIN C ON THE HEMATOLOGY, SEMEN QUALITY AND HORMONAL PROFILE OF TEDDY GOAT BUCKS IN ARSENIC TOXICITY

Muhammad Zubair, PhD

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(Presented By: Muhammad Zubair, Lecturer)

Ameliorative effects of vitamin C on the hematology, semen quality and hormonal profile of Teddy goat bucks in arsenic toxicity

The present environmental study was conducted to investigate the toxic effects of arsenic on male reproductive functions of Teddy bucks, and to examine whether these toxic effects are ameliorated by vitamin C. For this purpose, 12 adult Teddy bucks were randomly divided into three treatment groups viz; A (control), B (sodium arsenite), C (sodium arsenite + vitamin C), with four animals in each group. Sodium arsenite and vitamin C was fed with 5 and 200 mg/kg BW/day respectively. These treatments continued for 17 weeks. Semen quality parameters (volume, sperm motility, sperm count, acrosomal integrity, membrane functional integrity and DNA integrity) were evaluated on weekly. Hematological variables (red blood cells count, hemoglobin, packed cell volume and white blood cells), serum concentrations of male sex hormones (testosterone, LH, FSH) and cortisol were recorded fortnightly. The data were subjected to two-way analysis of variance, followed by Duncan test for multiple mean comparisons.

**Results:** We demonstrated that the increasing aggregation of fetal Leydig cells with the increasing doses of DBP delayed their involution, thus leading to the delayed development of the adult Leydig cells.

**Conclusion:** We demonstrated that the increasing aggregation of fetal Leydig cells with the increasing doses of DBP delayed their involution, thus leading to the delayed development of the adult Leydig cells.

### 23 IS IT POSSIBLE FOR SMOKING-ABSTINENCE TO REVERSE THE NICOTINE-INDUCED ALTERATIONS IN THE EPIDIDYMIS?

Panagiota Tsounapi PhD1, Masashi Honda PhD2, Fotios Dimitriadias PhD3, Katsuya Hikita PhD2, Nikolaos Sofikitis PhD, DMSci4 and Atsushi Takenaka PhD2

1Division of Urology Tottori University Faculty of Medicine; 2Division of Urology Tottori University Faculty of Medicine; 3Department of Urology Aristotle University; 4Department of Urology University of Ioannina School of Medicine

(Presented By: Panagiota Tsounapi, PhD)

Introduction and Objectives: Available data indicate that up to 13% of infertility is attributed to cigarette smoking. In the present study, nicotine was selected as a major addictive substance of tobacco smoke and the effects of nicotine-induced alterations in oxidative stress (OS) in the epididymis and the testis were examined. Furthermore, the impact of nicotine-abstinence was investigated alleviate these changes.

**Methods:** Adult Wistar rats were treated orally with nicotine (15 mg/kg). One group was administered nicotine for 10 weeks (Nico-group) and another group was administered nicotine for 7 weeks followed by 3 weeks of abstinence (Abst-group). The Control group had free access to fresh water. Tissue levels of malondialdehyde (MDA) and total antioxidant capacity (TAC) were evaluated both in the testis and the epididymis. Additionally, cotinine levels in the urine, serum and seminal vesicular fluid (SVF) were evaluated. Furthermore, testosterone was measured in the urine samples. Finally, immunohistochemistry was performed for OS-markers and Cytochrome P450 2A6 (CYP2A6) in epididymal tail samples.

**Results:** Nicotine treatment significantly increased MDA levels both in the testis and epididymis in Nico-group compared to Abst and Control groups. TAC was significantly decreased in both epididymis and testis in Nico group compared to Abst and Control groups. Cotinine concentrations in urine, serum and SVF
were significantly increased in Nico-group compared to Abst group. Testosterone levels in the urine in Nico group were significantly lower compared to Control-group, while there was no significant difference between Control and Abst-group, neither between Nico and Abst groups. OS-markers had stronger expression in epididymal samples from Nico-group compared with Abst and Control groups. CYP2A6 which is the primary enzyme responsible for the oxidation of nicotine and cotinine was expressed and localized in the epithelial cells of the epididymis in Nico-group. 

**Conclusions:** The present data show that the harmful effects of nicotine in the testis and epididymis can be reversed by abstinence. It is possible that additional treatment with an antioxidant reagent may enhance the antioxidant defenses of testis and epididymis, and further ameliorate the cigarette smoke-induced oxidative stress in both testicular and epididymal tissue. The present data may help clinicians to advice patients, especially those who attend assisted-reproductive programs, to quit smoking.

### 24 PURINERGIC MODULATION OF V-ATPASE-DEPENDENT PROTON SECRETION IN EPIDIDYMAL CLEAR CELLS

Maria Agustina Battistone PhD¹, Flavia Gombar Master², Maria Alejandro Peralta Bachelor¹, Nicolas DaSilva PhD², Dennis Brown PhD¹ and Sylvie Breton PhD¹

¹Program in Membrane Biology/Division of Nephrology, Massachusetts General Hospital, Harvard Medical School; ²Laboratory of Morphometry, Metabolism & Cardiovascular disease Department of Anatomy - IBrag - UERJ

(Presented By: Maria Agustina Battistone, PhD)

The epididymis maintains an optimum environment for sperm maturation. Elaborate communication networks between the different epithelial cell types (clear cells (CCs), principal cells (PCs) and basal cells) are important to establish an acidic luminal environment, which is required to maintain sperm dormant before ejaculation. CCs secrete H⁺ via the vacuolar H⁺-ATPase (V-ATPase) located in their apical membrane. This process is regulated by the cAMP/PKA and calcium/PKC pathways, which induce apical V-ATPase accumulation following redistribution of recycling sub-apical vesicles. We showed that CCs secrete ATP, which is hydrolyzed into adenosine by ectonucleotidases (EctoNs).

Immunofluorescence (IF) showed expression of the adenosine receptors, A1, A2A and A2B, and the ATP receptor P2X4 in the apical membrane of CCs. A2A and A2B increase cAMP, and P2X4 increases calcium, and we, therefore, studied their role in the regulation of V-ATPase in CCs. IF and Western blot following cell fractionation showed V-ATPase membrane accumulation when mouse epididymides were perfused in vivo with adenosine or an A2B agonist (BAY-60-6583; 100 µM), and with the non-hydrolysable ATP analog ATPγS or a P2X4 agonist (ivermectin; 100 µM). No effect was detected using an A2A activator, compared to control. These results indicate that V-ATPase-dependent H⁺ secretion in CCs is activated by adenosine via A2B and by ATP through P2X4.

Moreover, we detected a 3-fold increase in luminal adenosine concentration (<0.03) and a 50% reduction in ATP concentration (<0.05) after perfusion at 7.8 versus the control pH of 6.6, suggesting an increase in ATP hydrolysis by EctoNs at alkaline pH. Indeed, specific EctoN inhibitors (AMPCP and POM-1, 10 µM) decreased luminal adenosine levels measured at pH 7.8 (33 and 47% vs control, p<0.03). Perfusion of the cauda at alkaline pH 7.8 induces V-ATPase-dependent H⁺ secretion by CCs, which restores the pH towards 6.6. EctoN inhibitors partially prevented this recovery (control: 7.2±0.05, AMPCP: 7.5±0.03, POM-1: 7.6±0.04, p<0.01). These data suggest that ATP and adenosine are luminal modulators of H⁺ secretion by CCs and that the production of adenosine is itself modulated by luminal pH.

Altogether, our study reveals novel mechanisms by which CCs respond to luminal agonists via purinergic regulation, and provides new frameworks for the discovery of potential diagnostic targets of male infertility, and the development of novel methods for male contraception.

### 25 MAZ HAPLOINSUFFICIENCY ALTERS BACULUM MORPHOGENESIS IN MICE

Marisol O'Neill MS, Gene Huang MD, Meade Haller PhD and Dolores J. Lamb PhD

Baylor College of Medicine

(Presented By: Marisol Ann O'Neill, MS)

**Introduction and Objectives:** Hypospadias is a common congenital genitourinary (GU) anomaly affecting 1 in 125 males. Using array comparative genomic hybridization and the DECIPHER database, we identified myc-associated zinc finger (MAZ), which is highly expressed in the genital tubercle, as a candidate gene for GU development. MAZ copy number variants (CNVs) were identified in 6.5% of patients GU anomalies. Of the patients with Lower GU defects, micropenis and hypospadias were common in patients with duplications while cryptorchidism and hypospadias were common in patients with deletions suggesting MAZ may be a dosage sensitive gene. We hypothesized that MAZ haploinsufficiency would affect penile morphology in mice. Due to differences in anatomy of the murine and human penis, hypospadias in mice has been reported as a spectrum of morphometric changes not limited to defects of the urethral meatus. Using micro computed tomography (micr-CT), we phenotyped penises from Maz-Δ/Δ and wild type mice.

**Methods:** Murine Penises were fixed overnight in formalin followed by dehydration in 70% ethanol. To allow visualization of penises by micro-ct, fixed penises were submerged 0.1N iodine overnight. Stained penises were briefly rinsed with PBS to remove any loose iodine then embedded in 1% agarose. Imaging was performed using a SkyScan 1272 X-Ray Microtomograph using a 0.5 µm aluminum filter and 5 µm pixel size. Images were reconstructed using NRecon software; visualization and measurements of specimen were performed in 3D Slicer v4.

**Results:** Maz Δ/Δ mice are perinatal lethal therefore only Maz+/Δ mice were examined. Five wild type and seven Maz +/Δ adult penises were measured for changes in total penis length, MUMP length, and baculum length and width. While there was no difference in the total penis (5.65 ± 0.11 mm vs 5.74 ± 0.19 mm; p = 0.48) or MUMP (1.71 ± 0.06 mm vs 1.72 ± 0.05 mm;
ABSTRACTS

p=0.62) lengths of Maz+/Δ mice, the baculum had a 3% shorter length (4.12 ± 0.09 mm vs 3.99 ± 0.10 mm; p = 0.04) and 31% smaller baculum shaft width (0.35 ± 0.03 mm vs 0.24 ± 0.06 mm; p = 0.004) compared to wild type mice.

Conclusions: Baculum shaft width and length were significantly smaller in Maz+/Δ mice when compared to wild types. Baculum shaft width has been reported to be associated with reproductive success in male mice; further studies are required to confirm this association.

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26 CRITICAL ROLE OF REGULATORY SPERMATOZOAL TRANSCRIPTS IN EARLY EMBRYONIC DEVELOPMENT
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(Submitted By: Vidhu Dhawan, MBBS, MD)

Introduction: The knowledge of molecular and cellular events underlying fertilization and early embryonic development has increased substantially over years. A plethora of studies have been conducted in recent years to assess the role of paternal factors for successful fertilization and embryonic development. The presence of RNA in sperm has contradicted the previously held belief that paternal contribution is limited to one copy of the genome. Also the defects in sperm chromatin integrity are a potential cause of pregnancy losses.

Objectives: The present study was designed with an aim to evaluate the expression pattern of spermatozoal FOXG1B, RPS6, RBM9 and RPL10A in male partners of couples experiencing early pregnancy loss in both spontaneous as well as assisted conceptions. Seminal oxidative stress and DNA Fragmentation Index (DFI) was also assessed.

Methods: Semen sample was from male partners of couples experiencing recurrent pregnancy loss (RPL) (n=75), recurrent implantation failures (RIF) (n=30) and 30 fertile controls. Semen analysis was assessed by WHO (2010) criteria. Gene expression analysis was done by q-PCR analysis and the relative quantification of target genes was calculated after normalization to β-actin with 2-ΔΔCt method. Reactive oxygen species (ROS) levels (RLU/sec/million sperm) were assessed by luminol dependent chemiluminescence. The Sperm chromatin structure assay (SCSA) was performed by flow cytometry to determine DFI.

Results: The average DCt of FOXG1, RPS6, RBM9 and RPL10A genes was found to be 3.62, -0.58, 1.5, 3.25 in RPL patients and 5.41, 4.6, 4.3, 6.7 in RIF patients. However, the average DCt of healthy fertile controls was found to be 3.94, 2.2, -0.06 and 2.5. The mean ROS level in the cases was seen to be higher (>25) in 32% of RPL patients (356.9 ± 137.8) and 75% RIF patients (142.78 ± 75.6) with respect to controls (26.7 ± 9.8). The While the odds of occurrence of RPL was 0.77 times higher (>25) in 32% of RPL patients and RIF (41.3 ± 5.1) was significantly (P < 0.0001) higher as compared to controls (27.4 ± 6.4).

Conclusion: Sperm transcript dysregulation along with oxidative DNA damage are one of the main causes of early pregnancy loss. Regulation of oxidative stress and DNA damage following adoption of various complementary and alternative medicine therapies may help in normalization of transcript dysregulation.

28 ANALYSIS OF THE CELLULAR AND NUCLEAR INTEGRITY OF SPERM FROM PATIENTS WITH VARICOCELE
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Varicocele has a negative impact on seminal parameters and deleterious effects on sperm DNA fragmentation (SDF) and epigenetic changes. SDF and oxidative stress appear to be related to reduced sperm DNA methylation and decreased telomere content, which may lead to genomic instability. The aim of the present study was to verify the effect of varicocele on seminal quality, SDF, global DNA methylation and telomere length in varicocele. This is a case-control study with 40 volunteers, 20 men with varicocele (8 grade II and 12 grade III) and 20 men without the disease. The seminal quality was evaluated by spermogram and the SDF was analyzed by Halosperm G2® kit. Some samples were selected by the DNA quality, the sperm DNA methylation was evaluated by ELISA (Enzyme-Linked Immunosorbent Assay) and telomere content by real-time polymerase chain reaction (qPCR). The comparisons were performed using the non-parametric Mann-Whitney test (p <0.05). There were no differences in mean age between the groups (p> 0.05). There was a decrease in sperm concentration (p = 0.0033), progressive motility (p = 0.0041) and morphology (p = 0.0015) in varicocele group compared to the controls. Even without significant differences, a higher percentage of DNA fragmentation was observed in the varicocele group (Varicocele: 37 ± 2; Control: 26 ± 1) (p> 0.05). In the patients with the disease, despite to have lower percentage of sperm DNA methylation (49.74 ± 20.75) in relation to the control group (64.66 ± 17.08), we did not observe statistical difference (p> 0.05). No difference was observed in telomere content between the groups (p> 0.05). When varicocele group was separated according to degree (II and III), no differences were observed in any of the variables (p> 0.05). We showed that varicocele is associated with decreased in seminal quality and may be related to a higher percentage of DNA damage, regardless of the degree of disease. However, an increasing of sample size is necessary to confirm the results. Regarding the telomere length, a larger sample may answer the actual impact of the disease, and its relation to the sperm DNA fragmentation. However, this is the first study that sought to evaluate the effect of the disease on this parameter.
29 IMPACT OF INCREASED SEMINAL 8-HYDROXY-2'-DEOXYGUANOSINE LEVELS ON INCREASED RISK OF CHILDHOOD CANCER RETINOBLASTOMA
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(Presented By: Shilpa Bisht, MSc)

Introduction: Oxidative stress (OS) has been implicated in a wide array of diseases and pathophysiological conditions such as neurodegenerative disorders, inflammatory diseases and cancer. OS is the major cause of sperm DNA damage as it induces peroxidative damage to sperm plasma membrane and DNA fragmentation in sperm nuclear and mitochondrial genome. OS induced sperm DNA damage is associated with pathologies such as male factor infertility, recurrent pregnancy loss (RPL), and high frequency of childhood morbidities and childhood diseases such as complex polygenic diseases, dominant genetic disorders, neuropsychiatric debility and childhood cancers. OS induces production of mutagenic oxidative base adduct 8-OHdG (8-hydroxy-2'-deoxyguanosine) in sperm DNA. 8-OHdG has the ability to pair with adenine and results in G:C to T:A transversions which results in single and double strand DNA breaks in the sperm DNA and therefore, increased mutation rate. Retinoblastoma (RB) is the most common childhood intraocular cancer and the exact etiology for RB causation is not known in unilateral sporadic RB cases.

Objectives: The present study was planned with an aim to determine 8-OHdG levels in seminal plasma of fathers of children affected with unilateral sporadic RB which may predispose the sperm to develop de novo germline mutations and may be the underlying cause for the development of unilateral sporadic RB.

Methods: The present study is a case-control study. Semen sample were obtained from 60 fathers of children with RB and 60 fathers of healthy children followed by separation of seminal plasma. 8-OHdG levels were determined in the seminal plasma of cases and controls by ELISA (DNA/RNA Oxidative Damage EIA kit from Cayman Chemical, Ann Arbor, MI).

Results: The mean ages of cases and controls were 32.17±11.2 years and 29.5±4.54 years respectively. 8-OHdG plasma levels were found to be significantly higher (p value= 0.019) in fathers of RB patients (7281±28 pg/ml) as compared to the fathers of healthy children (5871±39 pg/ml).

Conclusion: Increased levels of 8-OHdG (a promutagen) were detected in seminal plasma of fathers of children with RB which may predispose to mutation in germline. Persistence of these mutagenic bases post fertilization increases incidences of mutation in embryo and thus, may be underlying cause for the development of unilateral sporadic RB in children.

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30 SIMPLE AND HIGHLY EFFICIENT POLYETHYLENIMINE TRANFECTION PROTOCOL FOR TRANSIENT TRANSFECTION IN MOUSE SPERMATOGONIAL STEM CELLS
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(Presented By: Chatchanan Doungkamchan, MD)

Introduction: In this study, we aimed to develop a simple transient transfection protocol for mouse spermatogonial stem cells (mSSCs) to facilitate downstream gene editing studies. Polyethylenimine (PEI) is a cationic transfection reagent that has been widely used to transiently transfect mammalian cells, but has not been tested in mSSCs. In this study, we developed a modified PEI protocol that allows simple, efficient, low toxicity transient transfection in mSSCs.

Methods: To assess transfection efficiency using PEI compared to Lipid-based reagent, established mSSC cultures from EF1a-EGFP mice were passaged; replated into 24-well plates; expanded until 80% confluent; and transfected with a chicken β-actin (CAG)-mCherry reporter plasmid. The transfection efficiency and cell viability were evaluated 48 hours after transfection by flow cytometry. Lipid-based reagent transfection was done using Superfect (Qiagen) according to manufacturer’s protocol. PEI transfection protocol was done by separately mixing 1 μg plasmid DNA with 10 μL of 50 mM sodium chloride (NaCl); and 10 μL of PEI with 5 μL NaCl. The mixtures were allowed to equilibrate for three minutes before the PEI/NaCl mixture was added into DNA/NaCl mixture and incubated for 30 minutes. The mixture was then mixed with 350 μL Iscove's Modified Dulbecco's Medium (IMDM) media and added to the mSSCs culture for six hours before replacing transfection media with 1 mL of supplemented IMDM media. To improve transfection efficiency, we modified PEI protocol (mPEI) by replacing NaCl with plain IMDM media.

Results: Transfection efficiency with PEI (46.90%±2.54) was significantly higher than Superfect (1.92%±0.15, p<0.0001). The viability after PEI transfection (55.50%±5.97) was significantly higher than Superfect (37.86%±1.72, p=0.0116). The transfection efficiency was improved further using the modified PEI protocol (65.40%±0.90, p=0.0023) without decreasing viability (58.23%±3.06, p=0.7048). To test the long-term survival and proliferation in vitro, the mCherry-positive cells from modified PEI protocol were sorted and cultured for at least 3 passages. Transplant experiments are underway to test the stem cell function of PEI transfected, FACS-sorted mSSCs.

Conclusion: We developed a transient transfection protocol for mSSCs using PEI (mPEI) that is simple, cost-effective, highly efficient and feasible in most labs. This work was supported by discretionary funds to KEO.
DNA methylation perturbation confers risk to offspring health. Investigation to identify specific mechanisms by which sperm conception range of offspring health disparities associated with pre-paternal smoke exposure and warrants further investigation to identify specific mechanisms by which sperm conception paternal smoking confers increased risk for a number of conditions in offspring. In order to study this process and explore possible therapies, our current method of SSC isolation and propagation have been adapted to KS (41,XXY) mouse model aiming to expand these cells in vitro and overcome the in vivo loss of SSC.

**Methods:** Putative SSCs were isolated and cultured from testes of normal (40, XY) mice aged 1-day old and 3-day old. The propagation of the cells was optimized comparing different culture medias, culture surfaces and seeding concentrations. Propagated cells were characterized using qPCR, Digital-PCR and Flow Cytometry analyses. Histological images were used to examine the evolution of cells morphology in culture. The optimized SSC isolation, culture and evaluation system established from normal mouse was then applied to 3-day old KS mouse testicular cells.

**Results:** The presence of SSC population was demonstrated in normal and KS cultured testicular cells by qPCR, and FACS. Quantification of undifferentiated spermatogonia by using Digital-PCR showed >15% ZBTB16 (PLZF) positive cells in culture. Preliminary data culturing KS mouse testicular cells showed a viable culture of slowly growing cells up to 60 days. Ongoing work is focusing on optimization of culture system and full characterization of cultured KS testicular cells as well as testing their transplantation efficacy to restore fertility.

**Conclusions:** This work overcomes the initial quiescent stage of neonatal germ cells loss in KS mouse testis to successfully expand them in vitro. Extension of this novel method may lead to new therapeutic options for KS patients.
The prognosis and clinical management of patients with 45,X/46,XY mosaicism differ from non-mosaic 45,X (Turner syndrome). Phenotypes range from apparently normal males, infants with genital ambiguity, or female external genitalia with an increased risk for gonadoblastoma. Gender assignment and prediction of reproductive potential for individual patients can be challenging in this mosaic genetic condition. To ascertain long term clinical outcomes, we compared cytogenetic findings and clinical manifestations and performed genotype/phenotype correlation in 50 cases diagnosed with 45,X/46,XY mosaicism at the University of Pittsburgh Medical Center between 1996-2016. All patients had a 45,X cell line along with a cell line containing one or two copies of normal or isodicentric Y chromosome as confirmed by fluorescence in situ hybridization (FISH) or microarray studies. In 43 patients with available clinical data, 13 (30.2%) resulted in spontaneous miscarriage or pregnancy termination; in 30 patients phenotype range included normal males (n=4, 9.3%), infertile males (n=4, 9.3%), infants with ambiguous genitalia (n=13, 30.2%) and females with premature ovarian insufficiency or Turner syndrome (n=9, 21%). In patients with cytogenetic studies involving multiple tissues, the proportion of each cell line was compared in cultured and uncultured peripheral blood samples, buccal cells and urinary epithelial cells. Gonadal tissue was assessed when available following prophylactic gonadectomy performed due to high risk of gonadal neoplasia. Interestingly, the level of mosaicism varied among different tissues of the same patient. Such discrepancy was also observed in prenatal vs. postnatal samples of affected newborns. This cytogenetic variation may contribute to the phenotypic heterogeneity among individuals with 45,X/46,XY mosaicism. We hypothesize that an individual’s reproductive phenotype reflects the gonadal cytogenetic findings rather than the peripheral blood karyotype. In our study, the 45,X/46,XY mosaic levels in urine samples appeared to correlate with percentage of abnormal cells in gonadal tissues. Thus, a noninvasive alternative method, direct genetic analysis of urinary epithelial cells may be helpful since urinary tract cells share similar embryonic origins with gonads. Further research will elucidate the consequences of the tissue-specific differences in the relative proportions of cells with different chromosome or genetic composition.
Introduction and Objectives: Deletions in the AZF region of the Y-chromosome, also known as Y-chromosome microdeletions (YCMD), are responsible for approximately 10% of male infertility cases. Well characterized YCMD include AZFa, AZFb, AZFα, and AZFAβ, which result in varying degrees of spermatogenesis dysfunction. In particular, deletions in the AZFa and AZFb regions are associated with azoospermia with poor prognosis for testicular sperm retrieval. On the other hand, deletions in the AZFc region can present with severe oligospermia or azoospermia and have more promising prognoses for testicular sperm retrieval. Recently, partial deletions have been described in the AZFc region. We aim to characterize the frequency and presenting phenotypes for these partial AZFc YCMD (b2/b3, b1/b3, and gr/gr).

Methods: A retrospective review of all YCMD testing performed on consecutive subfertile and infertile men was conducted. Patients with b2/b3, b1/b3, and gr/gr AZFc YCMD were identified and their charts analyzed for sperm concentration and hormone levels.

Results: A total of 3,195 subfertile or infertile men were screened for YCMD between 1997 and 2016. A total of 446 patients (14%) had YCMD identified. Amongst YCMD identified, the frequencies of b2/b3, b1/b3, and gr/gr AZFc YCMD were 2.7%, 1.1%, and 26%, respectively. While we did not have enough clinical data to analyze patients with b1/b3 AZFc YCMD, 89% of patients with b2/b3 AZFc YCMD presented with azoosperma while the remaining 11% presented with cryptozoosperma. Of patients with gr/gr AZFc YCMD, 81% presented with azoosperma, 6% presented with cryptozoosperma, 5% with oligospermia, and only 6% with normozoosperma. While serum testosterone levels were normal amongst men with b2/b3 and gr/gr AZFc YCMD (401+/−139ng/dl and 344+/−149ng/dl, respectively), FSH levels were markedly elevated in both groups (20+/−9mIU/mL and 22+/−16mIU/mL for b2/b3 and gr/gr, respectively).

Conclusions: Partial AZFc deletions, especially the gr/gr deletion and, to a lesser extent, the b1/b3 and b2/b3 deletions, are commonly seen YCMD in subfertile and infertile men. The overwhelming majority of patients with b2/b3 and gr/gr AZFc deletions present with severe dysfunction of spermatogenesis (either azoosperma or cryptozoosperma). More work is required to further characterize these partial AZFc YCMD in order to better understand their impact on testicular sperm extraction results and reproductive outcomes.

36 LOSS OF TRANSLATIONAL SUPPRESSION OF PRM1/2 VIA YBX2 IS A CULPRIT OF EARLY AND LATE MATURATION ARREST IN HUMANS.

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Introduction: YBX2 protein binds to Y-box promoters and mRNAs regulating translation of important mRNAs in pachytyne spermatocytes and round spermatids. CDK1 phosphorylation of YBX2 enhances binding to RNAs. Here, YBX2 binding provides temporal translational suppression of PRM1/2 and SCMP, as they expressed only as mRNAs in spermatocytes but not expressed as proteins until spermatids. Loss of YBX2 activity leads to male infertility due to loss of translational suppression. Our study aim was to analyze expression of known YBX2 promoter binding elements among well-defined histological categories of male infertility: Sertoli cell only syndrome, maturation arrest (MA)(early and late) and hypospermatogenesis.

Methods: RNAseq was performed using human testis samples from men with nonobstructive azoosperma (50) and 10 from normal controls. SYCP3 was used as a marker for spermatocyte quantity and CLGN for spermatids. Phantom5 was used to predict enhancers and inhibitors of YBX2 expression. Statistical analysis was performed using JMPGenomics. FDR<0.001 was used to identify differentially expressed genes.

Results: Expression of YBX2 was 207x less in men with eMA and IMA as compared to controls. Expression of PRM1/2 was 1.99E+10 and SCMP 2.33E+10x lower in MA than in controls. Both eMA and IMA have similar numbers of SYCP3 positive spermatocytes and CLGN positive spermatids as seen in normal testis (fold ratio 0.78). Thus, decreased expression of PRM1/2 and SCMP in eMA and IMA is not due to the loss of spermatocytes or spermatids. Expression levels of CDK1 were similar between MA and NL testes. Multifactorial regression analysis demonstrated a decrease in YBX2 expression in MA is due to decrease in COMP levels (p=0.0001). No additional YBX2 promoter regulators: CTCFL, EZH2, KDM5A, PPARG, CTBP1, E2F4, and USF1 were statistically different.

Conclusions: Decrease in YBX2 expression in men with eMA and IMA leads to release of translational suppression and loss of mRNAs typically sequestered by YBX2: PRM1/2 and SCMP. This finding has significant therapeutic implications; increasing YBX2 levels could restore PRM1/2 expression and potentially direct arrested spermatids toward maturation.

37 TESTICULAR PATHOLOGY IS NOT ALTERED IN OBESE INFERTILE MEN WHO PRESENT SEMEN ANALYSES, SPERM FUNCTIONAL TESTS, ELECTRON MICROSCOPY AND TESTIS HISTOLOGY IN OBESE INFERTILE PATIENTS

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relationship between obesity and male infertility; however, its physiological mechanisms are not well elucidated.

**Aims:** To evaluate the effect of obesity (BMI and body fat percentage evaluation) in seminal and functional parameters, testicular histology and hormonal profile.

**Methods:** We included data from 83 medical records of infertile patients aged 21 to 45 y.o., classified according to body fat percentage (BFP) according to bioimpedance values (eutrophic≤19% (n=27), high>19%(n=56)) and BMI (eutrophic (n=34); 18.5<BMI<24.9 kg/m2), overweight (n =31; 25.0<BMI<29.9 kg/m2) and obesity (n =18; BMI≥30 kg/m2). Patients were submitted to semen analysis and complementary sperm function tests: anti-sperm antibodies (ASA), creatine kinase activity (CK), reactive oxygen species (ROS) and ultrastructural morphology by electron microscopy (EM). Testicular histology according to Johnsen and Copenhagen criteria and sexual hormones were included. We were used Student's T test and analysis of variance for statistical analysis.

**Results:** Grade A motility decreased in overweight and obesity groups when compared to the eutrophic group. Grade C motility increased in overweight and obesity groups, compared to the control group. We observed an increase in percentage of anti-sperm antibodies in the overweight group (p<0.05). Patients with BFP>19% had a reduction in progressive motility and reduced sperm maturation by CK activity (p<0.05). We did not observe significant alterations in the hormonal profile, testis histology and maturation of sperm chromatin in patients with excess of fat tissue.

**Conclusion:** Excessive body fat has a negative effect on the final steps of spermatogenesis, demonstrated by reduced total progressive motility, increased forms of immature sperm and high anti-sperm antibodies.

**Financial Support:** Androscience/CNPq – PIBIC

**Keywords:** Male infertility, body mass index, body fat, semen, sperm.

**Ethics Committee Approval:** FMUSP Ethics Committee (n°859215/2014)

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**IMPROVING POST-THAW SPERM CRYOSURVIVAL RATES IN THE ANDROLOGY LAB: CHOOSING THE BEST PROCESSING TECHNIQUE PREVIOUS TO THE CRYOPRESERVATION PROCESS IS CRUCIAL**

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(Presented By: Beatriz Crossol Vicente De Campos)

**Introduction:** Seminal processing before cryopreservation is not always used, but depending on initial semen characteristics may be a crucial to improve post-thaw cryosurvival rates.

**Objective:** To determine the optimal pre-freeze semen processing method to improve post-thaw sperm quality.

**Methods:** Ninety-one normozoospermic men (19 to 68 y.o.) had seminal samples cryopreserved from 2002-2016. After routine initial analyses, samples were processed by three different methods: simple centrifugation, density gradient using Isolate® or human serum albumin (BSA®) by the liquid vapor freezing method. After 24 hours, a small sample was evaluated. The one-way ANOVA test was used for statistical analysis and adopted p <0.05.

**Results:** TYB samples were used as control group, with total motility = 72.82±8.64%, progressive motility = 53.51±12.93%, and cryosurvival (CS) = 18.29±16.64%. The association of density gradient processing and TYB + SSS showed an increase in grade B motility (49.33±11.19%, p=0.013) and in CS (36.51 ±31.42%, p=0.009) compared to control group. When evaluating the simple wash + SSS, a reduction of total motility (62.00 ±5.70%, p=0.019), progressive motility (43.00 ±15.24%, p = 0.094), grade A motility, p=0.040), grade B (35.00±16.20%, p=0.227), and in CS (8.10±6.59%, p=0.376) was observed. and increase in sperm motility (38.00±5.70%, p=0.018).

**Conclusion:** We conclude that the density gradient pre-freeze seminal processing associated with TYB+SSS resulted in better post-thaw sperm quality samples and may be considered as standard part of the protocol in normozoospermic patients who seek cryopreservation for several reasons.

**Financial Support:** Androscience

**Keywords:** Male infertility, cryopreservation, seminal processing, semen, sperm.

**Ethics Committee Approval:** FMUSP Ethics Committee (n° 031/13)

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**POSITIVE EFFECT OF MELATONIN AND CAFFEINE SUPPLEMENTATION IN STRUCTURAL AND FUNCTIONAL CHARACTERISTICS IN PRE-FREEZE AND POST-THAW SEMEN SAMPLES**

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(Presented By: Juliana Risso Pariz, BSc, MSc)

**Introduction:** Cryopreservation process can damage spermatozoa and impair structural and functional characteristics. Plasma, nuclear membranes and cellular organelles can suffer from freeze and thaw process.

**Objective:** To evaluate the effect of melatonin (MEL) and caffeine (CAF) supplementation in structural and functional characteristics in pre-freeze and post-thaw seminal samples.

**Methods:** Twenty-six semen samples from men between 22 and 54 years-old. All samples were normozoospermic according to WHO criteria. Samples were cryopreserved using Human Tubal Fluid modified without any supplement or with MEL 2mM. After
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41 VITAMIN E REDUCES INTRACELLULAR SUPEROXIDE ANION ACTIVITY IN CRYOPRESERVED HUMAN SEMEN

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Universidade Federal de São Paulo (Presented By: Larissa Belardin, MSc)

Introduction and Objective: Despite the long-term benefits of sperm cryopreservation in order to preserve male fertility, this technique still brings adverse effects to cells. The mechanism behind these modifications may be related to excessive reactive oxygen species (ROS) generation. While ROS are necessary for physiological sperm functions, unbalanced levels lead to important alterations, such as sperm DNA fragmentation. Aware of importance of balance between ROS and antioxidants levels, there is evidence that antioxidant supplementation protects sperm from cryodamage. Specifically, vitamin E is a potent chain-breaking lipophilic antioxidant. Thus, this study aimed to verify the possible protectant effect of vitamin E in human sperm during cryopreservation.

Methods: A prospective paired study was carried out including semen from 21 adult men. Fresh samples were analysed according to World Health Organization (2010) guidelines. The remaining semen volume was divided into two aliquots; one cryopreserved using a standard Test-Yolk Buffer, and one using the same buffer supplemented with 40µM alpha-tocopherol acetate. After a three-day storage period in liquid nitrogen, the cryopreserved samples were thawed and evaluated for mitochondrial activity, acrosome integrity, DNA fragmentation, intracellular superoxide anion activity, vitality and motility. Both groups were compared using a paired Student’s t test or a Wilcoxon test, when appropriate. An alpha of 5% was adopted.

Results: Pre-freeze and post-thaw results in non-supplemented samples: progressive motility (51.92vs7.27%; p<0.001). High mitochondrial activity sperm (25.30vs8.30%; p<0.001), sperm vitality (78.33vs41.67%; p<0.001), sperm hyperactivation (8.43vs0.69%; p=0.002). No statistical differences in ROS, SCSA pairs presented lower intracellular superoxide anion levels.

Conclusion: Vitamin E is able to improve intracellular oxidative stress in cryopreserved human semen. Because excessive superoxide activity may increase ROS levels, which in turn would lead to downstream alterations to sperm mitochondria, DNA, and acrosome integrity, and because tests were carried out immediately post-thaw, it may be that our analysis detected, by a sensitive method, initial alterations before they affected cellular alterations.

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42 SEMEN CRISP3 LEVELS IN THE ADULT VARICOCELE

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Introduction: Varicocele is the most prevalent treatable cause of male infertility, and its surgical treatment (varicocelectomy) has been shown to improve male fertility. We have demonstrated a higher expression of Cysteine-rich secretory protein 3 (CRISP3) in the seminal plasma of adolescents with varicocele. Because CRISP3 is related to fertilization and with inflammation and cancer, we hypothesized that CRISP3 in varicocele may be playing an inflammatory role. We aimed to verify seminal levels
of CRISP3 in adults with and without varicocele, and before and after varicocelectomy.

**Methods:** This prospective study included 83 adults, divided into two sub-studies to verify: (I) the effect of varicocele by comparing controls without varicocele (C, n=25) to men with varicocele (V, n=36), and (II) the effect of varicocelectomy by comparing men before (PRE) and six months after (POST) varicocelectomy (n=22). After seminal (WHO, 2010) and sperm functional analysis, 50 µg of seminal plasma total protein were utilized for Western blotting analysis for quantification of CRISP3. DJ1 [PARK7] was used as a loading control. Groups were compared by an unpaired Student’s T or Mann-Whitney test (sub-study I), and by a paired Student’s T or Wilcoxon test (sub-study II) (p<0.05).

**Results:** Results are presented in Table 1. For sub-study I, varicocele was associated to lower mitochondrial activity (DAB IV) and to increased seminal CRISP3 levels (nearly 100-fold increased in the unglycosylated form [29kDa], and a 7-fold increase in the glycosylated form [31kDa]). Varicocelectomy leads to an increase in sperm with normal morphology and mitochondrial activity (DAB I). CRISP3 levels decreased, both in the unglycosylated (5.6-fold) and the glycosylated (4.3-fold) forms.

**Conclusion:** In the presence of varicocele, there is a marked increase in seminal CRISP3 levels, more so in the unglycosylated form. Surgical intervention (varicocelectomy) decreases CRISP3 levels and improves semen quality.

**Financial Support:** São Paulo Research Foundation (process number: 2016/05487-3).

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**43 THE EFFECT OF TESTICULAR GERM CELL TUMORS ON FUNCTIONAL ASPECTS OF SPERM AND OXIDATIVE STRESS OF SEMINAL PLASMA**

Maria Beatriz Ribeiro de Andrade MSc, Paula Intasqui MSc, Larissa Belardin MSc, Danielle Tibaldi MSc, Ricardo Pimenta Bertolla DVM; PhD and Deborah Montagnini Spaine PhD
Sao Paulo Federal University
(Presented By: Maria Beatriz Ribeiro De Andrade, BSc, MSc)

**Introduction and Objective:** Testicular germ cell tumors (TGCT) can affect spermatogenesis and lead to alterations in semen quality and to sperm functional traits. This may be due to changes in tumor cells metabolism or to a local inflammatory process. Therefore, we wished to verify if men with testicular tumors present alterations in semen quality, sperm functional traits, and in seminal plasma oxidative stress.

**Materials and Methods:** A prospective study was carried out including 24 patients with TGCT who provided semen sample before orchiectomy, of which 14 non-seminoma and 10 seminoma. A control group was comprised of 17 normozoospermic men. Men with clinical varicocele, smoking, with systemic diseases (such as cancer and endocrinopathies and their treatments), endocrine disorders, genetic syndromes, or history of genitourinary disorders were excluded from the control group. Following semen analysis, an aliquot was used for analysis of (i) sperm DNA fragmentation (alkaline Comet assay, classified as low [Class I] to high [Class IV] DNA fragmentation); (ii) acrosome integrity (PNA-FITC); and (iii) mitochondrial activity (Grade I [all mitochondria active] to IV [all mitochondria inactive]). Seminal plasma MDA levels were measured as markers of oxidative stress. Groups were compared using one-way ANOVA followed by a Bonferroni post-hoc test, or Kruskal-Wallis, followed by a Games Howell post-hoc test, when appropriate (p<0.05).

**Results:** Results are presented in table 1. A decrease in sperm morphology (%) (p= 0.012), mitochondrial activity (p<0.0001) and sperm concentration (p=0.00002) were observed in the non-seminoma group when compared to controls. A decrease in sperm morphology (p=0.009), mitochondrial activity (p<0.0001), non-progressive motility (p=0.010) and sperm concentration (p=0.001) were observed in the seminoma group when compared to controls.

**Conclusion:** Based on our findings, a testicular germ cell tumor is associated to a decrease in sperm morphology, sperm mitochondrial activity, and sperm concentration. This demonstrates important alterations to spermatogenesis before removal of the affected testis.

**Acknowledgements:** M. B. Ribeiro de Andrade received a scholarship from CAPES.
ABSTRACTS

44 TRANSGENDER SPERM CRYOPRESERVATION: TRENDS AND FINDINGS IN THE PAST DECADE
Kai Li MD¹, Dayron Rodriguez MD¹, Scott Gabrielsen MD, PhD¹, Amy Blanchard², Grace Centola PhD² and Cigdem Tanrikut MD¹
¹Massachusetts General Hospital; ²New England Cryogenic Center
(Presented By: Kai Li, MD)

Introduction and Objective: Awareness and acceptance of transgenderism has increased in the last two decades. The 2001 World Professional Association for Transgender Health’s Standards of Care advocates discussion of reproductive issues with transgender patients prior to initiation of hormonal therapy. To date, there is limited literature regarding the incidence and semen characteristics of transgender individuals banking sperm. We sought to assess transgender sperm cryopreservation compared to the non-transgender population in the last 10 years. We also compared semen parameters between the two populations.

Methods: We performed a retrospective analysis of sperm cryopreservation performed at a single center from 2006 through 2016. We analyzed 194 transgender samples and 2327 non-transgender samples for a total of 84 unique transgender bankers and 1398 unique non-transgender bankers. Bankers who preserved multiple samples had the collective semen parameters averaged and the mean used for statistical analysis. Semen samples were analyzed according to WHO 4th and 5th edition guidelines based on year of sample production. Linear regression was used to compare the annual incidence of cryopreservation from 2006-2016 of transgender versus non-transgender. Semen parameters were compared using Student’s T-test.

Results: The number of transgender individuals pursuing sperm cryopreservation increased relative to non-transgender individuals from 2006 to 2016. The trajectory of the two groups was significantly different (Figure 1, p=0.001). There were no significant differences in ejaculatory volume, total sperm count, percent motility, or total motile sperm between the two groups.

Conclusions: This is the largest report to date on the incidence of transgender sperm cryopreservation and comparison of semen characteristics. The incidence of sperm cryopreservation by transgender individuals has increased in the last decade, paralleling the increase in awareness and acceptance, and may reflect increased discussion between transgender individuals and medical professionals. There were no significant differences in semen parameters.

45 NORMAL PREOPERATIVE FOLLICLE-STIMULATING HORMONE LEVEL IS ASSOCIATED WITH IMPROVEMENT IN SEMEN PARAMETERS FOLLOWING MICROSURGICAL VARICOCELECTOMY
Lunan Ji MD, Samuel Shabtaie, Nachiketh Soodana Prakash MD and Ranjith Ramasamy MD
University of Miami
(Presented By: Lunan Ji, MD)

Introduction: We investigated whether preoperative follicle-stimulating hormone (FSH) level is associated with changes in post-operative semen parameters following microsurgical varicocelectomy.

Methods: We identified 37 men who had undergone microsurgical varicocelectomy between August 2015 and June 2016. We compared semen parameters in men based on their pre-operative FSH level, normal <10 mIU/ml (n=25) and abnormal ≥10 mIU/ml (n=12). We compared varicocele grade, testis volume, prevalence of bilateral disease, pre-operative, and post-operative semen parameters (at 3 months) between men with normal and abnormal FSH.

Results: The age, varicocele grade, pre-operative testosterone levels were similar between men who underwent microsurgical varicocelectomy with normal and high FSH. Men with higher FSH had higher rates of bilateral disease. Men with FSH <10 mIU/mL had higher increases in absolute total sperm count

Table 1. Value of seminal analysis and DNA fragmentation (Comet), mitochondrial activity (DiB), acrosome integrity (PIA - IVIC) and lidropereination (TBA-IVC) were presented as mean ± standard deviation.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Non-transgender group</th>
<th>Transgender group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>(nmol/L)</td>
<td>(nmol/L)</td>
<td>(nmol/L)</td>
<td></td>
</tr>
<tr>
<td>Volume</td>
<td>30 ± 4.00</td>
<td>29 ± 4.00</td>
<td>0.62</td>
</tr>
<tr>
<td>Progressive (%)</td>
<td>49 ± 10.00</td>
<td>50 ± 10.00</td>
<td>0.77</td>
</tr>
<tr>
<td>Non-progressive (%)</td>
<td>10 ± 3.00</td>
<td>10 ± 3.00</td>
<td>0.62</td>
</tr>
<tr>
<td>Concentration (μg/mL)</td>
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<td>15 ± 20.00</td>
<td>0.39</td>
</tr>
<tr>
<td>Morphology (%)</td>
<td>4 ± 2.00</td>
<td>4 ± 2.00</td>
<td>0.62</td>
</tr>
<tr>
<td>Comet class (%)</td>
<td>0 ± 0.00</td>
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<td>Comet class (%)</td>
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<tr>
<td>Comet class (%)</td>
<td>0 ± 0.00</td>
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<td>0.62</td>
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<tr>
<td>D+B (%)</td>
<td>1 ± 0.00</td>
<td>1 ± 0.00</td>
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<tr>
<td>D+B (%)</td>
<td>1 ± 0.00</td>
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<td>D+B (%)</td>
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<tr>
<td>D+B (%)</td>
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<td>1 ± 0.00</td>
<td>0.62</td>
</tr>
<tr>
<td>DNA fragmentation (%)</td>
<td>5 ± 2.00</td>
<td>5 ± 2.00</td>
<td>0.62</td>
</tr>
<tr>
<td>MDA (μmol/L)</td>
<td>10 ± 3.00</td>
<td>10 ± 3.00</td>
<td>0.62</td>
</tr>
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</table>
Introduction and Objective: The World Health Organization (WHO) 2010 guideline defines >4% normal sperm morphology, by the Kruger strict criteria, as the lower limit of normal. While initially described as a strong predictor of diminished IUI pregnancy success rates. To assess the available evidence, we demonstrated no relationship between sperm morphology and IUI insemination success, several recent publications have initially described as a strong predictor of intrauterine pregnancy by the Kruger strict criteria, as the lower limit of normal. While WHO 2010 guideline defines >4% normal sperm morphology, <1%. Studies were assessed both overall and by WHO guideline Eras: pre−1999, 2000−2010, and post 2010. Estimates were pooled using random−effects meta−analysis.

Results: Data were extracted from 22 observational studies involving 41,585 cycles. Twenty studies reported sperm morphology >4% and ≤4% and nine studies reported sperm morphology >1% and <1%. When assessing the 4% threshold, a statistically significant difference was evident overall (≥4%: 14% vs. ≤4%: 12%, p = 0.03). However, no significant difference was seen in IUI success rate when the 1% sperm morphology threshold was assessed: (<1%; 14% vs. ≥1%; 14%, p = 0.97).

Conclusion: Abnormal sperm morphologies according to Kruger’s criteria are not predictive of diminished IUI pregnancy rates. Further, IUI pregnancies can be equally achieved in even men with <1% normal sperm morphology as compared to men with >1%. Thus, couples with abnormal sperm morphologies should not be excluded from a trial of IUI as long as the other semen parameters are within normal limits.

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A SYSTEMATIC REVIEW OF THE EFFICACY AND SAFETY OF TRANSURETHRAL SURGERY FOR EJACULATORY DUCT OBSTRUCTION−RELATED INFERTILITY
Clark Judge BA and Peter Stahl MD
Columbia University

(Presented By: Clark Judge, BA)

Objective: Our goal was to evaluate the efficacy and safety of transurethral surgery for EDO-related infertility.

Methods: Pubmed, Embase, and MEDLINE databases were searched for studies evaluating efficacy and safety of transurethral surgery for EDO-related infertility. We analyzed all studies of transurethral surgery in infertile men with complete or partial EDO. The impact of transurethral surgery on semen quality, pregnancy rates, and complications was analyzed by structured data synthesis, as heterogeneity of data reporting precluded meta-analysis.

Results: We identified 22 cohort studies, 8 case series, and 10 case reports that described outcomes of transurethral surgery for 482 infertile men with either complete or partial EDO. Surgical treatments used transurethral resection of the ejaculatory ducts (TURED) (399/482, 83.8%), transurethral incision of the ejaculatory ducts (TUIED) (11/482, 2.3%), unspecified TURED/TUIED (49/482, 10.2%), transurethral dilation of the ejaculatory ducts (21/482, 4.4%), and transurethral laser treatment (2/482, 0.4%). Sperm were detectable in the ejaculate postoperatively in 64.9% (244/376) of azoospermic patients treated surgically for complete EDO. The rate of achieving a normal semen analysis (SA) after surgery for complete EDO amongst men for whom full SA data were reported was 35.3%...
ABSTRACTS

(54/153), and the aggregate reported spontaneous pregnancy rate was 19.0% (56/294). In non-azoospermic men with partial EDO, the aggregate reported rates of semen quality improvement, achievement of normozoospermia, and spontaneous pregnancy were 77.4% (82/106), and 53.1% (17/32), and 29.6% (29/98), respectively. Aggregate data derived from studies that reported postoperative adverse events revealed significant complications in 14.0% (42/299). The most common reported complications were watery ejaculate (3.3%), epididymitis/orchitis (2.3%), prolonged hematuria requiring catheterization (2.3%), conversion to azoospermia (1.7%), and hematospermia (1.3%).

Conclusions: This systematic review demonstrated that transurethral surgery appears to be an effective treatment for complete or partial EDO that results in improved semen quality for the majority of patients. Spontaneous pregnancies have been reported in 19-30% of cases, and the risk of postoperative complications appears to be acceptably low. These data are valuable for counseling patients on treatment options for EDO-related infertility.

50 POLICY ON POSTHUMOUS SPERM RETRIEVAL: SURVEY OF 75 MAJOR ACADEMIC MEDICAL CENTERS
Nicholas Waler¹ and Ranjith Ramasamy MD²
¹University of Miami Miller School of Medicine; ²Department of Urology, University of Miami, Miami, FL
(Presented By: Nicholas Waler)

Introduction and Objectives: Very few studies have addressed attitudes on posthumous sperm retrieval due to the ethical and legal ramifications of the use of gametes after death. We evaluated the presence and content of a policy on posthumous sperm retrieval at the 75 major academic medical centers in the U.S.

Methods: We surveyed the 75 major academic medical centers as ranked for research in 2016 by U.S. News & World Report using a questionnaire based telephone/web survey. We gathered data on presence and content of posthumous sperm retrieval policies. If not published, we contacted the legal counsel for the medical center, the ethics and compliance offices, the Urology Department, as well as the infertility center for each institution, in that order.

Results: Out of the 75 major academic medical centers, we gathered data on posthumous sperm retrieval from 30 (40%). Of the 30 institutions, 10 (33%) had policies regarding posthumous sperm retrieval, 19 (60%) did not have a policy, and one center remained undisclosed. Five of the 19 medical centers without policies have discussed development of a policy but did not formalize it due to lack of legal guidance as a barrier to policy adoption. Out of the 10 centers that had a policy, four required prior written consent, while six allowed for verbal or inferred consent from the surviving life partner.

Conclusion: Very few, about 1/3, of the surveyed academic medical centers have policies on posthumous sperm retrieval. Medical centers can adopt individualized policies based on guidelines published by the American Society for Reproductive Medicine.

51 SERUM METABOLIC PROFILING IDENTIFIES CHARACTERIZATION OF NON-OBSTRUCTIVE AZOOSPERMIC MEN
Zhe Zhang MD, Yuzhuo Yang MD and Hui Jiang MD
Peking University Third Hospital
(Presented By: Zhe Zhang, MD)

Male infertility is considered a common health problem, and non-obstructive azoospermia with unclear pathogenesis is one of the most challenging tasks for clinicians. The objective of this study was to investigate the differential serum metabolic pattern in non-obstructive azoospermic men and to determine potential biomarkers related to spermatogenic dysfunction. Serum samples from patients with non-obstructive azoospermia (n = 22) and healthy controls (n = 31) were examined using high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). Serum metabolomic profiling could differentiate non-obstructive azoospermic patients from healthy control subjects. A total of 24 metabolites were screened and identified as potential markers, many of which are involved in energy production, oxidative stress and cell apoptosis in spermatogenesis. Moreover, the results showed that various metabolic pathways, including D-glutamine and D-glutamate metabolism, taurine and hypotaurine metabolism, pyruvate metabolism, the citrate cycle and alanine, aspartate and glutamate metabolism, were disrupted in patients with non-obstructive azoospermia. Our results indicated the serum metabolic disorders may contribute to the etiology of non-obstructive azoospermia. This study suggested serum metabolomics could identify unique metabolic patterns of non-obstructive azoospermia and provide novel insights into the pathogenesis underlying male infertility.
52 PENILE PROSTHESIS COMPLICATIONS: A DESCRIPTIVE STUDY OF THE DETROIT AFRICAN AMERICAN PATIENT POPULATION.

Mohammed Zaher DO¹, William Duscomb Medical Student², Maha Husainat Research Assistant¹, Ibraheem Malkawi Research Assistant¹ and Mazen Abdelhady MD¹
¹Detroit Medical Center; ²Michigan State University

Introduction: Failure and infection rates of inflatable penile prosthesis (IPP) implantation have been vastly studied with the largest studies showing reoperation rates ranging from 6-7%. In our previous study, we found a revision rate of 17% of which 70% of the failures were African American (AA) patients. The IPP mechanical failure and infection rate is not well researched in the AA population. In this study, we further evaluated the failure and infection rate of IPP implantation in this possibly high risk AA population. Our objective in this study was to determine which variables had an impact on penile implants in AAs and if the AA population had a higher failure rate.

Methods: This was a retrospective chart review of men ages 18 and older that had an IPP implanted at the Detroit Medical Center between 2000-2016. Variables included: all races, reason for IPP placement, type of IPP, IPP failure, reason for failure, and co-morbidities.

Results: A total of 150 patients were included, 93 were AA. The average age of our patients at time of surgery was 66 years (range 39-94). The average age of patients at time of IPP failure was 68 years (range 47-90). 39 had a failed IPP (26%), of those, the majority of the race being AA (69%, n=27). The most common reason for insertion of an IPP was organic erectile dysfunction (ED) (74%, n=111), while the most common cause for failure was IPP malfunction (67%, n=26). Other reasons for IPP failure were erosions (23%, n=9) and infections (10%, n=4), of which 78% (n=7) and 50% (n=2) were AA, respectively. Of the 39 patients who failed their first IPP, 36% failed again (n=14); of these patients majority were AA (71%, n=10) (p <0.05).

Conclusion: In our study, African Americans had an overall higher IPP mechanical failure as well as secondary revision rates compared to other races. These higher rates found in our AA patient population could be secondary to their high incidence of existing co-morbidities. Our research suggests that when considering an IPP placement for erectile dysfunction, the surgeon should take race and co-morbidities into account when discussing with patients the possible complications and failure rate.

53 SOCIOECONOMIC DISPARITIES IN THE TREATMENT OF ERECTILE DYSFUNCTION: A SYSTEMATIC REVIEW

Denise Asafu-Adjei MD, MPH¹, Mofan Gu MPH², Matthew Pagano MD³, Ifeanyi Onyeji MD¹ and Peter Stahl MD¹
³Columbia University Medical Center; ²Columbia University Mailman School of Public Health

Introduction and Objectives: Previous literature suggests that socioeconomic disparities exist between the rate and types of treatment for erectile dysfunction (ED). The objective of this study was to identify the various socioeconomic factors that contribute to these disparities, examine the mechanisms by which these factors interact, and propose ways to diminish the impact of these disparities as it pertains to patient outcomes.

Methods: A systematic literature search via PubMed was conducted, using a combination of keywords including socioeconomic status (SES) as well as treatment terms for ED. Articles were initially screened based on title and abstract, but were eliminated based on established exclusion criteria. The goal was to obtain articles with primary data and quantitative analysis that would allow for adequate extraction of data. A total of 1246 articles were obtained from PubMed and information was extracted from 15 articles for systematic review. The data were not amenable to meta-analysis and therefore a structured data analysis was performed.

Results: Six studies addressing treatment-seeking behavior showed that patients with higher income and educational status were more likely to seek active treatment for ED. Eight studies focused on ED treatment rates and the data suggest that men with higher incomes are more likely to seek treatment for ED. In terms of treatment type disparities, there is literature to suggest that African-American and Hispanic men are more likely to be treated with penile prosthesis than Caucasian men. Additionally, men with Medicaid or self-pay patients are more likely to be treated with semi-rigid rather than inflatable prostheses, as compared to men with commercial insurance.

Conclusions: There is a signal in the published literature that ED treatment rates and the types of treatments provided vary according to socioeconomic factors. It remains unknown whether the observed differences are due to patient choice, physician bias, differences in ED severity, and/or SES factors. However, the significant findings across multiple studies warrant further examination into the root causes of these published trends. In the future, greater patient and physician education and awareness may be necessary to address these disparities and implement standard-of-care algorithms across patient groups and institutions.
ABSTRACTS

54 TESTICULAR SPERM RETRIEVAL IN LATE ADOLESCENTS (AGED 15-19 YEARS) WITH NON-MOSAIC KLINEFELTER SYNDROME AND AZOOSPERMIA
Han-Yu Weng, Yung-Ming Lin PhD and Yu-Sheng Cheng
National Cheng Kung University Hospital
(Presented By: Han-Yu Weng, MD)

Introduction and Objectives: It has been shown that most men with Klinefelter syndrome (KS) are born with spermatogonia and the germ cells appear to undergo apoptosis during puberty. To date, controversy exist in the age of fertility preservation in adolescents with non-mosaic KS. WHO identifies adolescence as the period that occurs after childhood and before adulthood, from ages 10 to 19. Previous report revealed extreme low sperm retrieval rate (SRR) in early adolescents. The objective of this study is to retrospectively analyze the clinical characteristics and SRR of late adolescents (age 15-19 years) with non-mosaic KS in our clinic and to review the literature.

Methods: Three late adolescents who were referred for hypogonadism and fertility counselling underwent microsurgical testicular sperm extraction (microTESE). Their medical history, physical examination findings, testicular volume, serum hormone parameters, microTESE outcome were analyzed. Then, a comprehensive literature searches for systematic review using MEDLINE and PubMed was conducted. Exclusion criteria includes mosaic KS, aged 14 years or younger, aged 20 years or older, and no SRR as primary outcome.

Results: Increased serum FSH and LH levels as well as decreased testosterone levels were noted in our three patients. All three patients had bilateral testicular atrophy (less than 5 ml for each testicle). Spermatozoa were retrieved in two patients (66.7%). Two patients with complete Sertoli cell-only syndrome and one patient with hypospermatogenesis were noted in testicular histopathology. The literature search identified a total of 89 scientific papers. Eight publications and 85 late adolescents with age 15-19 years were enrolled in final analysis. A total of 88 late adolescents underwent testicular sperm retrieval, and 42 met with success (SRR: 47.7%).

Conclusion: Testicular SRR in late adolescents is not superior to those who undergo the procedure later in their life.

55 ANXA7 AND PSMA5 ARE SEMINAL BIOMARKERS OF SPERM ACROSOME INTEGRITY
Paula Intasqui MSc, Larissa Belardin MSc, Mariana Antoniassi MSc, Mariana Camargo PhD, Daniel S. Zylbersztejn PhD and Ricardo P. Bertolla PhD
Department of Surgery, Division of Urology, Sao Paulo Federal University
(Presented By: Paula Intasqui Lopes, MSc, BSc)

Introduction and Objective: The sperm acrosome is important for fertilization and, thus, for male fertility. Among proteins involved in acrosome formation (spermiogenesis) and reaction (capacitation), two proteins have been recently highlighted. Annexin A7 (ANXA7) is a Ca2+-dependent phospholipid binding protein with GTPase activity that facilitates vesicle transport and membrane fusion. It is important for acrosome reaction and sperm-zona pellucida binding. Proteasome subunit alpha type-5 (PSMA5) protein is part of the proteasome 20S core, and recent studies have demonstrated that this complex is important for acrosome formation, selection of sperm with intact acrosome, and exocytosis. Therefore, we aimed to evaluate expression of these proteins in seminal plasma and correlations with acrosome integrity in ejaculated sperm.

Methods: A cross-sectional study was performed including 155 normozoospermic men. After semen analysis (WHO 2010 guidelines), sperm acrosome integrity was evaluated using PNA-FITC staining. Samples were then divided according to acrosome integrity into control (> 82% sperm with intact acrosome, top 15%, n=23) and study (< 67% sperm with intact acrosome, bottom 15%, n=19) groups. The remaining semen volume was centrifuged for seminal plasma separation, in which ANXA7 and PSMA5 expression was evaluated by Western blotting. Data were normalized by a loading control. Groups were compared by an unpaired Student’s t test or by the Mann Whitney test.

Results: The low acrosome integrity group presented decreased percentage of sperm with intact acrosomes (64% ± 3.63 vs. 85.5% ± 4.01, p<0.001), as expected, as well as decreased sperm morphology (6.0% ± 2.04 vs. 9.0% ± 6.13, p=0.031) and percentage of sperm with active mitochondria (8.5% ± 3.81 vs. 9.5% ± 9.78, p=0.021). ANXA7 and PSMA5 expression data are presented in Figure 1. ANXA7 was significantly underexpressed, whereas PSMA5 was overexpressed in the study group. Moreover, PSMA5 negatively correlated with the percentage of intact acrosome (p=0.025, r=-0.180, Spearman’s correlation).

Conclusion: ANXA7 and PSMA5 are seminal biomarkers of acrosome integrity and damage, respectively.


Figure 1. Protein expression data of ANXA7 (A) and PSMA5 (B) in seminal plasma, by Western blot analysis. Control (high sperm acrosome integrity) and Study (low sperm acrosome integrity) groups were compared by an unpaired Student’s test.

56 EFFECTS OF VARICOCELE IN SPERM CAPACITATION
Rhayza Andretta PhD candidate¹, Larissa Belardin MSc¹, Letícia Castro DVM, MSc², Jheysson Moura BSc¹, Renato Fraitte DM, PhD¹, Fatima Okada PhD and Ricardo Bertolla DVM, PhD¹
¹Federal University of Sao Paulo ; ²University of Sao Paulo
(Presented By: Rhayza Andretta PhD candidate)

Introduction: Varicocele is defined as an abnormal dilation of the testicular veins in the pampiniform plexus with retrograde blood flow in the internal spermatic veins as a result of
incompetent or absent valves. It is considered one of the main causes of male infertility affecting 15-25% of the adult male population, and is responsible for the alterations to semen quality, leading to failures in the processes associated with fertilization, such as sperm capacitation. Sperm capacitation is characterized by physiological changes that occur mainly in the female reproductive system, rendering sperm functionally competent to fertilize the oocyte. Many changes occur during capacitation, such as increased plasma membrane fluidity, increased protein phosphorylation, changes in motility pattern, and acrosome reaction. However, it is not known if varicocele may affect these mechanisms.

Objectives: To evaluate the effect of varicocele on sperm capacitation.

Methods: Men were divided into 2 groups: controls without varicocele (n=17) and varicocele (grades II and III, n=32). Semen was collected by masturbation after 2-5 days of ejaculatory abstinence. One aliquot was used for seminal analysis (World Health Organization, 2010). The remaining volume was submitted to a discontinuous density gradient (45 to 90%) and centrifuged at 300 g for 20 minutes. The pellet was then washed in human tubal fluid (HTF). An aliquot was used to evaluate motility by computer-assisted sperm analysis (IVOS). Capacitation was then induced using HTF supplemented with 1% bovine serum albumin (BSA) for 2 hours at 37o C, 5% CO2. Following capacitation induction, the following measures were assessed: motility (IVOS), capacitation assay (chlorotetracycline), intracellular superoxide anion activity, and mitochondrial activity. Groups were compared using a Student’s t test or a Mann-Whitney test.

Results: Results are presented in table 1. Men with presented lower ejaculate volume. After capacitation, the varicocele group presented lower sperm motility and mitochondrial activity when compared to controls.

Conclusion: Our data suggest that varicocele may exert negative effects to sperm capacitation. Financial support: CAPES.

57 PROTECTIVE ROLE OF LYCOPODIUM CLAVATUM ON AGEING INDUCED CHANGES IN SPERM CHARACTERISTICS AND TESTICULAR OXIDATIVE DAMAGE: A DOSE-DEPENDENT STUDY IN WISTAR ALBINO RATS

Ganesh Lakshmanan BHMS, MSc¹ and Prakash seppan PhD²
¹University of Madras; ²Department of Anatomy, University of Madras.

(Presented By: Ganesh Lakshmanan, BHMS, MSc)

Objective: Aging in men leads to decline in reproductive capacity due to oxidative stress following a operative insufficiency in spermatogenesis and steroidogenesis. The crude ethanolic extract of Lycopodium clavatum commonly known as “club moss” has been reported to have good antioxidant properties. Traditionally lycopodium is used to treat sexual complaints and reproductive insufficiency of old aged men and considered as the ‘balm of old man’. However there is no scientific validation to confirm this effect. The aim of this study is to analyze the efficacy of ethanolic extract of Lycopodium clavatum on aging induced alteration in testicular function and to find its effective therapeutic concentration.

Materials and Methods: Aged male wistar albino rats (24 months) were randomly divided into five groups (n=12), first group received distilled water, and the other three groups received ethanolic extract of Lycopodium clavatum at dosage of 100, 250, 500, 1000 mg / kg. b.w daily for 60 days by gavage. At the end of experimental period, serum testosterone was estimated. Sperm parameters including count, viability, motility, membrane permeability and nuclear condensation were done. Biochemical analyses of testicular antioxidants were done. Testicular mRNA expression of antioxidants and apoptotic genes were estimated by qPCR. The results were statistically analysed.

Results: Aging induced pathological changes were noted in the aged untreated animals. Beneficial effects were significant in Lycopodium clavatum treated groups when compared to untreated aged rats. Depleted testosterone level in untreated aged rat was improved in all the treated rats however, significant improvement was seen with 500mg dosage. Sperm parameters were significantly improved in aged rats with 500 mg dosage when compared to the other treated aged groups. The gene expression studies emphasized the maximum beneficial effects under 500mg dosage.

Conclusions: This observation confirms that Lycopodium clavatum has protective effects on aging induced reproductive disorder and the effect seem to be dosage dependent. Thus results signifies that finding effective dose for given animal is a key factor for maximum therapeutic outcome.
58 OXIDATIVE STRESS EVALUATION IN LEUKOCYTOSPERMIC INFERTILE MEN: ROLE OF SEMINAL OXIDATION-REDUCTION POTENTIAL (ORP), 8-ISO-PGF2α AND PROTEIN CARBONYL CONTENT
Ahmet Ayaz PhD, Wayne J. Hellstrom MD, FACS and Suresh C. Sikka PhD, HCLD/CC
Tulane Medical Center, Department of Urology
(Presented By: Ahmet Ayaz PhD)

Oxidative stress due to leukocytospermia has a detrimental effect on sperm this can be assessed by measuring 8-iso-PGF2α (8-iso prostaglandin F2α) and protein carbonyl content in semen samples in addition to more established methods such as ROS-TAC, lipid peroxidation etc. Measurement of oxidation-reduction potential is a new electrochemical approach to monitor oxidative stress levels in biological samples. The original device (Redoxsys, Aytu Biosciences Inc) measuring sORP (static ORP) and cORP (capacity ORP) has recently been upgraded to MiOXsys and quantities only sORP. The goal of this study was to determine a) if the older Redoxsys system is comparable to the newer MiOXsys system in terms of ORP measurement and b) whether 8-iso-PGF2α and protein carbonyl content of semen samples reflect extent of oxidative damage in leukocytospermic. Semen samples (n=20) were collected from infertile patients attending our Andrology Clinic and evaluated as per WHO guidelines. These samples were divided into two groups: Leukocytospermia (LCS) with ≥2.0 million WBC/ mL and non-leukocytospermia (non-LCS) with 0 to 1 million WBC/ mL. sORP levels were measured by both Redoxsys and MiOXsys concurrently. Also, 8-iso-PGF2α was measured by the Elisa kit protocol (Enzo Life Sciences, Inc. Farmingdale, NY) and protein carbonyl content in the same sample was measured by the DNP tagging assay (Abcam, San Francisco, CA). Our data demonstrated no difference in sORP values by using Redoxsys (1.53±0.15 mV/million sperm/mL) and MiOXsys (1.44±0.14 mV/million sperm/mL) in all samples. Also there were no differences between LCS (Redoxsys: 1.45±0.24 mV/million sperm/mL, MiOXsys: 1.37±0.22 mV/million sperm/mL) and non-LCS (Redoxsys: 1.60±0.18 mV/million sperm/mL, MiOXsys: 1.51±0.18 mV/million sperm/ mL) semen samples (p>0.89). 8-iso-PGF2α and protein carbonyl content did not reveal any correlation with sORP in these semen samples for either LCS or non-LCS patients. Larger populations of LCS and non-LCS men need to be studied for confirmation of these findings.

59 POPULATION-BASED SEMEN ANALYSIS RESULTS AMONG PATIENTS WITH INFLAMMATORY BOWEL DISEASE
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(Presented By: Luke Martin, MD)

Introduction: Crohn’s disease (CD) and ulcerative colitis (UC) are chronic inflammatory conditions that impact an estimated 350,000 reproductive age men in the United States. Inflammatory bowel disease (IBD) is thought to negatively impact male fertility, but objective data are lacking. The objective of this study was to evaluate male fertility in IBD by examining semen analysis results and paternity from the SHARE study (subfertility health assisted reproduction and the environment), a population based cohort of over 40,000 semen analysis results from Utah men.

Methods: A population-based cohort of male IBD patients (n=3,196) was identified using the Utah Population Database (contains person level linked demographic, genealogical, and medical record information for 85% of Utahans) based on ICD-9 diagnosis codes recorded from 1996-2014, and validated by chart review (specificity 94%). The IBD cohort was then cross-linked (n=55) to a population dataset of semen analysis results. The semen analyses spanned WHO3-5 and contained comprehensive data. Semen analysis results from the cohort of IBD patients were compared to fertile, age-matched, paired (1:1) controls (n=47) using the Wilcoxon signed rank test. Paternity was evaluated though presence and number of linked offspring.

Results: Among IBD patients for whom semen analysis results and appropriate controls were available, 24 (51%) had a diagnosis of UC and 23 (49%) of CD. Offspring were identified in 71% of UC patients who had a mean of 2.5 children. Among CD patients, 61% had offspring, with a mean of 2.0 children. Semen analysis parameters among patients with UC were not significantly different compared to fertile, age-matched controls: concentration (p=0.73), total sperm (p=0.63), motility (p=0.59), vitality (p=0.78), total motile count (p=0.91), head morphology (p=0.41), tail morphology (p=0.98). Similarly, semen analysis parameters among patients with CD were not significantly different compared to fertile, age-matched controls: concentration (p=1), total sperm (p=1), motility (p=0.31), vitality (p=0.69), head morphology (0.99), tail morphology (0.11). In CD, total motile count trended toward a decrease but did not reach statistical significance (p=0.06).

Conclusions: Semen analysis values among those with IBD are not significantly impacted compared to age-matched controls. Male patients with IBD should be counseled that their disease likely does not significantly impact their semen analysis parameters.
implantation and pregnancies in both natural and assisted reproduction. However, until now there is no conclusive evidence proving a strong association between sperm DNA damage and ART outcomes.

**Objectives:** The purpose of this report was to update the evidence on the relationship between sperm DNA damage and pregnancy outcomes through a meta-analysis.

**Methods:** We conducted a meta-analysis of all studies published until August, 2016 on the association between sperm DNA damage assessed by SCSA, TUNEL, SCD and Comet assays and clinical pregnancy after IVF and/or ICSI treatment.

**Results:** We identified 142 relevant articles, from which we were able to calculate the odds ratios (ORs) from 70 studies (31 SCSA, 18 TUNEL, 13 SCD and 8 Comet assay). The meta-analysis included 17744 treatment cycles (9363 IVF, 6260 ICSI and 2121 mixed IVF+ICSI cycles). The combined OR (95%CI) of all the studies (1.15, 1.08-1.23; P<0.0001), for IVF studies (1.15, 1.05-1.27; P=0.0033), ICSI studies (0.89, 1.60-0.99; P=0.0254) and mixed IVF+ICSI studies (2.00, 1.66-2.41; P<0.0001) indicated that sperm DNA damage is associated with clinical pregnancy following ART. When studies were stratified according to the assays, we observed that the ORs differed according to assay type: TUNEL (1.85,1.52-2.26; P<0.0001), SCD (1.16, 1.02-1.32; P=0.0233), Comet (4.15, 3.04-5.68; P<0.0001) and SCSA (0.88, 0.80-0.96; P=0.0041). Direct method of sperm DNA damage measurement was strongly associated with pregnancy outcome (OR=2.40, 2.03-2.84; P<0.0001; 2,965 cycles) compared to indirect methods (0.99, 0.92-1.06; P=0.678; 14,779 cycles). However, indirect methods showed a significant association with pregnancy outcome in studies controlling for female age (1.25, 1.11-1.41; P=0.0003; 4210 cycles) and female factors infertility (0.65, 0.56-0.74; P<0.0001; 4033 cycles). When sperm DNA damage was above the threshold value, ICSI pregnancy rates were lower than IVF pregnancy rates, in studies controlled for female age (47.6% vs. 49.5%) or female factors infertility (49.2% vs. 56.8%).

**Conclusions:** The updated meta-analysis we have performed demonstrates that there is a potential adverse impact of sperm DNA damage on clinical pregnancy. The studies using a direct method of sperm DNA damage analysis showed a strong association between sperm DNA damage and pregnancy outcome following ART.

**61 COMPUTATIONAL FLOW CYTOMETRY REVEALS THAT CRYOPRESERVATION INDUCES SPERMPTOSIS BUT SUBPOPULATIONS OF SPERMATOZOA MAY EXPERIENCE CAPACITATION LIKE CHANGES**

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(Presented By: Fernando Juan Pena Vega, PhD)

The reduced lifespan of cryopreserved spermatozoa in the mare reproductive tract has been attributed both to capacitative and to apoptotic changes. However there is a lack of studies investigating both phenomena simultaneously. In order to improve our knowledge in this particular point, we studied in raw and frozen thawed samples apoptotic and capacitative markers using a wide battery of test based in flow cytometry. Apoptotic markers evaluated were caspase3 activity, externalization of phosphatidylserine (PS) and mitochondrial membrane potential. Markers of changes resembling capacitiation were membrane fluidity, tyrosine phosphorylation and intracellular sodium. Conventional and computational flow cytometry using non-linear dimensionally reduction techniques (t-SNE) and automatic classification of cellular expression by non-linear stochastic embedding (ACCENSE) were used. Most of the changes induced by cryopreservation were apoptotic, with increase in caspase 3 activation (p<0.01), PS translocation to the outer membrane (p<0.001), loss of mitochondrial membrane potential (P<0.05) and increase in intracellular Na+ (p<0.01). Average values of markers of capacitative changes were not affected by cryopreservation, however the analysis of the phenotype of individual spermatozoa using computational flow cytometry revealed the presence of subpopulations of spermatozoa experiencing capacitative changes. For the first time advanced computational techniques were applied to the analysis of spermatozoa, and this techniques were able to disclose relevant information of the ejaculate that remained hidden using conventional flow cytometry.

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**63 EFFECT OF GHRELIN ON MOUSE REPRODUCTIVE PERFORMANCE AND SPERMATOGENESIS**

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(Presented By: Enrica Bianchi, PhD)

**Introduction:** Cryptorchidism is a common congenital abnormality characterized by a failure to descend one or both testes into the scrotum, increasing the risk for developing male infertility and testicular cancer.

**Objectives:** The present study elucidated the effects of ghrelin or growth hormone secretagogue receptor (GHSR1a) deletion on mouse reproductive performance and evaluated the ability of ghrelin to protect mouse spermatogenesis.

**Methods:** Reciprocal matings of heterozygous / homozygous ghrelin and GHSR1a knockout mice were performed. Litter size and germ cell apoptosis were recorded and testicular histological evaluations were performed. Sperm count and motility were assessed in ghrelin KO and GHSR KO mice. Wild type and GHSR1a KO mice were subjected to heat-induced germ cell death resulting from surgical induction of cryptorchidism. Mice received intraperitoneal injections of ghrelin or saline twice a day for 20 days post-surgery. Normal and cryptorchid testes were collected to determine testis weights and for histopathological analyses including seminiferous tubule diameter, and the
percentage of seminiferous tubules with spermatids and giant cells.

**Results:** Our findings demonstrated that deletion of endogenous ghrelin altered male fertility and that exogenous ghrelin treatment protected the testis from damage. A significant increase in the percentage of seminiferous tubules with more than 3 TUNEL-stained cells and in testicular weights was observed in ghrelin KO mice but not GHSR KO mice. Furthermore, ghrelin treatment ameliorated testicular weight changes in cryptorchid testes. The percentage of seminiferous tubules containing spermatids and seminiferous tubule diameter was significantly increased in the ghrelin-treated GHSR KO mice compared to the control group. Increased GSH content levels were observed in ghrelin-treated cryptorchid testes of wild type and GHSR KO mice compared to saline-treated cryptorchid testes, confirming that the antioxidant properties of ghrelin are not mediated by the GHSR-1a receptor.

**Conclusion:** Deletion of ghrelin compromised male fertility, and ghrelin therapy attenuated cryptorchid-induced testicular damage in a GHSR1a receptor-independent manner.

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**64 DYNAMIC SUBCELLULAR LIPID ORGANIZATION IN HORMONE INDUCED MA-10 MOUSE TUMOR LEYDIG CELLS.**

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(Presented By: Sathvika Venugopal PhD)

Lipids play a role in numerous biological processes including membrane remodeling and signal transduction mediating hormone action in cell function. A detailed insight into the function of lipids in steriodogenesis requires an understanding of the subcellular organelle localization of individual lipids. For this, steroidogenic MA-10 mouse tumor Leydig cells were chosen because of their ability to rapidly produce progesterone in a hormone-inducible manner.

Mitochondria, endoplasmic reticulum (ER), cytoplasm, plasma membrane (PM), PM-associated membranes (PAMs) and mitochondria associated membranes (MAMs) were isolated from MA-10 cells in basal, hormone stimulated (treated for 2 hours with dibutyryl cAMP (dbcAMP), and steroidogenesis inhibited (treated with dbcAMP and cycloheximide) states. Lipidomic analyses were performed by direct infusion (shotgun lipidomics) using electrospray ionization tandem mass spectrometry of major membrane lipid categories. This analysis identified 2105 individual/isobaric species, including glycerophospholipids, lysoglycerophospholipids, shingolipids, cholesterol and its esters, and ceramides. Every isolated subcellular organelle membrane had a unique lipid composition and induction of steriodogenesis by dbcAMP caused a significant remodeling of the subcellular lipidome. For example, we noted a substantial increase in ceramide levels in PAM and PM compartments, suggesting a role of ceramides in signal transduction process mediating the induction of acute steriodogenesis. Ceramide levels remained elevated when compared to control and in the presence of cycloheximide, an inhibitor of cAMP-induced cholesterol transport into mitochondria and thus steriodogenesis. These data suggest that ceramide may play a role as a signaling molecule in PM. In addition, a drastic decrease in cholesterol ester levels was noted in the cytoplasm, ER and whole cell lipid extracts, suggesting that a significant amount of cholesterol esters are de-esterified and likely utilized for steroid biosynthesis. Abundant lipids such as phosphotidylcholine and sphingolipids were not affected by the various treatments.

The observed cAMP-induced dynamic changes in MA-10 cell subcellular membrane lipidome suggest that hormone-induced acute steroid hormone production is a process that involves extensive organelle remodeling. This study is one of the first to analyze lipid re-organization during steriodogenesis. (Supported by CIHR grant FRN-148659 and a CRC).

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**65 GONADOTROPIN INDEPENDENT ANDROGEN SYNTHESIS IN THE HUMAN PREPUBERTAL TESTIS: BREAKING THE DOGMA**

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(Presented By: Paula Aliberti)

In contrast with the well documented gonadotropin stimulated testicular androgen synthesis, in humans, prepubertal (Pp) intratesticular testosterone has been reported (Rivarola 1989) but not elucidated. It has been proposed that the insulin-like growth factor family could provide essential signals for testis development (Griffeth 2014).

The aim of this study was to evaluate the expression of steroidogenic enzymes and androgen receptor (AR) in human Pp testes, and analyze a possible relation with the IGF family. Eighteen Pp testes, confirmed by histology analysis, were collected at necropsy from 18 subjects without endocrine or metabolic diseases, and divided in 2 groups: Infancy n=8 (median age 1.3 mo, range 2 days-7 mo), and Childhood n=10 (median age 6 years, range 1-9 y). Protein expression of AR was analyzed by IHC, and of HSD3B2 and CYP11A1 by WB. The mRNA expression of the front and backdoor steroidogenic pathways (CYP17A1, HSD3B2, SRD5A1, SRD5A2, AKR1C1, AKR1C2, AKR1C3, AKR1C4) and the IGF family (IGF1, IGF1R, INSR) was assessed by RTqPCR.

Every sample expressed AR in peritubular and interstitial cells, including the Leydig cells present in neonatal and minipubertal samples. Sertoli cells were negative for AR in Infancy, by its expression increased gradually throughout Childhood starting at 3 years of age.

HSD3B2 and CYP11A1 protein expression was observed in all samples. SRD5A2 and AKR1C4 mRNAs were not detected in...
any sample while all other analyzed genes were expressed in every tissue. CYP17A1 mRNA expression was significantly higher in Infancy than in Childhood (p<0.01), while IGFI, SRDS5A1 and AKR1C3 were significantly higher in Childhood (p<0.05). Multiple correlation studies revealed in Infancy a strong negative correlation between IGFI and CYP17A1 expression and a positive correlation between the enzyme AKR1C3 and both AKR1C1 and AKR1C2. In Childhood, a positive correlation with age was found for CYP17A1 as well as for AKR1C3. Both enzymes SRDS5A1 and AKR1C1 correlated positively with AKR1C3 and AKR1C2. A negative correlation was obtained between both receptors. IGFI correlated positively with CYP17A1 while INSR negatively with CYP17A1 and AKR1C3. To our knowledge, we are the first to report the Pp testicular expression of genes involved in androgen synthesis and its gonadotropin independent increase throughout childhood. Also, our results hint to a possible role of the IGFs in the testis steroidogenic maturation previous to central puberty onset.

**66 THE ROLE OF HMGN5 IN SPERMATOGENESIS**

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(Presented By: Boryana Zhelyazkova)

**Introduction:** Male factor infertility contributes to about half of the total cases, yet a third to half of these patients are still classified as idiopathic. Thus, identifying the need to better understand the genetic bases of this condition. Array comparative genomic hybridization analysis for copy-number variations (CNV) was performed on 20 non-obstructive azoospermic (NOA) men, which revealed one patient harboring a microdeletion that encompassed the gene, HMGN5 (High Mobility Group Nucleosome Binding Domain 5). Located on the X-chromosome, HMGN5 binds to nucleosome particles and can act as transcriptional regulator. The mouse and human genes are highly homologous and differ from other members of the HMGN family by a much longer C-tail. The HMGN5 gene expression is upregulated in various human tumors and confers tumor oncogenic effects in many cancer models. Knock-down of HMGN5 in human cancer cells resulted in cell cycle arrest and enhanced apoptosis. HMGN5 is highly expressed in the testes and may play a role in spermatogenesis via cell cycle modulation.

**Methods:** The mouse and human genes are highly homologous; therefore, we investigated the mouse gene in testis development. Expression levels were evaluated via qPCR. Cell growth analysis was preformed via cell counts post Hmgn5 siRNA mediated knock-down in mouse testicular cell lines C18-4 and GC-1.

**Results:** Analysis of various mouse tissues showed very high expression levels in the testes over more moderate expression in other tissues. Knockdown of Hmgn5 in the testicular cell lines C18-4 and GC-1 showed a statistically significant delay in cell growth based on two-way ANOVA analysis three to four days post knock down. In addition, Cyclin b1 and Bcl2 expression levels were downregulated by 40% and 50% respectively.

**Conclusion:** The results suggest that down-regulation of Hmgn5 in testicular cell lines leads to cell cycle changes that might be result of altered apoptosis. This may underlie some cases of non-obstructive azoospermia.

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**67 MULTIPLE NUCLEAR RECEPTORS AND SIGNALLING PATHWAYS ARE AFFECTED BY INHIBITION OF SERTOLI CELL SUMOYLATION**

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(Presented By: Keumsil Hwang, BS, MS)

**Introduction/Objectives:** Small ubiquitin-related modifiers (SUMOs) proteins are posttranslational modifiers. Recent data are consistent with important roles for SUMOs in human and rodent spermatogenesis. To further evaluate the role of SUMOs in Sertoli cell (SCs), this study used a well-characterized primary paradigm and treatment with a small molecule trihydroxyflavone SUMO inhibitor to prevent transfer of required E2 (Ubc9) enzyme thioester conjugates to substrates. SC dose-responsiveness to retinoid receptor signaling was evaluated.

**Methods:** SCs isolated from testes of 18-day-old SD rats were purified. Primary SCs (≥97% pure) were established in defined serum-free conditions as previously reported. On day 3 ex vivo, 24h pretreatment with the SUMO E2 Ubc9 Inhibitor 2D08 (100μM) or matched-vehicle (control) preceded a second 24h treatment period with 2D08 +/- doses of all--trans–Retinoic acid (ATRA; 1-100μM), a ligand for retinoic acid receptor (RAR) and retinoid X receptor (RXR). Endpoint analyses, day 5. Triplicate SC samples were analyzed for RNA and protein. Gene expression was quantified by Q-RT-PCR analyses and normalized to 18S/sample. Whole cell lysate proteins were separated by SDS-PAGE followed by sequential Western blotting with activity-specific immunoreagents. Specific activity signals for phosphorylated proteins were normalized with respective pan-antibodies. β-actin was used to normalize protein/sample. Data reported at statistical significance, p≤0.05.

**Results:** 2D08 vs. vehicle-treated control (A) mRNA/18S: Nuclear Receptors No change: androgen receptor (AR); Nuclear Receptor Coactivator 1 (SRC-1); RARγ1,2. Decrease: progesterone receptor (PGR); RARα; RXRa,γ. Increase: estrogen receptors (ESR1,2) α,β; RXRβ. (B) Protein: Increase: AR. Decrease: RXRa,β.

ATRA treatment alone vs. vehicle-matched control (C) mRNA/18S: Nuclear Receptors No change: RARγ1,2. Decrease: ESR2, RARγ; RXRa,β Increase: RXRβ. (D) Protein: Increase: ERβ, PGR, RARγ but not AR; Decrease: RARα, RXRa, RXRβ. 2D08+ATRA vs. ATRA (E) mRNA/18S: Decrease: RARα, RARγ; and RXRa,β were further reduced. (F) Protein: Decrease: AR; ESR2; PGR; RXRa,γ; RXRa,β

**Conclusions:** These data show that inhibition of SUMOylation results in significant changes in SC expression of distinct nuclear
ABSTRACTS

receptors and transcription factors. SC effects include ATRA responsiveness. These findings are consistent with a role for SUMOylation in directly regulating SC function and thereby, germ cells.

68 DEFECTS OF USP42 CAUSE MALE INFERTILITY AND ARE ASSOCIATED WITH NONOBSTRUCTIVE AZOOSPERMIA IN MEN
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(Presented By: Bo Zheng, Jr., PhD)

Ubiquitin-mediated protein degradation and modification are required for mammalian functional spermatogenesis. Normal spermatogenesis is dependent on the balance of ubiquitination and deubiquitination. Deubiquitination is a reverse process of ubiquitin-mediated by deubiquitinating enzymes (DUBs). However, the underlying mechanistic links between DUBs and spermatogenesis remain largely unexplored. Here, we identified ubiquitin-specific peptidase 42 (USP42) gene as a potential candidate for maintaining spermatogenesis. USP42 is a deubiquitinating enzyme belonging to ubiquitin-specific processing proteases (USP) family. We found Usp42-deficient mice were infertile, exhibiting disarranged ectoplasmic specialization (ES) junctions, abnormal spermatid heads shaping and failed spermiation. High-throughput comparative proteomic profile identified a large-scale shift between wild-type (WT) and Usp42 knock-out (KO) testes. In further study, we demonstrated USP42 could regulate ES assembly by deubiquitinate retinoic acid induced 14 (RAI14) in a K48-linked degradation pathway. Altogether, our study indicates that USP42 is crucial for spermiogenesis and provides novel insight into the role of DUBs in male reproduction.

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69 3 DIMENSIONAL HUMAN TESTIS ORGANOID SYSTEM CREATED FROM IMMATURE TESTICULAR CELLS
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(Presented By: Nima Pourhabibi Zarandi, MD)

Introduction: Creating miniature 3 dimensional (3D) organ-like structures from human cells mimicking the function of native organs and eventually develop a "body on a chip" is eagerly desired. We have recently developed an in vitro 3D human testis organoid system from mature human testicular cells with the potential for in vitro differentiation of spermatogonial stem cells (SSC) and androgen production. The main objective of this study is to show the feasibility of establishing the same 3D organoid system, using immature testicular cells. This has a potential application of fertility preservation in prepubertal male cancer survivors and genetically impaired boys who are at risk of infertility.

Material and Methods: Isolated cells from immature (prepubertal) testicular tissue were cultured in 2 Dimensional (2D) condition for 50 days and 5 passages. Specific genes expression assay was used to prove the presence of all 4 cell types including SSCs, Sertoli, Leydig and peritubular cells, as well as confirming undifferentiated condition of spermatogonial cells. Flow cytometry analysis showed the quantity of each cell type. We integrated 2D cultured cells into 3D spherical culture via hanging drop method, using 10,000 cells per organoid. Over 5 weeks of 3D culture the functionality of organoids was evaluated using live/dead cell staining, ATP production assay, post-meiotic genes expression and androgen production.

Results: Specific markers for spermatogonia including ZBTB16 (PLZF) , PGAP9.5 (UCHLI), THY1 (CD90), CD9, FGFR3 and SSEA4; GATA4, SOX9, Clusterin and CD49f for Sertoli cells; STAR, TSPO and Cyp11A1 for Leydig cells; and CD34 for peritubular cells; all together approved the presences of different cell types in the cells that isolated, cultured and integrated into 3D organoid. The 3D testis organoids system maintained their structure, viability, metabolic activity and produced androgen over 5 weeks of culture. PRM1 expression showed that this 3D system was able to differentiate SSCs to post meiotic germ cells.

Conclusions: Human 3D testicular organoid system was generated successfully by using isolated human SSC, Sertoli, Leydig and peritubular cells from immature testis and maintained long term in 3D culture. The system was able to produce androgen and push SSCs toward early differentiation. Future directions will include optimizing the system and testing implanted organoids in vivo, as well as evaluating their use as a novel testicular toxicity model.

70 CLONAL DEVELOPMENT OF SPERMATOGONIA IN RHESUS TESTES
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(Presented By: Adetunji Fayomi, DVM)

Introduction and Objectives: Undifferentiated spermatogonia in rodent testes are described by clone size (Asingle, Apaired, Aaligned) and molecular markers that they express. Spermatogonia in nonhuman primate (NHP) testes are described by nuclear morphology and intensity of staining with hematoxylin (Adark, Apale). There is limited information about how the dark and pale descriptions of nuclear morphology correlate with clone size or molecular markers in primates, which makes it difficult to compare rodent and primate data. The aim of this study is to learn molecular characteristics of Adark and Apale spermatogonia and use them as molecular markers to characterize stage-specific clonal development of undifferentiated and differentiating spermatogonia in the rhesus seminiferous epithelium.
Methods: We used colorimetric immunohistochemistry (IHC) to characterize UTF1, ENO2 and cKIT expression in Adark, Apale and B spermatogonia of the Rhesus testis. We performed IHC co-staining in section and whole mount to determine the extent of overlap between these markers and correlate their expression with clone size. 5-ethyl-2′-deoxyuridine (EDU)-labeling was used to mark cells at S-phase and establish a tool for staging NHP seminiferous tubules in whole mount.

Results: We found that UTF1 and ENO2 are markers of Adark and Apale undifferentiated spermatogonia in the Rhesus tests. We also demonstrated that irrespective of the stage of seminiferous epithelium, most of the undifferentiated spermatogonia (UTF1+/cKIT- cells) exist as clones of 1, 2 or 4 cells. Clones of 4 cells were more prevalent in stage V, which coincide with the stage with the highest frequency of UTF1+/cKIT+ transitioning spermatogonia. UTF1+ spermatogonia rarely express cKIT during stages I-IV of the seminiferous epithelium. cKIT expression occurs mostly in Larger UTF1+ clones (2-4 cells). Highest frequency of EDU+/UTF1+ clones were observed in stages X-XI.

Conclusion: Similar to rodents, rhesus spermatogonia develop in interconnected clones of cells and increased clone size is associated with increased spermatogonial differentiation (cKIT+). Undifferentiated (UTF1+/cKIT-) spermatogonia were observed in clones of 1-4 cells and rarely in clones of 8, suggesting that Rhesus has fewer transit amplifying divisions in the pool of undifferentiated spermatogonia than rodents.

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VITAMIN A DEFICIENT LECITHIN RETINOL ACYLTRANSFERASE (LRAT) MICE SERVE AS AN INDUCIBLE MODEL OF SERTOLI CELL ONLY SYNDROME

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Introduction: Sertoli cell only (SCO) syndrome by definition indicates loss of germ cells; however, our data in humans indicate preservation of spermatogonial stem cell (SSC) markers in men with SCO. Therefore, SCO may be the earliest arrest of spermatogenesis with block of entry of SSCs into meiosis. Sertoli cell dysfunction and/or primary errors in SSCs may lead to SCO but the etiology of SCO remains under investigation. The aim of our study was to evaluate the utility of Lecithin:Retinol Acyltransferase (LRAT) knock out (KO) mice as an animal model to study SCO. LRAT KO mice fed a Vitamin A deficient diet have been shown to develop SCO.

Methods: 18 animals were used in this study, 3 in each group: wild type (WT) fed vit A deficient diet (Adef), WT fed A sufficient diet (Asuf), LRAT KO Asuf, LRAT KO Adef at 6 and 8wks time points were sacrificed and testis tissue were procured. Histology and immunofluorescence were performed for cellular characterization. Next generation RNA sequencing was performed to assess expression of gene transcripts among germ cells, SSCs, Sertoli cells, and Leydig cells. Expression profiles were compared to data obtained from our analysis of human testes from men with SCO.

Results: Normal histology and spermatogenesis were seen among 6wk WT Asuf, WT Adef, and LRAT ASuf mice. However, 6wk LRAT ADef mice demonstrated hypospermatogenesis. At 8 wks, LRAT ASuf demonstrated normal spermatogenesis while LRAT Adef mice demonstrated largely SCO with some pockets of conserved spermatogenesis, pattern similar to one observed in human SCO. At 8wks LRAT Asuf and ADef testes stained positive for markers of SSCs: PLZF and OCT4. However, only LRAT Asuf testes stained positive to SYCP3 indicating ADef mice lack differentiating cells beyond spermatogonia (SPG). Analysis of 1903 known transcripts mapped to testis and expressed in both human and mouse testes confirmed similarities between LRAT KO Adef and human SCO profile. 8wk LRAT ADef mice demonstrated greater ITFA6 expression corresponding to undifferentiated SSCs, greater ZBTB16 expression corresponding to undifferentiated SPG, and less PCNA, DDX4, and SYCP3 corresponding to less expression of SPG, and primary spermatocytes respectively.

Conclusion: LRAT KO mice fed a Adef diet for more than 8 wks develop arrest beyond SSCs entry into meiosis, similar to that observed in men with SCO. LRAT KO mice fed an ADef diet serve as a valuable inducible animal model of SCO to better understand its biology.

KNOWLEDGE OF IFT140 MAY DISRUPT SPERMATOGENESIS BY DYSREGULATING THE NFKB SIGNALING PATHWAY

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Introduction and Objective: A homozygous, six nucleotide deletion in exon 22 of the intraflagellar transport 140 (IFT140) gene in a consanguineous family of non-obstructive azoospermic brothers was identified using whole-exome sequencing. Significant changes in the expression of key genes in the NFkB pathway (decreased Fas and increased Bcl2) were present upon Ift140 knockdown in mouse male germ cells, suggesting the presence of an anti-apoptotic milieu. The objective of this study was to define the functional consequences of Ift140 knockdown on the NFkB pathway signaling genes.

Methods: Ift140 function was silenced in C18-4, a mouse spermatogonial cell line. Ift140 mRNA levels were evaluated using quantitative real-time PCR. Gene expression studies were performed in technical triplicates on an oligonucleotide array of 84 key genes related to NFkB pathway signaling. Changes in gene expression that were more than 1.5x up or down relative to control were considered dysregulated. Results were validated and analyzed for statistical significance using REST software (Qiagen). Knockdown and control cultures were treated with Sunitinib (2μM, 8 hours) to induce apoptosis, and a cell survival

were immotile. Histologic studies showed impaired short and bend tails, round heads. All mutant sperm examined spermiogenesis in the mutant mice. Immunofluorescent staining revealed that Y68 is a key amino acid that controls MEIG1 migration to the manchette to transport cargo proteins for sperm flagella formation.

Mouse meiosis-expressed gene 1 (mMEIG1) is a key player in the regulation of mouse spermiogenesis and sperm flagella formation. In male germ cells, it is expressed in the whole cell body of spermatocytes and round spermatids, but is recruited to the manchette of elongating spermatids by another spermiogenesis regulator, PACRG. The MEIG1/PACRG complex is essential to transport cargo, including sperm associated antigen 16 (SPAG16) to build sperm flagella. Nuclear magnetic resonance (NMR) studies revealed that mMEIG1 adopts a unique fold that provides a large surface for interacting with other proteins. Among the 12 exposed and conserved amino acids, four of them, W50, K57, F66, particularly Y68 mediate binding to PACRG. To study the role of Y68 in vivo, we mutated this amino acid using the CRISPR/cas9 system. DNA sequencing of the RT-PCR product revealed that only the amino acid was mutated in the mutant mice.

RESULTS: Ift140 knockdown was 90.3% efficient in C18-4 cells at 72 hours. Twenty-four NFKB genes were down-regulated and eight genes were up-regulated. Dysregulated genes encoded 11 ligands and receptors upstream of the NFKB pathway, a member of the intermediate signaling complexes; a tyrosine kinase; and 6 pathway responsive genes that modulate the immune response and apoptosis. After Sunitinib treatment, 63.4% of Ift140-silenced cells survived 8 hours compared to 25.7% of scramble-control cells (p<0.05) underscoring the significance of increased expression of apoptosis-related NFKB signaling genes.

Conclusion: Statistically significant changes in the expression of key genes in the NFKB pathway occurred upon Ift140 knockdown. Dysregulated genes encoded inflammatory ligands and receptors that activate the NFKB pathway, an intermediate signaling complex member, tyrosine kinase, and pathway responsive genes that modulate the immune response and apoptosis. These changes suggest increased NFKB activity following Ift140 knockdown with negative feedback on activating ligand genes and increased expression of apoptosis related genes.

73 MUTATION OF A SINGLE AMINO ACID OF MEIOSIS-EXPRESSED GENE 1 BY CRISPR/CAS9 SYSTEM RESULTS IN IMPAIRED SPERMIOGENESIS AND MALE INFERTILITY IN MICE
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(Submitted By: Shiyang Zhang, Master)

Mouse meiosis-expressed gene 1 (mMEIG1) is a key player in the regulation of mouse spermiogenesis and sperm flagella formation. In male germ cells, it is expressed in the whole cell body of spermatocytes and round spermatids, but is recruited to the manchette of elongating spermatids by another spermiogenesis regulator, PACRG. The MEIG1/PACRG complex is essential to transport cargo, including sperm associated antigen 16 (SPAG16) to build sperm flagella. Nuclear magnetic resonance (NMR) studies revealed that mMEIG1 adopts a unique fold that provides a large surface for interacting with other proteins. Among the 12 exposed and conserved amino acids, four of them, W50, K57, F66, particularly Y68 mediate binding to PACRG. To study the role of Y68 in vivo, we mutated this amino acid using the CRISPR/cas9 system. DNA sequencing of the RT-PCR product revealed that only the amino acid was mutated in the mutant mice. Western blot analysis demonstrated that MEIG1 protein was expressed, however, the level was reduced in the testis compared to the controls. All homozygous mutant mice examined were completely infertile, and sperm count was dramatically reduced. The developed sperm displayed multiple abnormalities, including short and bend tails, round heads. All mutant sperm examined were immotile. Histologic studies showed impaired spermiogenesis in the mutant mice. Immunofluorescent staining revealed that the mutant MEIG1 is still present in the whole cell body of spermatocytes, but accumulated in the acrosome region of round spermatids. No MEIG1 signal was discovered in the manchette of the elongating spermatids. Similarly, SPAG16L is expressed in the cytoplasm of spermatocytes and round spermatids, and is present in the manchette of the elongating spermatids of the control mice. In the mutant mice, SPAG16 is still expressed in the cytoplasm of spermatocytes and round spermatocytes; it is no longer present in the manchette of elongating spermatids. These findings suggest that Y68 is a key amino acid that controls MEIG1 migration to the manchette to transport cargo proteins for sperm flagella formation.

ABSTRACTS

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ABSTRACTS

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testes, suggesting that changes intrinsic to the old cells were responsible at least in part for their reduced T production. 2) When cultured away from their in vivo testicular environments, cells from old regressed but not old normal testes increased their steroidogenic function significantly, suggesting that extrinsic factors associated with the seminiferous tubules also may affect Leydig cell aging.

Supported By: NIH grant AG25037 (BZ) and National Natural Science Foundation of China grants NSFC81471411 (HC) and NSFC81102150 (LY).

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TSEP7, A SMALL PROTEIN ENCODED BY A PUTATIVE LONG NONCODING RNA, NEGATIVELY REGULATES PROLIFERATION OF UNDIFFERENTIATED SPERMATOGONIA BY AFFECTING CHROMATIN STRUCTURE

Mingxi Liu PhD
Nanjing Medical University
(Presented By: Mingxi Liu, PhD)

Short proteins can be concealed within small open reading frames (sORFs) on RNAs that appear to be noncoding in biosphere from plant to animal. In mammals, the number and function of these short proteins are remained unclear. Due to LncRNAs are enriched in testis, we perform a proteomic analysis on mouse testis to discover novel Testicular sORF-encoded proteins (TSEPs). We have identified 57 novel TSEPs. One of these short proteins, TSEP7, is encoded by LncRNA n277827, could be only detected in testis by western blot, but LncRNA n277827 could be detected in multiple tissues. Lack of TSEP7 cause an enlargement of undifferentiated spermatogonia pool in mouse testis. We demonstrate that N-terminal of TSEP7 interacted with histone H2B; C-terminal of TSEP7 is associated with distribution of TSEP7 in cell nuclear. Histone H2B K20 acetylation (H2B-K20ac) is reduced in testis of TSEP7 null mice, while expression of germ cell differentiation gene are significantly reduced. These data suggested that TSEP7 interaction with H2B affect histone modification and negatively regulates proliferation of undifferentiated spermatogonia.

This work was supported by the National Basic Research Program of China (2014CB943202) and National Key Research and Development Program of China (2016YFA0500902).

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WHOLE EXOME SEQUENCING OF A CONSANGUINEOUS TURKISH FAMILY IDENTIFIES A MUTATION IN GTF2H3 IN BROTHERS WITH MALE FACTOR INFERTILITY

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(Presented By: Raul Clavijo, MD)

Introduction: Up to 80% of patients with a diagnosis of nonobstructive azoospermia (NOA) have a negative result on genetic testing. We sequenced the exomes of four members of a consanguineous Turkish family comprised of the mother, father and their seven sons. The exomes sequenced were those from two sons who had NOA and two who were oligospermic. Standard genetic testing revealed no karyotype abnormalities or Y microdeletions.

Objective: Using whole exome sequencing (WES), we sought to investigate the genetic cause of abnormal semen parameters in the affected sons.

Methods: Extraction of DNA was performed from blood samples followed by whole exome sequencing. Variants were annotated using the ANNOVAR software tool. The filter based annotation feature was used to assess variants for rarity, deleterious nature, conservation, and confirmed familial segregation as well as absence in the control population.

Results: A non−synonymous mutation in “general transcription factor TFIIH subunit 3” (GTF2H3) was identified in this consanguineous family. This mutation in chromosome 12 (12chr: 124144111 T>C) of GTF2H3 is a nonsynonymous SNP and likely a disease−causing mutation as it is predicted to be damaging (SIFT 0.009, mutation taster score 1/D, and Polyphen2 0.97), is a rare variant (ExAC allele frequency of <0.01%), segregates with the disease, and is highly conserved (GERP 5.28). Family segregation of the variants showed the presence of the homozygous mutation in the brothers with NOA and heterozygous mutation in the oligospermic brothers.

Conclusions: Using WES, we identified a mutation in GTF2H3 as a likely disease−causing variant in a Turkish family with several sons with NOA and oligospermia. Our data reinforce the clinical role of WES in the molecular diagnosis of highly heterogeneous genetic diseases, where conventional genetic approaches have previously failed to define a genetic diagnosis.

Financial Support: The John P. Hussman Institute for Human Genomics
WHOLE EXOME SEQUENCING IDENTIFIES X-LINKED FHL1 MUTATION IN CONSANGUINEOUS TURKISH FAMILY WITH NON OBSTRUCTIVE AZOOSPERMIA AND CHEST WALL DEFORMITIES.

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(Presented By: Samuel Michael Cohen)

Introduction/Objectives: To investigate the genetic cause of nonobstructive azoospermia (NOA) in a consanguineous Turkish family through targeted exon whole-exome sequencing followed by homozygosity mapping and filtering analysis to identify genetic variations.

Patients: We sequenced the exomes of a consanguineous Turkish family comprised of the mother and father, who are cousins, and their four sons, two of whom have NOA and the other two sons have chest wall deformities and low sperm count. See Figure 1.

Methods: DNA extraction followed by whole exome sequencing. Data was put through several databases and filter based annotation software. After homozygosity matching, we identified all variants that pass filter criteria, namely rarity, deleterious nature, and conservation, and confirmed familial segregation as well as absence in the control population. Funding for the project came from the John P. Hussman Institute for Human Genomics.

Results: A non-synonymous mutation in “four-and-a-half lim domains 1” (FHL1) was identified in a consanguineous family from Turkey. This mutation in exon 6 (Xchr:135292164 G>A) of FHL1 is a nonsynonymous SNP and likely a disease-causing mutation as it is predicted to be damaging (SIFT 0.026, mutation taster score 1/D, and Polyphen2 0.846), is a rare variant (ExAC allele frequency of 1.11%), and segregates with the disease and is highly conserved (GERP 5.57). Family segregation of the variants showed the presence of the homozygous mutation in the brothers with NOA and low sperm counts, heterozygous mutation in mother, and homozygous wild type in the father indicating an X-linked inheritance pattern.

Conclusions: Using WES, we identified an X-linked mutation in FHL1 as a likely disease-causing variant in a Turkish family diagnosed with NOA. Our data reinforce the clinical role of WES in the molecular diagnosis of highly heterogeneous genetic diseases, which conventional genetic approaches have previously failed to conclude a molecular diagnosis.

FGF21 PROMOTES DIFFERENTIATION OF RAT STEM LEYDIG CELLS WITHOUT AFFECTING THE PROLIFERATION

Ren-Shan Ge MD, Yiyan Wang MD, Chunyan Jin PhD, Lanlan Chen MD, Tiantian Song MD, Jingjing Guo MD and Xingwang Li MD
The Second Affiliated Hospital and Yuying Children’s Hospital of Wenzhou Medical University
(Presented By: Ren-Shan Ge, MD)

Introduction: Fibroblast growth factor 21 (FGF21) was reported to be expressed in the testis. However, little is known about the effects of FGF21 on the proliferation and differentiation of stem Leydig cells. In this study, we examined the roles of FGF21 in Leydig cell development in rats.

Methods: An established seminiferous tubule isolation and culture model with ethylene dimethanesulfonate (EDS) treatment to eliminate adult Leydig cells was used to study the effects of FGF21 on stem Leydig cell proliferation and differentiation by measuring testosterone production, mRNA and protein levels of steroidogenic genes, and the number of proliferating Leydig cells.

Results: FGF21 increased testosterone production and steroidogenic gene expression levels of Lhcgr, Scarb1, Cyp11a1, Cyp17a1 and Hsd11b1. Click-iT EdU staining showed that FGF21 had no significant effect on the proliferation of stem cells. A specific and FGF21 inhibitor PD173074 was utilized to further confirm FGF21 action. Consistently, in vivo EDS-treated Leydig cell regeneration model in rat testes showed that FGF21 promoted differentiation, judged by the increasing serum testosterone level and the expression levels of steroidogenesis-related genes. However, double staining of PCNA (proliferating cell nuclear antigen) and CYP11A1 (Leydig cell marker) showed that FGF21 failed to stimulate the proliferation of Leydig cells in vivo.

Conclusion: These data indicate that FGF21 plays a role during Leydig cell development by promoting the differentiation of stem Leydig cells without affecting the proliferation in rat testes. Funding: This work is supported by NSFC (31171425 and 81300471) and Zhejiang Provincial NSFC (LY15H310008)
ABSTRACTS

78 FGF1 INCREASES THE PROLIFERATION OF RAT STEM LEYDIG CELL BUT INHIBITS ITS DIFFERENTIATION
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(Presented By: Xiao-Heng Li, MS)

Introduction: Fibroblast growth factor 1 (FGF1), also called, alpha-fibroblast growth factor, exists in the rat testis. However, its function on proliferation and differentiation of rat Leydig cells is unknown.

Methods: We used a Leydig cell-depleted seminiferous tubule culture system to evaluate the effects of FGF1 on stem Leydig cells in vitro. We also evaluated the effects of FGF1 on the androgen production by rat progenitor, immature, and adult Leydig cells. Recombinant FGF1 (1-100 ng/ml) concentration-dependently stimulated the EdU incorporation into the stem Leydig cells, indicating that it stimulates the proliferation of stem Leydig cells.

Results: FGF1 significantly delayed the differentiation of the stem cell into the Leydig cell lineage, as judged by the more than 50% reduction of testosterone production, the down-regulation of steroidogenesis-related gene (Lhcg, Scarb1, Star, Cyp11a1, Hsd3b1, and Cyp17a1) and reduced number of Leydig cells stained by 17b-hydroxysteroid dehydrogenase 10. FGF1 also inhibited the androgen production by progenitor, immature, and adult Leydig cells.

Conclusion: FGF1 stimulates the proliferation of stem Leydig cells but inhibits their differentiation as well as the androgen production in the Leydig cell lineage.

Funding: This work is supported by NSFC (81601266 & 81300471) & Health & Family Planning Commission of Zhejiang Province (2017KY483, 2017KY473) & Wenzhou Science & Technology Bureau (Y20150111).

Key Words: cell proliferation, rat stem Leydig cells, the Leydig cell lineage

79 METABOLIC AND HORMONAL PROFILE IN MALE INFERTILITY: THE ROLE OF INSULIN, HIGH DENSITY LIPOPROTEINS, FSH ON TESTOSTERONE LEVELS AND SPERM PARAMETERS
Elaine MF Costa MD; PhD1,2,3,4, Juliana R Pariz MSc, PhD student1,2,4 and Jorge Hallak MD, PhD1,2,4

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Introduction: It is well established that sperm concentration and quality depends on testosterone levels and low testosterone identifies men with an adverse metabolic phenotype.

Objective: To evaluate the influence of hormonal and metabolic profile in male fertility.

Methods: One hundred and one non-obese men were recruited from a private Andrology reference clinic. They were divided into fertile (n=44) and infertile groups (n=57). Semen was analyzed according to WHO guidelines and sperm functional tests were performed. Blood samples were obtained to measure basal serum FSH, LH, free testosterone, total testosterone, SHBG, LDL and HDL total cholesterol, triglycerides, fasting glycaemia, insulin and glycated hemoglobin. Statistical analysis was performed by SPSS program version 19.0 (SPSS Inc., Chicago, IL). T-test was used for unpaired samples and Spearman test for correlation analysis. Statistical significance was considered with P value < 0.05.

Results: Varicocele was found in 24% of infertile patients (14/57pts) and in 18% of fertile men (8/44pts). The mean age was similar in both groups (42.4±10.4 and 40.9± 11.7 y.o.), as well as the BMI (29.0±4.5 and 26.6±3.9 respectively). No difference was found in cholesterol and glucose profiles. Concerning hormone measurements, FSH levels lean toward to be higher in infertile group (6.0 ± 6.1 UI/L versus 4.1±2.3 UI/L; p= 0.086 ), although without significance due to small sample size. Total testosterone levels were significantly lower in the infertile group (468±181 ng/dL vs. 599±269 ng/dL; p=0.01) but free testosterone levels were similar in both groups. We identified a positive correlation of testosterone levels with free testosterone, total cholesterol and HDL levels, sperm volume, motility and velocity, however, there was a negative correlation with insulin levels and BMI. Additionally, FSH levels was inversely correlated with sperm velocity and adult Leydig cells.

Conclusion: Lower testosterone associated with higher FSH levels in infertile patients suggest that besides varicocele there are other factors that lead to a hypogonadal state and affects testis function. Concerning metabolic features, our results suggest that higher total cholesterol and HDL levels associated with lower BMI and insulin levels contribute to higher total testosterone levels in better functioning testis.

80 THE UV-FILTER BENZOPHENONE-1 INHIBITS HUMAN TESTIS RETINALDEHYDE DEHYDROGENASE 1 MEMBER A1 AS A POTENTIAL ENDOCRINE DISRUPTING CHEMICAL
Hongqin Zhang MD1, Xiaoheng Li MSc2, Ren-shan Ge MD3, Ying Zhong MD1 and Siyao Liu MD1

¹Jinjiang Maternity and Child Health Hospital; ²The Second Affiliated Hospital and Yuying Children’s Hospital of Wenzhou Medical University

Introduction: The increased incidence of both male and female infertility could be caused by the wide-spread use of chemicals. The exposure to these chemicals may inhibit some critical enzymes for germ cell development. One family of these enzymes is retinaldehyde dehydrogenase (ALDH). Retinaldehyde dehydrogenases, especially ALDH1, ALDH2 and ALDH3, are responsible for catalysis of the formation of retinoic acid. Retinoic acid is critical for germ cell development. One member...
ALDH1A1 is critical for the earlier stage development of germ cells.

Methods: In the present study, we tested UV-filter benzophenone-1 for its inhibition of human ALDH1A1 and the inhibitory mode of action. Benzophenone-1 is added to sun lotion as a UV filter to prevent the UV burn from the sun. We cloned human ALDH1A1 and used propionaldehyde as the substrate of the enzyme and NAD+ as the cofactor and measured the formation of NADH to judge the effects of benzophenone-1.

Results: Benzophenone-1 potently inhibited ALDH1A1 with IC50 value of 35.253 +/- 0.123 uM. Benzophenone-1 competitively inhibited human ALDH1A1 when propionaldehyde was used as the substrate and inhibited the enzyme in a mixed mode when cofactor NAD+ was used. Molecular docking study demonstrated that benzophenone-1 bound to the propionaldehyde binding pocket of the enzyme.

Conclusion: Our data clearly shows that benzophenone-1 is a potent and competitive inhibitor of human ALDH1A1, potentially disrupting germ cell development.

Keywords: retinoic acid; human ALDH1A1; benzophenone-1, competitive inhibition

ABSTRACTS

81 KNOCKDOWN OF IFT140 DECREASES TESTOSTERONE PRODUCTION IN MLTC-1 CELLS
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(Presented By: Amin S. Herati, MD)

Introduction and Objective: We previously identified a homozygous, six nucleotide deletion in exon 22 of the intraflagellar transport 140 (IFT140) gene in a consanguineous family of non-obstructive azoospermic (NOA) brothers using whole-exome sequencing. IFT140 was expressed in the Leydig cells of human and murine testis sections. The objective of our study is to determine if the IFT140 modulates testosterone production.

Methods: Ift140 function was studied in MLTC-1, a hormonally responsive mouse Leydig cell line. Transient knockdown was performed using Ift140 siRNA and a scrambled control (GE Dharmacon). Testosterone levels were subsequently measured using an ELISA. To stimulate steroidogenesis, samples of both knockdown and scramble were treated with 0.05 IU hCG for four after 68 hours of transfection and compared to untreated controls. Ift140 mRNA levels and steroidogenesis pathway genes (3β-HSD, Cyp11a1, Cyp17a1) were evaluated using quantitative real-time PCR (qPCR). Transient knockdown, ELISA, and gene expression studies were all performed in biological triplicate. Gene expression results were analyzed for statistical significance using REST software (Qiagen).

Results: Ift140 knockdown was 94% efficient in MLTC-1 cells at 72 hours. Knockdown of MLTC-1 cells using Ift140 siRNA resulted in lower testosterone with and without hCG stimulation compared to scramble (Table 1). Gene expression of steroidogenic genes were compared between hCG treated knockdown and scramble samples with significantly higher expression of Cyp17a1 by 66% (Standard error range 49-87%) with a p value p=0.0001. No significant difference was present for 3β-HSD or Cyp11a1.

Conclusion: We observed lower but not statistically significant normalized testosterone production with and without hCG stimulation in the knockdown. This suggests possible steroidogenic impairment with Ift140 mutations.

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<th>Table 1. Normalized Testosterone Production in MLTC Cells after 72 hour Ift140 Knockdown (μg testosterone / μg protein ± SEM)</th>
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82 BREAKING PARADIGMS: MARIJUANA IS NOT A HARMLESS RECREATIONAL DRUG AND IS WORSE THAN TOBACCO ON SPERM AND TESTICULAR FUNCTION
Jorge Hallak MD, PhD¹,²,³,⁴, Juliana R Pariz MSc, PhD¹,²,³,⁴, Elaine MF Costa MD, PhD¹,²,³,⁴ and Paulo HN Saldiva MD, PhD⁵
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(Presented By: Jorge Hallak, MD, PhD)

Introduction: Over the last 15 years we have been focused on studying the effects of marijuana consumption on sperm and testicular function. It is anecdotal and deeply accepted by users that marijuana is a relaxing and inoffensive habit and that the real harm comes from cigarette smoking. In fact, this is the argument used by cannabis addicts to avoid any further criticism or investigation and by multibillion-dollar industry that is willing to decriminalize its use.

Objective: To evaluate and compare marijuana and cigarette consumption with smoking and non-smoking fertile patients on sperm parameters and hormonal levels.

Methods: We studied 57 male subjects who came for an initial andrological evaluation and who self-reported regular use of marijuana and 374 fertile men (pre-vasectomy candidates or no risk factors for sperm/testicular dysfunction). The patients were classified as group I (263 non-smokers, fertile pre-vasectomy patients – control group), group II (111 smokers, fertile pre-vasectomy patients), group III (41 marijuana only consumers) and group IV (16 marijuana and tobacco combined users). We performed ANOVA and interaction tests of seminal parameters and hormone profile between the groups. P value adopted <0.05.

Results: A significant reduction on sperm concentration (p=0.001), total sperm number (p=0.018), total motile sperm count (0.012), total motility (p=0.001), total progressive motility (p<0.001), morphology by strict and WHO criteria (p<0.001) and increased pH (<0.001) in group III when compared to group I. Group II showed reduction on sperm morphology by both WHO
and strict criteria (p<0.05). LH (p<0.001) and FSH (p=0.001) were significantly higher in group III and even higher in group IV compared to control. Testosterone levels were diminished in group IV (p=0.045) and prolactin levels were higher in group III (p=0.038).

Conclusion: We were surprised with the results that are arising from 15 years of observation in marijuana and tobacco smokers. These results are astonishing evidence that marijuana has adverse effects on both sperm parameters in a higher degree than tobacco and that the common combination of both substances have even higher deleterious consequences on hormonal levels and testicular function.

Financial support: Androscience

Keywords: marijuana, cigarette, tobacco, sperm, testis, hormones.

Ethics Committee Approval: FMUSP n° 859.215

83 ZIRAM COMPETITIVELY INHIBITS HUMAN TESTIS RETINALDEHYDE DEHYDROGENASE 1A1
Ling Wang MD1, Xiaoheng Li MS2, Ren-Shan Ge MD2 and Ying Zhong MD1
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(Presented By: Li Wang, MD)

Introduction: More evidence indicates that retinoic acid induces germ cells to express the pre-meiotic marker Stra8 and enter meiosis. Retinoic acid is synthesized by a series of retinoic acid-synthesizing enzymes (retinaldehyde dehydrogenases), especially the ALDH1A1. Null mutation of ALDH1A1 causes the delay of the onset of germ cell meiosis in ovaries and testes. Many environmental endocrine disrupters may block the germ cell meiosis via inhibiting ALDH1A1. One of these endocrine disruptors is ziram (zinc dimethyldithiocarbamate). Ziram is primarily utilized in the agricultural field as a fungicide to prevent the spread of fungal infections in fruits and crops.

Methods: In this study, we cloned human ALDH1A1 and tested the effects, and the action mode of ziram on human ALDH1A1. We used propionaldehyde as the substrate of the enzyme and NAD+ as the cofactor and measured the formation of NADH.

Results: We found that human ALDH1A1 catalyzed propionaldehyde with Vmax of 373.6 +/- 20.76 nmol/mg protein/min and Km of 49.55 +/- 6.76 uM. Ziram potently inhibited ALDH1A1 with IC50 value of 2.26 +/- 0.10 uM. Ziram showed competitive inhibition on the enzyme against propionaldehyde and mixed inhibition on the enzyme against cofactor NAD+.

Conclusion: Our data shows that ziram is a potent and competitive inhibitor of human ALDH1A1, potentially disrupting germ cell meiosis.

Funding: This work is supported by Health & Family Planning Commission of Zhejiang Province (11–CX29). Corresponding author Ying Zhong: yzhong08@yahoo.com.

84 GINSENSIDE RG3-ENRICHED KOREAN RED GINSENG EXTRACT ALLEVIATES DOXORUBICIN-INDUCED TESTICULAR DAMAGE IN RATS BY MODULATING INFLAMMATION AND AUTOPHAGY - AN EXPERIMENTAL STUDY
Jae Yup Hong, Kyu-Min Song1, Kyung Hwa Choi1 and Si-Kwan Kim1
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(Presented By: Jae Yup Hong, MD, PhD)

Introduction and Objectives: It is well known that anticancer agent triggers cytotoxicity predominantly in actively proliferating organs like testes and Korean Red Ginseng (KRG; steamed and dried Panax ginseng Meyer) plays protective role in carcinogenesis and proliferation of cancer cells. We investigated effect of KRG-WE on mRNA expression levels of molecules related to antioxidant enzymes, spermatogenesis and sex hormone receptors. Further more, we analyzed expression levels of marker molecules related to inflammation, autophagy and apoptosis from the DOX-treated testis.

Methods: In the present study, alleviative effect of KRG water extract (WE) against doxorubicin (DOX)-induced testicular toxicity in rats was investigated. DOX (1 mg∙mL−1∙kg−1∙week−1) was administrated intraperitoneally for 8 weeks and KRG-WE was given orally for 9 weeks (100 or 200 mg/kg/day) since 1 week before DOX-exposure. Messenger RNA expression levels of molecules related to antioxidant enzymes, spermatogenesis and sex hormone receptors (AR, LH, FSHR) were investigated. Marker proteins associated with inflammation, autophagy and apoptosis were also monitored.

Results: Data indicated that DOX induced marked genetic alteration in spermatogenesis-related testicular biomarkers and KRG demonstrably ameliorated the disorders by modulating the mRNA expression levels related to antioxidant, spermatogenesis and sex hormone receptors. In addition, KRG-WE attenuated inflammatory responses and stimulated autophagy in DOX-exposed rat testis.

Conclusions: KRG can be used as a functional food or adjuvant for the prevention of chemotherapy-induced male reproductive disorder.

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ABSTRACTS

85 PERINATAL EXPOSURE TO 2,2',4,4'-TETRABROMODIPHENYL ETHER IMPAIRS MALE REPRODUCTIVE HEALTH AND SPERM EPIGENOME IN ADULT RATS

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Polybrominated diphenyl ethers (PBDEs) is a group of environmental brominated flame retardants used in production of a diversity of polymers. PBDE were recently withdrawn from commerce in North America and Europe. However, generations that were exposed perinatally to the highest environmental doses of PBDE account for one-fifth of the total U.S. population. Toxicity of PBDE for the male reproductive system has been demonstrated in several human and animal studies, however long lasting effects of developmental exposures on male reproduction are still poorly understood. In this study, pregnant Wistar rats were exposed to 0.2 mg/kg 2,2',4,4'-tetrabromodiphenyl ether (BDE-47) from gestation day 8 until postnatal day 21 and male reproductive outcomes and sperm epigenome were analyzed on postnatal day 120 in offspring. Exposed animals had significantly smaller testes, displayed trend towards decreased sperm motility and classificati

86 ENVIRONMENTAL TEMPERATURE AND PARTICULATE MATTER ARE CORRELATED WITH SEMEN PARAMETERS: A BIG-DATA APPROACH

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Background: Recently, we demonstrated an influence of environmental temperature but not a clear effect of air pollution on sperm number.

Aim: To assess the relationship between air pollution, environmental parameters and quality-related sperm variables, using a big-data approach.

Methods: Seminal parameters from 5131 men, environmental temperature (T) and particulate matter (PM) of the province of Modena were acquired into a data-warehouse. The period of exposure was considered from 3 months before (Jan 2010) to 3 months after the last semen collection (Mar 2016). A meteorological model, developed under the project ERACLITO at ARPA Hydro Meteorological Service, was used to extrapolate T in the town of residence.

Results: 5573 semen analyses were collected. Both maximum and minimum T registered on the day of collection were inversely related to total sperm number (p<0.005), non-progressive (NP) motility (p<0.05), typical forms (p<0.005). Results were confirmed considering T in the 30 and 60 days before collection, but not in the 90 days before collection. Sperm number was lower in summer/autumn (p<0.001). PM10 and PM2.5 were directly related to NP motility (p<0.001) and typical forms (p<0.001). Random tree models were used in sub-datasets on the basis of environmental parameters. A threshold level of 21.25 μg/m3 was found for PM2.5 in the sub-dataset of typical form.

Discussion: Here we demonstrate an influence of environmental T and PM on semen parameters on the largest dataset available so far. Higher T in the 60 days before semen collection is inversely related to sperm parameters. PM10 and PM2.5 influence sperm motility and classification models recognize a PM2.5 threshold able to divide sperm typical forms.
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PHTHALATE EXPOSURE DURING SPERMATOGENESIS IN ADULT MICE AND SPERM EPIGENETIC DYSREGULATION.

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Background: Phthalates, a class of endocrine disrupting compounds (EDCs) used in plastics and personal care products, are ubiquitous environmental contaminants resulting in widespread human exposure. Phthalate exposure in males is associated with poor sperm quality and more recently, with longer time to pregnancy. A growing body of compelling data demonstrates that environmental exposures can be embodied within the male germ cell via epigenetic marks during spermatogenesis; however, these studies are mostly limited to dietary manipulation. Thus, our objective is to examine the effect of DEHP exposure in adult mice on the sperm methylome.

Methods: Adult reproductive age (8-12 wks old) male C57BL/6J mice (N = 4 per group) was treated with 0 or 2.5 mg/kg body weight/day of DEHP in 50% DMSO for 70 days with surgically implanted osmotic pumps. Sperm was collected from the caudal epididymis via swim-up assay for 30 min at 37°C followed by a 40% PureCeption gradient to remove any residual somatic cells. Sperm DNA was isolated through our published protocol. Libraries were prepared using Ovation RRBS Methyl-Seq System (Nugen), pair-end sequenced on a HiSeq 2000 and differential methylated regions (DMRs) were analysed via DMAP program.

Results: We achieved an average of 10.2 million uniquely mapped reads per sample after excluding on average 3% N6 PCR duplicates. Restricting to loci with a minimum of 10x coverage depth, greater or equal to 5% methylation change and q value < 0.05, DEHP exposure resulted in 445 DMRs compared to vehicle controls. Functional annotation analyses via DAVID revealed significant enrichment (FDR < 0.05) for phosphophostere, alternative splicing, cell projection and cytoskeleton classes of genes. Interestingly, while we saw no significant difference in average methylation across all loci (p-value = 0.19), we found that 82% of the sperm DMRs were hypomethylated in DEHP exposed males as compared to controls. The majority (55%) of DEHP-induced sperm DMRs were associated with regions with intermediate methylation levels (e.g., 20-80%).

Discussion: Our findings indicate that paternal environmental exposure encountered in adulthood may influence the epigenome of mature sperm in mice. Ongoing work is investigating the inheritance of sperm-induced DMRs in early embryonic tissue.

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PERIPUBERTAL DIOXIN CONCENTRATIONS AND SUBSEQUENT SPERM METHYLOME PROFILES OF RUSSIAN YOUNG ADULTS

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Background: Dioxins are a group of persistent and structurally-related endocrine disrupting compounds (EDCs) that are generated as unwanted by-products of chemical industrial processes and incineration and are linked with adverse male reproductive health. Compelling animal data in the past few years have demonstrated that the epigenome of the male germ cell is sensitive to environmental conditions at specific windows of development; however, the associations of peripubertal environmental exposures on the sperm methylome in humans is less understood. Thus, we sought to examine the association of peripubertal TCDD exposure with subsequent profiles of DNA methylation via whole genome bisulfite sequencing (WGBS) from semen samples collected in early adulthood.

Methods: The Russian Children Study is a prospective cohort of 516 old boys who were enrolled at 8 to 9 years of age and resided in Chapaevsk, Samara region, between 2003-2005. TCDD was measured at the Centers for Disease Control and Prevention in serum collected at ages 8-9. We randomly selected 4 subjects with highest and 4 with lowest peripubertal TCDD levels who provided semen samples at ages 18-19. Sperm DNA was extracted by our newly published protocol. Libraries for WGBS were constructed using TruSeq DNA methylation kit (Illumina). After SNP removal, differential methylated regions (DMRs) were identified via DMAP package with the following parameters: a minimum of 10x coverage depth, 10% methylation change and q value < 0.05.

Results: Peripubertal blood TCDD concentrations for the low and high exposure group were 0.39 ± 0.07 pg/g lipid and 10.4 ± 1.76 pg/g lipid, respectively. We achieved an average of 136 million uniquely mapped reads per sample with an average coverage depth of 4X. We identified 55 DMRs that distinguished low and high peripubertal TCDD exposure. 6% were located in gene, 7% in promoters and 27% in intergenic regions. Gene ontology analyses revealed enrichment in terms such as phosphoprotein and cytoplasm.

Conclusion: To our knowledge, this is the first study to examine the associations of peripubertal exposure to persistent EDCs on subsequent sperm methylation in humans. Ongoing work is expanding our analyses of the associations between sperm methylation and peripubertal exposures to replicate our findings.

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MALE REPRODUCTIVE HEALTH OF AN INSECTICIDE EXPOSED POPULATION IN A MALARIA AREA IN SOUTH AFRICA (2003-2016).

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(Presented By: Christiaan de Jager, BSc, MSc, PhD)

Introduction: Exposure to environmental endocrine disrupting chemicals (EDCs) often used in industry, agriculture and domestically is linked to altered spermatogenesis, urogenital abnormalities and decreased reproductive health. Contemporary insecticide exposures, primarily low-level environmental (eg. p,p’-DDE) or occupational exposures, are associated with adverse male reproductive health, due to their EDC potential.

Aim: To determine changes between p,p’-DDE plasma concentrations and seminal parameters over time, while considering related factors.

Methods: A cross-sectional study was conducted by recruiting more than 700 young males, between 2003 and 2016, from DDT sprayed and non-sprayed communities in a malaria endemic area. DDT, other relevant insecticides and metabolites were measured in blood plasma and urine respectively. Semen analyses was done according to WHO (1999), sperm chromatin integrity was determined using the SCSA method and linear regression analyses were performed.

Results: Significant differences in end points were found between men from DDT sprayed and those from non-sprayed villages. In sprayed villages p,p’-DDE concentrations decreased significantly from 216.9±210.6 ug/g (mean±SD) during 2003-2008 (n=303) to 6.3±6.8 ug/g during 2012-2016 (P<0.001)(n=100). Similarly p,p’-DDE concentrations were lower in men from non-sprayed villages 2.8± 4.3 ug/g (n= 234) compared to 1.8± 3.8ug/g (n=99) for the same periods (P<0.001). Similar to 2003-2008, logistic regression analyses of 2012-2016 data indicate men with p,p’-DDE levels between 0.26 and 2.25 µg/g are 2.6 times more likely to present with oligozoospermia than men with either lower or higher p,p’DDE levels (P<0.030). The results also point to a weak association between p,p’-DDE plasma concentrations, seminal parameters and sperm chromatin defects (%DFI) in the participants from the sprayed villages (p<0.010).

Discussion: p,p’-DDE levels indicate a trend of continuous exposure with a decline over a 13 year period. Despite the decline in exposure levels over time, seminal parameters and chromatin integrity were affected. In utero or early life exposures may therefore adversely affect reproductive health, due to the potential synergistic and additive effects of known EDCs in malaria areas. While still dependant on DDT for malaria vector control affected populations should be educated to limit exposure while safer alternatives are developed.

TESTICULAR AND METABOLIC EFFECTS OF PRENATAL EXPOSURE TO 1,2-CYCLOHEXANE DICARBOXYLIC ACID DIISONONYL ESTER (DINCH) IN YOUNG AND OLD SPRAGUE DAWLEY MALE RATS

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(Presented By: Enrico Campioli, PharmD, PhD)

Plasticizers are commonly added to plastic polymers to enhance the pliability, durability, and elastic properties. Phthalates, the most common class of plasticizers, have been associated with the development of endocrine and reproductive disorders. In 2002, the plasticizer 1,2-Cyclohexane dicarboxylic acid diisononyl ester (DINCH) was introduced in the European market for use in plastic materials and articles that come into contact with food. Although DINCH received final approval from the European Food Safety Authority in 2006, there is limited knowledge about its potential endocrine-disrupting properties. Preliminary studies from our lab showed that in utero exposure to DINCH significantly reduced testosterone production and testicular gene expression in PND 60 offspring. The purpose of the present work was to assess whether in utero exposure to 1, 10 and 100 mg DINCH/kg/day from gestational day 14 until birth would affect testicular function of the offspring at PND 60 (young) and PND 200 (old).

At PND 60, exposure to DINCH affected the anogenital distance and seminal vesicle weight, in addition to reducing circulating testosterone levels. These morphological changes were correlated with changes in the expression of testicular Star, Tspp, Cyp11a1, Ar, and Plzf. At PND 200, the exposed offspring showed a significant reduction of testosterone production and seminal vesicle weight, altered expression of Cyp11a1 and Pgdfra, and random appearance of small and liquid testes containing degenerating tubules.

DINCH-exposed male offspring at PND 60 exhibited increased random serum glucose concentrations which were not associated with impaired glucose utilization as determined by the administered glucose tolerance test. Serum analysis of liver markers confirmed that DINCH might have an effect on hepatic function since the albumin/globulin ratio, total bilirubin, and total protein levels were altered. These changes were not sustained in the PND200 progeny, most likely due to the progressive aging of the animals. Although more studies will be required to evaluate DINCH’s impact on the various tissues, these results, taken together, suggest that in utero exposure to DINCH from gestational day 14 until birth might have a direct effect on Leydig cell function,
causing premature aging of the testis, and impairing liver metabolic capacity. These effects may be attenuated with the physiological aging of the animal. (Supported by CIHR grant FRN-148688 and a CRC).

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FETAL EXPOSURE TO GENISTEIN (GEN) AND DI-(2-ETHYLHEXYL) PHTHALATE (DEHP) ALTERS JAK/STAT SIGNALING IN RAT TESTIS  
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(Presented By: Martine Culty, PhD)

Introduction and Objectives: Perinatal phases of development have been shown to be particularly sensitive to chemical exposures. Fetal exposure to chemicals with endocrine disruptor properties is believed to predispose males to reproductive abnormalities. The purpose of the current study was to investigate the possibility that a mixture of two common compounds, the phytoestrogen genistein (GEN) and the phthalate plasticizer DEHP, administered to pregnant rats at doses relevant to humans, would change signaling cascades in the testes of their offspring.

Methods: Pregnant SD rats were gavaged with corn oil (vehicle) or 10 mg/kg/day of DEHP, GEN or their mixture, from gestation day 14 to birth. Male offspring were sacrificed at Postnatal day (PND)3 and 120, and total RNA was extracted from the testes, using offspring from three different dams per treatment. Affymetrix 2.0 ST microarray analysis was conducted by Genome Quebec. Pathway analysis (DAVIDS, Ingenuity, KEGG) and key word searches in PubMed were used to identify candidate genes for further validation and expression studies.

Results: Gene array and pathway analyses revealed that fetal exposure to GEN, DEHP and their mixture resulted in distinct gene expression patterns in the JAK/STAT, PI3K/AKT/mTOR and MAPK pathways, highlighting several genes uniquely disrupted by the mixture. Moreover, different sets of genes were affected in neonatal and adult testes, with GEN+DEHP mixture significantly upregulating JAK/STAT pathway genes in neonatal testes.

Conclusion: These data suggest that fetal exposure to an environmentally relevant dose of GEN and DEHP mixture disturb signaling pathways in neonatal and adult testes, potentially affecting downstream cascades critical for cell cycle and cell survival, which finally may contribute to testicular dysfunction.

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CHARACTERIZATION OF PRIMARY CILIA OF THE EPIDIDYMIS DURING POSTNATAL DEVELOPMENT  
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(Presented By: Agathe Bernet)

Primary cilia (PC) are solitary and non-motile antennas present at the cell surface and taking their origin from a mother centriole. In most organ systems, these signalling organelles play the role of mechano-sensors responsive to extracellular stimuli. Although the mutation of Pkd1/2 genes encoding constituents of PC causes developmental reproductive dysfunctions, little is known about the role of PC in the control of reproductive tissue homeostasis and sperm fertilizing capacities. Objective. Our objective is to characterize and assess the role of PC along the male reproductive system, particularly in the epididymis, the organ in which spermatozoa acquire their ability to fertilize the oocyte. Methods. To ascertain the detection of PC, we used complementary transmission electron microscopy (TEM) and confocal microscopy/3D-reconstruction approaches on a double transgenic mouse model expressing endogenous fluorescence in PC and centrioles (Arl13b-mcherry/Cnetr2-eGFP). Specific location of PC throughout the different epididymal segments was investigated by immuno-fluorescent staining during post-natal development. Several PC parameters (e.g. length, density, and orientation) were quantified by using an image-processing pipeline from whole organ confocal images. Results. Axonemal microtubules (9+0) typical of non-motile PC were detected by TEM at the apical pole of epididymal principal cells of adult mice. In addition, striated fibers from the PC-associated-centriole were observed in smooth muscle cells surrounding the epithelium. The presence of PC in the epididymis was confirmed by confocal microscopy and 3D-reconstruction in Arl13b-mcherry/Cnetr2-eGFP mice, which showed a cell type-specific localization of PC during postnatal development. For instance, at birth, short PC were localized at the apical pole of undifferentiated cells. At puberty, PC were present both at the apical pole of differentiated cells and associated with cytokeratin-V positive basal cells. In adult, PC were found elongated, at a higher density in the corpus region, and exclusively associated with basal cells. Conclusions. Our study showed for the first time a dynamic and cell-specific localization of PC during postnatal development of the epididymis. Although the function of this signaling organelle remains to be explored in this organ, our preliminary studies open the door to a better comprehension of the control and maintenance of epididymal functions and male fertility.

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NEW INSIGHTS ON THE CELLULAR DISTRIBUTION OF BETA-DEFENSINS DURING EPIDIDYMAL MORPHOGENESIS  
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(Presented By: Lucas G.A. Ferreira, MSc Student)
ABSTRACTS

Objectives: β-defensins are components of host defense, with antimicrobial and pleiotropic immunomodulatory properties. A gradient of region- and cell-specific expression of different β-defensins is observed in the epithelium of postnatal and adult epididymis of different species. We reported that the expression pattern (mRNA and protein level) of the β-defensin SPAG11C (sperm-associated antigen 11C) drastically changed as the rat epididymis develops from prenatal to postnatal life. Prenatally, SPAG11C was mainly detected in the mesenchymal cells of the rat Wolffian duct (WD), the embryonic precursor of epididymis. Recombinant SPAG11C affected ex vivo cultured WD morphogenesis by regulating epithelial cell proliferation, suggesting a role for this β-defensin in the androgen-induced morphological differentiation of WD. To gain further insights into the biological role of β-defensins in epididymal development, here we investigated the expression of two other β-defensins, named SPAG11E (also known as BIN1B) and DEFB2 (β-defensin 2) in the rat WD. These two proteins were chosen due to their known involvement in reproductive tasks in adult rats.

Methods: Immunohistochemistry was performed on paraffin-embedded tissue sections from whole male fetuses at embryonic day (e) 20.5 and epididymides from adult (120-days-old) Wistar rats. RT-qPCR studies were conducted with total RNA extracted from isolated e20.5 WDs. Ethics Approval: CEUA Unifesp-EPM N. 1776201213.

Results: Defb2 mRNA was detected in WDs at e20.5. Different from SPAG11C (used as positive control), DEFB2 immunostaining pattern was observed in both mesenchymal and epithelial cells in WDs at e20.5. In the adult rat, this β-defensin exhibited a region-specific immunodistribution mainly detected in the epithelial cells from the initial segment and caput region. In contrast, SPAG11E was not readily detected at either mRNA or protein level in the WDs at e20.5. The SPAG11E-positive immunostaining pattern was restricted to epithelial cells from the adult caput epididymis, as reported in the literature, confirming the effectiveness of the antibody used.

Conclusions: The present results shed light on the potential physiological role for different β-defensins in the modulation of events in the developing epididymis during prenatal-to-postnatal transition.


94 TRANSLANTATION OF SPERMATOGONIAL STEM CELL (SCC) IN STALLIONS

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(Presented By: Minjung Yoon, PhD)

Castration of stallions is performed to tone down their stallion-like behavior as well as to make them more trainable. As a result, geldings having superior genetic values lose their fertility. Development of techniques that can be utilized to produce donor SSC derived sperm in the recipient stallions may provide a solution for this dilemma. Thus, the objective of this study was to test if donor SSC derived sperm can be produced through SSC transplantation by ultrasound-guided rete testis injection. Six Thoroughbred stallions were used as recipient stallions. Three of recipients were treated with intra-testicular injection of 70% glycerin. In contrast, in the control group of 3 stallions were treated with PBS. At 10 weeks after treatment, the rates of Sertoli cell only seminiferous tubule cross section were 12.53±9.25 and 1.27±0.78% in 70% glycerin and PBS treated testses, respectively. Transplantation was performed on 11 week post-treatment. For donor SSCs, testses were obtained from 5 pre-pubertal Jeju crossbred (Jeju horse x Thoroughbred) during the routine castration. Single germ cells were isolated from donor testses using two-enzyme digestion procedure. The viability of isolated germ cells were (87.3±1.72). Five hundred million viable germ cells in 14.85 ml of MEMα with 10% FBS supplemented with 0.15 ul of DNase were transplanted by ultrasound-guided rete testis injection. Semen of recipient stallions were collected from two months after transplantation at various frequency and duration (8-25 times for 5-9 months). Microsatellite DNA fingerprinting analysis with 17 markers were performed to detect the presence of donor SSC derived sperm in the sperm collected from recipient stallions. As a result, the genetic information of donor derived sperm was not identified in the sperm of recipient stallions. The ablation of recipient germ cells and the timing of transplantation appear to be the key factors for the production of donor SSC derived sperm in the recipient stallions.

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95 IMPACT OF THE GENETIC BACKGROUND ON THE REPRODUCTIVE PHENOTYPE OF CRISP1 AND CRISP4 KNOCKOUT MICE

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IBYME
(Presented By: Mariana Weigel Munoz)

Epididymal CRISP1 and CRISP4 associate with sperm during maturation and participate in fertilization very likely through their ability to regulate critical sperm Ca2+ channels. In spite of this, CRISP1 and CRISP4 knockout (KO) mice are fertile. As it has been reported that a single mutation can produce markedly different phenotypes, including fertility, depending on the genetic background of the animals, the aim of the present work was to study the reproductive phenotype of CRISP1 and CRISP4 KO mice having a different genetic background. The CRISP1 and CRISP4 KO mice used in this study had a homogeneous C57BL6 background (generated by backcrossing the original 129SvEv/C57BL6N mice), and a mixed C57BL6/DBA background, respectively. Fertility was evaluated by mating, total motility by CASA, tyrosine phosphorylation (pTyR) by Western blot, cAMP levels by RIA, intracellular Ca2+ levels by flow cytometry, and fertilizing ability by IVF. Results revealed that males from the new CRISP1 and CRISP4 KO colonies remained fertile but their sperm exhibited changes in several parameters compared to the original colonies. Differently from CRISP1 KO sperm from the mixed genetic background which had clearly
ABSTRACTS

96 EXPOSURE TO TERTIARY-BUTYL HYDROPEROXIDE (TBHP) - DOWN REGULATES THE EXPRESSION OF USP9Y IN MATURE MICE TESTIS

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(Presented By: Pegah Mokhtari, MA)

Introduction: Infertility is a major worldwide reproductive problem that affects approximately 15% of young couples. The male infertility is responsible for approximately 40% of these cases. Two major causative factors of male infertility are oxidative stress (OS) and genetic factors. Reactive Oxygen Species (ROS) can increase oxidative stress. Increase OS can be destructive effects on reproductive system functions such as Fragmentation of sperm DNA and alteration gene expression which involved in spermatogenesis. Us9y gene is one of the important azoospermia factor (AZF) genes in Y chromosome. AZF deletion causes a severe block in spermatogenesis which affects the proliferation of spermatogonia, and consequently male infertility. The expression profile of Us9y gene was evaluated in testis tissues of Balb/c mice after OS induction.

Materials and Methods: A model of oxidative stress in adult male Balb/c mice testis by injection of the 1:10 concentration of tertiary-butyl hydroperoxide (TBHP) was created. Case group included treated mice by TBHP for 2 weeks and control group treated only by injection of dH2O. Induced ROS levels in testes tissue samples of all mice were measured by flow-cytometry. Consequently the expression of Us9y gene was quantitatively measured in samples of both groups by real-time PCR.

Results: According to flow-cytometry results, an increase of OS in TBHP treated mice in comparison to control group was observed. The gene expression of Us9y in testis was significantly down regulated in OS-exposed and ROS induced mice (P < 0.01).

Conclusion: Our results indicated that Us9y may be a major target gene of OS and the down regulated expression of Us9y can be closely related to male reproductive toxicity induced by TBHP.

Key Words: Male infertility, Oxidative stress, TBHP, Us9y.

99 NOVEL COMPOUND HETEROZYGOUS DNAAF2 MUTATION CAUSE PRIMARY CILIARY DYSKINESIA IN A HAN CHINESE FAMILY

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(Presented By: Minghan Sun, MD, PHD)

Primary ciliary dyskinesia (PCD) [MIM 242650] is a genetically heterogeneous recessive disorder with an incidence of 1 in 20,000-60,000 live births and characterized by the combination of recurrent respiratory tract infections, sinusitis, bronchiectasis and male infertility. The DNAAF2 gene have been associated with Primary ciliary dyskinesia. This study was aimed to identify the DNAAF2 mutations responsible for autosomal recessive Primary ciliary dyskinesia (PCD) in a Han Chinese family. A three generation family from Sichuan Province of China was recruited in this study. The coding sequence of CBS was amplified by polymerase chain reaction (PCR), followed by direct DNA sequencing. All available members of the family underwent comprehensive medical examinations. Among all the family members, one affected individuals showed typical clinical features of PCD. Genomic DNA was collected from peripheral blood of all the participants. The Exome sequencing was performed on the proband of this family and direct Sanger sequencing on other family members and normal controls was followed to confirm the causal mutations. Two novel compound heterozygous mutations in the DNAAF2 gene, c.156C>A (p.Tyr52Ter) and c.26C>A (p.Ser9Ter), were identified by sequencing analysis in this family. Both of the two nonsense mutation were detected in the proband, but not present in other family members and 600 normal controls. Another two normal members in the family were found to carry this heterozygous mutation. This study provides a mutation spectrum of DNAAF2 resulting in PCD a Chinese population, which may shed light on the molecular pathogenesis and clinical diagnosis of DNAAF2-associated PCD.
A MULTIDISCIPLINARY MODEL OF EARLY FERTILITY PRESERVATION IN KLINEFELTER PATIENTS: DESCRIPTION AND UPDATE OF A PROGRAM
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¹Wake Forest Institute for Regenerative Medicine, Department of Urology; ²Wake Forest Institute for Regenerative Medicine; ³Section of Pediatric Endocrinology; ⁴Section of Medical Genetics; ⁵Department of Pathology; ⁶Center for Reproductive Medicine; ⁷Department of Radiology; ⁸Department of Urology

Introduction: Klinefelter Syndrome affects 1/500-1/1000 males and is the most common genetic disorder compromising male fertility. Previous studies of its physiopathology have shown a dramatic loss of germ cells including spermatogonial stem cells (SSC) following the onset of puberty.

Material and Methods: To establish a multidisciplinary referral program to offer clinical and experimental fertility preservation options to Klinefelter patients of all ages. Klinefelter patients diagnosed at any age including prenatal, infancy, prepubertal, adolescence and adult are referred by either pediatric endocrinologists or medical genetics consultants to a male reproductive medicine and surgery clinic. After initial consultation, each patient is enrolled in a long term follow up program to monitor his endocrine profile (Testosterone, FSH, LH, E2, Inhibin B and AMH), pubertal development (Tanner stage) and testicular structure to detect early fibrosis with Elastography and Ultrasound. At Tanner stage III or higher, a one step fertility intervention is offered, including semen collection (by penile vibration stimulation or electroejaculation), microsurgical testicular sperm extraction (micro TESE) and SSC cryopreservation. The extracted sperm is stored in a clinical setting for future IVF/ICSI and his testicular tissue containing SSCs is stored in our experimental autologous testicular tissue bank for possible future in vitro or in vivo spermatogenesis trials.

Result: From December 2014 to January 2016, 15 patients have been enrolled in this program. Two patients (11 & 13 years old; XXY and XXY respectively) met our criteria for intervention and went through electroejaculation and semen was collected successfully, however no sperm found in their semen. Micro TESE was performed immediately in both testes of each patient and no testicular sperm were found in either specimen by an embryologist presented in the operating room to evaluate the ejaculate and testicular biopsy samples. A biopsy from each testis was stored to preserve SSCs. Diagnostic pathology examination performed by a dedicated testicular pathologist confirmed the absence of testicular sperms at all specimens and presence of spermatogonia in fewer than 10% of tubules in both patients.

Conclusion: We have established an effective, comprehensive and safe multidisciplinary team program for potential early fertility preservation in Klinefelter boys.

YOGA AND MEDITATION PROMOTES QUALITY OF LIFE BY DECREASING DEPRESSION SEVERITY AND CELLULAR AGING IN MALE INFERTILITY: RANDOMIZED CONTROLLED TRIAL
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Introduction: Unhealthy modern lifestyle and environmental factors play a major role in infertility including idiopathic and unexplained infertility. Decreased quality of life, depression, and accelerated aging are associated with this group.

Objective: To evaluate the effect of yoga and meditation on quality of life, depression and cellular aging in infertile males.

Methods: Seventy-four males with infertility for more than 6 months were randomized into two groups: yoga (36): practicing Yoga and Meditation based lifestyle intervention (YMLI) in addition to routine expectant management for 12 weeks; control (36): routine expectant management only. All subjects were assessed both pre and post intervention using World Health Organization Quality of Life Scale (WHOQOL-BREF); Beck Depression Inventory-II scale (BDI-II); and assay kits for cellular aging biomarkers in peripheral blood. Cellular aging biomarkers included: 8-hydroxy 2'-deoxyguanosine (8-OHdG) for DNA damage; reactive oxygen species (ROS) and total antioxidant capacity (TAC) for oxidative stress; telomere length and telomerase activity for telomere attrition.

Results: Quality of life significantly improved while depression and cellular aging biomarkers significantly decreased in yoga
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A FRESH PERSPECTIVE ON AN OLD MODEL: SEGMENTALLY ORGANIZED HAIRPIN-LOOP CHROMOSOME CONFIGURATIONS WITHIN THE 3D SPERM NUCLEUS
Helen Tempest PhD and Dimitrios Ioannou PhD
Florida International University
(Presented By: Helen Ghislaine Tempest, PhD)

Introduction: Genomes are nonrandomly organized within nuclei. Sperm cells are proposed to have a unique hairpin-loop arrangement that has been hypothesized to be critical for the ordered exodus of the paternal genome following fertilization. Early studies suggest centromeres cluster in the nuclear center forming a chromocenter, with p- and q-chromosome arms stretching toward the nuclear periphery forming a hairpin-loop structure.

Objectives: This study examines whether evidence can be provided to support this model of chromatin organization in sperm using 3D modeling.

Materials and Methods: This study was approved by the local IRB, five normozoospermic males were recruited. Three color fluorescence in-situ hybridization targeted the centromere and p- and q-arms of eight different chromosomes (2, 3, 6, 8, 10, 12, 16, and 18). 3D modeling was employed. The radial organization of each probe was assessed by measuring the distance of the geometric center of each loci to the nearest nuclear periphery. Hairpin-loop configurations were determined by the angle created between p- and q-arms. A minimum of 30 cells per subject, per chromosome were studied. Nonrandom radial organization was established using Chi-squared goodness-of-fit test (p<0.05).

Results: Distinct reproducible chromosome-specific patterns of organization emerge. All chromosomes possessed nonrandom radial organization (p<0.05). Chromosome arms were found to form discrete hairpin-loop configurations. Three categories of hairpin-loops were observed: narrow (<40°: 2, 10, 12, 18), intermediate (>40°<60°: 3, 8), and wide (>60°: 6, 16). Six centromeres (2, 3, 6, 10, 12, 18) were more peripherally localized than their chromosome arms.

Conclusion: Reproducible nonrandom hairpin-loop organization of chromosomes in sperm was observed to support the previously proposed model. However, our findings suggest that this model needs to be redefined. We do not find evidence to support the existence of a centralized chromocenter with 75% of investigated centromeres being more proximal to the nuclear periphery than their respective chromosome arms. This suggests the sperm nucleus is more segmentally organized; resulting in specific genomic regions being exposed, remodeled and activated first following fertilization. The sequential exodus and remodeling of chromatin could impact patterns of gene activation observed within the early embryo, perturbations in which, could negatively impact fertilization and early embryogenesis.

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CHANGES IN SPERM BANKING RATES WITHIN THE FIRST SEVEN MONTHS OF A FORMAL MALE ONCOFERTILITY PROGRAM
Diana M Lopategui MD, Emad Ibrahim MD, Raphael Yechiel MD, Nancy Brackett MD and Ranjith Ramasamy MD
University of Miami
(Presented By: Diana Maria Lopategui, MD)

Introduction and Objectives: A male fertility preservation program can help address the reproductive needs of patients receiving oncologic treatments with risk of infertility. Our institution initiated a formal fertility preservation program in June of 2016. This study examined sperm banking rates within the first seven months of this program, versus sperm banking rates prior to this program, in men diagnosed with cancer.

Methods: A single institution, retrospective chart review was performed for men with newly diagnosed cancer. Rates of sperm banking were assessed from January 1, 2011 to May 30, 2016, prior to initiation of a fertility preservation program, and again from June 1 to December 31, 2016, after the implementation of a standardized program that included nursing and physician education directed at fertility preservation.

Results: Prior to the initiation of the program, 30 of 902 male oncologic patients underwent sperm banking prior to their treatment (3.3%). After the program was implemented, 21 of 102 male oncologic patients underwent fertility preservation (20.6%). In this group, patients’ mean age ± standard deviation (SD) was 25.9±6.9 years (range 14-62 years), with 2 pediatric patients. 17 of the samples (76.7%) were obtained by masturbation. When viable sperm could not be obtained from ejaculation, patients underwent either testicular or epididymal sperm extraction (4 cases).

Conclusions: The rate of sperm banking increased after institution of a formal fertility preservation program. This increase was seen within a relatively short period of time, i.e., within the first 7 months of the program’s existence. These results emphasize the clinical need for such a program at academic institutions. Oncofertility is a relevant part of the care for oncologic patients, and should be considered as part of counseling before cancer treatment.

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12 YEARS EXPERIENCE TRANSURETHRAL CATHETERIZATION OF THE EJACULATORY DUCTS FOR TREATMENT OF PROSTATIC OBSTRUCTIVE AZOOSPERMIA.
Oleksandr Knigavko MD, PhD, Volodymyr Lesovoy MD,PhD,DS, Andriy Arkatov MD,PhD and Mykola Panasovskyi MD,PhD
Kharkiv National Medical University
(Presented By: Oleksandr Volodymyrovych Knigavko, MD,PhD)
A frequent complication of chronic prostatovesiculitis is prostate fibrosis and obstruction of ejaculatory ducts (EjD). Clinically it is manifested obstructive azoospermia (OA) and male infertility.

**Materials and Methods:** For the treatment of recent (less than 1 year) obstruction EjD, we’ve developed and implemented a method of transurethral catheterization and balloon dilation of the ducts. In 2005-2016, on the base of andrological department of Kharkiv Regional Clinical Center of Urology and Nephrology117 patients with prostate fibrosis and obstructive azoospermia were undertaken of transurethral catheterization (TUC) and balloon dilatation of EjD on the background of antibacterial treatment of prostatitis. During urethrocystoscopy we found and catheterized the orifices of EjD by ureteral catheter 3 Ch. Then we performed balloon dilatation them by catheter Foggarti. After 2 and 12 weeks, then 6 months were carried out a survey and semen analysis.

**Results:** In 41 patients (35%) 2 weeks after TUC spermatozoa were found in semen. After 3 months the spermatozoa still detected in 47 (40.2%) another patients, general 88 patients with appearance of spermatozoa (75.2%). In 52 wives this patients (44/4%) diagnosed through a 1-4.5 year natural pregnancy.

**Conclusion:** Transurethral catheterization EjD is a new effective method for treatment of recent obstructive prostatic azoospermia (75.2%) patients with chronic prostatovesiculitis.

**ABSTRACTS**

### 106 OPEN EPIDIDYMAL SPERM ASPIRATION (OESA): RESULTS OF A TWELVE-YEAR EXPERIENCE

**Background and Aim:** Obstructive azoospermia accounts for 40% percent of all azoospermia cases and 2% of all infertility cases in the Western world. Several surgical procedures for the retrieval of spermatozoa exist. After some negative results with percutaneous epididymal sperm aspiration (PESA) in patients we on beforehand expected to have good results (e.g. proven fertile men after vasectomy), we decided to perform open epididymal sperm aspiration (OESA) at our facility. By government decree, testicular sperm retrieval was not allowed. Here, we report sperm retrieval rates (SRR) and reproductive outcomes of OESA in our hospital.

### 107 INFLUENCE OF 5A-REDUCTASE INHIBITOR (5-ARI) USAGE ON REPRODUCTIVE FUNCTION IN MEN OF MARRIED COUPLES

Seung-Hun Song MD, Dong Suk Kim MD, Sung Han Shim PhD and Jae Yup Hong MD
CHA Gangnam Medical Center
(Presented By: Seung-Hun Song, MD)

**Introduction:** Finasteride is a 5a–reductase inhibitor that blocks the conversion of testosterone (T) to dihydrotestosterone (DHT) and has been has been approved to treat androgenic alopecia. There have been concerns about the potential negative effects of this hormonal agent on male reproductive function. We investigated the effect of finasteride usage on the reproduction function in male partners of married couples.

**Materials and Methods:** We compared the reproductive function between those who takes finasteride more than 6 months and no medication group, who visited our andrology center for fertility evaluation. Each group consisted of 25 cases. In addition to basic fertility evaluation, semen and reproductive hormone data were compared between two groups. Semen samples were collected with abstinence period of more than 48 hours. Patients with varicocele, previous scrotal surgery, underlying medical disease were excluded.
**ABSTRACTS**

**Results:** The mean patient age was 36.8 years (range: 32–51 years). All of the study group was taking low-dose (1–1.25 mg) finasteride for androgenic alopecia. The mean duration of treatment with finasteride was 22.12 months (range: 6–84 months). There was no significant difference between two groups in regards to semen parameters. (sperm volume: 2.25 ± 1.31 vs 2.51 ± 0.89 ml, p = 0.43; sperm concentration: 105.73 ± 56.27 vs 84.52 ± 44.53, p = 0.15; sperm motility: 50.8 ± 11.96% vs 56.32 ± 10.29%, p = 0.09; sperm strict morphology: 7.04 ± 0.93% vs 7.44 ± 1.88%, p = 0.18, respectively). There was no significant difference in regards to serum reproductive hormonal level between groups. One patient complained of weak ejaculation and reduced semen volume while taking finasteride.

**Conclusions:** Our study suggests that low dose finasteride does not have a negative effect in regards to male reproductive function. However, further large scale investigation is warranted.

**108 TESTICULAR DAMAGE AND ALTERATION IN SEMINAL QUALITY BY CHANGES IN TESTICULAR MICROCIRCULATION IN SPONTANEOUSLY HYPERTENSIVE RATS.**

Lucas Giglio Colli BSc; PhD candidate¹, Larissa Belardin MSc², Stephen Fernandes de Paula Rodrigues PhD¹, Mariana Antoniassi MSc², Rhayza Andretta MSc², Ricardo Bertolla DVM; PhD² and Maria Helena Catelli de Carvalho PhD¹

¹Universidade de São Paulo - USP; ²Universidade Federal de São Paulo - UNIFESP (Presented By: Larissa Belardin, MSc)

**Introduction:** Microcirculation abnormalities are one of the key points that cause damage in target organs due to arterial hypertension (AH). In the testis, the microcirculation phenomenon denominated vasomotoricly (alternation between rapid or slow flow/without flow periods) plays an important role on the exchange of transvascular fluids and nutrients. Because this organ is poorly vascularized, which results in low O2 tension, any disturbance in its microvasculature may result in fertility alterations. With that in mind, in this study we aimed to identify the possible influences of AH in spontaneous hypertensive rats (SHR) testis, evaluating semen quality, testicular morphology and its microvasculature. Methods: 5 SHR and 5 controls (Wistar rats – WT with 24-26 weeks old (300-450 grams) were used. For morphological analysis and measure of blood flow in testicle arterioles (n° of flow stops/minutes – nPF) standard histological techniques and intravital microscopy were utilized. Sperm morphology, concentration, motility, acrosomal integrity (PNA-FITC in flow cytometer), DNA fragmentation (Comet assay), intracellular oxygen reactive species (ROS) (DHE) and mitochondrial activity (DAB) were assessed. Groups were compared using a Student’s T-test (α=5%). Results: Histological alterations in blood vessels and in the germinal epithelium of specific regions of the testis in SHR were observed. There was a decrease in sperm quality in SHR, demonstrated by decreased in mitochondrial activity, acrosome integrity, concentration and motility and an increase in intracellular ROS generation. No differences in basal arteriolar blood flow were observed between groups (WT: 6.7±2.06 x SHR: 6.4±0.97 nPF/min; however topic application of norepinephrine on the testis increased nPF only in SHR (SHR Basal: 7.3±0.57 x SHRne: 8.5±0.57 nPF/min, p=0.0025). Prazosin (α1 antagonist) application was capable of reverting the nPF value in SHRne at similar levels to WT (SHRpr: 4.7±1.5 x WT: 6.7±2.06 nPF/min).

**Conclusion:** Alterations in semen quality and in testicular morphology were observed in SHR rats, which may be associated to testicular blood flow alterations, mediated by norepinephrine action via α1 adrenergic receptors.

**Table 1. Seminal and functional analysis of sperm.**

<table>
<thead>
<tr>
<th></th>
<th>WT</th>
<th>SHR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperm concentration (x10⁶/mL)</td>
<td>19.42 (6.66)</td>
<td>10.75 (5.69)</td>
<td>0.638*</td>
</tr>
<tr>
<td>Motile sperm (%)</td>
<td>10.42 (3.39)</td>
<td>2.47 (3.71)</td>
<td>0.0196*</td>
</tr>
<tr>
<td>Morphology (%) normal</td>
<td>98.5 (1.28)</td>
<td>98.5 (1.28)</td>
<td>0.113</td>
</tr>
<tr>
<td>DHE positive (%)</td>
<td>0.5 (0.86)</td>
<td>5.4 (3.19)</td>
<td>0.0072*</td>
</tr>
<tr>
<td>PNA (intact) (%)</td>
<td>96.54 (1.22)</td>
<td>94.50 (1.98)</td>
<td>0.6564</td>
</tr>
<tr>
<td>PNA (non-intact)</td>
<td>97.60 (2.60)</td>
<td>97.20 (2.67)</td>
<td>0.0011*</td>
</tr>
<tr>
<td>DAB I (%)</td>
<td>97 (2.60)</td>
<td>97 (2.60)</td>
<td>0.004*</td>
</tr>
<tr>
<td>DAB II (%)</td>
<td>3.3 (1.26)</td>
<td>5.9 (2.16)</td>
<td>0.0610</td>
</tr>
<tr>
<td>DAB III (%)</td>
<td>1.1 (1.29)</td>
<td>5.1 (1.67)</td>
<td>0.0026*</td>
</tr>
<tr>
<td>DAB IV (%)</td>
<td>0.2 (0.24)</td>
<td>1.2 (0.83)</td>
<td>0.0462*</td>
</tr>
</tbody>
</table>

* – statistically significant difference.

**109 THE MALE CONTRACEPTION INITIATIVE’S STRATEGY FOR MALE CONTRACEPTIVE RESEARCH AND DEVELOPMENT**

David Sokal MD, Edward Eddy MS, PhD, Carol Sloan MS and Aaron Hamlin
Male Contraception Initiative (Presented By: Aaron Hamlin)

**Introduction:** The Male Contraception Initiative (MCI) is a 501(c)3 non-profit organization with two main goals: Publicize the need for a new, reliable, and reversible male contraceptive; and Support research on new male contraceptives through initiatives in the areas of policy, networking, and funding.

**Objectives:** Develop and implement a strategy to facilitate bringing a new male contraceptive to market.

**Methods:** Examining (a) the history of contraceptive development, (b) major constraints, and (c) major opportunities.

**Results:** Here are five strategic considerations, and how we plan to address them.

1-Commercialization: Big pharma is likely to shun commercialization of male contraceptives because of the potential liability from unanticipated adverse events among a healthy population. With help from others, we hope to engage small pharma companies in discussions about male contraception.

2-Myths and skepticism: The perception of low acceptability of male contraceptives may inhibit interest of pharma companies. Lack of knowledge limits the understanding of market potential. MCI’s upcoming consumer survey will provide representative
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on June 20, 2017, from https://www.journals.oup.com/andrology/

data to identify men’s contraceptive preferences and the
prevalence of unmet need among population segments to inform
estimates of market potential.

3-Regulatory guidance: This is a novel product category and
researchers and pharma need guidance. MCI plans to engage the
United States Food and Drug Administration in proactive
discussions.

4-Scientific breakthroughs: New knowledge and new
technologies present a major opportunity to develop contraceptive
approaches that affect sperm function and sperm transport, rather
than sperm production. MCI has issued a Request for Proposals to
fund such research and plans to award at least one multi-year grant
in 2017 of up to approximately $500,000.

5-Desired characteristics: Potential advantages of focusing on
sperm function and transport include: a. more rapid onset of
action and greater acceptability; b. greater specificity and fewer
side effects; c. lower risk of developmental concerns; and d. lower
risk of irreversible sterility. MCI’s support focuses on research
with these characteristics.

Conclusion: We have developed a strategy to support the
development of new, reliable, and reversible male contraceptives.
Implementing this strategy is a long-term effort. “The best time to
plant a tree was 20 years ago. The second-best time is now.”
Chinese Proverb

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SEARCH FOR NEW PREDICTIVE PARAMETERS OF
ASSISTED REPRODUCTION OUTCOMES THROUGH
ANALYSIS OF MALE GAMETE

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biologist, Fanfani Laura biologist², Benini Francesca biologist²,
Pellegrini Sandra MD², Maggi Mario MD, PhD³ and Baldi
Elisabetta PhD³

¹Department of Experimental and Clinical Biomedical Sciences;
²Department of Experimental and Clinical Biomedical Sciences
(Submitted By: Lara Tamburrino, PhD)

Introduction and Objectives: Infertility is a worldwide health
problem affecting about 15% of couples. A widely used treatment
option for couple infertility is assisted reproduction technique
(ART). Despite recent improvements, ART success is still low
and identification of predictive markers is one of the main goals
of current research. We evaluated sperm chromatin maturity
status and expression of CatSper, a sperm-specific calcium
channel involved in several sperm functions, as possible
predictors of ART outcomes.

Methods: 206 semen samples from male partners of couples
undergoing ART were included. Sperm chromatin status was
evaluated by determination of histones persistence (Aniline Blue
(AB) staining) and protamination degree (Chromomycin A3
(CMA3) staining). CatSper expression was determined by
immunofluorescence method coupled with flow cytometry. ART
outcomes considered were: Fertilization rate (FR), Embryo
quality (EQ) and pregnancy achievement.

Results: sperm percentage of AB and CMA3 positivity were
 correlated (r=0.5, p<0.0001, n=147). AB positive sperm were
negatively associated with FR (r=-0.2, p=0.004, n=163; β=-0.2,
p=0.01 after adjustment for female age and female factor). CMA3
positivity was significantly lower in couples with higher EQ
(median value: 12.0 [6.00÷31.00] in EQ ≥0.5, n=9 vs 23.0
[7.00÷69.00] in EQ<0.5, n=133, p=0.005). CatSper expression
was significantly higher in high quality embryos (median value:
5.3 [3.05÷11.10] in EQ≥0.5 n=16 vs 4.3 [2.00÷14.3] in EQ<0.5,
n=120, p=0.02). All results were confirmed in couples with
women ≤ 35 years (median age), where an association between
CatSper and achievement of pregnancy was revealed (median
value 5.2 [3.3÷11.1] in pregnant, n=20 vs 4.1 [2.0÷12.7] in non-
pregnant, n=44, p=0.02).

Conclusion: Despite the close association between the two
measures, AB and CMA3 are related to different ART outcomes
suggesting detection of different aspects of chromatin status.
These tests are low cost and rapid to perform, and could be easily
introduced in couple infertility work-up. This is the first study
evaluating the association between CatSper expression and ART
outcomes. Our data suggest a role of the channel in the
achievement of a good EQ. In the subgroup of younger women,
where the importance of male factor is unmasked, the association
between CatSper and EQ became stricter revealing also an
association with pregnancy achievement.

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STAT III STAIN CAN BE A COST EFFECTIVE
ALTERNATIVE TO DIFF-QUIK ANDROLOGY STAIN

Daniele Stawkey BSc, Dorina Dulaj MSc, Sule Dogan PhD,
Kamran Ullah MD, Michael Fakih MD, Nicholas Shamma MD,
Ahmad Hammoud MD, Jonathan Ayers MD and Iqbal Khan MD
IVF Michigan Fertility Center

(Presented By: Daniele Stawkey, BSc)

Objective: The purpose of this study was to evaluate sperm
morphology with Stat III andrology stain versus Diff-Quik
andrology stain.

Background: Sperm morphology is incorporated within the basic
semen analysis as it aids in determining quality of spermatozoa.
Previous studies have shown that abnormal sperm morphology
can cause infertility in males. Abnormal sperm morphology was
also shown to be associated with a lower sperm count and a lower
motility [1]. Therefore, evaluating sperm morphology with the
most effective method is critical to understanding male fertility. A
lot of different methods and stains have been used to evaluate
sperm morphology in routine semen analysis so far [2]. Diff
Quick and STAT III stains are based on Wright's and Wright's
Giemsas hematology stain, and especially Diff Quick has been
most commonly used morphology stain.

Materials and Methods: These two andrology stains were used to
assess sperm morphology in this study: Diff-Quik (Siemens
Healthcare Diagnostics Inc.) and Stat III (Origio- MidAtlantic
Devices, Inc). We randomly selected 42 males (n) with unknown
fertility during a three months period between June and August
2016. Basic semen analysis was performed, and sperm
morphology was recorded with both stains after splitting the
samples. Data were analyzed using one way ANOVA.

Results: The sperm parameters, including age, sperm
concentration (106/ml), progressive motility (%) sperm
morphology with Diff-Quik (%) and, sperm morphology with Stat
III (%) with the descriptive statistics of mean and standard error
were found 35±1.5, %51±9, %59±3, %4±1, and %4±1,
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respectively. According to our findings, two morphology stains were not statistically different from each other (p> 0.05).


112 VALIDATION OF TESTIS EXPRESSED 101 (TEX101) PROTEIN AS A POTENTIAL CAPTURE ANTIGEN IN LIVE SPERMATOZOA SORTING.

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1CREAte Fertility Centre; 2Department of Lab Medicine & Pathobiology, University of Toronto; 3Murray Koffler Urologic Wellness Centre, Mount Sinai Hospital, Toronto; 4CREAte Fertility Centre, Toronto

(Presented By: Junyan Zhang, MSc)

Introduction: TEX101 is a plasma membrane-associated protein specific to mouse and human testicular germ cells. In mouse, TEX101 is located on the plasma membrane of spermatocytes, round and elongated spermatids and testicular spermatozoa. Although TEX101 remains on the cell surfaces of later stage of spermatids, it is enzymatically processed and shed from most sperm in the caput epididymis. Knowledge is limited about TEX101 expression in human ejaculated spermatozoa. We have generated monoclonal antibodies that can detect the native form of TEX101 and aimed to validate this marker as a potential capture antigen to eliminate ejaculated spermatozoa with residual TEX101 in expectation to enrich samples for highest quality of mature spermatozoa.

Methods: Spermatozoa were obtained with written informed consent from waste material of patients undergoing semen analysis. Motile spermatozoa were isolated by density gradient centrifugation. We examined the expression pattern of TEX101 in normal human ejaculate sperm by immunofluorescent microscopy using two clones of anti-TEX101 monoclonal antibodies. TEX101+ and TEX101− fractions of sperm were separated using magnetic-activated cell sorting (MACS) and the sperm count, motility and morphology of each fraction was compared.

Results: TEX101 was detected in approximately 15-20% of human ejaculated spermatozoa by immunofluorescent microscopy. 90% of ejaculated sperm were recovered after MACS. In concordance with immunocytochemistry, approximately 20% of total spermatozoa were found in the TEX101 positive and 80% in the TEX101 negative fraction. TEX101 negative fraction showing greater normal morphology with higher progressive motility of 60% vs 15% in TEX101 positive fraction.

Conclusion: Our preliminary data support the use of TEX101 as a candidate capture antigen to design microfluidics-based strategies for mature sperm enrichment. The quality and maturity of TEX101 positive vs TEX101 negative spermatozoa will be characterized further with regards to viability, sperm DNA fragmentation and protamination/residual histone levels.

113 FERTILITY ATTITUDES AMONG MEN WITH KLINEFELTER SYNDROME

Sergio Lizama MD4, Swaytha Yalamanchi MD2 and Adrian Dobs MD, MHS3

1Department of Internal Medicine, St. Agnes Hospital; 2Division of Endocrinology, Diabetes, and Metabolism, Johns Hopkins University School of Medicine

(Presented By: Sergio A. Lizama, MD)

Introduction: Infertility is a well-recognized complication of Klinefelter syndrome (KS). However, numerous options for addressing this comorbidity exist. We hypothesize that men with KS are not uniformly counseled on fertility options despite an interest in reproductive potential.

Methods: We adapted a questionnaire used in an oncology population, to evaluate attitudes towards fertility among men with KS. We administered these surveys at the Association for X and Y Variations Syndrome (AXYS) conference in 2015. The survey included demographics, fertility history, attitudes about fertility, cryopreservation, and about testicular sperm extraction (TESE)/intracytoplasmic sperm injection (ICSI).

Results: Nine men (mean age 46 years) were included. No men had biologic children. Seven had previously been interested in having children. Six had discussed options to conceive; adoption was the most popular answer reported. Among these men, five considered adoption. Only one man chose to adopt children and 2 had children of partners in prior relationships. No men attempted sperm banking, TESE/ICSI, or in vitro fertilization (IVF). Eight were aware of infertility (6 were told by their healthcare provider; mean age 22 years). Three reported options for parenthood were never discussed. Five were counseled on adoption and 5 on TESE/IVF/ICSI. Three were offered cryopreservation and 3 had discussed the option of sperm donor. None of them reported attempting these options. Five men felt that their diagnosis of KS would make them better fathers. Two felt that KS limited their mate potential, with one man reporting that penis size/appearance had caused relationship problems. Two reported feeling more anxious about the health of their children due to KS, but none felt that their children were at increased risk of KS. Four reported that they wanted to have a biological child regardless of risk of KS. One reported that because of this fear, he preferred to use either donor sperm or adoption.

Conclusion: Our study demonstrated that the majority of men with KS have previously been interested in fathering children. Amongst men that are offered fertility options, men in our study did not pursue these opportunities. This may in part be related to perception of how KS affects role as fathers and the risk conferred to their children. A more nuanced understanding of
attitudes about fertility among men with KS will enable clinicians to better counsel patients about their options.

115 SEMINAL PLASMA PROTEOMIC MECHANISMS – ONE YEAR FOLLOW-UP AFTER VARICOCELECTOMY

Mariana Camargo PhD¹, Larissa Belardin MSc¹, Paula Intasqui MSc¹, Valdemir Carvalho PhD², Karina Cardozo PhD² and Ricardo Bertolla PhD¹

¹Sao Paulo Federal University; ²Fleury Group
(Presented By: Mariana Camargo, MSc, BSc)

**Objective:** We previously observed that at three months post-varicocelectomy the seminal plasma proteome demonstrates a shift back to homeostasis, with no difference in semen quality. Thus, we aimed to verify if 1-year follow-up of these patients demonstrates improved semen quality, and its relation with the proteomic profile.

**Methods:** Twenty-five men with varicocele provided one semen sample before (Pre) and another one year after (Post) bilateral subinguinal microsurgical varicocelectomy. An aliquot was used for semen analysis (WHO, 2010, evaluation of mitochondrial activity, DNA fragmentation, and acrosome integrity). For proteomic analysis, individual paired (Pre and Post) samples were submitted to mass spectrometry-based quantitation using dimethyl labelling. Post/Pre ratios were calculated and a one sample T-test analysis was performed. Functional enrichment analysis was performed by Cytoscape software. For semen analysis a paired Student’s T-test was performed (α=5%).

**Results:** Seminal results are presented in Table 1. Patients presented improved sperm total count, sperm morphology and mitochondrial activity, and increased ejaculate volume. In total, 698 proteins were found in this study, of which 62 proteins were under-represented, among which 4 different proteasome proteins (PSMD2, PSMA6, VCP, PSA1) were over-represented after varicocelectomy, among which proteins related to cell migration (FN1, SDCB1 and NRP1) and endopeptidase activity (SEMG1, SEMG2 and PLG).

**Conclusion:** Varicocelectomy leads to improved testicular function, demonstrated by increased semen volume and sperm morphology and mitochondrial activity, also demonstrated by proteomic analysis. Varicocelectomy decreases oxidative stress, which led to increased cell migration. Besides, phospholipases are essentials for sperm fertilization, and its inhibition was over-represented before the surgery.

**Support:** Sao Paulo Research Foundation (FAPESP) (Scholarship #2012/15039-7).

### Table 1. Semen and sperm functional analysis of pre and 1 year post-varicocelectomized men (data are mean, standard deviation).**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre group</th>
<th>Post group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (mL)</td>
<td>3.6 ± 1.3</td>
<td>3.9 ± 1.3</td>
<td>0.045</td>
</tr>
<tr>
<td>Progressive motility (%)</td>
<td>45.7 ± 14.8</td>
<td>40.1 ± 12.6</td>
<td>0.294</td>
</tr>
<tr>
<td>Sperm concentration (millions)</td>
<td>13.5 ± 23.5</td>
<td>16.8 ± 28.4</td>
<td>0.485</td>
</tr>
<tr>
<td>Sperm total count (million)</td>
<td>82.1 ± 25.1</td>
<td>87.4 ± 18.3</td>
<td>0.045</td>
</tr>
<tr>
<td>Sperm morphology (% normal)</td>
<td>2.1 ± 1.0</td>
<td>3.7 ± 1.9</td>
<td>0.045</td>
</tr>
<tr>
<td>Mitochondrial activity (% total)</td>
<td>7.1 ± 4.0</td>
<td>13.9 ± 2.3</td>
<td>0.015</td>
</tr>
<tr>
<td>DNA fragmentation (a.g.)</td>
<td>43.4 ± 22.4</td>
<td>32.0 ± 8.7</td>
<td>0.091</td>
</tr>
<tr>
<td>Acrosomal integrity (% normal)</td>
<td>75.5 ± 9.8</td>
<td>72.6 ± 10.5</td>
<td>0.021</td>
</tr>
</tbody>
</table>

*significant difference

116 ERYTHROPOIETIN AND A FEEDER CELL-FREE HYDROGEL-LAMININ SCAFFOLD PROMOTE THE EXPANSION AND MAINTENANCE OF HUMAN SPERMATOGONIAL STEM CELLS IN CULTURE

Sarayu Ratnam¹, Robert Brannigan² and Christopher Payne²

¹Ann & Robert H. Lurie Children's Hospital of Chicago; ²Northwestern University Feinberg School of Medicine
(Presented By: Christopher Payne, PhD)

Conditions that permit the long-term culture of mouse spermatogonial stem cells (SSCs) were established more than a decade ago. However, human (h)SSC cultures are not yet optimized. Most studies reporting hSSC propagation cite a maximum limit of 2-6 weeks. Maintenance of hSSCs declines over this period of time. Changes to current culture conditions are warranted in order to promote hSSC propagation in culture beyond 6 weeks. To address this compelling need, we focused on revising the culture medium and substrate used for hSSCs. A serum-free medium based on the Iscove Modified Dulbecco formulation (IMDM) with supplementation promotes mouse SSC expansion and maintenance favorably in our hands, but does not support the culture of hSSCs. Likewise, a substrate of pure laminin maintains mouse SSCs under feeder cell-free conditions, but does not support hSSC maintenance. Our two objectives of this study were to identify a novel scaffold-based substrate on which hSSCs could be supported without the need for feeder cells, and to determine whether supplementing IMDM culture medium with additional growth factor(s) would promote hSSC expansion and maintenance beyond 2-6 weeks. Donor hSSCs were obtained from adult human testis tissue. When hSSCs were grown on pure laminin in IMDM, very few survived at 2 months (<1 x 103 cells on day 60 versus 4.7 x 104 cells on day 0). In contrast, hSSCs grown on a hydrogel-laminin scaffold (HyStem-C) exhibited a modest expansion in number (9.2 x 104 cells on day 60 versus 4.5 x 104 cells on day 0). Previous studies revealed that erythropoietin (EPO) induced an expansion of undifferentiated spermatogonia in mammalian testes, and that the EPO receptor was expressed in germline-derived cells in vitro. We therefore supplemented IMDM culture medium with various concentrations of recombinant EPO. After 2 months in culture, hSSCs exposed to 1 ng/ml EPO exhibited significantly greater cell numbers (3.6 ± 0.7 x 105 cells on day 60 versus 5.5 ± 1.8 x 104 cells on day 0) than control hSSCs (8.1 ± 0.6 x 104 cells on day 60) versus 4.9 ± 1.1 x 104 cells on day 0). Previous studies revealed that erythropoietin (EPO) induced an expansion of undifferentiated spermatogonia in mammalian testes, and that the EPO receptor was expressed in germline-derived cells in vitro. We therefore supplemented IMDM culture medium with various concentrations of recombinant EPO. After 2 months in culture, hSSCs exposed to 1 ng/ml EPO exhibited significantly greater cell numbers (3.6 ± 0.7 x 105 cells on day 60 versus 5.5 ± 1.8 x 104 cells on day 0) than control hSSCs (8.1 ± 0.6 x 104 cells on day 60) versus 4.9 ± 1.1 x 104 cells on day 0). Immunocytochemistry and western blot analysis confirmed that the EPO receptor is present in cultured hSSCs. Quantitative RT-PCR analysis revealed that hSSC self-renewal gene expression was maintained during culture. We conclude that EPO and the HyStem-C-laminin scaffold together promote the expansion and maintenance of human spermatogonial stem cells in culture for at least 2 months.
EVALUATION OF DYNAMIC FcR EXPRESSION PATTERNS ON HUMAN SPERMATOZOA: A POTENTIAL NOVEL DIAGNOSTIC TEST AND METHOD FOR DETERMINING OPTIMAL TIMING FOR INTRAUTERINE INSEMINATION (IUI),

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1CReAtE Fertility Centre; 2Department of Medicine, University of Toronto; 3Department of Obstetrics & Gynaecology, University of Toronto; 4Arex Life Sciences LLC, Watertown, MA; 5Department of Obstetrics and Gynaecology, University of Toronto; 6Department of Gynaecology, Women’s College Hospital, Toronto, Canada

Introduction: Unexplained infertility accounts for approximately one-third of infertility cases. IUI is often utilized as a first line therapy for both unexplained and male factor infertility. Despite decades of clinical use, success rates for IUI remain relatively low. In addition, a weak correlation exists between sperm quality and IUI outcome. In livestock, FcR expression status has been shown to correlate with IUI success. The mechanism for this is thought to be the ability of spermatozoa to release FcRs, creating a decoy effect by binding potentially harmful antibodies in the female reproductive tract. The objective of this study was to correlate FcR expression kinetics in human ejaculates to IUI outcome.

Methods: Institutional REB approval was obtained. A fluorometric Kinetix assay™ was used to assess FcR expression in spermatozoa left over after clinical use from men attending the CReAtE Fertility Centre, Toronto, Canada, either at semen analysis or prior to IUI. Ejaculates (n= 40) were analyzed at 10 min intervals to assess shifts in sperm membrane FcR expression over a 2.5h time period. IUI samples (n=30) were analyzed following density gradient sperm isolation. Female factor infertility cases were excluded from the study. Those performing IUIs were blinded to FcR expression level at the time of IUI.

Results: 70 ejaculates were analyzed. The majority of samples (73%) displayed a normal FcR expression pattern with multiple peaks and valleys, while 27% of samples showed atypical FcR expression. Of 30 IUI cases, 6 became pregnant (26%), and one of these miscarried (16%). No patients with initially abnormal FcR expression achieved pregnancy. When retrospectively analyzed, 10 patients, by chance, had had their insemination timing during a FcR expression peak (which is less successful in livestock insemination), and 0/10 of these achieved pregnancy, while 10 had optimal IUI timing at a nadir of FcR release, and 60% of these achieved pregnancy (p<0.001).

Conclusion: This is the first translational study to link sperm FcR expression kinetics in humans to pregnancy outcome after IUI. While the sample size is still small, all pregnancies occurred within a +/-15-minute window of an FcR expression trough, consistent with animal data. Therefore, we hypothesize that IUI pregnancy outcome may be improved if the timing of IUI is coordinated with FcR status. In addition, FcR expression kinetics may also have diagnostic value in selecting patients suitable for IUI.

INTRODUCTION: AND OBJECTIVE: Varicoceles have been shown to affect testicular function through alterations in spermatogenesis and decrease in testosterone production. It is therefore not surprising that varicoceles are found in approximately 35-40% of infertile men. Men who are infertile and have a varicocele are found to have abnormal semen analysis parameters, increased percentage of sperm DNA fragmentation, and reactive oxygen species. Surgical correction of the varicocele may not always be sufficient to allow for natural conception; however, may improve success rates of alternative means of pregnancy such as in vitro fertilization (IVF). We evaluated different management options to allow for family building in the couple with azoospermic/severe oligozoospermic males with a varicocele using a cost effectiveness analysis model.

Methods: A model-based cost-utility analysis was performed estimating the mean cost and quality adjusted life years (QALYs) in all couples with infertility, male history of varicocele, and azoospermia/severe oligozoospermia over a 1 year time period. The model was constructed evaluating fertility outcomes utilizing IVF on 1 surgical model: varicocelectomy. Model QALY estimates were obtained from the literature: 0.56 for an infertile couple and 0.63 for an infertile couple who becomes pregnant. Average patient charges for varicocelectomy, testicular sperm extraction, and IVF were obtained. Success rate for IVF in a couple with oligozoospermia/azoospermia and male history of varicocele was obtained from the literature. TreeAge was utilized as the modeling software.

Results: The surgical option for the male resulted in 2 fertility strategies: varicocele repaired followed by IVF and IVF without varicocele repair. The table below lists the cost/QALY for the 2 different fertility strategies.

Conclusion: Varicocele repair has been shown to improve the success rate of IVF and is more cost effective in the severely oligozoospermic/azoospermic couple that requires IVF compared to the couple with a varicocele who does not have it repaired.
ABSTRACTS

120 SUSTAINED IMPROVEMENT OF ERECTILE AND VOIDING FUNCTION IN OBESE HYPOGONADAL MEN TREATED UP TO 8 YEARS WITH TESTOSTERONE THERAPY (TTH) WITH TESTOSTERONE UNDECANOATE INJECTIONS (TU) IN COMPARISON TO AN UNCONTROLLED GROUP

Farid Saad DVM, PhD, Ahmad Haider MD, PhD, Karim Haider, Gheorghe Doros PhD and Abdulmaged Traish PhD

Introduction and Objectives: Many obese men suffer from erectile and voiding dysfunction. We investigated effects of long-term TTh in obese hypogonadal men in a urological setting compared to an untreated hypogonadal control group.

Methods: Registry study in 656 men with testosterone ≤12.1 nmol/L and hypogonadal symptoms. 371 men (57%) with obesity, defined by BMI ≥30 kg/m2 were analysed. 248 received TU 1000 mg/12 weeks following an initial 6-week interval (T-group). 123 men opted against TTh and served as controls (CTRL). 8-year data are presented. Changes over time between groups were compared by a mixed effects model for repeated measures with a random effect for intercept and fixed effects for time, group and their interaction. Changes were adjusted for age, weight, waist circumference, blood pressure, fasting glucose, lipids and quality of life to account for baseline differences between groups.

Results: Mean age: 61.3±6.2 years. In the T-group, IIEF-EF (maximum score: 30) increased from 19.7±4.9 to 26.1±2.6. The improvement was statistically significant vs. previous year for the first 4 years. In CTRL, IIEF-EF declined from 19.9±3.6 to 11.8±1.9. Estimated adjusted difference between groups: 14.4 (p<0.0001 for all).

In the T-group, IPSS decreased from 7.5±3.9 to 2.1±1.0. The improvement was statistically significant vs. previous year for the first 7 years. In CTRL, IPSS increased from 4.7±1.9 to 6.6±2.3. Difference between groups: -4.8 (p<0.0001 for all).

In the T-group, men lost 20.0% weight and 10.6% waist circumference while CTRL patients gained 1.0% and 0.9%, resp. Adherence to testosterone was 100% as all injections were administered in the office and documented. No patient dropped out. In CTRL, there were 51 (41%) major adverse cardiovascular events (MACE): 14 MIs (11%), 19 strokes (15%), and 18 deaths (15%). There were no MACE in the T-group.

Conclusions: In obese hypogonadal men, TTh improves and preserves erectile and voiding function for a prolonged period of time. TTh improves weight and waist circumference and may reduce major adverse cardiovascular events and mortality.

121 SEXUAL ACTIVITY IN MEN IN NORTHERN REMOTE NON-INDUSTRIALIZED BRAZILIAN AMAZON IS HIGHLY MAINTAINED THROUGHOUT LIFESPAN EMPHASIZING THE ROLE OF GOOD HABITS, NATURAL NUTRITION AND AN UNPOLLUTED ENVIRONMENT IN SEXUAL HEALTH

Thiago ACC Teixeira MD, MSc, Maira TST Nazima MD, PhD, Jorge Hallak MD, PhD

Introduction: Amazon covers 67% of Brazil and is a cradle of biodiversity of fauna and flora, also where different ethnic groups have specific lifestyle and sexual habits.

Objective: To define the mean sexual quality of life of 18-69 y.o. men living in an non-industrialized and non-polluted city of northern remote Brazilian Amazon and to evaluate the influence of aging in their sexual function.

Methods: This cross-sectional quantitative probability sample study was performed in a demographically representative population (n=385) at Macapa (Amapa) with data collected privately by male researcher at participants’ houses, including Portuguese-speaker men who were sexually active for a minimum of 6 months. Foreigners were excluded. The city preserves a mixture of Indigenous/African cultures with urban habits were fish consumption and local typical fruits are highly appreciated. The Amazon River insulates it, so there are no roads to the more developed cities. Intact rainforest covers 90% of State territory.

To measure sexual satisfaction and function of different aspects of male sexuality, it was used a Brazilian-designed and validated questionnaire named Male Sexual Quotient (MSQ), which ranges on a 100-point scale with higher values indicating better sexual quality of life. Kruskal-Wallis test was performed to determine the central tendency measures and to verify the level of significance (P<0.05).

Results: Response rate was 81.69%. Mean age=36.0±12.95 years, with predominance of brown-skinned men (63.1%), self-employed workers (42.1%), monthly earned income of US$0 to 371.3 (46.7%) and singles (36.1%). Mean MSQ score=80.4±12.1 (Highly satisfied). Sexual quality of life is statistically significant when compared with age (P<0.01). In what concerns the sexual domains, desire (P<0.01), partner satisfaction (P=0.04) and erection quality (P<0.05) were statistically significant.

Conclusion: Regardless of age and the aging process, Amazonian men in this population have an excellent sexual quality of life, probably justified by environmental, socio-cultural and nutritional aspects. There is a strong association of sexual quality of life and aging, highlighting 3 domains: desire, partner satisfaction and erection quality.
ABSTRACTS

Variation of Male Sexual Quotient per Age

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10 YEARS USING MICROSURGICAL PENILE DENERVATION FOR TREATMENT SEVERE PREMATURE EJACULATION
Oleksandr Knigavko MD, PhD
Kharkiv National Medical University
(Presented By: Oleksandr Volodymyrovych Knigavko, MD, PhD)

Introduction: Premature ejaculation (PE) is a common problem for sexually active men. Traditionally for its treatment sexologists use Selective Serotonin Reuptake Inhibitors (SSRI) on-demand (dapoxetine) or long-term (sertraline, paroxetine, fluoxetine...). But in some cases these medicines are not effective or have some side effects. That is why we decide to investigate the effectiveness, safety and long-term results of microsurgical denervation of penis glans - selective neurotomy (SNT).

Methods: During 2007-2016 years on the base of andrological department of KRCCUN 649 patients with PE were examined and treated. For this part of investigation we picked out 146 patients with severe (Intravaginal Ejaculation Latency Time (IELT) less than 60 sec) primary PE without neurological factors (anxiety, depression, etc.). All patients in this group have positive lidocaine test (increasing IVLT more than 1.5 time after using condoms or sprays with lidocaine or articaine). Most of these patients were unsatisfied with previous treatment with SSRI (insufficient increasing of IVLT or side effects of medicines). These patients were undertaken microsurgical denervation of penis glans using microscope with 10 time enlargement. After circumcision we cut 50-80% branches of penile nerve in Bach fascia (more often 6 from 9 branches). Three weeks patients restart their sexual intercourses. We investigate sensiveness of penis glans, IELT and sexual satisfaction throw 1 and 6 months after surgery.

Results: The average IELT these patients before SNT consisted 47.4+4.3 sec. All patients feel reduce of sensitive penis glans throw one month (by their sexual feeling and by results of biothesometry) after surgery. 143 from 146 patients (96.5%) were satisfied with iELT and their sexual life. Average IELT after surgery was 6 min 51 sec+ 33 sec.

Conclusion: Selective neurotomy is safe, profitable and high effective method of treatment of PE and may prove to be a last resort for traditional treatment when patients have severe side effects, pharmacological ineffectiveness and want more permanent solution for premature ejaculation.

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MINIMALLY INVASIVE SURGICAL TREATMENT OF VENO-OCCCLUSIVE FORM OF ERECTILE DYSFUNCTION.
Said Kaziiev PhD student¹ and Oleksandr Knigavko PhD, A professor²
¹Kharkiv National Medical University, Department of Urology, Nephrology and Andrology; ²Kharkiv National Medical University
(Presented By: Said Kaziiev, PhD student)

Introduction: ED veno-occlusive form is more likely to occur in men, young or middle age. When patients have distal venous leakage through deep dorsal veins and Santorini plexus, sclerotherapy of deep veins by R.Hervig shows good results. Unfortunately there are not officially registered sclerosant in Ukraine. That is why for stop pathological blood flow we use embolization with metallic spiral. But if the patients have proximal venous leak we suggest better effectiveness of treatment by ligation of the pathologic shunts.

Materials and Methods: On the basis of the Kharkiv Regional Clinical Center of Urology and Nephrology n.a. V.I. Shapoval, a comprehensive examination and treatment of 76 patients suffering from ED, veno-occlusive form and bilateral varicocele was conducted. The average patient age of 38.5 +4.4 years. This form of ED is diagnosed by medical history and by Doppler mode ultrasound of the scrotum and penis. The patients with proximal venous leak were underwent surgical treatment: bilateral operation of "Marmar" with ligation of the veins (pathological shunts) coming from the penis to the spermatic cord and vena dorsal penis. Before the operation we injected 10 mg of alprostadil and 1 ml of papaverine into the penis for enlargement and better searching of the pathological shunts.

Results: The efficacy of surgical treatment of the subjective (questionnaires on IIEF) - 85.2%, the objective –in the absence of venous shunt on Doppler US -94%.
Conclusions: 1) Bilateral varicocele in young men with erectile problems is a marker and one of the reasons of veno-occlusive form of ED.
2) Modified (with ligation of the dorsal and communicating veins) duplex operation of Marmara is a highly effective (85-95%) method of treatment for patients with proximal venous leak.
3) Angiosurgery with embolisation of the deep pelvic vein is a satisfactory method (68%) for treatment of ED in patients with distal venous leak.

124 INVESTIGATING THE ROLE OF THE CAENORHABDITIS ELEGANS GENE M05D6.2, AN ORTHOLOG OF HUMAN T-COMPLEX PROTEIN 11 (TCP11), IN SPERM FUNCTION AND FERTILITY
Emily Lopes and Matthew Marcello PhD
Pace University
(Presented By: Emily Lopes)

Human t-complex protein 11 (TCP11) is a testis-specific gene product that is hypothesized to be necessary for proper sperm capacitation, acrosome reaction, and sperm morphology. M05D6.2 is the Caenorhabditis elegans ortholog for human TCP11. C. elegans have two sexes: hermaphrodite and male. Sperm from hermaphrodites and males must undergo proper sperm activation, which includes processes similar to sperm capacitation and acrosome reaction in mammals, to migrate to and fertilize the egg. We have used RNA interference (RNAi) to disrupt the gene function of M05D6.2 in C. elegans. Hermaphrodites subject to M05D6.2 RNAi-treatment show no reduction in fertility. However, when male C. elegans are subject to M05D6.2 RNAi-treatment our preliminary results indicate that they have a significant decrease in fertility. We also investigated hermaphrodites with single nucleotide polymorphisms (SNPs) at conserved nucleotides in M05D6.2 and found that these animals did not have the same number of progeny as controls. Currently, we are investigating potential defects in spermatogenesis in animals lacking function M05D6.2. Our goal is to understand the conserved biological function of TCP11.

125 COMPREHENSIVE PELVIC FLOOR PHYSICAL THERAPY FOR MEN WITH IDIOPATHIC CHRONIC PELVIC PAIN SYNDROME: A PROSPECTIVE STUDY
Thomas Masterson MD¹ and Ranjith Ramasamy MD²
¹University of Miami; ²University of Miami Miller School of Medicine
(Presented By: Thomas Masterson, III, MD)

Introduction: Male Chronic Pelvic Pain Syndrome (CPPS) is a heterogeneous constellation of symptoms that causes significant impairment and is challenging to treat. A multimodal treatment approach achieves the best outcomes. Previously published studies have shown benefit when incorporating pelvic floor physical therapy (PFPT) into treatment algorithms for CPPS. In this prospective study, we evaluated men with CPPS who underwent comprehensive PFPT. We used the previously validated modified NIH-Chronic Prostatitis Symptom Index (NIH-CPSI) to measure outcomes.

Methods: 14 men who underwent PFPT for idiopathic CPPS from October 2015 to October 2016 were identified. Men with clearly identifiable causes of pelvic pain, such as previous surgery, chronic infection, trauma, prostatitis and epididymitis were excluded. Patients were evaluated by two physical therapists trained in PFPT. Treatment included: manual therapy of pelvic floor and abdominal musculature; pelvic floor exercises; patient education; biofeedback to facilitate strengthening and relaxation of pelvic floor; therapeutic ultrasound and electrical stimulation for pelvic floor muscle for strengthening/relaxation and pain relief. Patients’ progress was evaluated with the modified National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) administered at initial evaluation, every subsequent 10th visit, and discharge. Higher scores reflect worse symptoms. Previous validation of the modified NIH-CPSI calculated a reduction of 7 points to predict robust response (sensitivity 100%, specificity 76%) and a 4 point change to predict modest response. Data are presented as medians (ranges).

Results: 10 patients completed 10 visits. Four patients completed between 5 and 9 visits. Baseline Modified NIH-CPSI scores at initial evaluation had a median of 30.8 (range 16-39). Tenth visit scores had a median of 22.2 (range of 7-37). Five patients (50%) in the study had a reduction of greater than 7 points, and two (20%) had a change of greater than 4. Three patients (30%) did not have any meaningful change. Treatment duration appears to correlate with treatment response.

Conclusion: Male CPPS is difficult to treat and often requires a multimodal approach. Based on the results of our study, PFPT may be an effective treatment option for select patients. A larger study with a control group is needed to validate the routine use of PFPT in men with CPPS and predict characteristics of men who would respond to therapy.
Conclusion: Oxidative Stress (OS) impacting the male reproductive tract is the leading cause of poor semen parameters as well as DNA damage in spermatozoa. Men with high levels of OS may be subfertile or infertile, expose their female partners to higher risk of miscarriage, and pass on de novo genetic and epigenetic changes to their offspring potentially compromising the health of future generations. To combat OS, a number of natural antioxidant ingredients have found widespread use in the management of male infertility but often without sufficient scientific or clinical evidence. Naturally synthesized by all animals, Coenzyme CoQ10 (CoQ10) is a critical component to the mitochondrial electron transport chain. The bioenergetic and antioxidant role of this molecule suggest possible involvement in sperm biochemistry and therefore the male fertility potential. However, the beneficial use of exogenous CoQ10 supplementation in the management of male infertility remains controversial. This review focuses on the latest evidence from human clinical trials but also closely examines the evidence from biochemical studies documenting the importance of CoQ10 molecule to male reproductive health.

Objective: To evaluate if oral supplementation with CoQ10 improves semen parameters and male fertility potential.

Materials & Methods: A systematic and detailed review of the scientific literature including analysis of human clinical trials, in vitro/vivo studies and a stringent set of medicinal and pharmacological criteria were used to critically examine the role of CoQ10 in the management of male infertility.

Main Results: To date, 15 low-medium grade clinical trials have been performed. Only three trials were randomized, placebo-controlled, double-blind studies but only one reports minor improvement in sperm motility with no rise in pregnancy or live-birth rates. Additionally, the oral intake of CoQ10 is allied with a rise in mitochondrial concentration of α-tocopherol (common form of Vitamin E). Interestingly, as an antioxidant, CoQ10 only has 1/10th the reactivity of α-tocopherol with much poorer oral bioavailability.

Conclusion: The evidence supporting the use of CoQ10 in male infertility is inadequate, but its oral intake appears to augment mitochondrial α-tocopherol content.
128 THE ROLE OF SUBCLINICAL GENITOURINARY INFECTIONS IN MALE INFERTILITY
Juliana R Pariz BSc, MSc, PhD1,2,3,4, Rosa Alice C Monteiro BSc1,4 and Jorge Hallak MD, PhD1,2,3,4
1Androscience – High Complexity Clinical and Research Andrology Laboratory, Brazil; 2Dept. of Urology, USP, Brazil; 3Reproductive Toxicology Unit, Dept. of Pathology, USP, Brazil; 4Oswaldo Cruz German Hospital, Brazil (Presented By: Juliana Risso Pariz, BSc, MSc)

Introduction: Genitourinary tract infections are the most common disease affecting male reproductive health, frequently do not have clear symptoms, therefore are not properly investigated neither diagnosed nor treated. Bacteria, protozoa and yeasts may interact directly with spermatozoa, resulting in sperm agglutination, motility and morphological alterations to sperm.

Objective: To determine genitourinary infections frequency in asymptomatic patients in as part of a routine andrological evaluation.

Methods: 981 tests were performed in patients evaluated between 2012 and 2016 who presented with any alteration on anamnesis and/or physical examination: pain in the external genitalia, symptoms of urethritis, burning sensation in the perineum, urethral discharge, pain, etc. After initial evaluation, a prostatic massage followed by microbiological analysis on urethral secretion (collected by swab), urine (medium–jet urine) and semen (collected by masturbation). Were used Student’s T test for statistical analysis and adopted p<0.05.

Results: Twenty-one percent (239/981 samples) had some microorganism both semen, secretion, urine. Of these, 6.28% (15/239) reported testicular pain and 43.52% (104/239) had a clinical sign on physical exam that could be associated with any kind of infection. When diagnosed during clinical evaluation, epididymitis was suspected in 24.26% patients (10.46% epididymitis only, prostatitis in combination with epididymitis 11.29%, and 2.51% orchiepididymitis). In addition, 10.46% had urethritis, 5.02% prostatitis and 3.76% orchitis. Enterococcus ssp, E. coli, Staphylococcus ssp and Klebsiella ssp. were the most frequent microorganisms. Antibiograms revealed that only 58% of the available antibiotics in the market were effective against these infections.

Conclusion: Male genitourinary tract infections should be a concern by the andrologists when seeking for a diagnosis and correct treatment for male infertility. Often difficult to diagnosis due to the lack of a readily available and well equipped andrology laboratory. Much higher incidence of epididymitis, support the hypothesis that the epididymis is a physiological barrier against testicular infections. Appropriate antibiotic treatment should be given before investigating every other possible cause of infertility, since the presence of infections impact negatively on seminal quality.

Financial Support: Androscience
Ethics Committee Approval: FMUSP n°859215/2014

129 CASE REPORT AND REVIEW OF THE LITERATURE: BILATERAL TESTICULAR DIFFUSE LARGE B-CELL LYMPHOMA
Janeske Vonkeman BSc1 and Gavin Langille MD FRCS2
1MD Candidate, Dalhousie University; 2Assistant professor, Dalhousie University, Dept. of Urology (Presented By: Janeske Vonkeman BSc)

Introduction: We report a 61-year old male with a painful left testicular swelling failing to respond to oral antibiotics who was referred in for assessment. Additional symptoms included fevers, chills, and night sweats. Scrotal ultrasound showed multiple bilateral hypoechoigenous testicular lesions, more prominent in the left testicle. Staged orchectomy revealed bilateral testicular diffuse large B-cell lymphoma. The patient received testosterone therapy to prevent hypogonadal symptoms. Chemotherapy with six cycles of R-CHOP and three cycles of high-dose Methotrexate was initiated, and the patient remains free of disease at 1 year of follow-up.

Methods: Consent was obtained from the patient for case report. For the literature review, Pubmed queries were designed to retrieve reports on bilateral testicular diffuse large B-cell lymphoma.

Results: Fifteen case reports of bilateral testicular diffuse large B-cell lymphoma were identified. The average age at the time of diagnosis was 64 years. Testicular swelling and palpable mass were most frequent presenting complaints. Orchitectomy was used for definitive pathologic diagnosis. Chemotherapeutic treatment regimens among the reported cases were variable.

Conclusion: This case report and review of the literature serves to describe the presentation and treatment modalities for bilateral testicular diffuse large B-cell lymphoma, an uncommon cause of testicular enlargement. It is important for clinicians to include this as a differential diagnosis when approaching testicular masses. When performing orchitectomy, surgeons must remember to send such samples to the pathologist without fixation to facilitate the diagnosis of lymphoma.

130 EFFECT OF MUCUNA PRURIENS (LINN.) ON SPERM DAMAGE INDUCED BY HYPERCHOLESTEROLEMIA: AN EXPERIMENTAL STUDY USING WISTAR ALBINO RAT
Prakash Seppan PhD1, Anuradha Murgesh PhD1, Ibrahim Muhammed PhD1, Karthik Ganesh Mohanraj PhD2, Ganesh Lakshmanan MSc1, Dinesh Premavathy MSc1, Sakthi Jothi Mathu MSc1 and Khayinmi Wungpam MSc1
1University of Madras; 2Saveetha University (Presented By: Seppan Prakash, MSc, PhD)

Introduction: Hypercholesterolemia has detrimental effect on normal physiological. The present study was intended to analysis the nature of reproductive damage inflicted during intake of fat diet and evaluate the therapeutic effect of the Mucuna pruriens (M.pruiriens), a leguminous plant identified for its properties like aphrodisiac and improving fertility, including androgenic and anticholesterol properties.

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Objective: The objective of this study was to evaluate the therapeutic potential of the Mucuna pruriens on hypercholesterolic induced reproductive disorder in Wistar albino rat.

Methods: Grouping: Control, hypercholesterolemia induced rat (feeding with high fat diet), hypercholesterolemia +M.pruniens and Control+M.pruniens (ethanolic extract of the seed at dose of 200 mg/kg b.w for 60 days). Epididymal sperm were collected and following analyses were done; motility, morphology and morphometry, chromatin integrity, Biochemical estimation of enzymatic and non-enzymatic antioxidants, Reactive Oxygen Species (ROS), Lipid Peroxidation, chromosomal integrity by fluorescent staining and mitochondrial membrane potential were estimated using the fluorescent cationic dye rhodamine 123.

Results and Conclusion: Hypercholesterolemia animal sperm showed reduced motility, increased sperm abnormalities including amorphous, microcephalic, acephalic, increase cytoplasmic remnant, loss of chromosomal integrity and increase in mitochondrial membrane permeability when compare to control animal sperm. Increased ROS levels indicated by decreased antioxidants defense system. High ROS level increases the mitochondrial membrane permeability; this in turn affects the respiratory chain, by diminish ATP production. The inability of the sperm cell or the epididymal cell to overcome the excessive ROS insult produced by the abnormal sperm or/and abnormal function of epididymal cells, thence leading to increase in the levels of LPO, DNA/chromosomal integrity in the hypercholesterolemic animals Thus, motility in hypercholesterolemic rat sperm was reduced due to altered axoneme phosphorylation. These observation shows that, free radical mediated damage along with poor anti-oxidant defense system in sperm would substantially contribute related pathophysiological changes. These pathologies were remarkably reduced or recovered in M.pruniens treated hypercholesterolemic rats. No pathology or toxicity was seen in control +M.pruniens.

131 THE EFFECT OF SEMINAL PLASMA AND POTENTIATORS OF DNA DAMAGE ON STALLION EPIDIDYMAL SPERM
Rosanna Serafini DVM, PhD, Dickson Varner, Terry Blanchard, Sheila Teague and Charles Love
Department of Large Animal Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, Texas, USA
(Presented By: Rosanna Serafini, DVM)

Introduction: Freezing and thawing can induce oxidative stress in sperm DNA. Ejaculated sperm are exposed to seminal plasma, which may influence sperm susceptibility to oxidative stress.

Objective: This study examined effects of direct and indirect (enzymatic) potentiators of oxidative DNA damage on fresh (FR) and frozen-thawed (FT) epididymal sperm +/- prior exposure to seminal plasma.

Methods: DNA injury was measured by detecting the percentage of 8-hydroxy, 2’deoxyguanosine-positive sperm (%8OHdG; Gibb et al., 2014). Sperm were obtained from the cauda epididymis of 12 stallions. Recovered sperm were exposed or unexposed to seminal plasma for 15 min. Sperm were processed as FR or FT specimens, and subjected to the following treatments: 1) control (FR sperm with no exposure to seminal plasma or potentiators; Tx1); 2) FeSO4 (10 µM) and H2O2 (20 µM); Tx2; or 3) DNAse I (200 U/mL) and MgCl2 (5 µM); Tx3, for 1 h at 37 °C. All samples were then treated with dithiothreitol (DTT, 2 mM) for 30 min at 37 °C, fixed in 2% (w/v) paraformaldehyde and stored at 4 °C for 24 h prior to analysis by flow cytometry. Data were subjected to an ANOVA procedure.

Results: For sperm with no seminal plasma, %8OHdG was higher for Tx2 in FR (23%) and FT (55%), as compared to Tx1 (5%), but higher in Tx2 for FT than FR (P<0.05). %8OHdG was similar for Tx1 (5%) and Tx3 in FR (15%) and FT (18%; P>0.05). For sperm with seminal plasma, %8OHdG was higher (P<0.05) for Tx2 in FR (19%) or FT (27%), as compared to Tx1 (5%), but similar between FR and FT for Tx2 (P>0.05). %8OHdG was similar between Tx1 (5%) and Tx3 (17%) for FR (P<0.05), but was higher for Tx3 (22%) in FT than Tx1 (P<0.05). Overall, %8OHdG was higher (P<0.05) in Tx2 for FT with no seminal plasma (55%) than in all other treatment groups (range 5-27%).

Conclusion: %8OHdG was most highly affected by direct oxidation (FeSO4+H2O2) in frozen-thawed sperm not exposed to seminal plasma. The seminal plasma protected sperm from direct oxidative (FeSO4+H2O2), but not enzymatic, stressors. This effect may be due to the presence of iron-binding proteins (i.e., lactoferrin and transferrin) present in equine seminal plasma. Response to oxidative potentiators was similar between treatments FR and FT for sperm exposed to seminal plasma, a condition which simulates ejaculated semen. As such, frozen-thawed semen may be used to measure this form of oxidative injury in clinical ejaculates.

132 HOW CAN PSYCHOSOCIAL STRESS IMPACT ON NATURAL MALE FERTILITY? AN HYPOTHESIS EMERGED FROM OUR CLINICAL PRACTISE
Julia Irene Ariagno Bioq¹, Gabriela Ruth Mendeluk PhD¹, Herberto Repetto Biochemist, Specialist in Andrology¹, Dario Jacobsen Biochemist, Specialist in Endocrinology², Diego Gonzalez Biochemist, Specialist in Endocrinology², Martin Repetto PhD², Gabriela Berg PhD² and Bibiana Fabre PhD²
¹Laboratory of Male Fertility, Hospital de Clínicas “José de San Martín”, Faculty of Pharmacia and Biochemistry, University of Buenos Aires, Bs. As., Argentina.; ²Clinical Biochemistry Department, INFIBIOC, Faculty of Pharmacia and Biochemistry, University of Buenos Aires, Bs. As., Argentina.
(Presented By: Julia Irene Irene Ariagno, Sr., Professor)

Psychosocial stress is an increasing worldwide health problem. Several researches have shown that individuals with fertility problems experience psychosocial problems (Aflakseir and Zarei, 2013). The question of whether stress contributes to conception delay is a controversial issue that has received much attention in recent years. What remains unclear is the role that stress, defined as a physiological or psychological response to a positive or negative external stimulus, may play in reproductive function, in part due to an inability to separate cause and effect. Physiological compensatory linkages have been elucidated between the hypothalamic pituitary adrenal (HPA) axis and the hypothalamic pituitary gonadal axis (Chrousos, Torpy & Gold, 1998)).
ABSTRACTS

While considering male natural fertility, sperm motility plays a crucial role. A new tool has been introduced in the Andrology Laboratory, the computer-assisted sperm analysis (CASA) systems. It allows assessing the motility of individual spermatozoa, generating huge datasets. The aim of our work was to characterize sperm motility of a paradigmatic case of psychosocial stress by the employment of a CASA System. Our purpose was to highlight one probable effect of psychosocial stress on male natural fertility. The design arises from our clinical practice, where we could identify a paradigmatic case of secondary infertility due to psychosocial stress. While the patient (37 years old) revealed a flat profile of saliva cortisol, no other changes in his hormone profile were observed. Serum cortisol was 31.9 µg/ml (Reference Value: 5.25-25 µg/ml). He showed a particular type of sperm motility characterized as having high energy but low progressiveness. His sperm kinetic (SCA-Microoptic) could be contrasted to a group of proven fertility (n: 19). In terms of sperm kinetic, he was in the 5th percentile for rapid progressive sperm and in the 90th percentile for amplitude of lateral head displacement, achieving the 75th percentile for the beat cross frequency (BCF). In a group of infertile patients (n: 79) a significant correlation was found between the absolute seminal value of cortisol (µg/ejaculate) and BCF (r: 0.242; p: 0.038). According to our results we can hypothesize that psychosocial stress may cause a particular type of asthenozoospermia, the most frequent feature in Clinical Andrology Laboratory, with direct impact on natural fertility.

Introduction:
In the last ten years DNA fragmentation (DNA-f) is becoming the gold standard in spermatozoa nuclear evaluation however standardization is still needed. Sperm are highly specialized cells with DNA specifically programed and condensed to be released during the fertilization process. The events required for DNA condensation expose the genetic material to possible damage. Our study suggests that DNA-f and age are strongly correleated. We believe the decreasing levels of testosterone in older patients affect the DNA packaging process due to lack of stimulation on nuclear testosterone receptors. Advanced age may increase the rate of abnormalities in the anatomic structure involving spermatogenesis. We found an association between DNA-f and age however we need a larger population to evaluate the impact of age on nuclear development and to understand the pathophysiology behind these abnormalities.

Conclusions: Our study suggests that DNA-f and age are strongly correlated. We believe the decreasing levels of testosterone in older patients affect the DNA packaging process due to lack of stimulation on nuclear testosterone receptors. Advanced age may increase the rate of abnormalities in the anatomic structure involving spermatogenesis. We found an association between DNA-f and age however we need a larger population to evaluate the impact of age on nuclear development and to understand the pathophysiology behind these abnormalities.

133 DNA FRAGMENTATION, A NUCLEAR EVALUATION FOR SPERM PRODUCTION DROUGHT DURING LIFE YEARS.
Héctor Salvador Godoy Morales MD1, Karina Cázarez Pérez MD1, José Alfonso Gutiérrez Frusch MD2, Paola Berenice Merchand Álvarez MD2, Ricardo Mera Mejía Biology2 and José Manuel Lozano Sánchez MD2

Methods: Semen samples where obtained by masturbation. Samples were analyze using WHO 2010 parameters and a commercial COMET assay was used to evaluate DNA fragmentation following manufacturer’s instructions. Statistical analysis was done using JMP 12; normalization of population using Shapiro-Wilk and Spearman correlation (p<0.05) was used to determine significance.

Results: 347 samples were studied with a non-normal distribution. Median age was 38 years (22-58); median DNA-f was 27%(19-36%). There was a positive Spearman correlation between age and DNA-f 0.219 (p=0.001). Figure 1

Fig 1. Scatter graph array

134 EFFECTS OF A MICRONUTRIENT SUPPLEMENTATION COMBINED WITH A PHOSPHODIESTERASE TYPE 5 INHIBITOR ON SPERM QUANTITATIVE, QUALITATIVE, AND FUNCTIONAL PARAMETERS: A RANDOMIZED, CONTROLLED TRIAL

Fotios Dimitriadis Ast Professor1, Panagiota Tsounapi Ast Professor2, Masashi Honda Ast Professor3, Athanasios Zachariou MD3, Sotirios Skouros MD3, Katsuya Hikita MD2, Irene Matthiaiu MD3, Gergji Semini MD1, Charalampos Mamoulakis Ast Professor1, Apostolos Kaponis Ast Professor3, Georgios Antonakis Ass Professor5, Nikolaos Sofikitis Professor1 and Atsushi Takenaka Professor2

Methods: One hundred thirty two oligoasthenospermic men were treated daily for an experimental period (EP) of 90 days with either an MISP (45 men, group A, experimental group), L-carnitine (44 men, group B, positive control group), MISP plus avanafil (43 men, group C, experimental group); a further group of 42 men with oligoasthenospermia (group D, negative control group) received no treatment.

Introduction and Objectives: The objective of the current study was to evaluate the effects of a micronutrient supplementation (MISP) combined with avanafil on sperm function.

Methods: One hundred thirty two oligoasthenospermic men were treated daily for an experimental period (EP) of 90 days with either an MISP (45 men, group A, experimental group), L-carnitine (44 men, group B, positive control group), MISP plus avanafil (43 men, group C, experimental group); a further group of 42 men with oligoasthenospermia (group D, negative control group) received no treatment.
ABSTRACTS

The present study was initially scheduled to include 174 idiopathic oligoasthenospermic men. When each patient was recruited they were randomly assigned to one of the four above-mentioned groups.

Sperm quantitative, qualitative, and functional (outcome of the hypooosmotic swelling test and the percentage of hyperactivated spermatozoa after incubation under conditions known to induce sperm capacitation) parameters were evaluated before the treatment and after the end of treatment in each group A, B, or C, respectively. The same sperm parameters were measured in each participant of group D before and after the 90-day EP. Hypooosmotic swelling test (HOST) and sperm hyperactivation assay were performed as previously described (Andrologia 1997; 29:303). A probability P smaller than 0.05 was considered to be statistically significant. Wilcoxon test for paired observations was employed for statistical analysis.

**Results:** Within group A and within group C, the percentage of motile spermatozoa (%MS), the HOST-result, and the percentage of hyperactivated spermatozoa (%HS) were significantly greater after MISP or MISP plus avanafil treatment than before each of the two respective treatments. Furthermore, within group B and within group D, differences in the %MS, HOST-outcome, and %HS, between the beginning of the EP and the end the EP were not significant.

**Conclusions:** We suggest that MISP or MISP plus avanafil - combined administration improves sperm membrane permeability with an overall result improvement in sperm motility, outcome of HOST, and an increase in the %HS.

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**EVALUATION OF AN IN-HOME SEMEN TESTING SYSTEM BY COUPLES PARTICIPATING IN AN INTERNET-BASED PRECONCEPTION STUDY**

Greg Sommer PhD¹, Tiffany Trinidad BS¹, Ulrich Schaff PhDD, Michael Eisenberg MD², Amelia Wesselink MPH³, Elizabeth Hatch PhD³ and Lauren Wise ScD³

¹Sandstone Diagnostics; ²Stanford University School of Medicine; ³Boston University School of Public Health

(Presented By: Greg Sommer, PhD)

**Objective:** To evaluate the utility of the Trak Male Fertility Testing System – a new FDA-cleared device for in-home semen parameter measurements – to gather individual semen data from men participating in the Boston University Pregnancy Study Online (PRESTO) study of couples trying to conceive in the general population.

**Methods:** PRESTO couples with less than 3 months of pregnancy attempt time were invited to participate in the Trak sub-study. Consenting participants were mailed a Trak Engine and two test kits (consumables for home measurement of sperm concentration and semen volume). Users self-reported and uploaded smartphone images of their test results via an online questionnaire. Data were correlated to subject responses from the baseline PRESTO questionnaire.

**Results:** During 4 months of recruitment, 45 of 82 (55%) men invited to the sub-study agreed to participate. 36 men (82%) successfully uploaded their 1st set of semen results and completed the usability survey, with 96% reporting they believed the results were accurate. Mean device “ease of use” score was 1.29 on a Likert scale (1=very easy, 5=difficult). A total of 27 men uploaded both sets of results (i.e., completed study) and received a $20 e-gift card. The distribution of semen parameters was as expected for a population-based cohort of men aged 24-40 (semen volume: median=3.0, interquartile range (IQR): 2.5-4.2; sperm concentration: median=60.0, IQR: 26.5-90.0; total sperm count: median=157.5, IQR: 71.3-330.0). 6 men (17%) reported abnormal concentration or volume results (< 15 M/mL or < 1.5 mL) further emphasizing utility of early testing. Table 1 shows mean values for selected semen parameters reported using Trak according to selected lifestyle, anthropometric, socioeconomic, and medical history variables. These data provide early evidence that the semen results are consistent with findings from the literature for several health and lifestyle variables and that a geographically diverse group of men from the general population will participate in semen studies.

**Conclusion:** The Trak System provides a convenient, reliable, easy-to-use, and cost-effective means to measure semen parameters for epidemiological research by allowing men to test at home.

**Table 1. Differences in mean semen parameters by selected characteristics, PRESTO / Trak pilot study.**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (SD)</th>
<th>Median (Q1,Q3)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at baseline, years</td>
<td>30.8 (5.7)</td>
<td>30.4 (29.0, 32.2)</td>
<td></td>
</tr>
<tr>
<td>Abstinence, days</td>
<td>10.5 (7.9)</td>
<td>10.4 (9.0, 13.0)</td>
<td></td>
</tr>
<tr>
<td>Less than college education vs.</td>
<td>1.05 (1.3)</td>
<td>1.10 (1.0, 1.3)</td>
<td></td>
</tr>
<tr>
<td>White vs. Non-Hispanic, Other</td>
<td>0.79 (0.28)</td>
<td>0.77 (0.17, 0.77)</td>
<td></td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td>0.29 (0.09)</td>
<td>0.30 (0.07, 0.32)</td>
<td></td>
</tr>
<tr>
<td>BMI 23-29 vs. BMI &gt;30 kg/m²</td>
<td>0.99 (0.68)</td>
<td>1.00 (0.96, 1.02)</td>
<td></td>
</tr>
<tr>
<td>Tobacco use vs. non-smoker</td>
<td>0.66 (0.26)</td>
<td>0.67 (0.44, 0.90)</td>
<td></td>
</tr>
<tr>
<td>Vigorous physical activity</td>
<td>0.07 (0.34)</td>
<td>0.12 (0.05, 0.19)</td>
<td></td>
</tr>
<tr>
<td>Prevalence Score (100-0)</td>
<td>0.02 (0.10)</td>
<td>0.02 (0.00, 0.05)</td>
<td></td>
</tr>
<tr>
<td>Major Depression Inventory (MED)</td>
<td>0.13 (0.36)</td>
<td>0.17 (0.07, 0.31)</td>
<td></td>
</tr>
<tr>
<td>Job hours worked per week</td>
<td>0.56 (0.47)</td>
<td>0.83 (0.51, 1.15)</td>
<td></td>
</tr>
<tr>
<td>Lifting use on leg/hours/week</td>
<td>0.10 (0.35)</td>
<td>0.56 (0.10, 0.57)</td>
<td></td>
</tr>
<tr>
<td>Waist to hip ratio (w:h)</td>
<td>0.35 (0.41)</td>
<td>0.40 (0.32, 0.51)</td>
<td></td>
</tr>
<tr>
<td>Sperm concentration</td>
<td>60.0 (26.5)</td>
<td>62.5 (30.0, 90.0)</td>
<td></td>
</tr>
<tr>
<td>Total sperm count (10⁶/mL)</td>
<td>157.5 (71.3)</td>
<td>157.5 (71.3, 330.0)</td>
<td></td>
</tr>
</tbody>
</table>


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**LOCALIZATION PATTERNS OF THE GANGLIOSIDE GM1 IDENTIFY SPERM CAPABLE OF UNDERGOING CAPACITATION AND ACROSOME EXOCYTOSIS**

Alexander J. Travis VMD, PhD², Cristina Cardona PhD², Melissa A. Moody MS¹, Alana J. Simpson BS², Romeo Mendoza BS² and Charles G. Ostermeier PhD²

¹Cornell University, NY; ²Androvia LifeSciences, NY (Presented By: Alexander J. Travis, VMD, PhD)

**Introduction:** Sperm must first capacitate and then undergo acrosome exocytosis (AE) to fertilize. Localization patterns of GM1 change in response to capacitation stimuli (Cap-Score™) and track strongly with human clinical fertility. This indirect evidence supported the notion that individual human sperm showing “capacitated” GM1 patterns represent capacitated sperm. Here, we examined directly if “capacitated” GM1 patterns represent cells that are capacitated and can undergo AE.

**Methods:** 10 semen samples were collected from fertile men (pregnant partner or recent father). Samples were liquefied, washed, and aliquots incubated under non-capacitating (NC) and capacitating (CAP) conditions. For 7 of these samples, a CAP+calcium ionophore A23187 treatment was used to induce AE. Cells were then attached to slides and dual labeled with PNA, a lectin that binds specific carbohydrate residues associated with...
**ABSTRACTS**

The sperm flagellum is essential for sperm motility during their journey through the female reproductive tract. In addition, once near the egg, sperm experience a dramatic change in their motility called hyperactivation that involves a highly asymmetrical movement of the tail and high amplitude bending of the head. The similar cylindrical appearance between axons and the sperm tail, together with the scarce information about actin organization in sperm, sparked our interest in studying the structure of the actin cytoskeleton in the sperm flagellum. In the present work, we used STORM super resolution microscopy to investigate actin structures in the sperm tail. We found that mouse sperm flagellum possesses a compartmentalized actin cytoskeleton different in the midpiece that in the principal piece. While in the mid-piece polymerized actin forms a double-helix that accompanies mitochondria, actin in the principal piece forms short bundles radially distributed from the axoneme to the plasma membrane. Actin-binding proteins spectrin and adducin are also found in these structures.

**138 IMPROVEMENT OF SEMEN ANALYSIS QUALITY - SLOWLY MOVING FORWARD?**
Lars Björndahl MD PhD, Rebecka Holmberg PhD, Biomedical Scientist, Ulrik Kvist MD, PhD, John Flanagan PhD and Stefan Arver MD, PhD
ANOVA, Karolinska University Hospital and Karolinska Institutet
(Presented By: Lars Björndahl, MD, PhD)

**Introduction:** The reliability and usefulness of human semen analysis results has been in focus for at least 80 years. Both laboratory techniques and the possibility to compare results from different laboratories is in general still not satisfactory. WHO provides a basis for acceptable laboratory investigations of men with reproductive problems as well as for scientific studies using semen analysis results.

**Objectives:** The aim of this presentation is to highlight reasonable development aiming at improved quality in basic semen analysis.

**Methods:** A systematic evaluation of the scientific basis of some important aspects of semen analysis has been done in a WHO project to develop recommendations for the investigation of the infertile couple. We have also collected data on resources available for andrology laboratories to train and maintain competence. We have also observed the level of competence expressed in manuscripts reviewed for publication in different scientific journals.

**Results:** It is possible to get reliable data for the choice of continued investigations by one proper semen analysis. Using multiple parameters for the interpretation of semen analysis results gives useful predictive measures both for spontaneous and assisted conceptions. Training courses and programmes exist in several regions, although the compliance with science based recommendations vary. This is also the matter concerning schemes for external quality assessment.

Despite a long history of awareness of quality problems in semen analysis, concomitant with recommendations of adequate laboratory techniques, many laboratories still don’t comply with...
**ABSTRACTS**

acceptable standards. Another aspect is that in manuscripts submitted for publication, and sometimes also in published articles, the scientific level in the laboratory work is insufficient.

**Conclusion:** A probable common cause for the present situation is that the WHO manuals are not formal ISO standards, meaning that accreditation bodies cannot examine the compliance with the WHO recommendations. Therefore, both the clinical management of men in infertile couples and the scientific development of andrology would benefit if science based ISO standards for human semen analysis were developed. Another step forward that the development of andrology would benefit from is if scientific journals could adopt reviewing instruments that will raise the standards of published studies, e.g. by true compliance with WHO standards.

**139 PRSS50: A SERINE PROTEASE REQUIRED FOR PROPER SPERM FLAGELLUM ASSEMBLY**

Carolina Jorgez PhD

Baylor College of Medicine

(Presented By: Carolina Jorgez, PhD)

Technologies, used in clinical genetics laboratories to identify mutations and copy number variations (CNV) for many types of genomic disease, are not routinely used to diagnose infertile men. Thus, except for Y chromosome microdeletions, karyotype anomalies and CFTR mutations, genetic causes of male infertility are rarely defined. Twenty infertile men were evaluated by array comparative genomic hybridization (aCGH) to identify CNVs and a 58Kb microdeletion at chromosome 3p21.31 was identified in 4 men. Validation and analysis by qPCR of 203 infertile men identified 32 infertile men with this microdeletion (9 of whom have a homozygous deletion) and 7 with a microduplication. None of the 241 controls tested have a homozygous deletion. This homozygous deletion was unique to infertile men and significant when compared to fertile controls (p=0.001). This intergenic region is flanked on the 5' site with the genes PRSS50, PRSS46 and PRSS45 and on the 3' site with the gene PRSS42. Of the 4 PRSS genes, the only gene highly expressed in germ cells is PRSS50. In the mouse, Prss50 expression begins at postnatal day 14 in spermatocytes with the first wave of spermatogenesis and expression continues through adulthood. In the sperm Prss50 immunoreactivity was restricted to the midpiece. As in mouse, human express PRSS50 in the spermatocytes and in the sperm midpiece. Prss50-KO mice were generated with CRISPR/Cas9 genome editing. Prss50-KO male mice were subfertile with a lengthened pregnancy time and smaller litter sizes (p<0.05). Prss50 deficiency in mice had no apparent effect on testicular germ cell development, although increased numbers of residual bodies were present in the seminiferous tubules. Prss50-KO sperm have reduced fertilizing ability due to a significant decrease in motility. The phenotype worsens with aging. Prss50-KO sperm display several tail defects ranging from two-headed sperm conjoined by a single tail and sperm with multiple tails or midpieces. Mitotracker (labeling mitochondria in the midpiece) and ΔGtubulin (labeling the entire flagellum) demonstrated gaps in the principal piece and abnormal mitochondria localization in Prrs50-KO sperm. These defects were also observed at the ultrastructural level. Sperm showed a heterogeneous mixture of flagellar abnormalities involving the mitochondria and the microtubules. These results indicated that Prss50 is involved in spermiogenesis and flagellum structure and function.

**140 SLO3 K+ CHANNEL PH AND CA2+ SENSITIVITY ALTERED IN A NATURAL VARIANT**

Yanyan Gang PhD¹, Juan Ferreira BS², Victor Dzikunu BS³, Alice Butler MS⁴, Pascale Lybaert PhD⁵, Pen Yuan PhD⁶, Karl Magleby PhD⁷, Lawrence Salkoff PhD⁷ and Celia Santi MD PhD⁸

¹University of Miami. Dept. of Physiology & Biophysics; ²Washington University. Dept. of Obstetrics and Gynecology; ³Washington University. Dept. of Neurosciences; ⁴Washington University School of Medicine. Dept of Obstetrics and Gynecology; ⁵Washington University. Dept of Cell Biology; ⁶University of Miami. Dept of Physiology and Biophysics; ⁷Washington University. Dept. of Obstetrics & Gynecology

(Presented By: Celia Santi, MD, PhD)

Sperm-specific pH-sensitive SLO3 channels are responsible for membrane potential changes in mouse sperm critical for fertilization. However, in human sperm, the major K+ conductance is Ca2+ sensitive as well as pH-sensitive. It’s been debated whether Ca2+ sensitive SLO1 channels substitute for hSLO3 in human sperm, or whether human SLO3 channels have acquired Ca2+ sensitivity. Here we show that hSlo3 is rapidly evolving, and reveal a natural structural variant with enhanced Ca2+ and pH sensitivities. This variant allele (C382R) alters an amino acid side chain at a principal interface between the intramembrane gated pore and the cytoplasmic gating ring of the channel. Since the gating ring contains sensors to intracellular factors such as pH and Ca2+, the effectiveness of transduction between the gating ring and the pore domain appears to be enhanced. It is not yet known whether C382R affects sperm fertilization capacity.

**141 CLAUDIN FAMILY EXPRESSION IN TESTIS; A DYNAMIC MEMBRANE BEHAVIOR FOR SPERM FORMATION IN PATIENTS WITH INFERTILITY**

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(Presented By: Alejandro Sandoval Travesi, MD)

**Introduction:** Human spermatogenesis is regulated through paracrine and endocrine activity, cell interaction with Sertoli promotes spermatogenesis. These cell–cell signaling promotes the modification and expression of different type of proteins. That includes the Claudins family whose involved with sperm and Sertoli cells connections. The goal of this study is to demonstrate the presence and its localization of the Claudins family (1,3,4 and 6) at human testicle biopsies obtained by TESE.
ABSTRACTS

Objectives: Demonstrate the presence of Claudin family at TESE in human samples of infertile couples. Determine the location of expression and its correlation with pathology diagnosis.

Methods: Testicular biopsies were obtained by TESE, with previous diagnosis of azoospermia, genetic causes were excluded. Claudin family expression was evaluated by immunohistochemistry. Evaluation the expression divided the sample in two groups (with germ cells and without germ cells) to evaluate Claudin family expression at stroma and tubules conducted by pathology evaluation.

Results: We studied twenty testes biopsies of couples with infertility in TESE; They were divided in two groups: group 1: 7 patients with azoospermia and group 2: 13 with presence of spermatogenesis, immunohistochemically analysis of the biopsies was performed with monoclonal and polyclonal antibodies reactive to claudins 1,3,4 and 6. The results showed that claudin 1 express nuclear at Sertoli cells, and in positive in sperm cell at group 2. Claudin 3 positive nuclear mark at Sertoli cells and germ cells.(Fig 1) Claudin 4 expression at the basal membrane with Sertoli cells.Claudin 6 were negative mark. At azoospermia group, they were Claudin 3 negative mark the rest Claudin family expression were the same, independently the level of the arrest at germ cell.

Conclusions: The claudin family is positive express at human testes. The interaction with Sertoli cells involve claudin 3 and 4. But also indicates that sperm have its personal claudin for interaction with Sertoli cells Claudin 1, claudin 6 negative mark at this experiment. Tight junctions indicate that sperm membrane modifies during its maturation improving sperm quality as a messenger for nuclear development.

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GONADOTROPIN REGULATION OF RETINOIC ACID ACTIVITY IN THE TESTIS
Seyedmehdi Nourashrafeddin, Batool Hosseini Rashidi and Tony M. Plant
(Presented By: SeyedMehdi Nourashrafeddin)

Spermatogenesis initiates at puberty in primates by an increase in gonadotropins, FSH and LH. Before puberty the testis contains only undifferentiated germ cells. However, spermatogonial differentiation and spermatogenesis can be initiated prior to puberty after stimulation with exogenous LH and FSH. Retinoic acid (RA) signaling is considered to be a major component that drives spermatogonial differentiation. We were interested in evaluating the relative role of LH and FSH, either alone or in combination, in regulating the retinoic acid signaling in monkey testes. Sixteen juvenile male rhesus monkeys (Macaca mulatta) were infused with intermittent recombinant single chain human LH (schLH) or recombinant human FSH (rhFSH) or a combination of both for 11 days. We analyzed the expression of the several putative RA signaling pathway related genes; i.e. RDH10, RDH11, ALDH1A1, ALDH1A2, CYP26B1, CRABP1, CRABP2, STRA6, STRA8 in the testis after 11 days of stimulation with vehicle, LH, FSH and combination LH/FSH using qPCR. The qPCR results analysis showed that administration of the gonadotropins affected a significant change in expression of some RA signaling related genes in the monkey testis. These findings are the first evidence that the activity of retinoic acid signaling in the monkey testis might be regulated through gonadotropins (LH/FSH) levels.

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SUMOYLATION MAY REGULATE TRANSCRIPTION AND PHOSPHORYLATION EVENTS IN MOUSE SPERMATOCYTES, AND IS REQUIRED FOR G2/M MEIOTIC TRANSITION IN VITRO.
Margarita Vigodner PhD¹, Benjamin Lucas PhD² and Elana Molcho BSc²
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(Presented By: Margarita Vigodner, PhD)

Introduction: Identification of SUMO targets in purified mouse spermatocytes by our laboratory has provided initial insights into the functional importance of sumoylation during male meiosis in mice. The identified proteins are involved in the regulation of transcription, stress response, microRNA biogenesis, cell cycle control, DNA breaks, and other processes. Notably, the largest identified group was of proteins regulating transcription, including those important for spermatogenesis. Interestingly, some kinases have also been identified by our screen as SUMO targets. This finding is consistent with growing evidence that phosphorylation and sumoylation interact at multiple levels.

Methods and Results: Our preliminary data in purified mouse spermatocytes demonstrate that the inhibition of sumoylation arrests the G2/M1 transition in mouse spermatocytes. In the control culture, treatment with Okadaic acid (OA, an inhibitor of the serine/threonine protein phosphatases PP1 and PP2A) induced condensation of chromosomes accompanied by massive H3Ser10 phosphorylation and full disassembly of the SC. In contrast, the addition of GA prevented chromosome condensation and disassembling of the SC. Similar to the results in somatic cells, inhibition of sumoylation significantly affected the global pattern of tyrosine phosphorylation. The timing of the meiotic arrest was similar to the one observed upon inhibition of tyrosine phosphorylation. It must be noted that, similar to sumoylation, the role of tyrosine phosphorylation in meiotic prophase and G2/M transition is not well understood. Global changes in serine/threonine (Ser/Thr) phosphorylation were less prominent,
probably due to the poor quality of the antibodies. Therefore, we used specific antibodies against either activating (PLK1, AUR, ERK, AKT) or inhibitory (CDC) phosphorylation on several Ser/Thr kinases implicated in the regulation of meiosis as well as kinase assays for some of them. Our results revealed that the activity of PLK1 and Aurora kinases were negatively regulated by inhibition of sumoylation during OA-induced G2/M1 meiotic transition, while the activity of ERKs and AKT were not affected or increased.

Conclusions: Both AURB and PLK1 are being "at the right time and at the right place" to at least, in part, explain the meiotic arrest obtained in the spermatocyte culture. AURB is responsible for phosphorylation of H3 on Ser10 and PLK1 is responsible for the disassembly of the SC.

ABSTRACTS

144 CRISPR/CAS9-MEDIATED TSPO GENE MUTATIONS LEAD TO REDUCED MITOCHONDRIAL MEMBRANE POTENTIAL (ΔΨM) AND STEROID FORMATION IN MA-10 MOUSE LEYDIG TUMOR CELLS

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The rate-determining step in steroidogenesis is the conversion of cholesterol to pregnenolone by the mitochondrial CYP11A1. This reaction is dependent upon delivery of cholesterol from intracellular stores into mitochondria. A wealth of evidence implicates the mitochondrial Translocator Protein (TSPO), a high affinity cholesterol binding protein, as a mediator in this process. However, recent studies of genetic deletion of Tspos in mice have provided conflicting data on the role of TSPO in steroidogenesis. Moreover, conflicting data have been generated in MA-10 mouse Leydig cells; knocking down TSPO expression using antisense oligonucleotides was shown to reduce the ability of the cells to form steroids, whereas CRISPR/Cas9-guided Tspos deletion was reported to have no effect on steroid synthesis.

We re-assessed the role of TSPO in steroidogenesis by introducing Tspos-specific mutations in MA-10 cells using CRISPR/Cas9. Experiments were performed using wild-type (WT) vs. Tspos-mutated cells (nG1); and a MA-10 sub-cell line Mito-H cells (generated by introducing reduction-oxidation sensitive green fluorescent protein roGFP) vs. cells with TSPO deficiency (G2G). Cells carrying a Tspos deletion (nG1 and G2G) were obtained via FACS of cells transfected with two guide RNAs designed specifically to target the exon2 of Tspos gene. The loss of TSPO was confirmed by gene-specific RT-PCR, immunoblot analysis, confocal live cell imaging and immuofluorescence staining. Cells with TSPO deficiency produced significantly lower progesterone than the corresponding WT cells; one failed to produce steroids in response to dbcAMP treatment and the other showed a 50% reduced response to dbcAMP. These changes correlated with disturbed neutral lipid homeostasis. The mitochondrial membrane potential (ΔΨm) of cells with Tspos mutations was significantly reduced. Steroidogenic acute regulatory (STAR) protein levels were induced in Tspos-mutated cells prior to and independently of dbcAMP simulation, suggesting an effort by the cells to compensate for the lack of TSPO or abnormal STAR mitochondrial import. Considering that ΔΨm is required for cAMP-stimulated steroidogenesis, these results (i) provide additional, strong evidence for a role of TSPO in mitochondrial steroid biosynthesis, and (ii) suggest that TSPO or a TSPO-associated partner involved in ΔΨm regulation is necessary for STAR action and import in steroidogenesis. (Supported by CIHR grants MOP-125983 and FRN-148659, and a CRC).

146 CHARACTERIZATION OF THE COOPERATION BETWEEN THE NUCLEAR RECEPTORS COUP-TFII AND SF1 IN LEYDIG CELL GENE EXPRESSION

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CHU de Quebec Research Centre - Laval University

The insulin-like 3 (INSL3) hormone produced by fetal and adult Leydig cells regulates testicular descent and bone metabolism. Despite these important roles, little remains known about the mechanisms regulating Insl3 expression in Leydig cells. Previous work has revealed that most regulatory elements are located within the proximal Insl3 promoter region, which contains several binding sites for nuclear receptors. Not surprisingly, most transcription factors known to regulate Insl3 transcription in Leydig cells are nuclear receptors and include steroidogenic factor 1 (SF1, NR5A1), NUR77 (NR4A1) and chicken ovalbumin upstream promoter-transcription factor 2 (COUP-TFII, NR2F2). As for other genes, Leydig cell-specific Insl3 expression is believed to be the result of cooperation between transcription factors. Consistent with this, we recently identified a functional cooperation between COUP-TFII and SF1 in Insl3 promoter activation in MA-10 Leydig cells. The goal of the present study was to further characterize the SF1/COUP-TFII cooperation. We first determined the binding site requirement for the cooperation using various Insl3 reporters either wild-type or harboring mutations in the COUP-TFII and/or SF1 elements. In MA-10 Leydig cells COUP-TFII (6-fold) and SF1 (4-fold) individually activated the wild-type mouse Insl3 promoter, and a cooperation of 15-fold was observed when both factors were combined. The SF1/COUP-TFII cooperation was lost only when both the COUP-TFII and SF1 elements were inactivated. Similar results were obtained in heterologous CV-1 fibroblast cells. These data indicate that at least one intact element (SF1 or COUP-TFII) is required and sufficient for the SF1/COUP-TFII cooperation. The requirement of only one functional element can be explained by the fact that COUP-TFII and SF1 physically interact as revealed by co-immunoprecipitation assays. We next tested whether this cooperation was also observed with nuclear receptors related to COUP-TFII and to SF1 or if it is specific to these two nuclear receptors. SF1 was found to also cooperate with COUP-TFII (NR2F1) on the Insl3 promoter. However, the SF1-related nuclear receptors LRH-1 (NR5A2) and NUR77 (NR4A1) did not cooperate with COUP-TFII. In conclusion, our results provide a
better understanding of the cooperation between COUP-TFII and SF1 in the regulation of Insl3 expression, a unique marker of Leydig cells and an informative clinical parameter of gonadal function. Supported by CIHR.

147 EFFECT OF EARLY TYPE 2 DIABETES ON MALE FERTILITY.
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(Presented By: Jannette Dufour, PhD)

Diabetes is a major epidemic with the number of affected individuals increasing at unprecedented rates. In the United States, it is the 7th leading cause of death affecting 9.3% of the population. Type 2 diabetes (T2D), which traditionally appeared in individuals over 40, is now emerging in young adults. For instance, in Ohio and Arkansas, African-American children with T2D represent up to 70-75% of new pediatric diabetes cases. In males, diabetes is associated with infertility, low testosterone levels and altered testicular morphology. Since T2D is now affecting more people who are still within their reproductive years, it is important to learn if T2D in its early stages reduces an individual’s ability to reproduce. Thus, we hypothesized that high blood glucose levels would affect cellular morphology and testosterone levels in the testis in an early type 2 diabetes mouse model. Male C57BL/6J mice were categorized into low fat diet (LFD) or high fat diet (HFD) groups. Mice in LFD or HFD were fed a diet containing 10 or 65% energy from fat, respectively, for 14 weeks. To determine impaired glucose tolerance and insulin resistance, intra peritoneal glucose tolerance and intra peritoneal insulin tolerance tests were performed, respectively. At the end of the study, body weight was measured and blood was collected. Testes and pancreas were collected for protein extraction and immunostaining. ELISA was performed to measure testicular and serum testosterone levels. Body weight was significantly higher in HFD mice compared to LFD. Additionally, HFD mice had impaired glucose tolerance and insulin resistance. In the Pancreas, total cellular insulin and islet cell morphology were not affected by the HFD, indicating an early diabetes model. Analysis of the testis tissue revealed that tubule diameter and Sertoli cells and Leydig cells were not different between LFD and HFD groups. No significant difference in the number of interstitial macrophages was detected. On the same note, testicular or serum testosterone levels were not different between the groups. Since no measurable differences in somatic cells, immune cells and testosterone levels were detected between HFD and LFD groups, it can be concluded that fertility is not affected during the early stages of T2D. This is promising for young adults who have early T2D or pre-diabetes. If they receive treatment early that prevents progression to chronic diabetes, their reproductive capabilities may not be affected.

148 THE TESTICULAR EXPLANT SYSTEM PROVIDES AN ALTERNATIVE PLATFORM TO ASSESS THE IMPACT OF GERM CELL TOXICANTS AND PATHOGENS.
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(Presented By: Prabagaran Esakky, PhD)

Spermatogenesis is a highly complex, dynamic, and hormone dependent cellular process that results in production of haploid sperm in the testis. In vitro differentiation of male germ cells in cell culture methods has the inherent inability of reproducing in vivo cellular activities. Alternatively, the testis organ culture appears to be of a potential platform to in vivo spermatogenesis as it can preserve tissue architecture, intercellular communication, germ cell physiology, and produce haploid sperm. We hypothesize here that testicular explant model is a suitable alternative to understand the process of spermatogenesis, determine the toxicity of germ cell toxicants and assess the impact of male germ cell pathogens such as ZIKA virus (ZIKV). We have recently developed and characterized a mouse neonatal testicular explant system that supports the production of haploid sperm. We validated the structural and functional integrity of our testicular explant system by using stage and cell-type specific markers of spermatogenesis. This was further confirmed when the explant system failed to undergo meiotic progress following exposure to the reversible bromodomain inhibitor, JQ1. Analysis of the expression of several growth indicators following exposure to cigarette smoke condensate suggested that the neonatal spermatogenesis is susceptible to germ cell toxicants of cigarette smoke. ZIKV infection of the explant system indicates the susceptibility of male germ cells in the ex vivo model. Thus, the testicular explant system is a suitable alternative to assess the toxicity of germ cell toxicants and pathogens on the progress of spermatogenesis.

149 THYROID HORMONES AND CELL SERTOLI PROLIFERATION AND DIFFERENTIATION IN PROGENIES FROM CBZ-TREATED RATS DURING PREGNANCY AND LACTATION
Rhayza Andretta PhD candidate, Renato Tessier PhD, Camila Paccola PhD, Taiza Stump PhD, Samara de Oliva PhD and Sandra Miranda PhD
Federal University of Sao Paulo
(Presented By: Rhayza Andretta PhD candidate)

Carbamazepine (CBZ) is a widely-utilized drug in the control of seizure and affective disorders, causing hypothyroidism in patients. The role of thyroid hormone on the Sertoli cell proliferation and differentiation is a central issue since these cells regulate the germ cell differentiation and proliferation. The clinical aspects must also be considered since epileptic fertile women continuously use CBZ. Data related to side effects of CBZ treatment during pregnancy and breastfeeding on male offspring reproduction are scarce. Our previous study showed that CBZ provokes late reproductive alterations in rats treated from
the weaning until puberty and adulthood. To evaluate the side effects of CBZ on seminiferous epithelium of rat offspring from dams treated during whole pregnancy and lactation, as well as the probable thyroid hormone involvement in this event, the following parameters were analyzed: 1-plasma TSH and T3 thyroid hormone levels in rat dams (n=12) and their pups; 2-Sertoli cell proliferation and differentiation using adequate immunolabeling and 3-the resulting testis alterations in different phases of sexual maturation of the offspring. Rat dams received CBZ (20mg/Kg/day; CBZ group) or propylene glycol (Control group) intraperitoneal injections during whole gestation and breastfeeding. Testicular cross-sections of the offspring were submitted to PCNA and Ki67 immunolabeling for evaluation of Sertoli cell proliferation. Differentiation and function of the Sertoli cells were respectively evaluated using anti-p27kip1 and anti-transferrin immunolabeling. Progenies (Control and CBZ groups, n=12/age) were euthanized at 4, 14, 41, 63 and 93 days post-partum (dpp) for these analyses. Testis morphometry was carried out. Plasma dosages of T3 and TSH were obtained by ELISA method. CBZ exposure affected the volume density of transferrin-positive labeling in the seminiferous epithelium at 63 dpp (late puberty) but did not change the numerical densities of PCNA and Ki67-positive Sertoli cells or the T3 level in any age. However, there was a significant reduction of p27kip1-positive Sertoli cell numerical density at 14 dpp, a rise of TSH level at 14 dpp and of some testicular morphometric parameters at 4 dpp in CBZ rats. These last results altogether suggest that CBZ may cause a light and transient hypothyroidism leading to a delay of Sertoli cell differentiation in infant rats and an altered Sertoli cell function at late puberty. FAPESP-2012/05905-9

150 TESTIS HISTOLOGY IN MEN SUBMITTED TO MICROSURGICAL CORRECTION OF SUBCLINICAL VARICOCELE WITH LONG REFUX AS A VARIABLE TO UNDERSTAND IMPROVEMENT IN SPERM QUALITY POST-TREATMENT

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(Presented By: Jorge Hallak, MD, PhD)

Introduction: Subclinical varicocele with long reflux can damage spermatogenesis and cause sperm abnormalities. The challenge in subclinical varicocele approach is the identification of subjects who will benefit from surgical treatment, since many patients do not show improvement in semen analysis.

Objective: To identify testicular histological pattern as prognostic value of improved reproductive capacity in patients with subclinical varicocele submitted to microsurgical correction.

Methods: We retrospectively analyzed testicular biopsies of 20 men diagnosed with subclinical varicocele. The diagnosis of subclinical varicocele was carried out through bilateral testicular palpation, auscultation of long and continuous venous reflux by Doppler stethoscope with and without Valsalva maneuver and confirmation by color Doppler sonography. The determination of the testicular histological pattern was performed by the creation of cut-off values that associate Johnsen scores, Copenhagen index and testicular volume with improvement in semen parameters. To determine cut-off points of predict fertility improvement, Receiver Operating Characteristic (ROC) curves were created combining histological scores, hormones and semen parameters.

Results: Johnsen score must be >8.2 (left testicle) and right testicular volume >12.8 mL to improve sperm concentration. Johnsen score must be >8.2 (bilateral testsit) and Copenhagen index (digit II) must be <2.5 in both testis to total sperm motility improvement. To increase progressive motility, Johnsen score must be >9.1 bilaterally and right testicular volume >13.6 mL.

Conclusion: We could determine parameters to evaluate which patients can benefit from surgical treatment of subclinical varicoceles with very long reflux.

Financial Support: Androscience/Capes-DS

Ethics Committee Approval: FMUSP nº047/2012

151 THE FUNCTION OF EPIDIDYMAL CYSTEINE-RICH SECRETORY PROTEINS (CRISPS)

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(Presented By: Jinghua Hu, MSc)

It has been demonstrated that epididymal CRISP1 and CRISP4 are individually required for full sperm function, but mice null for either gene remain fertile, suggesting that there may be redundancy between the two genes. In contrast to mice, humans possess a single epididymal CRISP. In order to define the function of CRISPs in epididymis as a family, and thus their likely relevance to human fertility, we produced Crisp1/Crisp4 double knockout mouse model to study the influence of epididymal CRISPs absence on male fertility. Crisp1/Crisp4 homozygous null males are fertile, however, computer assisted sperm analysis (CASA) revealed that epididymal CRISPs are necessary for sperm to acquire the capacity for rapidly progressive motility, and a normal ability to undergo the progesterone-induced acrosome reaction in vitro and thus, likely normal acrosome reaction ability in vivo. Further, we have shown that with increased age, 23 weeks, double knockout mice epididyemides contained significantly reduced numbers of sperm compared to their wild type counterparts. This, and an association between CRISP-related proteins and immune tolerance in lower order species, suggests that epididymal CRISPs may function to protect sperm against immune-mediated sperm elimination in epididymis. Ongoing studies are dissecting the relationship between epididymal CRISPs and immune regulation.
Differential Tolerogenic Capacity of the Epididymis and Testis in Mice with Conditional Deletion of TGFBR2 in Dendritic Cells

Fernando Pierucci-Alves¹, Monica T. Midura-Kiela², Sherry D. Fleming³, Bruce D. Schultz¹ and Pawel R. Kiela²
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Sperm are immunogenic and peripheral tolerance mechanisms are necessary for reproductive success. Initial data revealed prominent physiological signaling by transforming growth factor beta (TGFβ) in murine epididymis, where large networks of dendritic cells (DCs) and macrophages exist. This study’s overarching hypothesis is that TGFβ-signalizing in epididymal DCs maintains immunotolerance to sperm in the epididymis and disruption of this signaling pathway breaks sperm tolerance through impaired or insufficient regulatory T cell (Treg) function. In male mice with DC-specific TGFβ receptor 2 deletion (Tgfb2ΔDCFoxP3GFP-KI), we detected severe epididymal leukocytosis with sperm granulomas, antisperm antibodies but no apparent testicular pathology at the histological level. To further observe these observations, we quantified leukocytes (CD45+) and Tregs (FoxP3/GFP+) in epididymides, testes and kidneys from 4 Tgfbr2ΔDCFoxP3GFP-KI males and control littermates by flow cytometry. We used kidneys as a sperm reservoir because they are partially resistant to CP-induced apoptosis. Thus, we conclude that HNt mice are viable, fertile and smaller in size (BW:28.5±2.2g) with an average of 18% decrease in body weight (BW) as compared to WT (BW:34.9±10.3g) mice. The testis weight (TW:88±10.1mg, p=0.007) in HNt mice was significantly lower than WT (TW:105.2±9.3mg) mice. There was no difference in cauda epididymal sperm count between HNt (1.3±0.03 million/mg cauda) and WT (1.3±0.03 million/mg cauda) mice. Testis histological examination in HNt mice showed normal histology with the baseline germ cell apoptosis rates reminiscent of WT levels. HNt mice have similar plasma T levels (0.6±0.4ng/ml) as WT (0.7±0.5ng/ml) controls. Two days after CP treatment, there were no marked changes in body and testis weight, and plasma T levels. The germ cell apoptosis rate in WT mice was significantly (p<0.001) increased at spermatogenic stages I-III (AI:46.1±4.6), VII-VIII (AI:20.6±0.9) and XI-XII (AI:56.9±4.8) as compared to non-treated WT mice (stages I-III AI: 9.5±2.1; VII-VIII:2.5±0.6; XI-XII:17.5±1.8). In HNt mice, CP treatment significantly increased germ cell apoptosis at stages XI-XII (AI: 23.7±2.9; p=0.03), but not at stages I-III (AI:14.9±2.3) and VII-VIII (AI:4.8±1.1) as compared to baseline levels of HNt mice (stages I-III AI:3±1.8; VII-VIII:3.8±0.8; XI-XII:13.3±3.2), suggesting that male germ cells in HNt mice were partially resistant to CP-induced apoptosis. Thus, we conclude that HN 1) is cytoprotective hormone; and 2) mimics the effects of caloric-restriction on metabolism and chemotherapy-protection.
ABSTRACTS

1 (Oral/Poster)
DIFFERENTIAL TOLEROGIC CAPACITY OF THE EPIDIDYMIS AND TESTIS IN MICE WITH CONDITIONAL DELETION OF TGFBR2 IN DENDRITIC CELLS
Fernando Pierucci-Alves¹, Monica T. Midura-Kiela², Sherry D. Fleming¹, Bruce D. Schultz¹ and Pawel R. Kiela³
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(Presented By: Fernando Pierucci-Alves, DVM)

Sperm are immunogenic and peripheral tolerance mechanisms are necessary for reproductive success. Initial data revealed prominent physiological signaling by transforming growth factor beta (TGFβ) in murine epididymis, where large networks of dendritic cells (DCs) and macrophages exist. This study’s overarching hypothesis is that TGFβ-signaling in epididymal DCs maintains immunotolerance to sperm in the epididymis and disruption of this signaling pathway breaks sperm tolerance through impaired or insufficient regulatory T cell (Treg) function. In male mice with DC-specific TGFβ receptor 2 deletion (Tgbr2ΔDCFoxP3GFP-KI), we detected severe epididymal leukocytosis with sperm granulomas, antisperm antibodies but no apparent testicular pathology at the histological level. To further these observations, we quantified leukocytes (CD45+) and Tregs (FoxP3/GFP+) in epididymides, testes and kidneys from 4 Tgbr2ΔDCFoxP3GFP-KI males and control littermates by flow cytometry. We used kidneys as a sperm-free organ of the genitourinary tract, and as an additional control. Compared to controls, the epididymis of Tgbr2ΔDCFoxP3GFP-KI mice had 3.4 times more infiltrating CD45+ leukocytes (P<0.05), while the Tgbr2ΔDCFoxP3GFP-KI testis and kidney exhibited 1.2- and 1.5-fold increase in infiltrating leukocytes (P<0.05), respectively. Tregs were 5-6 times more abundant in epididymis and kidney of Tgbr2ΔDCFoxP3GFP-KI mice, while the testis exhibited 53 times more Tregs – compared to controls. These data suggest the epididymis is most susceptible to inflammation when the DC/TGFβ-signaling axis is disrupted, and that the testis maintains alternative robust immunosuppressive mechanisms to fend off autoimmune responses. Additional studies are addressing how loss of TGFβ-signaling disrupts epididymal and testicular DC tolerogenic capacities and testing whether there is differential induction and function between epididymal and testicular Tregs. Supported by P20GM103418 (K-INBRE); Johnson Cancer Research Center

2 (Oral/Poster)
HUMANIN TRANSGENIC MICE ARE PROTECTED FROM CYCLOPHOSPHAMIDE-INDUCED MALE GERM CELL APOPTOSIS
YanHe Lue MD¹, Hemal Mehta MS², James Hoang BS¹, Kelvin Yen PhD², Junxiang Wan PhD², Ronald Swerdlaff MD¹, Pinchas Cohen MD² and Christina Wang MD¹
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(Presented By: YanHe Lue, MD)

Humanin (HN) is a cytoprotective peptide encoded by a mitochondrial gene. We have previously demonstrated that the pharmacological administration of HN or its analogue HNG protects male germ cells against cyclophosphamide (CP)-induced apoptosis in mice. To examine the role of endogenous HN in the cytoprotection of male germ cells from chemotherapy, we generated HN transgenic (HNT) mice expressing a CMV-promoter driven humanin transgene. After genotyping by PCR, 1) groups of 7 adult (5-10 month-old) HNT and age-matched wildtype (WT) mice were used for the characterization of male reproductive phenotype, and 2) groups of 6 adult HNT and age-matched WT mice were treated with a single-dose of CP injection (i.p. 200mg/kg) to examine male germ cell apoptosis (quantified as apoptotic index (AI): the number of apoptotic germ cells/100 Sertoli cells). The plasma testosterone (T) was measured by RIA. HNT mice were viable, fertile and smaller in size (BW:28.5±2.2g) with an average of 18% decrease in body weight (BW) as compared to WT (BW:34.9±10.3g) mice. The testis weight (TW:88±10.1mg, p=0.007) in HNT mice was significantly lower than WT (TW:105.2±9.3mg) mice. There was no difference in cauda epididymal sperm count between HNT (1.3±0.07 million/mg cauda) and WT (1.3±0.03 million/mg cauda) mice. Testis histological examination in HNT mice showed normal histology with the baseline germ cell apoptosis rates reminiscent of WT levels. HNT mice have similar plasma T levels (0.6±0.4ng/ml) as WT (0.7±0.5ng/ml) controls. Two days after CP treatment, there were no marked changes in body and testis weight, and plasma T levels. The germ cell apoptosis rate in WT mice was significantly (p<0.001) increased at spermatogenic stages I-III (AI:46.1±4.6), VII-VIII (AI:20.6±0.9) and XI-XII (AI:56.9±4.8) as compared to non-treated WT mice (stages I-III AI: 9.5±2.1; VII-VIII:2.5±0.6; XI-XII:17.5±1.8). In HNT mice, CP treatment significantly increased germ cell apoptosis at stages XI-XII (AI: 23.7±2.9; p=0.03), but not at stages I-III (AI:14.9±2.3) and VII-VIII (AI:4.8±1.1) as compared to baseline levels of HNT mice (stages I-III AI:8.3±1.8; VII-VIII:3.8±0.8; XI-XII:13.3±3.2), suggesting that male germ cells in HNT mice were partially resistant to CP-induced apoptosis. Thus, we conclude that HN 1) is cytoprotective hormone; and 2) mimics the effects of caloric–restriction on metabolism and chemotherapy–protection.
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