2011 American Physiological Society Conference

Physiology of Cardiovascular Disease: Gender Disparities

MEETING PROGRAM AND ABSTRACTS

University of Mississippi Medical Center
Jackson, Mississippi
October 12-14, 2011

www.the-aps.org/gender2011
2011 APS Conference
Physiology of Cardiovascular Disease: Gender Disparities

APS Council

President
Joey P. Granger

Past President
Peter D. Wagner

President-Elect
Susan M. Barman

Kenneth M. Baldwin
Ida Llewellyn-Smith
Jane F. Reckelhoff

David P. Brooks
Patricia E. Molina
Curt D. Sigmund

Dennis Brown
Usha Raj
Alan F. Sved

Ex officio Members

Pamela K. Carmines
Joseph R. Haywood
Hershel Raff

John C. Chatham
Ronald M. Lynch

Martin Frank
Thomas A. Pressley
Jeff M. Sands

Conference Organizers

Jane F. Reckelhoff (Chair)
Univ. of Mississippi Med. Ctr.

Michael J. Ryan (Co-Chair)
Univ. of Mississippi Med. Ctr.

Barbara T. Alexander
Univ. of Mississippi Med. Ctr.

C. Noel Bairey Merz
Cedars-Sinai Med. Ctr.

Christine Marie-Bilkan
Univ. of Mississippi Med. Ctr.

Meir Steiner
McMaster Univ., Canada

Acknowledgements

The Conference Organizers and The American Physiological Society gratefully recognize the generous financial support from the following:

Women’s Health Research Center, University of Mississippi Medical Center
Faculty Scholarship Exchange Program, University of Mississippi Medical Center
Council of High Blood Pressure Research, American Heart Association
Council on Clinical Cardiology, American Heart Association
Isis Cardiovascular Network
Society for Women’s Health Research
NIH, National Institute of Diabetes and Digestive and Kidney Diseases
### 2011 APS Conference
**Physiology of Cardiovascular Disease: Gender Disparities**
**October 12—14, 2011, University of Mississippi Medical Ctr., Jackson, Mississippi**

<table>
<thead>
<tr>
<th>Wednesday, October 12</th>
<th>Thursday, October 13</th>
<th>Friday, October 14</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>7:00 – 9:00 PM</strong></td>
<td><strong>7:00 AM</strong></td>
<td><strong>7:00 AM</strong></td>
</tr>
<tr>
<td><strong>Opening Reception</strong></td>
<td><strong>Breakfast/Registration</strong></td>
<td><strong>Breakfast/Registration</strong></td>
</tr>
<tr>
<td>Historic King Edward Hotel</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>8:00 – 8:40 AM</strong></td>
<td><strong>Plenary Lecture: From Stem Cells and Cadaveric Matrix to Engineered Organs</strong></td>
<td><strong>8:00—9:00 AM</strong></td>
</tr>
<tr>
<td>Doris Taylor, Univ. of Minnesota</td>
<td></td>
<td><strong>Symposia V:</strong></td>
</tr>
<tr>
<td><strong>8:40 – 9:40 AM</strong></td>
<td><strong>Symposia I:</strong></td>
<td><strong>Gender Disparities in Cardiology</strong></td>
</tr>
<tr>
<td><strong>Aging and CVD</strong></td>
<td>Heddwon Brooks, Univ. of Arizona</td>
<td>C. Noel Bairey Merz, Cedars-Sinai Med. Ctr.</td>
</tr>
<tr>
<td>Rhian Touyz, Univ. of Ottawa, Canada</td>
<td></td>
<td>Nanette Weuger, Emory Univ.</td>
</tr>
<tr>
<td><strong>9:40—10:00 AM</strong></td>
<td><strong>Break</strong></td>
<td><strong>9:00—9:40 AM</strong></td>
</tr>
<tr>
<td><strong>10:00—11:00 AM</strong></td>
<td><strong>Symposia II:</strong></td>
<td><strong>Selected Abstract Oral Presentations</strong></td>
</tr>
<tr>
<td><strong>Gender Disparities in Renal Disease</strong></td>
<td></td>
<td><strong>9:40—10:00 AM</strong></td>
</tr>
<tr>
<td>Sharon Elliot, Univ. of Miami</td>
<td></td>
<td><strong>Break</strong></td>
</tr>
<tr>
<td>Vesna Garovic, Mayo Clinic</td>
<td></td>
<td><strong>10:00—11:00 AM</strong></td>
</tr>
<tr>
<td>Michal Schwartzman, New York Med. Coll.</td>
<td></td>
<td><strong>Symposia VI:</strong></td>
</tr>
<tr>
<td><strong>11:00 AM—11:50 AM</strong></td>
<td><strong>Selected Abstract Oral Presentations</strong></td>
<td><strong>Cardiovascular Disease and Inflammation</strong></td>
</tr>
<tr>
<td><strong>11:50 AM—1:00 PM</strong></td>
<td><strong>Lunch and Poster Session I</strong></td>
<td>David Harrison, Vanderbilt Univ.</td>
</tr>
<tr>
<td><strong>1:00—2:00 PM</strong></td>
<td><strong>Symposia III:</strong></td>
<td>R. Anwar Ahmed, Virginia Tech.</td>
</tr>
<tr>
<td><strong>Diabetes, Obesity and Cardiovascular Disease</strong></td>
<td></td>
<td>Jennifer Sullivan, Med. Coll. of Georgia</td>
</tr>
<tr>
<td>Willis Samson, St. Louis Univ. Sch. of Med.</td>
<td></td>
<td><strong>11:00—11:50 AM</strong></td>
</tr>
<tr>
<td>David Parkes, Amylin Pharmaceuticals, Inc.</td>
<td></td>
<td><strong>Selected Abstract Oral Presentations</strong></td>
</tr>
<tr>
<td>John Hall, Univ. of Mississippi Med. Ctr.</td>
<td></td>
<td><strong>11:50 AM—1:00 PM</strong></td>
</tr>
<tr>
<td><strong>2:00—2:40 PM</strong></td>
<td><strong>Selected Abstract Oral Presentations</strong></td>
<td><strong>Lunch and Poster Session II</strong></td>
</tr>
<tr>
<td><strong>2:40—3:00 PM</strong></td>
<td><strong>Break</strong></td>
<td><strong>1:00—2:00 PM</strong></td>
</tr>
<tr>
<td><strong>3:00—4:00 PM</strong></td>
<td><strong>Symposia IV:</strong></td>
<td><strong>Symposia VII:</strong></td>
</tr>
<tr>
<td><strong>Neuro Mechanisms and Depression in Cardiovascular Disease</strong></td>
<td></td>
<td><strong>Gender Differences in Vascular Function</strong></td>
</tr>
<tr>
<td>Virginia Brooks, Oregon Hlth. and Science Univ.</td>
<td></td>
<td>Marilyn Cipolla, Univ. of Vermont</td>
</tr>
<tr>
<td>Meir Steiner, McMaster Univ., Canada</td>
<td></td>
<td>Christopher Minson, Univ. of Oregon</td>
</tr>
<tr>
<td>Nabil Alkayed, Oregon Hlth, and Science Univ.</td>
<td></td>
<td>Sandra Davidge, Univ. of Alberta, Canada</td>
</tr>
<tr>
<td><strong>4:00—4:50 PM</strong></td>
<td><strong>Selected Abstract Oral Presentations</strong></td>
<td><strong>2:00—2:40 PM</strong></td>
</tr>
<tr>
<td><strong>5:00—6:00 PM</strong></td>
<td><strong>Career Session:</strong></td>
<td><strong>Selected Abstract Oral Presentations</strong></td>
</tr>
<tr>
<td><strong>Careers in Physiology Trainee Session</strong></td>
<td></td>
<td><strong>2:40—3:00 PM</strong></td>
</tr>
<tr>
<td>Jennifer Sasser, Univ. of Florida</td>
<td></td>
<td><strong>Break</strong></td>
</tr>
<tr>
<td><strong>6:30—10:00 PM</strong></td>
<td><strong>Dinner</strong></td>
<td><strong>3:00—4:00 PM</strong></td>
</tr>
<tr>
<td><strong>Historic King Edward Hotel</strong></td>
<td></td>
<td><strong>Symposia VIII:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Cardiovascular Disease and Fertility</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sarah Berga, Emory Univ.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Babbette LaMarca, Univ. of Mississippi Med. Ctr.</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>4:00—5:00 PM</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Selected Abstract Oral Presentations</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>6:30 PM</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Closing Dinner and Awards Presentation</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fairview Inn</td>
</tr>
</tbody>
</table>
Location:
The 2011 APS Conference, Physiology of Cardiovascular Disease: Gender Disparities will be held October 12—14, 2011 at the University of Mississippi Medical Center, 2500 N. State Street, Jackson, MS 39216, telephone (601) 984-2103 FAX: (601) 984-2105

Onsite Registration Hours:
    Thursday, October 13 ………7:00 AM—5:30 PM
    Friday, October 14…………..7:00 AM—5:00 PM

On-Site Registration Fees:
    APS Member……………………………………$350
    Retired Member………………………………$250
    Nonmember……………………………………$400
    Postdoctoral……………………………………$250
    Student…………………………………………$250

The registration fee includes entry into all scientific sessions, opening reception, lunches and dinners.

Payment Information:
Registrants may pay by institutional or personal check, traveler’s check, MasterCard, VISA or American Express. Checks must be payable to “The American Physiological Society” and drawn on a United States bank payable in US dollars.

Student Registration:
Any student member or regularly matriculated student working toward a degree in one of the biomedical sciences is eligible to register at the student fee. Nonmember postdoctoral fellows, hospital residents and interns, and laboratory technicians do not qualify as students. Nonmember students who register onsite must provide a valid university student ID card. APS student members should present their current APS membership card indicating their student category status.

Postdoctoral Registration:
Any person who has received a Ph.D. degree in physiology or related field, within four years of this meeting, as attested to by the department head is eligible to register at the postdoctoral fee. A statement signed by the department head must accompany the registration form and remittance when registering.

Press:
Press badges will be issued at the APS registration desk, only to members of the working press and freelance writers bearing a letter of assignment from an editor. Representatives of allied fields (public relations, public affairs, etc.) must register as nonmembers.

Ancillary Session:
Career Workshop: This special session entitled: “Careers in Physiology Trainee Session” will be presented by Jennifer Sasser, University of Florida.

Program Objective:
The role that sex steroids and gender play in the physiology and pathophysiology of cardiovascular and renal disease (CVRD) is becoming an increasingly more important area of research. The program will be balanced to include both basic science and clinical studies, ranging from the gene to the whole animal or human. The global aspect of the conference is to gather a critical mass of scientists with interests and expertise in the role of sex steroids and/or the gender differences in the physiology of CVRD, and to promote an exchange of ideas to foster collaboration that will further advance this important line of scientific investigation. In addition, this conference will be to increase the awareness of sex disparities in CVRD that need to be understood in order to ultimately improve clinical outcomes for men and women and promote individualized health care.

Target Audience:
The intended audience for this conference includes all levels of researchers working in the field of gender disparities in cardiovascular disease. Furthermore, this conference will provide a diverse program that covers many of the organ systems in which sex steroids and gender have been shown to be important in cardiovascular diseases.

Daily Shuttle Bus Schedule

Thursday, October 13, 2011:
Departs the Historic King Edward Hotel at 7:00 AM and 7:30 AM
Departs UMMC at 5:00 PM, 5:30 PM and 6:00 PM for the Historic King Edward Hotel.

Friday, October 14, 2011:
Departs the Historic King Edward Hotel at 7:00 AM and 7:30 AM
Departs UMMC at 5:00 PM, 5:30 PM for the Historic King Edward Hotel.
Departs the Historic King Edward Hotel at 6:15 PM for the Fairview Inn.
THURSDAY, OCTOBER 13, 2011

Plenary Lecture

**1.0 PLENARY LECTURE**
Thurs., 8:00-8:40 AM, A/B.

Chair: Michael Ryan, Univ. of Mississippi Med. Ctr.

8:00 AM  
1.1  Sex Cells and Matrix: Cardiac Regeneration in 2011. Doris Taylor, Univ. of Minnesota.

Symposia I

**2.0 AGING AND CVD**
Thurs., 8:40-9:40 AM, A/B.

Co-Chairs: Rudy Ortiz, Univ. of California, Merced. Virginia Huxley, Univ. of Missouri, Columbia.

8:40 AM  
2.1  Diabetes and Metabolic Syndrome: Progression Across the Perimenopause Transition. Heddwen Brooks, Univ. of Arizona.

9:00 AM  
2.2  Early Menopause and Cardiovascular Disease. Pamela Ouyang, Johns Hopkins Univ.

9:20 AM  
2.3  Cardiovascular Remodelling, Hypertension and Sex Hormones in Follicitropin Receptor Knockout (FORKO) Mice. Rhian Touyz, Univ. of Ottawa, Canada.

9:40 AM Break

Symposia II

**3.0 GENDER DISPARITIES IN RENAL DISEASE**
Thurs., 10:00 AM-12:00 Noon, A/B.

Co-Chairs: Kathryn Sandberg, Georgetown Univ. Jing Li, Univ. of Mississippi Med. Ctr.

10:00 AM  
3.1  Sex Differences in Renal Injury: Role of Podocytes. Sharon Elliot, Univ. of Miami.

10:20 AM  
3.2  Podocyturia as an Early Predictive Marker of Pre-eclampsia. Vesna Garovic, Mayo Clinic.

10:40 AM  

11:00 AM  

11:10 AM  
3.5  Sex Steroids and Renal Sodium Transport in Mice Consuming 1% and 4% Salt Diet. Al Rouch, Oklahoma State Univ. Ctr. for Hlth. Sci. (4.2).

11:20 AM  
3.6  Aldosterone Escape is Influenced by Sex Chromosomal Complement in Mice. Carolyn Eccelbarger, Georgetown Univ. (4.3).

11:30 AM  
3.7  GPR30 Agonist G-1 Restores Megalin Expression and Reduces Proteinuria in Salt-sensitive mRen2.Lewis Females. Sarah Lindsey, Wake Forest Univ. Sch. of Med. (4.4).

11:40 AM  
3.8  Collecting Duct-derived Renin Exhibits Sex Differences During Normal Salt and High Salt Diets in Sprague-Dawley Rats. Vicky Rands, tulane Univ. (4.5).

Poster Session I

**4.0 POSTER SESSION I**
Thurs., 11:50 AM-1:00 PM, C/D

Board #  

1  

2  
4.2  Sex Steroids and Renal Sodium Transport in Mice Consuming 1% and 4% Salt Diet. A. Rouch, K. Curtis, L. Fan and L. Kudo, Oklahoma State Univ. Ctr. for Hlth. Sci.

3  
4.3  Aldosterone Escape is Influenced by Sex Chromosomal Complement in Mice. C. Eccelbarger, R.M. Garikepati, H. Ji, A. Arnold, K. Sandberg and L. Li, Georgetown Univ. and UCLA.

4  
4.4  GPR30 Agonist G-1 Restores Megalin Expression and Reduces Proteinuria in Salt-sensitive mRen2.Lewis Females. S. Lindsey, L. Yamaleyeva and M. Chappell, Wake Forest Univ. Sch. of Med.

5  
4.5  Collecting Duct-derived Renin Exhibits Sex Differences During Normal Salt and High Salt Diets in Sprague-Dawley Rats. V. Rands, D. Seth and M. Prieto, Tulane Univ.

6  

7  
4.7  GPR30 Activation Increases ACE2 Expression in Diabetic Ovariectomized mRen2.Lewis Females. H. El-Bassossy, S. Lindsey, L. Yamaleyeva and M. Chappell, Wake Forest Univ. Sch. of Med.

8  

9  
4.9  The Effects of Streptozotocin-induced Diabetes and Gender on the Rat Aortic Endothelial Function. X. Han, L. Anderson and R. Rahimian, Univ. of the Pacific.

10  
4.10  Withdrawn.
DAILY SCHEDULE

Board #

11  4.11 Central Blockade of Angiotensin I-7) or Angiotensin II Receptor Type 2 (AT2) Enhances Aldosterone/Salt-induced Increases in Blood Pressure in Female Rats. B. Xu, Z. Zhang, F. Guo, M. Hay and A. Johnson. Univ. of Iowa and Univ. of Arizona.


16  4.16 Fetal Programming of Hypertension Induced by Zinc Restriction in Fetal Life: Gender Differences in Early Effects on Kidney. C. Arranz, A. Sofia, V. Luciana, A. Costa and A. Tomat. Univ. of Buenos Aires, Argentina.


Don’t forget to join your colleagues for the poster sessions held daily in room C/D—lunch is included!

Symposia III

5.0 DIABETES, OBESITY AND CARDIOVASCULAR DISEASE

Thurs., 1:00-2:40 PM, A/B.

Co-Chairs:  Mark Chappell, Wake Forest Univ. Sch. of Med.
<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Title</th>
<th>Speaker</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:00 PM</td>
<td>5.1</td>
<td>Novel Pancreatic Peptides Control Glucose Homeostasis and Appetite.</td>
<td>Willis (Rick) Samson</td>
<td>St. Louis Univ.</td>
</tr>
<tr>
<td>1:20 PM</td>
<td>5.2</td>
<td>Translational Cardiovascular Benefits of Exenatide-Preclinical and Clinical Evidence.</td>
<td>David Parkes. Amylin Pharma., Inc.</td>
<td></td>
</tr>
<tr>
<td>1:40 PM</td>
<td>5.3</td>
<td>Pathophysiology of Hypertension in Obesity/metabolic Syndrome.</td>
<td>John Hall.</td>
<td>Univ. of Mississippi Med. Ctr.</td>
</tr>
<tr>
<td>2:10 PM</td>
<td>5.5</td>
<td>GPR30 Activation Increases ACE2 Expression in Diabetic Ovariectomized mRen2-Lewis Females.</td>
<td>Mark Chappell. Wake Forest Univ. Sch. of Med.</td>
<td>(4.7).</td>
</tr>
<tr>
<td>2:30 PM</td>
<td>5.7</td>
<td>The Effects of Streptozotocin-induced Diabetes and Gender on the Rat Aortic Endothelial Function.</td>
<td>Xiaoyuan Han. Univ. of the Pacific</td>
<td>(4.9).</td>
</tr>
<tr>
<td>2:40 PM</td>
<td>Break</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Symposia IV**

**NEURO MECHANISMS AND DEPRESSION IN CARDIOVASCULAR DISEASE**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Title</th>
<th>Speaker</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>3:20 PM</td>
<td>6.0.2</td>
<td>Sex Differences in Depression and Cardiovascular Disease.</td>
<td>Meir Steiner. Mcmaster Univ.</td>
<td>Canada</td>
</tr>
<tr>
<td>4:00 PM</td>
<td>6.0.4</td>
<td>Heme Oxygenase-1 as a Potential agent for the Treatment of Pre-eclampsia.</td>
<td>Eric George. Univ. of Mississippi Med. Ctr.</td>
<td>(4.29).</td>
</tr>
<tr>
<td>4:10 PM</td>
<td>6.0.5</td>
<td>Central Blockade of Angiotensin (1-7) or Angiotensin II Receptor Type 2 (AT2) Enhances Aldosterone/Salt-induced Increases in Blood Pressure in Female Rats.</td>
<td>Baolian Xue. Univ. of Iowa.</td>
<td>(4.11).</td>
</tr>
<tr>
<td>4:30 PM</td>
<td>6.0.7</td>
<td>GPR30 is involved in the Regulation of the KCa1.1 Channel Current in a Gender Specific Population of Myelinated Vagal Afferents.</td>
<td>John Schild. Indiana Univ-Purdue Univ. Indiana-polis.</td>
<td>(4.13).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Title</th>
<th>Speaker</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>5:00 PM</td>
<td>7.0.1</td>
<td>CAREER SESSION</td>
<td>Jennifer Sasser. Univ. of Florida, Gainesville.</td>
<td></td>
</tr>
</tbody>
</table>

**Dinner on Thursday, October 13th will be held at the Historic King Edward Hotel at 6:30 PM**

**FRIDAY, OCTOBER 14, 2011**

**Symposia V**

**GENDER DISPARITIES IN CARDIOLOGY**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Title</th>
<th>Speaker</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:00 AM</td>
<td>8.0.1</td>
<td>Women and Ischemic Heart Disease.</td>
<td>C. Noé Bairéy-Merz. Cedars-Sinai Med. Ctr.</td>
<td>Los Angeles.</td>
</tr>
<tr>
<td>8:40 AM</td>
<td>8.0.3</td>
<td>The Feminine Face of Heart Disease: What Do We Know About Angina in Women?</td>
<td>Nanette Wenger. Emory Univ.</td>
<td></td>
</tr>
<tr>
<td>9:00 AM</td>
<td>8.0.4</td>
<td>Dietary Genistein Induces Sex-dependent Cardiovascular Effects in Mice.</td>
<td>Layla Al-Nakash. Midwestern Univ.</td>
<td>(4.30).</td>
</tr>
<tr>
<td>9:10 AM</td>
<td>8.0.5</td>
<td>Antioxidant Tempol Exacerbates Pressor Response to Stress in Multiparous Rats.</td>
<td>Susan Jacobs-Kaufman. Univ. of Alberta, Canada</td>
<td>(10.2).</td>
</tr>
</tbody>
</table>
DAILY SCHEDULE


9:40 AM  Break.

Symposia VI

9.0  CARDIOVASCULAR DISEASE AND INFLAMMATION
Fri., 10:00-11:50 AM, A/B

Co-Chairs: Kate Denton, Monash Univ., Australia.
           Analia Loria, Georgia Hlth. Sci. Univ.

10:00 AM  9.1 Inflammation, Immunity and Hypertension. David Harrison, Vanderbalt. Univ.


11:00 AM  9.4 Inflammation-Induced TLR4 Expression and Reactive Oxygen Species are Attenuated by Dihydrotestosterone in Human Primary Vascular Smooth Muscle Cells. Rayna Gonzales, Univ. of Arizona Coll. of Med. (10.5).

11:10 AM  9.5 Bone Marrow-derived Angiogenic Progenitor Cells are Dysfunctional in Chronic Ang II Infusion Rat Model of Hypertension. Mohan Raizada, Univ. of Florida, Gainesville. (10.1).

11:20 AM  9.6 Testosterone Induces Leukocyte Migration by COX2 and NADPH Oxidase-dependent Pathways. Rheurre Lopes, Univ. of São Paulo, Brazil (10.7).

11:30 AM  9.7 Sex-Dependent Immune-Protection with Minocycline after Experimental Embolic Stroke. Irina Sazonova, Georgia Hlth. Sci. Univ. (10.8).

11:40 AM  9.8 Estrogen Promotes Cardiac Stem Cell Paracrine Action and thus Facilitates CSC-mediated Protection Following Hypoxia. Meiijing Wang, Indiana Univ. Sch. of Med. (10.9).

Poster Session II

10.0  POSTER SESSION II
Fri., 11:50 AM-1:00 PM, C/D

Board #

1  10.1 Bone Marrow-derived Angiogenic Progenitor Cells are Dysfunctional in Chronic Ang II Infusion Rat Model of Hypertension. J. Y. Jun, J. Zubevcevic, A. Afzal, G. Lamont, J. Marulanda, J. Mocco and M. Raizada, Univ. of Florida, Gainesville.

2  10.2 Antioxidant Tempol Exacerbates Pressor Response to Stress in Multiparous Rats. S. Jacobs-

Board #

Kaufman and J. Levasseur. Univ. of Alberta, Canada.


6  10.6 Withdrawn.


DAILY SCHEDULE

2:10 PM  11.5  20-HETE-Induced Vascular Remodeling in the Model of Androgen-Induced Hypertension. Yan Ding, New York Med. Coll. (10.11).


2:30 PM  11.7  Sex Differences in Downstream TGF-beta Signaling in the Arteries of Spontaneously Hypertensive Rats. Ashlee Tipton, Georgia Hlth. Sci. Univ. (10.13).

2:40 PM  Break.

Symposia VIII

12.0  CARDIOVASCULAR DISEASE AND FERTILITY
Fri., 3:00-5:10 PM, A/B

Co-Chairs: Jeffrey Gilbert, Univ. of Oregon. Mark Cunningham, Univ. of Florida, Gainesville.

3:00 PM  12.1  PCOS, Stress-Induced Anovulation, and CVD. Sarah Berga, Emory Univ.

3:20 PM  12.2  Hypertension in Response to Placental Ischemia: Role of Agonistic Autoantibodies to the Angiotensin II Type 1 Receptor. Babbette LaMarca, Univ. of Mississippi Med. Ctr.


4:00 PM  12.4  Gender Differences in the Intergenerational Transmission of Hypertension Associated with Uteroplacental Insufficiency in Rats. Linda Gallo, Univ. of Melbourne, Australia. (10.14).

4:10 PM  12.5  Exposure of Neonatal Female, but not Male Mice to Testosterone Promotes Angiotensin II-Induced Abdominal Aortic Aneurysms. Xuan Zhang, Univ. of Kentucky. (10.15).

4:20 PM  12.6  ACE2 Deficiency is Associated with Impaired Gestational Weight Gain and Fetal Growth Restriction. Lilya Yamaleyeva, Wake Forest Sch. of Med. (10.16).


4:40 PM  12.8  A Novel Reproductive Hormone, Cospeptin. Gina Yosten, St. Louis Univ. (10.18).


This meeting has been made possible through the generous support from:

Women's Health Research Center at the University of Mississippi Medical Center

Faculty Scholarship Exchange Program at the University of Mississippi Medical Center

Council of High Blood Pressure, American Heart Association

Council on Clinical Cardiology, American Heart Association

Isis Cardiovascular Network

Society for Women's Health Research

NIH, National Institute of Diabetes and Digestive and Kidney Diseases

Dinner on Friday, October 14th will be held at the Fairview Inn at 6:30 PM
2011 APS Conference
Physiology of Cardiovascular Disease: Gender Disparities

Abstracts of Invited and Contributed Presentations

1.0 Plenary Lecture
2.0 Aging and CVD
3.0 Gender Disparities in Renal Disease
4.0 Poster Session I
5.0 Diabetes, Obesity and Cardiovascular Disease
6.0 Neuro Mechanisms and Depression in Cardiovascular Disease
8.0 Gender Disparities in Cardiology
9.0 Cardiovascular Disease and Inflammation
10.0 Poster Session II
11.0 Gender Differences in Vascular Function
12.0 Cardiovascular Disease and Fertility

Author Index
1.0 PLENARY LECTURE

1.1 SEX CELLS AND MATRIX: CARDIAC REGENERATION IN 2011
Doris Taylor

Ctr. for Cardiovascular Repair, Univ. of Minnesota, Minneapolis, 312 Church St. S.E., 7-105A NIH, Minneapolis, MN, 55455.

Sex differences in symptomatology, risk, and even the effectiveness of therapies exist. It’s no surprise to think about sex differences in response to cells, genes, molecules, and every aspect of cardiovascular repair. Evaluating these differences in cutting edge therapies as they emerge will be critical to developing effective therapies. One novel therapy that is bone marrow mononuclear cell delivery for coronary artery disease (atherosclerosis) and acute myocardial infarction. I will describe our preclinical and early clinical data on the composition and function of bone marrow in individuals with cardiovascular disease. I will also discuss our more recent data on beginning to engineer whole organs for treatment of endstage organ failure and how sex differences are present even at the level of the extra cellular matrix. It’s no surprise that men and women differ. What is emerging as intriguing is that those differences exist at the level of cells, at the level of genes, and at the level of organs and tissues. Capitalizing on those differences should allow us to create personalized healthcare solutions at a level previously unimaginable.

2.0 AGING AND CVD

2.1 DIABETES AND METABOLIC SYNDROME: PROGRESSION ACROSS THE PERIMENOPAUSE TRANSITION
Hedvigen Brooks1, Melissa Romero-Aleshire1, Maggi Diamond-Stanic, Patricia Hoyer1

1Physiology, Univ. of Arizona, MRB, Tucson, AZ, 85718.

The 4-vinylcyclohexene diepoxide (VCD) model of menopause progresses gradually through perimenopause to post-menopause and preserves postmenopausal ovarian production of androgens. Studies in the VCD-model of menopause have shown that loss of ovarian function leads to the rapid development of the metabolic syndrome and diabetic kidney disease. To model metabolic syndrome, both control and VCD-treated mice were fed a high-fat diet. Menopausal mice on the high-fat diet demonstrated greater weight gain, higher circulating insulin levels, and had increased insulin resistance relative to cycling mice on the high-fat diet. On a standard diet, menopausal mice also had impaired glucose tolerance which improved with estrogen re-placement. When treated with streptozotocin (STZ) to induce diabetes, induction of diabetes post-ovarian failure resulted in higher blood glucose levels than induction in perimenopause. Renal damage was accelerated in post-menopause along with an increase in macrophage infl-tration and glomerular hypertrophy. The VCD model of menopause provides a model for the impact of the menopause transition on diabetic kidney disease and the metabolic syndrome (NIH RO1 DK073611, RO1 AG021948). References: Romero-Aleshire, M.J., Diamond-Stanic, M.K., Hasty, A.H., Hoyer, P.B., Brooks, H.L. 2009. Loss of ovarian function in the VCD mouse-model of menopause leads to insulin resistance and a rapid progression into the metabolic syndrome. AJP Reg. 297, 587–592. Diamond-Stanic, M.K., Romero-Aleshire, M.J., Hoyer, P.B., Greer, K., Hoying, J.B., Brooks, H.L. 2011. Midkine, a heparin-binding protein, is increased in the diabetic mouse kidney postmenopause. AJP Renal 300, F139-46.

2.2 EARLY MENOPAUSE AND CARDIOVASCULAR DISEASE
Pamela Oviano1

1Medicine, Johns Hopkins Univ., JH Bayview Med. Ctr., 4940 Eastern Ave, 301 Mason Lord Dr., Ste. 2400, Baltimore, MD, 21224.

Cardiovascular disease (CVD) is the leading cause of death in women. Current risk stratification tools have limitations in identifying younger women at moderate to high risk for CVD. Aspects of reproductive health or disorders may add additional predictive information in women. Studies have shown an increase in coronary heart disease (CVD) mortality in women with early menopause (<45 years) compared to women with average menopausal age (49 years or more). The Nurses' Health Study reported that early menopause was associated with increased risk for myocardial infarction. These studies have included mostly Caucasian women. The MultiEthnic Study of Atherosclerosis enrolled women of white, African-American, Hispanic and Chinese ethnicity, who were age 45 to 84 yrs and free of clinical atherosclerotic disease. This longitudinal study evaluates factors related to progression of subclinical disease. There were 693 women with self-reported early menopause (at age <46 yr) and 1816 women without early menopause, with mean followup of 57 months. We evaluated the association between early menopause and incident CHD (definite or probable MI, resuscitated cardiac arrest, and definite CHD death) and stroke (fatal and nonfatal). Early menopause is an independent predictor of CHD (HR 2.08) and stroke (HR 2.02) even after adjustment for traditional CVD risk factors. Support: NIH contracts N01-HC-95159 through N01-HC-95169, K23-HL-87114. Reference: Hoyer, P., Grodstein F, Hennekens C, et al. Age at natural menopause and risk of cardiovascular disease. Arch Intern Med 1999;159:1061-6.

2.3 CARDIOVASCULAR REMODELLING, HYPERTENSION AND SEX HORMONES IN FOLLITROPIN RECEPTOR KNOCKOUT (FORKO) MICE
Rhim Touy1


In physiological conditions, regulated production of reactive oxygen species (ROS) plays an important role in signal transduction and cellular function. In pathological conditions oxidative stress (increased ROS) contributes to oxidative damage, implicated in hypertension and end-organ damage. Oxidative stress also plays a role in gender-differentiated differences in cardiovascular disease and in menopause-associated hypertension. This has been attributed to increased ROS generation related to elevated androgen and/or to decreased estrogen levels. Estrogen deficiency may also contribute to reduced antioxidant capacity, which further exacerbates oxidative stress. Of the sex-steroids, including dianabol, progesterone and glutathione, thioestrin (Trx) is one of the most abundant. Thioestrin-interacting-protein (TrxIP) is an endogenous Trx inhibitor. Independent of its anti-oxidant properties, Trx also functions as a signaling molecule by modulating kinases involved in cell growth/apoptosis. In particular ASK-1, which is pro-apoptotic, is inhibited by Trx. Changes in Trx status have been implicated in various cardiovascular pathologies, including atherosclerosis and hypertension. We demonstrated that the Trx system is downregulated in FORKO mice, a model of menopause-associated hypertension. In particular Ang II-activated cardiovascular hypertrophy/fibrosis is associated with reduced Trx activity and upregulation of Trx-sensitive ASK-1/caspase signaling. These data suggested that in estrogen-deficient states, protective actions of Trx are blunted. Such phenomena may contribute to reduced-risk cardiovascular remodeling and target-organ damage, important in menopause-associated hypertension. (J Hypertens 2007:25:1263/Am J Physiol.2008;295:H1481; Hypertension 2009:54:427.)

3.0 GENDER DISPARITIES IN RENAL DISEASE

3.1 SEX DIFFERENCES IN RENAL INJURY: ROLE OF PODOCYTES
Sharon Elliot1, Paula Catanu1a

1Surgery, Miller Sch. of Med., Univ. of Miami, 1600 NW 10th Ave, R104, RMB 1038B, Miami, FL, 33136.

Steptoe modulates the development and progression of chronic kidney disease (CKD) not related to diabetes. Clinical studies have demonstrated that the severity and rate of progression of renal damage is greater in men, compared with women. Experimental studies also support the notion that female sex is protective and male sex permissive, for the development of CKD in non-diabetics, through the opposing actions of estrogens and testosterone. While multiple experimental studies have suggested that 17β-estradiol (E2) treatment may protect the glomerulus against injury, most studies have focused on mesangial cells. Recently, our laboratory has studied podocytes, the cell type whose role may include in-tiation of progressive diabetic renal disease and other kidney diseases. We showed that E2 treatment ameliorated type 2 diabetic glomerular disease part by preventing deleterious signaling and increasing estrogen receptor β expression in podocytes. We have now found that E2 administration to diabetic female mice stabilizes podocyte F actin through a decrease in Hsp-25 activation and an increase in Rac1 expression. In addition, E2 treatment increases Akt activation and decreases caspase expression. These data sug- gest that E2 treatment may prevent podocyte loss and effacement by preserving the actin cytoskeleton and decreasing apoptosis. Support: NIH AG017170-12. References: Catanu P, Doublier S, Fornoni A,Lupia E, Berho M, Striker GE, Xia X, Karl M, Elliot SJ. 17β-estradiol and Tamsulosin upregulate estrogen receptor β and regulate podococyte signaling pathways in a model of type 2 diabetes. Kidney Int. 75:194-201, 2009.

3.2 PODOCYTURIA AS AN EARLY PREDICTIVE MARKER OF PRE-EMCPLASMIA
Vesna Garovic

1Nephrology and Hypertension, Mayo Clinic, 200 First St. SW, Rochester, MN, 55905.

Preeclampsia is a syndrome of hypertension and proteinuria that occurs after 20 weeks gestation. Recent work shows that podocyturia, the shedding of live podocytes in the urine, is present at the time of delivery in preeclamptic patients. We aim to test whether podocyturia is predictive of preeclampsia and whether it can differentiate between preeclampsia and other hypertensive disorders of pregnancy. We prospectively enrolled 122 patients at first obstetric presentation. Urine samples were obtained at presentation, second trimester, delivery, and 4-6 weeks post-partum. Urine sediment was cultured for 24 hours to select for viable cells. Podocytes were then identified on the basis of podocin staining. The presence or absence of podocyturia was then correlated with the later development of preeclampsia or high risk pregnancy, including gestational hypertension, gestational diabetes, and/or high risk pregnancy. At delivery, podocyturia was consistently present in all 10 women with preeclampsia and absent from the 19 women with high risk pregnancy disorders. None of the 93 women with normal pregnancies developed podocyturia at delivery. At mid-gestation, all 10 women who later developed preeclampsia had podocyturia. In addition the women with high risk pregnancy disorders who did not develop preeclampsia and those with normal pregnancy did not develop podocyturia at mid-gestation. Podocyturia may be helpful in the diagnosis of preeclampsia at delivery and in differentiating women with proteinuria from other high risk preeclampsia patients. At mid-gestation, the presence of podocyturia may identify women at risk of developing preeclampsia later in pregnancy. Garovic VD, Wagner SJ, Turner ST, et al. Urinary podocyte excretion as a marker for preeclampsia. Am J Obstet Gynecol 2007 Apr; 196(4):320.e1-320.e7.
ROLE OF ANDROGENS AND 20-HETE IN RENAL SODIUM TRANSPORT

Kathryn Sandberg1, Lijun Li

1Dept. of Integrative Biology and Physiology, UCLA, 1417 LSIB, Los Angeles, 90024.

Differences in sensitivity to aldosterone may play a role in blood pressure (BP) disparity between males and females. In order to evaluate the role of the sex chromosomal complement (SCC) in determining sex differences in BP, we used ovariectomized (OVX) Sprague-Dawley (Sy) mice (sex-determining gene) was translocated from the Y chromosome to an autosomal chromosome. Mice of 4 distinct genotypes: 1) XX-F, 2) XY-F, 3) XX-M, and 4) XY-M were gonadectomized to remove masking effects of sex steroids. On a high-sodium diet (0.085%), mice were implanted with osmotic minipumps to infuse aldosterone and later switched to a high-NaCl diet (5%). By day 2 of high-NaCl diet, mice of the XX SCC demonstrated a significantly more robust aldosterone-escape effect, as evidenced by higher urinary sodium excretion (mMolNa+/g b.w.): 3.5 ± 0.9 (XX-F), 1.5 ± 0.2 (XY-F), 2.1 ± 0.3 (XX-M), and 1.5 ± 0.4 (XY-M), P < 0.028 for SCC. This significantly-increased excretion of sodium in the XX SCC was maintained on day 3 of high-NaCl diet (p = 0.031 for genotype). Interestingly, potassium excretion was also significantly increased in the XX SCC on day 3 (p = 0.045). These results suggest early-stage XX SCC are more aldosterone sensitive, leading to early sodium retention necessitating greater pressure natriuresis or 2) XX SCC have a greater efficiency of escape mechanisms relative to XY. Studies to evaluate BP in this model are currently ongoing. Overall, these studies highlight important differences due to SCC in renal sodium handling in response to high-NaCl diet with aldosterone infusion. This finding may be particularly relevant in the absence of sex steroids, e.g., postmenopausal.

4.4 GPR30 AGONIST G-1 RESTORES MEGALIN EXPRESSION AND REDUCES PROTEINURIA IN SALT-SENSITIVE MRENZ-LEWIS FEMALE MICE

Lilya Yamaleyeva1, Mark Chappell1


Female mRen2.Lewis (mRen2) rats maintained on high salt (HS, 4% sodium) exhibit markedly higher systolic blood pressure and significant end organ injury in the kidney, vasculature and heart. We previously reported that chronic treatment with the GPR30 agonist G-1 improved renal hypertension and creatinine clearance while reducing proteinuria and oxidative stress in HS females. The current study assessed renal GPR30 expression and its relationship with megalin, an endocytic receptor for filtered proteins. In mRen2 females fed HS for 10 weeks, cortical GPR30 protein increased approximately 6-fold (0.6 ± 0.3 vs. 4.0 ± 0.8; P < 0.01) compared to the normal salt (NS) group; however, cortical ERα isoforms (46, 66, and 36 kDa) were not changed. Immunofluorescence revealed co-localization of GPR30 and megalin on the luminal surface of proximal tubules. HS reduced megalin by 58% (P < 0.01, n=4-5) in comparison to the normal group while G1 treatment restored its expression (P < 0.05 vs. HS), as well as reduced tubulointerstitial oxidative stress (4-HNE staining). Meas. estimate, megalin was negatively associated with both proteinuria (r = -0.47, P < 0.005) and 8-isoprostane excretion (r = -0.64, P < 0.05). We conclude that the GPR30-induced renoprotective effects may involve restoration of megalin-mediated protein reabsorption through attenuation of oxidative stress within the proximal tubules of the salt-sensitive female mRen2 rat. Funding: NBHI 56973, HL51952, HL103974; AHA 0825515.

4.5 COLLECTING DUCT-DERIVED RENIN EXHIBITS SEX DIFFERENCES DURING NORMAL SALT AND HIGH SALT DIETS IN SPRAGUE-DAWLEY RATS

Vicky Rands1, Dale Seth1, Minolfa Prieto2

1Department of Medicine, Emory University, 1430 Tulane Ave., Atlanta, GA, 30322.

In contrast to the inhibitory effect of high salt (HS) on renin from the juxtaglomerular cells, renin from the collecting duct (CD renin) is not suppressed in male rats fed HS. To determine if CD renin exhibits sex disparity in response to HS, we measured the impact of a high-salt diet on CD renin expression. CD renin expression was reduced in male rats, but not females (F: 4.3 ± 1.7 vs. M: 5.2 ± 0.9, P < 0.01). These data suggest that CD renin expression may be dependent on sex hormones, which may play a role in the sex difference in renal sodium handling in response to high-salt diet.
females, the greater urinary renin activity in males, suggest greater capability to form intratubular Ang I and ultimately Ang II, in males. Tulane-BIRCWH (K12HD043451).

4.6 ASSOCIATION BETWEEN MENOPAUSE, OBESITY AND COGNITIVE IMPAIRMENT
Judith Zilberman1, Miledín Del Sueldo1, Gustavo Cerezo1, Stella Castellino2,3
1Human Hlth. Commission, 2Dept. of Physiology and Pharmacology, Univ. of the Pacific, 3Dept. of Biomed. Sci., Univ. of the Pacific, Arcos 1563, Buenos Aires, 1426, Argentina, 2Human Hlth. Commission, Sept. Res. Grp, Arcos 1563, Buenos Aires, 1426, Argentina, 3Human Hlth. Commission, Sept Res. Grp, Entre Rios 1359, Cordoba, 5900, Argentina, 4Programa Corazón Sano, Municipalidad de Villa Maria, Mendoza 18736, Córdoba, 5900, Argentina. Background: Obesity (Ob) has been associated with cognitive decline (CD). The protective role of estrogen on cognition is controversial. Aims: To evaluate the association between CD and Ob in menopausal women (MW). Methods: We included 578 women ≥51 y, 141 premenopausal, and 437 postmenopausal participating in the Preventive Program "Healthy Heart 2" (Villa Maria, Córdoba, Argentina). Design: cross-sectional and observational study. Multistage sampling stratified (sex and age) and call voluntary. The validated survey was used. Anthropometric data were recorded. Definition: MW as amenorrhea ≥1 y, Ob as waist circumference (WC) ≥88 cm or body mass index (BMI) ≥25, Cognitive assessment: Minimal Cognitive Examination (MCE) that includes: Mini-Mental Statement Examination (MMSE) (global cognition), Clock Drawing Test (executive function) and Boston abbreviated test (memory). Results: The average age 59.8 ± 9.4 y. The MWC prevalence was 44.3% (n=300) and Ob 52.6% (n=168). BMI was positively correlated with: MMSE (coef. Pearson (r) 0.09, p 0.019) and MCE (r 0.21, p 0.03). There was equal correlation between WC and MMSE (r 0.04, p 0.02) and MCE (r 0.10, p 0.03). Conclusions: The prevalence of Ob in MW was higher, both overall and abdominal. There was positive correlation between Ob and better cognition. The result was attributable to the hypothesis that increased production peripheral estrogen (adipose tissue) is protective.

4.7 GPR30 ACTIVATION INCREASES ACE2 EXPRESSION IN DIABETIC OVARIECTOMIZED MREN2.LEWIS FEMALES
Hans El-Basoussi1, Sarah Lunde1, Liliana Yanevlevska2, Mark Chappell1
1Hypertension and Vascular Res. Ctr., Wake Forest Univ. Sch. of Med., Medical Ctr. Blvd., Winston Salem, NC, 27157-1032. We previously reported that activation of the estrogen receptor GPR30 by the selective ligand G-1 reduced proteinuria and angiotensinogen expression in estrogen-depleted (O VX), diabetic mRen2.Lewis (mRen2) rat. The present study evaluated the influence of diabetes on ACE2 and nephrin (NPE) expression, two key enzymes involved in Ang II and Ang-(1-7) metabolism, within the kidneys of intact and OVX-mRen2. Diabetes was induced with a single dose of streptozotocin (STZ 65 mg/kg; ip) for 4 weeks without insulin replacement and kidneys removed for analysis of GPR30, ACE2 and NPE expression. Tubular expression of GPR30 increased significantly in the intact STZ mRen2 and was correlated with an increase in ACE2 protein expression (r=0.65, p<0.05). Both GPR30 and ACE2 were localized to the apical region of proximal tubules. NEP expression was significantly increased in intact STZ mRen2 (p<0.05) but did not correlate with GPR30 expression. In contrast, estrogen-depletion alone increased GPR30 expression, and diabetes had no further influence on the receptor or peptidase expression. GPR30 expression was reduced in aorta of diabetic rats, but the extent of decrease was greater in diabetic females. Furthermore, diabetic females were characterized by an increased sensitivity to ACh after indo compared with other groups. Incubation of aortic rings with L-NAME potentiated PE responses in all groups. However, aorta from control females showed a greater potentiation of the PE after NOS inhibition than in other groups. These data suggests the predisposition of female rat aorta to vascular injury in diabetes, possibly via altered NO production and COX metabolites (Supported by NIH/NIDCR).

4.10 Withdrawn.

4.11 CENTRAL BLOCKADE OF ANGIOTENSIN(1-7) OR ANGIOTENSIN II RECEPTOR ENHANCES ALDOSTERONE-SALT-INDUCED INCREASES IN BLOOD PRESSURE (BP) IN FEMALE RATS
Baojun Xue1, Zhongming Zhu1, Fang Guo1, Meredith Hay1, Alan Johnson1
1Psychology, Univ. of Iowa, 11E Seashore Hall, Iowa City, IA, 52242, 2Physiology, Univ. of Arizona, Administration Bldg., 512, Tucson, AZ, 85721-0066, 3Psychology, and the Cardiovascular Ctr., Univ. of Iowa, 11E Seashore Hall, Iowa City, IA, 52242. In comparison to male rats, females are protected against Ang II- and Aldo-induced hypertension (HT). However, the mechanism underlying this protective effect is not well-understood. Recent studies show brain-selective overexpression of ACE2 or AT,R attenuates Ang II-induced HT in male mice. ACE2- and AT,R-expression in the kidney is also higher in female rats than males, and may account for attenuated BP induced by systemic ANG II in females. Our study tested if central blockade of ACE2 or AT,R enhances Aldo-induced increase in BP in female rats. Systemic infusion of Aldo (0.75 μg/h, 4) weeks into females with 1% salt as a sole drinking fluid resulted in a slight increase in BP (Δ7.5±1.2 mmHg). But females receiving this same treatment along with iv infusions of ANG (1-7) receptor antagonist (A-779) or AT,R antagonist (PD123,191) showed a greater augmented pressure effects (Δ20.1±8.1 and Δ18.9±4.6 mmHg, respectively). RT-PCR analysis of brain revealed a significant increase in mRNA expression of renin (1.4-fold), Aldo synthesize (1.5-fold), 1-1 β-hydroxylase (2.9-fold), ACE2 (1.5-fold) and AT,R (2.5-fold). Yet neither AT,R nor ACE2 in LT or PVE changed in Aldo/salt-treated females compared to basal conditions. Our results suggest an anti hypertensive arm of the brain RAS (ACE2/ANG (1-7) Mas/AT,R) may play an important compensatory role in development of Aldo/salt induced HT in females. (HL-13438, HL-98207, DK-66086, and MH-80241).

4.12 SEX DIFFERENCE IN THE β-ADRENERGIC CONTRACTILE RESPONSE ROLES OF ADENYL CYCLASE AND PHOSPHODIESTERASE
Victoria McIntosh1, Robert Laskey2
1Physiology, Wayne State Univ. Sch. of Med., 1129 Elliman Bldg., 421 E. Canfield, Detroit, MI, 48201, 2Physiology, Wayne State Univ. Sch. of Med., 1104 Elliman Bldg., 421 E. Canfield, Detroit, MI, 48201. Female hearts exhibit a blunted contractile response to β-adrenergic receptor (β-AR) stimulation as compared to male hearts. The roles of adenylyl cyclase (AC), phoshodiesterase (PDE) and cAMP signaling in generating these sex-dependent differences were examined in dose response studies in isolated perfused hearts from male and female mice using AC agonist forskolin, PDE inhibitor isobutylmethylxanthine (IBMX), and a non-hydrolyzable form of cAMP, cyclic-AMP. Females showed a modestly lower contractile response to forskolin as compared to males at 5 μM (left ventricular systolic pressure in 5% change from baseline, 62.5±5 vs. 77±2), but there were no sex differences in the contractile responses to IBMX or cAMP-cAMP. Ad- ditionally, there were no sex differences in the responses to radical scavengers – α-tocopherol, αToc, or GSH, determined using western blotting. Paradoxically, expression of adenylyl cyclase V/VII in ventricular membranes is 78% greater in females than males. The re-
reduce contractile re-response to forskolin seen in females is not due to lower AC expression, and is likely only a minor com-potent in generating sex differences in the Jα-AR response. A plausible explanation for the paradoxical observation of greater AC expression but reduced contractile responses to forskolin could be sex differences in regulation of AC activity by protein kinases. Future studies will address sex differences in the complex regulation of the Jα-AR contractile response by PDEs and protein kinases. This work was sup-ported by National Heart, Lung, and Blood Institute Grant, RO1HL066132 (Robert D. Lasley).

14.13 GPRI3 IS INVOLVED IN THE REGULATION OF THE KCa1.1 CHANNEL CURRENT IN A GENDER SPECIFIC POPULATION OF MYELINATED VAGAL AFFERENTS

John Schild1, Baivan Li1

1Biomed. Engineering, IUPUI, SL220, 723 W. Michigan St., Indianapolis, IN, 46236. Autonomic nervous system control of cardiovascular function is sexually dimorphic. Our lab has a long-standing interest in cardiovascular function and recently showed that female rats have a unique and functionally distinct class of low threshold myelinated (Ah-type) aortic baroreceptor neurons (ABN) that is rarely ob-served in age-matched males. Furthermore, we have shown that the sensitivity and ex-citability of Ah-type ABN are markedly reduced in an ovarectomized rat model (OVX). Here, we test two hypotheses: 1) regulation of BK-type KCa (KCa1.1) ion channels underlies the loss of excitability in these gender specific afferents, and 2) a GPRI3 dependent pathway is involved in the regulation of KCa1.1 channels. Voltage and current clamp protocols were carried out using the patch clamp technique on vagal neurons (VGN) from aged matched female (NF, n = 10) and OVX (n = 10). The whole cell KCa1.1 (ibotenic acid sensitive) current in OVX was ~50% greater than that measured in NF. Companion current clamp studies in OVX revealed that repetitive discharges in Ah-type ABN were abolished as a result of OVX. Application of G-1, a selective agonist of the G-protein coupled estrogen receptor GPRI3, restored the excitability of Ah-type afferents to near control levels. Application of G-1 to voltage clamped VGN reduced the whole cell KCa1.1 current in Ah-type neurons from GCm levels measured in NF. Collectively, these studies impli-cate that the GPRI3 is involved in the regulation of KCa1.1 currents in myelinated Ah-type VGN. We contend that this gender specific population of myelinated vagal afferents may provide, at least in part, a neurophysiological explanation for the sexual dimorphism in neurocirculatory control. NIH HL081819 and HL072012.

14.14 ANGIOTENSIN PEPTIDES AND FMD: DOES SEX MATTER?

Yashesh Shah1, Margaret Zimmerman 2, Breana Berry 1, Thomas Poore 1, Jennifer Sullivan1, Ryan Harris1

1Georgia Prevention Inst., Georgia Hlth. Sci. Univ., 1120 15th St., Augusta, GA, 30912, 2Vascular Biology Ctr., Georgia Hlth. Sci. Univ., Sanders Bldg., CB 3330, 1120 15th St., Augusta, GA, 30912. The prevalence of cardiovascular disease is greater in men than in women, and al-though the mechanism responsible is unknown, sex differences in Angiotensin (Ang) concentrations of Ang(1-7) are associated with FMD. A total of 29 subjects par-ticipated in the flow-mediated dilation (FMD) test represents a bioassay of NO-de-pendent lipoprotein (HDL), low density lipoprotein (LDL). Very low density lipoprotein more relevant in hypertensive menopausal subjects. In our environment, diverse Hypertension and menopause are independent risk factors for dyslipidaemia. In Nigeria, we hypothesize that there is a gender difference in the expression but reduced contractile responses to forskolin could be sex differences in the complex regulation of the AC activity by protein kinases. Future studies will address sex differences in the response to fetal and lactation zinc deficiency. Methods: We has determined renal ROS activity with L-(14C)-arginine (pmol/min/g tissue) and protein abundance by western blot (% density/beta antigen), renal thiothriobarbituric acid-reactive substances (TBARS, nmol/mg prot.), glutathione concentration (GLUT, mg/g prot.), superoxide dismutase (SOD, U/mg prot ), catalase (CAT, nmol/mg prot) and glutathione peroxidase activity (GPO, pmol/min/g prot) in 21 days female (f) and male (m) offspring of Wistar rats exposed from pregnancy up to weaning: low(L, 8 ppm) or control(H, 300 ppm) diet (n = 6). Results: Renal ROS activity was decreased in Bm (237±5) and Fo (245±7) compared with Cm (302±5) and Cf (317±11) respectively. It was not associated with lower exression of eNOS, nNOS, INOS protein. *p<0.01 vs Cf; †p<0.01 vs Cm. Kidney morphological alterations observed in this model may be associated with nitric oxide system and oxidative stress of Ang(1-7). Lower ROS activity is not due to a decrease in protein expression so we suggest that other mecha-nisms may be involved, like alteration in NO zinc cluster, cofactors or the oxidative stress. The impairment of antioxidant enzymes due to this deficiency is more evident in female than in male rats.

14.15 GENDER DIFFERENCES IN RENAL OXIDATIVE STRESS ENZYMES IN DAHL SS RATS: EFFECTS OF SALT AND OVARIECTOMY

Damian Romero1, Jane Reckelhoff2, Licy Yanes3

1Biochemistry, Univ. of Mississippi Med. Ctr., 2500 North State St., Jackson, MS, 39216, 2Physiology and Biophysics, Univ. of Mississippi Med. Ctr., 2500 North State St., Jackson, MS, 39216, 3Medicine, Univ. of Mississippi Med. Ctr., 2500 North State St., Jackson, MS, 39216. Experimental and clinical data have failed to show a definite link between oxidative stress and cardiovascular diseases. Contradictory clinical studies showed either a pro-tection or a lack of effect of antioxidants in cardiovascular diseases. We had previ-ously shown that male SHR rats have higher blood pressure (BP) and oxidative stress than females. Antioxidant treatment decrease BP in male but not female SHR rats. We hypothesize that there is a gender difference in renal oxidative stress enzymes ex-pression under low (LS) or high (HS) salt in Dahl salt sensitive (SS) rats and that difference is due to sex hormones. Male, female and ovariectomized (OVX) SS rats (n=6/group) were maintained on LS phy-toestoferogen-free diet (0.28% NaCl) until 17 wk of age. Then, rats were placed on LS or HS diet (8% NaCl) for 4 wks. Renal cortices and medulla oxidative stress enzyme mRNA expression was quantified by qPCR. Males had higher levels of Nox4 and gp91phox compared to females on LS and HS diets. OVX rats had higher levels of Nox4 and gp91phox on LS but did not differ on HS. gp91phox levels were higher in males on LS and did not change with HS, whereas Nox4 had a similar pattern to male rats. EC-SOD levels were significantly higher in females compared to males, and OVX abolished that difference. Our data suggest that female rats may be unresponsive to oxidative stress secondary to high levels of renal SOD expression and that estradiol and/or progesterone may be involved in this protective mechanism.

14.16 SEX HORMONES MODULATE RESPONSES TO OXIDATIVE STRESS IN RENAL PROXIMAL TUBULE CELLS

Istvan Arany1, Jeb Clark1, Dustin Reed1, George Booz2, Luis Juncos3

1Vanderbilt University, 2Stanford University, 3University of Texas at Austin. Sex hormones were proposed that the oxidant-sensor adaptor protein p66shc may aggravate while the acti-vation is not due to a decrease in protein expression so we suggest that other mecha-nisms may be involved, like alteration in NO zinc cluster, cofactors or the oxidative stress. The impairment of antioxidant enzymes due to this deficiency is more evident in female than in male rats.

14.17 GENDER DIFFERENCES IN RENAL OXIDATIVE STRESS ENZYMES IN DEVELOPING AtheroscleROSIS:

Diana Alarcon1, 2, Ana Cecilia Barrera3, Maria de los Angeles Alvarado2, Rocío Sánchez2, 4

1Musicology, 2Psychology, 3Neuroscience, 4Biophysics, UNAM, Mexico City, Mexico. Sex differences in total cholesterol, HDL, LDL, VLDL and HDL/LDL ratio between the two groups (P> 0.05). However there were statistically significant differences in tri-glycerides and the atherogenic index of plasma (P<0.05). Simultaneous occurrence of menopause and hypertension leads to alteration in lipid profile that favours the use of triglyceride based indices (instead of HDL/LDL ratio) in determining the risk of developing atherosclerosis. Funding: This project was self sponsored.

2011 APS Conference: Physiology of Cardiovascular Diseases: Gender Disparities ABSTRACTS OF INVITED AND VOLUNTEERED PRESENTATIONS

October 26-30, 2011 APS Conference: Physiology of Cardiovascular Diseases: Gender Disparities ABSTRACTS OF INVITED AND VOLUNTEERED PRESENTATIONS
hormones on these factors in cultured renal proximal tubule cells. Dihydrotestosterone (DHT) treatment induced the p60src promoter and exacerbated endogenous as well as H2O2-induced ROS production and co-incident injury. DHT also augmented TGFβ-mediated induction of the promoter of the profibrotic αSMA gene and attenuated IL-6-induced tyrosine phosphorylation of STAT3. In contrast, 17β-estradiol (E2) treatment augmented tyrosine phosphorylation of STAT3 but inhibited TGFβ-mediated induction of the αSMA promoter. Thus, sex hormones may differentially regulate expression/activity of signaling molecules involved in survival or injury that can substantiate gender-specific responses to injury in the kidney. Funding: AHA GIA (10GRNT3790019, I. Arany), R01HL88101-04 and R01HL88810-02S1 (G.W. Booz) and DK74054 (L.A. Janczewski).

4.19 EXAGGERATED ANGIOTENSIN II-INDUCED HYPERTENSION IN MALE RATS EXPOSED TO EARLY LIFE STRESS DEPENDS ON TESTOSTERONE-LEVELS

Anaíla Loria1, Daílson Pollock1, Jennifer S Pollock1


Previously, we reported that male rats exposed to maternal separation (MS), a model of early life stress, displayed enhanced sensitivity to angiotensin (Ang) II infusion (65 ng/day, 2 weeks) compared to non-MS control (C) male rats. This enhanced AngII-induced hypertension was also present in female MS rats, but significantly attenuated. The aim of this study was to investigate the role of sex hormones underlying the sensitivity to AngII MS was performed in male and female WKY rats 3 hrs/day from day 2 to 14 of life. At the age of 12 weeks in baseline conditions, plasma testosterone (Ts) was similar in C and MS male rats (2456±377 and 2270±436 ng/ml, respectively) as well as in C and MS female rats (513±5 and 523±3 pg/ml). Also, estrogen (E2) was similar in C and MS male rats (4.0±0.5 and 3.4±0.5 ng/ml) as well as in C and MS female rats (14.2±1.8 and 13.3±2.5 pg/ml). In female C and MS rats, 14 days of AngII infusion reduced Ts (37.3±42±pg/ml) and E2 (61±5 and 1±2 pg/ml) similarly. However, in AngII-infused male rats, Ts was higher in MS than in C rats (1000±187 vs. 579±63 ng/ml, p<0.05). E2 was below detection in MS compared to C male rats. In castrated male rats, AngII infusion increased blood pressure in C and MS rats similarly (129±6mmHg and 125±6 mmHg) in contrast to the enhanced AngII-induced hypertension observed in non-castrated MS rats. These data suggest that Ts plays an important role in the mechanism underlying exaggerated AngII-induced hypertension due to early life stress.

4.20 ANDROGEN INDUCES THE EXPRESSION OF CYP4F2, A MAJOR 20-HETE PRODUCING ENZYME IN HUMAN, VIA ACTIVATION OF THE ANDROGEN RECEPTOR

Victor García1, Yumiko Lin2, Cheng-Chia Wu1, Michal L. Schwartzman1

220-Hydroxyicosatetraenoic acid (20-HETE) is a cytochrome P450 (CYP) 4-derived arachidonic acid metabolite and a vasoconstrictor found in the renal, cerebral and hepatic microcirculation. The pro-inflammatory and vasoconstrictor activity of 20-HETE has been associated with smooth muscle contractions, endothelial dysfunction and activation and hypertension. Androgen has been shown to induce cypr4a12 and cypr4a18 expression in mice and rats, respectively, resulting in 20-HETE-mediated hypertension. It remains to be determined whether androgen induces CYP4a in humans in whom androgen has contributed to gender differences in hypertension. To study this paradigm in an in vitro system, we used a well-established androgen-responsive human prostate cancer cell line, LNCaP, which has the capability of producing 20-HETE (570±140 pg/mg). 20-HETE synthesis in LNCaP cells pretreated with charcoal stripped medium followed by androgen replacement with 5α-dihydrotestosterone (DHT) increased by 65% when compared to vehicle-treated cells. CYP4F2 and CYP4F3 mRNA levels increased by 2.3- and 2-fold higher in DHT-treated LNCaP as compared to vehicle, while CYP4A11 and CYP4A22 mRNA levels decreased by 70-80%. The increase in CYP4F2 and CYP4F3 was attenuated by co-treatment with Flutamide. To further examine whether this association exists in non cancer cells, primary human coro-nary vascular smooth cells were treated with DHT/Flutamide. DHT increased CYP4F2 mRNA levels by 2-fold and was attenuated with Flutamide.

4.21 PROFILE OF ANTIOXIDANT AND PRO-OXIDANT ENZYMES AND MARKERS IN THE KIDNEY CORTEX (KC) DURING RAT PREGNANCY

Mark Cunningham1, Jennifer Sasser2, Chris Bas1

2The increased metabolic demand of pregnancy may result in oxidative stress (OS), a risk factor for pregnancy complications. In the pregnant rat, increases in renal Na re-absorption occur by midterm leading to increased KC oxygen consumption. Here, we examined enzymes and markers of OS in early (E), mid (M) and late (L) pregnancy (P) (days 3, 12, 20) compared to virgin (V). Protein abundance of endothelial nitric oxide synthase (eNOS), the NADPH oxidase subunit p22phox, and extracellular (EC), cytosolic (CuZn), and mitochondrial (Mn) superoxide dismutase (SOD) as well as hydrogen peroxide (H2O2) and nitrotyrosine (NT) levels were measured in KC. The only variable altered by P was a reduction in NT at LP vs V (by one-way ANOVA; Table). That this fall at LP was due to 4 days of partum (PP) vs V (test; Table). Conclusion: Despite increased renal metabolism during P, there is no change in KC antioxidant SODs or eNOS, pro-oxidant p22phox or H2O2 levels. The fall in NT at LP, which is maintained PP, suggests a fall in KC OS in normal P. This needs to be confirmed with other OS markers, and the mechanisms remain to be determined.

*P<0.05 vs V. Protein abundance as integrated optical density normalized to total protein loaded and internal standard.
injury. Systemic and renal hemodynamic parameters were determined in male and female NBW and LBW adult rats after mild renal I-R (15 minutes of ischemia). Renal superoxide production and renal cortical actinase isoenzyme activities were also assessed. Mild renal I-R did not alter renal parameters, in male or female NBW rats as well as in female LBW rats. However, male LBW rats show significant changes comparable with renal injury, (Table I). Thus, these findings suggest that LBW female rats are protected against the stress sensitivity in renal injury induced by ischemic.

### Parameters/Rat ID

<table>
<thead>
<tr>
<th>Male-NBW</th>
<th>Male-LBW</th>
<th>Female-NBW</th>
<th>Female-LBW</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (mmHg)</td>
<td>125±2</td>
<td>160±17</td>
<td>117±5</td>
</tr>
<tr>
<td>GFR (ml/min/1.73 m²)</td>
<td>0.9±0.1</td>
<td>0.3±0.1*</td>
<td>0.8±0.1</td>
</tr>
<tr>
<td>Basal Superoxide (RFU)</td>
<td>1692±128</td>
<td>4233±190*</td>
<td>1342±135</td>
</tr>
<tr>
<td>NAADP-on derivate superoxide</td>
<td>2245±414</td>
<td>407±395*</td>
<td>1845±292</td>
</tr>
<tr>
<td>Renal Injury Score</td>
<td>0.5±0.1</td>
<td>2.8±0.7*</td>
<td>0.5±0.2</td>
</tr>
</tbody>
</table>

*P<0.05 vs. All other groups.

### 4.25 SEX DIFFERENCES IN ACE MODULATES ANG 1-7 LEVELS IN NORMOTENSIVE WKY RATS

Kanchan Bhatia1, Margaret Zimmerman2, Jennifer Sullivan2


The goal of this study was to determine 1) if there is a sex difference in Ang (1-7) levels in the renal cortex of normotensive rats, and 2) to measure the activity of the major enzymes that regulate Ang (1-7) formation. 12 week old male and female WKY were studied; the renal cortex was isolated to measure Ang II, Ang (1-7), ACE and ACE2 activities. Female WKY had greater Ang II (336±36 vs. 261±32 pg/g cortex, p<0.05 vs. control). In summary, ACE inhibitor enalapril resulted in a larger decrease in Ang II levels in males than females, while significantly decreased ACE activity in females (Ang II: 155±21 vs. 104±40 RFU/mg protein, p<0.05 vs. control), and significantly decreased ACE activity in females (Ang II: 95±16 pg/g cortex, p<0.05 vs. control). This was associated with a significant decrease in Ang II and Ang (1-7) levels in males (Ang II: 95±16 ng/g cortex, Ang (1-7): 336±36 vs. 261±32 pg/g cortex, p<0.05 vs. control). In summary, enalapril resulted in a larger decrease in Ang II levels in males than females, while females had a greater decrease in Ang (1-7).

### 4.26 A ROLE FOR ETHNIC DISPARITY: ENDOTHELIN-1 SECRETION BY HUMAN PLACENTAS FROM FETUSES COMPLICATED BY PRE- ECLAMPSIA

Kedra Wallace1, Krystal Frazier1, William Bennett3, James Martin1, Babbette LaMarca1

OB/Gyn, Univ. of Mississippi Med. Ctr., 2500 N. State St., Jackson, MS, 34216.

It has been shown that preeclamptic women have high levels of circulating endothelin-1 (ET-1) during the later stages of pregnancy. We examined activation of placental and vascular ET-1 from women with preeclampsia (PE) compared to controls. Placentas were collected from 40 women (20 normotensive, 20 PE) and placental explants were exposed to conditioned media from placental explants to assess endothelial cell activation, measured by ET-1 secretion and PPET mRNA. Placental explants from PE secreted significantly more ET-1 (82.10±12.76 pg/ml, p<0.05) compared to controls (31.84±7.47 pg/ml, p<0.05), however, ACE activity was comparable between the sexes. We hypothesized that greater ACE activity in females contributed to greater Ang (1-7) levels. Additional rats were treated with the ACE inhibitor enalapril (10mg/kg/day, 14 days). Enalapril abolished ACE activity in males (-21±8 RFU/mg protein, p<0.05 vs. control), and significantly decreased ACE activity in females (104±40 RFU/mg protein, p<0.05 vs. control). This was associated with a significant decrease in Ang II and Ang (1-7) levels in males (Ang II: 95±16 ng/g cortex; Ang (1-7): 336±36 vs. 261±32 pg/g cortex, p<0.05 vs. control) and females (Ang II: 155±46 ng/g cortex, Ang (1-7): 154±33 pg/g cortex, p<0.05 vs. control). In summary, enalapril resulted in a larger decrease in Ang II levels in males than females, while females had a greater decrease in Ang (1-7).

### 4.27 DIFFERENTIAL PROGRAMMING OF ENDOTHELIN RECEPTOR EXPRESSION CONTRIBUTES TO SEX DIFFERENCES IN ADULT BLOOD PRESSURE REGULATION IN INTRAUTERINE GROWTH RESTRICTED OFFSPRING

Suttira Intapad1, F Lee Tull1, John Henry Dansiger1, Norma Ojeda1, Barbara T Alexander1

1Physiology and Biophysics, Univ. of Mississippi Med. Ctr., 2500 North State St., Jackson, MS, 34216; 2Pediatrics, Univ. of Mississippi Med. Ctr., 2500 North State St., Jackson, MS, 34216.

Endothelin (ET) and its receptor subtypes play a key role in control of blood pressure in an age- and sex-specific manner. Intravenous growth restriction (IUGR) programs hypertension and enhanced sensitivity to acute angiotensin II (ANG II) in male rats. Selective ET,R blockade (ABT-627) at the dose of 10 mg/kg/min attenuates the acute ANG II pressor response in male control rats and abolishes the enhanced pressor response to acute ANG II in adult male IUGR rats. Yet, this same dose of ET,R blockade did not reduce the increase in MAP in response to acute ANG II in female control or female IUGR. Thus, the goal of this study was determine whether IUGR programs sex-specific expression of the ET receptor subtypes. Protein expression of ET,R was significantly increased in the kidney of male IUGR relative to male control (cortex: 6 fold and medulla: 2.7 fold; P<0.05). Expression of ET,R was significantly increased in male IUGR (cortex: 3.5 fold and medulla: 2.7 fold; P<0.05). In contrast, the expression of ET,R did not differ in the kidney cortex and medullar of female IUGR and female control rats; but, protein expression of ET,R was significantly reduced in the medulla of female IUGR relative to female control (0.5 fold; P<0.05). In summary, these studies indicate differential programming of ET receptor expression and suggest that sex-specific differences in the ET system may contribute to contribute to acute ANG II sensitivity.
600G increased serum levels of insulin (2.9±0.5 ng/dL, n=6), compared to 0G controls (1.8±0.4 ng/dL, n=6, P<0.05) and decreased glucose (177.5±15.9 mg/dL, n=6, compared to 227±24.2 mg/dL, n=6, P<0.05). No effects in females. In males, 600G decreased body weight (by ~2.7 g, n=6, P<0.05), with no change in females. In females, 600G decreased systolic blood pressure (107±13.5 mmHg, pulse pressure (27.5±1.6 mmHg) and cardiac work (18.9±1.2 mmHg beats/min), compared to 0G (115±17.2 mmHg, 33.4±1.9 mmHg and 22.7±1.6 mmHg beats/min respectively, n=15, P<0.05). Aortic contractility was increased with 600G in both males and female isolated aorta (P<0.05). These data suggest that a one month diet with 600G has disparate beneficial effects on cardiovascular parameters in males and female mice. Joshi Martin was supported by the Midwestern University Summer Fellowship Program. Layla Al-Nakkash was supported by NIH (1R15DK071625-01A2).

5.0 OBESITY AND CARDIOVASCULAR DISEASE

5.1 NOVEL PANCREATIC PEPTIDES CONTROL GLUCOSE HOMEOSTASIS AND APPETITE

William Jamieson1, Gina Yost1


While the incidence of diabetes in the North American population does not display a chroomosomal sex bias, a major cause of insulin resistance, obesity, does. Traditionally the effect of obesity on insulin sensitivity is studied at the level of glucose transport and insulin signaling. The causes of obesity are more diverse including diet, exercise, and partitioning of fuel sources. We have studied two of those potential causes: appetite regulation and the insulin response to ingested carbohydrates and focused on novel islet factors that may co-ordinate both. Neftalin-1 is produced in beta cells of the pancreas and acts there to increase the insulin response to glucose. It is also produced widely in brain where it exerts potent, physiologically relevant anorexigenic actions. Neuronostatin, on the other hand, is produced in delta cells of the pancreas and acts in the paraffine to influence the glucagon-producing alpha cells. In an as yet to be determined mechanism those intra-islet effects of neuronostatin result in decreased insulin response to glucose. While the physiologic relevance of this action is not known, whole animal studies have confirmed the in vitro findings. Like nefitsalin-1, neuronostatin also potently inhibits food intake, acting via the central melanocortin system. Both neftalin-1 and neuronostatin act in brain to alter autonomic function, suggesting a third mechanism by which these peptides might influence the appearance of increased obesity risk in females, versus males.

5.2 TRANSLATIONAL CARDIOVASCULAR BENEFITS OF EXENATIDE-PRECLINICAL AND CLINICAL EVIDENCE

David Parke1

1In Vivo Pharmacology, Amylin Pharmaceuticals Inc., 9360 Towne Ctr. Dr., San Diego, CA, 92121.

Exenatide (Ex) is a naturally-occurring GLP-1 receptor agonist that exhibits anti-diabetics effects in type 2 diabetic patients via glucose-dependent insulinotropism, slowing of gastric emptying, glucagon suppression and reduced food intake. Animal studies support a role for Ex in improving cardiac function, hepatic and dynamics and survival. We have shown that Ex can reverse corticosterone-induced hypertenison independent of changes in body weight in rats. Furthermore, we have recently reported that the Ex analog, AC3174, significantly improved animal survival in be in IP-induced hypertension, and in MI-induced hearts at risk. Marked improvements in cardiac function/remodeling, hypertension, insulin sensitivity and renal function were evident following AC3174 treatment. These findings are now translating into the clinic in patients with Type 2 diabetes. In humans, Ex lowers systolic blood pressure in type 2 patients with hypertension. The data are consistent with moderate obesity and blood pressure reduction, correlated with the degree of elevation at baseline. A recent database analysis of ~39,000 patients reported that Ex treatment was associated with a lower risk of CV events and hospitalizations than treatment with other glucose-lowering therapies. Ongoing five-year CV outcome studies with Ex examining the incidence of major adverse CV events will validate the relevance of these short term (6-12 month) improvements in CV function. Over-all, these described benefits of Ex may have important clinical implications regarding therapeutic choices for patients with type 2 diabetes and associated CV co-morbidities.

6.0 NEURO MECHANISMS AND DEPRESSION IN CARDIOVASCULAR DISEASE

6.1 BAROREFLEX FUNCTION IN FEMALES: CHANGES WITH THE REPRODUCTIVE CYCLE AND PREGNANCY

Virginia Brooks1

1Physiology & Pharmacology, Oregon Hlth. & Sci. Univ., 3181 SW Sam Jackson Park Rd., Portland, OR 97239.

In females, baroreflex function fluctuates with the reproductive cycle, with baroreflex sensitivity or gain (BRG) reaching its peak when gonadal steroids are elevated. The estrogen surge likely mediates the increase in BRG, since ovariectomy in rats abolishes the variations in BRG induced by the estrous cycle, while estrogen increases BRG. In contrast, normal pregnancy markedly impairs the baroreflex. Two aspects of the sigmoidal baroreflex relationships between arterial pressure and heart rate or sympathetic nerve activity are attenuated: the maximal level of heart rate or sympathetic activity when arterial pressure is lowered and the maximal slope of the most linear segment of the curve, an index of BRG. Increased brain levels of the neurosteroid, 3-alpha-hydroxy-dihydroprogesterone, contribute to the decreased baroreflex maxima. Recent data suggest that the decrement in BRG is mediated by insulin resistance and decreases in brain insulin. These findings include that 1) the decreases in insulin sensitivity and BRG are correlated during pregnancy; 2) treatment of pregnant animals with the insulin sensitizing drug, rosiglitazone, improves insulin sensitivity and BRG; 3) brain insulin levels are decreased in pregnant animals; and 4) intracerebroventricular infusion of insulin normalizes BRG in pregnant rats. In further experiments, the arcuate nucleus at the brain site at which insulin increases BRG. Thus, during pregnancy, decrements in the levels or action of insulin in the arcuate nucleus may contribute to the impaired BRG. Review: Brooks VL, Dampney RAL & CM Heesch. Pregnancy and the endocrine regulation of the baroreceptor reflex. Am.J.Physiol. 595: R439-R451, 2010.

6.2 SEX DIFFERENCES IN DEPRESSION AND CARDIOVASCULAR DISEASE

Merr Stein1

1Psychosocial & Behavioural Neurosciences and Obstetrics & Gynecology, McMaster Univ., 301 James Street South, Hamilton, ON, L8S 3B6, Canada.

It has been long established that depression is an independent risk factor for cardiovascular disease (CVD) and that CVD is a risk factor for depression (Gruppo & Johnson 2009). Three lines of evidence have been proposed to date in order to explain the comorbidity of CVD and mood, as well as anxiety disorders: 1) the epidemiological evidence for a causal role of depression in the evolution and progression of CVD; 2) the biological evidence for the plausibility of an etiologic role of depression in CVD; and 3) both depression and CVD are manifestations of a common underlying pathophysiologic process (Rudisch & Nemeroff 2003). The goal of this presentation is to briefly review and synthesize the evidence for the above proposed explanations with a special focus on the roles of serotonin, platelets and the immune system. Sex and gender can influence the mood and CVD mechanisms and sex differences in the relevant of these differences as they pertain to women will be emphasized. References: Gruppo, A.J. & Johnson, A.K. 2009. Stress, depression and cardiovascular dysregulation: a review of neurobiological mechanisms and the integration of research from preclinical disease models. Stress 12, 1–21. Rudisch, B. & Nemeroff, C.B. 2003. Epidemiology of comorbid coronary artery disease and depression. Biol Psychiatry 54, 227–240.

6.3 MECHANISM OF THE SEX DIFFERENCE IN ENDOTHELIAL DYSFUNCTION AFTER STROKE

Nabil Alkayed1


We evaluated cerebrovascular eicosanoid signaling as a mechanism underlying the sexually dimorphic response to cerebral ischemia. Young adult female mice sustained smaller infarcts after middle cerebral artery occlusion (MCAO) compared to age-matched males. The difference in infarct size was associated with lower expression and activity of soluble epoxide hydrolase (sEH) in cerebral microvessels, and was abolished by sEH gene deletion and pharmacological inhibition. sEH is a key enzyme in the metabolic conversion and inactivation of neuroprotective and vasodilator eicosanoids called epoxyeicosatrienoic acids (EETs). Accordingly, EETs levels were higher in wild-type (WT) females vs. males and in sEH knockout (KO) vs. WT males. Prostaglandin in WT female vs. male and in sEHKO vs. WT male mice was associated with higher cerebrovascular perfusion. Similarly, transgenic (Tg) overexpression of P450 epoxygenase under the endothelial Tie2 promoter was protective against ischemic brain injury in male but not female mice, with higher cerebrovascular perfusion in Tg vs. WT male mice. Endothelin-dependent vasodilation was attenuated after MCAO in WT male mice and mice with endothelial-specific overexpression of sEH. Post-ischemic cerebrovascular endothelial dysfunction in male mice was rescued by sEH deletion in sEHKO mice. We conclude that the sex difference in ischemic brain injury after MCAO in mice is in part linked to higher endothelin-derived EETs and improved post-ischemic endothelial function in females. (R01 NS44313 & R01 NS070837). Davis CM, Siler DA, Alkayed NJ. Endothelin-dependent hyperpolarizing factor in the brain: influence of sex, vessel size and disease stage. Womens Health (Lond Engl) 7:293-303.

8.0 GENDER DISPARITIES IN CARDIOLOGY

8.1 WOMEN AND ISCHEMIC HEART DISEASE

C. Noel Bairey Merz1, Raffael Bagiardini1, Leslie Shaw1


Sex differences in coronary heart disease (CHD) demonstrates that prevalence, symptom manifestation, and pathophysiology for CHD varies between women and men. Given the lower burden of obstructive coronary artery disease (CAD) and preserved systolic function in women contrasted by higher rates of myocardial ischemia and more severe near-term mortality in men, the term ischemic heart disease (IHD) is more appropriate for this discussion specific to women, rather than CAD or CHD. This paradoxical sex difference where women have lower rates of anatomical cardiac disease but worsened symptoms, ischemia and outcomes appears to be linked to sex-specific pathophysiologic activity which includes microvascular dysfunction. For women with obstructive CAD, near-term risk (i.e., in-hospital through 30 days) is elevated for females compared to men, and while longer-term risk
management strategies are equally effective, women are less likely to receive guidelines-indicated therapies. For women with evidence of ischemia but no obstructive CAD, anti-anginal and anti- ischemic therapies can ameliorate symptoms, improve endothelial function, and quality of life, however trials to evaluate impact on adverse cardiac events are needed. Ongoing research using proposed models for application of emerging knowledge to clinical practice, as well as new hypotheses, such as sex differences in stem cell therapy, are being tested. Continued attention is indicated to devise therapeutic regimens to improve symptom burden and reduce risk in women with stable and unstable IHD symptoms.

**8.2 PREGNANCY COMPLICATIONS PREDICT INCREASED RISK OF CARDIOVASCULAR DISEASE IN WOMEN: IS THIS USEFUL TO KNOW?**

Janet Rich-Edwards¹

¹Dept. of Med., Brigham & Women’s Hosp. and Harvard Med. Sch., 1620 Tremont St., Boston, MA 02120.

More than 20% of women who have born children have experienced at least one common pregnancy complication associated with increased risk of cardiovascular disease in majority: preterm delivery, hypertensive pregnancy, gestational diabetes, or fetal growth restriction. To date, most of the evidence linking pregnancy complications with CVD events has been derived from data linkage of statistical birth, hospital, and mortality registries. These registries lack information on CVD risk factors, such as family history and body mass index that may predate both pregnancy complications and CVD events. Most analyses have also lacked data to determine the extent to which pregnancy complications predict CVD events above and beyond traditionally measured risk factors such as hypertension, diabetes, and dyslipidemia. We will present data from the longitudinal national Nurses’ Health Study II on the extent to which common pregnancy complications predict CVD events independent of known risk factors that have been recorded prospectively for 18 years in this cohort. We will discuss the extent to which a history of complex pregnancy may be useful to identify young women who might benefit from targeted screening and intervention to prevent future CVD events. Reference: Rich-Edwards JW, McElrath TF, Kurzmarzicki A, Seely EW. (2010). Breathing life into the lifestyle course: pregnancy history and cardiovascular disease in women. Hypertension; 56:331-4.

**8.3 THE FEMININE FACE OF HEART DISEASE: WHAT DO WE KNOW ABOUT ANGINA IN WOMEN?**

Janet Rich-Edwards¹

¹Cardiology, Emory Univ. Sch. of Med., 49 Jesse Hill Jr. Dr. SE, Atlanta, GA, 30303.

Angina is the predominant initial and subsequent presenting symptom of coronary heart disease in women, in contrast to myocardial infarction and sudden death for men. Only recently appreciated are non-chest-pain symptoms of myocardial ischemia, termed anginal equivalents, including shortness of breath, fatigue and weakness, lightheadedness, diaphoresis, nausea, and vomiting; these are more common in women than in men, in older than in younger patients, and in diabetics than in non-diabetics. Myocardial ischemia in women and its symptomatic consequences may relate to macrovascular disease (obstruction of the epicardial coronary arteries) or microvascular disease; a common clinical characteristic of these 2 may be present. Despite a lesser degree of obstructive epicardial coronary artery disease at angiography, women have greater morbidity and mortality from angina. Treatment options include optimal medical therapy encompassing lifestyle and other risk factor interventions and pharmaceuticals, as well as various revascularization options. Randomized summary, angina is highly prevalent in women, is multifactorial in etiology, and imparts considerable morbidity and lethality. It is suboptimally recognized and treated. Sex-specific basic and clinical research is warranted to enhance clinical outcomes. References: Wenger NK. Angina in Women. Curr Cardiol Rep 12:307-314, 2010.

**9.0 CARDIOVASCULAR DISEASE AND INFLAMMATION**

**9.1 INFLAMMATION, IMMUNITY AND HYPERTENSION**

David Harrison¹, Heinrich Lob², Paul Marvar³, Meena Madhur⁴


There is increasing evidence that inflammation, and in particular components of the adaptive immune response, contribute to hypertension. Stimulation of angiogenin II, salt and emotional stress cause T cell activation and the accumulation of these cells in the periglomerular tissues and the kidney. These cells release cytokines that contribute to NADPH oxidase activation, entry of other inflammatory cells, vasocostriction and renal sodium absorption. We propose that these induce an inflammatory response that promotes a second wave of more severe and sustained hypertension. The nature of the macrophage, trauma, the precise role of reactive oxygen species, the characteristics of the neutrophils and the ultimate effect of immune cells in hypertension still require substantial study, however these considerations raise the possibility of new therapeutic approaches to treat this common disease. References: Guzik TJ, Hoch NE, Brown KA, Maslove DM, LaRosa J, Dighton S, Corony J, Weyand C, Harrison DG. Role of the T cell in the genesis of angiotensin II induced hypertension and vascular dysfunction. J Exp Med. 2007;204:2449-2460. Harrison DG, Guzik TJ, Lob HE, Madhur MS, Marvar PJ, Thabet SR, Vitha A, Weyand CM. Inflammation, immunity, and hypertension. Hypertension. 2011;57:132-140.

**9.2 UNIQUE IMMUNE CAPABILITIES BETWEEN MALES AND FEMALES: IMPLICATIONS FOR HEALTH AND AUTOIMMUNE DISEASES**

S. Ansar Ahmed¹, Deena Khan¹, Riuan Dai²


An intriguing long-standing experimental and clinical observation is that the immune system of females is different. There are innate sex differences in the levels of immunoglobulin (IgM), cytokines, and lymphocyte subsets, as well as in their abilities to respond to antigens, infections and vaccines. Overall, the female immune system tends to be more reactive and responds better to antigens than their male counterparts. The provocative question is what is the biological relevance of these sex differences in the immune system? Does the stronger immune defense capabilities in females may contribute to increased longevity of females? This female “immuno- logical superiority” is not without consequences. The female immune system also reacts vigorously against it’s own self-antigens. Consequently, a majority of auto-immune diseases occur predominately in females in both animal models as well as in humans. Underlying reasons for the physiological and pathological sex differences in immune system are a subject of intense investigations. Potentially, they can be distilled into three main possibilities: (i) sex hormonal, (ii) Sex Chromosomal, and (iii) epigenetic and environmental influences. Of these, perhaps the most studied is the effect of sex hormones on immune response. In both hypertensive males and females, which cells have receptors for sex hormones and which cells do not?

**10.0 POSTER SESSION II**

**10.1 BONE MARROW-DERIVED ANGIogenic PROGENITOR CELLS ARE DISFUNCTIONAL IN CHRONIC ANG II INFUSION RAT MODEL OF HYPERTENSION**

Joo Yun Jun, Jasenka Zubcevic, Aqeela Afzal, Gwyneth Lamont, Jessica Marulanda, J. Moreno and Mohan K. Rairada

1Biomedical Sciences and Pathobiology, Virginia Tech, Blacksburg, VA 24061.

Introduction: Bone marrow (BM)-derived angiogenic progenitor cells (APCs) contribute to the repair of endothelial damage and thus play a key role in the maintenance of the vascular homeostasis. Therefore, their dysfunction has been implicated in the vascular pathophysiology of hypertension and cardiovascular disease. In view of this, we propose the following hypothesis: BM APCs are dysfunctional in the chronic rat model of angiotensin II-induced neurogenic hypertension and this is due to an imbalance in the vasculo-protective and vasocoagulant axes of the renin-angiotensin system (RAS). Methods: SD rats infused with AngII (200ng/kg/min, s.c.) for 4, 6 and 12 weeks, and their age-matched SD controls were used as a rodent model for neurogenic hypertension. BM was determined by FACS. Numbers were observed in the blood. This was associated with significant increases in females may lead to better blood pressure control in both sexes. Reference: Sullivan JC, Parideck JL, Doran D, Zhang Y, She JX, Pollock JS. Greater fraktaline expresssion in mesenteric arteries of female spontaneously hypertensive rats compared to males. Am J Physiol 296:H1080-1088, 2009; Harrison DG, Guzik TJ, Lob HE, Madhur MS, Marvar PJ, Thabet SR, Vinh A, Weyand CM. Inflammation, immunity and hypertension. Hypertension 57(2):132-40. 2011.
proliferation of APCs was decreased by 40%-50% at 6 weeks (p<0.05), and by 44%-55% at 12 weeks (p<0.05) of Ang II infusion compared to control. Conclusion: These data demonstrated that the numbers of APCs in BM and the ratio of APC/C in both blood and BM is significantly decreased in hypertension as a result of a decrease in APCs and concomitant increase in ICs. In addition, APCs in Ang II-induced hypertension are dysfunctional.

10.2 ANTIOXIDANT TEMPOL EXACERBATES PRESSOR RESPONSE TO STRESS IN MULTIPAROUS RATS
Susan Jacobs-Kaufman1, Jody Levasseur2


Multiparous (MP) women are at increased risk for cardiovascular disease. We have previously shown that MP rats have a greater pressor response to stress than virgin rats, due to oxidative stress-induced endothelial dysfunction rather than to augmented sympathetic activation. We examined whether an antioxidant would normalize the response. MP rats and age-matched virgins were administered Tempol (1mM in drinking water, 8x/8) and implanted with telemetry blood pressure and renal nerve activity devices. In response to stress (anest 10 sec) there was a triphasic response: a small transient rise in blood pressure, 0.1-1 sec, followed by a marked transient pressor response with partial recovery (1.5-6.0 sec), and a slow decline (6.5-10 sec). Tempol augmented the second phase of the response in the MP rats (Tempol: 47.9±6.6 mmHg; Control 33.4±3.3 mmHg; P<0.05; this was associated with an attenuation index reduction in heart rate Tempol: -22.1±10 bpm vs. Control: -118±31 bpm at 2.5 sec and sympathetic nerve activity (Tempol: 4.8±0.4 spikes/sec vs. Control: 2.2±1.0 spikes/sec at 2.5 sec). No such phenomenon was observed in the virgin animals. We conclude that Tempol exacerbates the pressor response to stress in MP rats due to a impairment of endogenous outflow and locally generated ROS. These data suggest that unanticipated central neural effects may limit the efficacy of antioxidants such as Tempol in reducing cardiovascular disease in at-risk individuals.

10.3 ESTROGEN RECEPTOR BETA-MEDIATED ANTI-INFLAMMATORY EFFECTS OF DIHYDROTESTOSTERONE IN VASCULAR SMOOTH MUSCLE CELLS
Kristen Zolova1, Robert Handal2, Rayna Gonzalez1


Vascular inflammation plays a key role in the etiology of cardiovascular disease, particularly stoke. Previous studies have demonstrated that sex steroids modulate vascular inflammation. Our recent studies show that, in human vascular smooth muscle cells, chronic treatment with the potent androgen dihydrotestosterone (DHT) decreases expression of the proinflammatory mediator cyclooxygenase-2 (COX-2) during cytokine-induced inflammation or hypoxia via an androgen receptor independent mechanism. Since DHT can be converted to 3β-diol, an estrogen receptor (ER) β-specific agonist, we hypothesized that DHT would decrease IL-1β induced COX-2 expression in primary human brain vascular smooth muscle cells (HBVSMC) via conversion to 3β-diol and subsequent activation of ERβ. Expression of sex steroid receptors and metabolizing enzymes was confirmed in HBVSMC via quantitative PCR. Pre-treatment for 18h with either DHT (10nM) or its estrogenic metabolite 3β-diol and subsequent activation of ERβ. Expression of sex steroid receptors and metabolizing enzymes was confirmed in HBVSMC via quantitative PCR. Pre-treatment for 18h with either DHT (10nM) or its estrogenic metabolite 3β-diol (10mM) reduced IL-1β-induced increases in COX-2 expression. Pre-treatment with the AR antagonist bicalutamide (1µM) did not block the effect of DHT. Both the non-nuclear and ER antagonist ICI 182,780 (1µM) and the selective ERβ-antagonist PHTPP (1µM) inhibited the effect of DHT. In conclusion, DHT appears to be protective during cerebral ischemia and to decrease arteriole oxidative stress. Because toll-like receptor 4 (TLR4) has been shown to be involved in many inflammatory pathways, we hypothesized that DHT alleviates inflammation by attenuating TLR4 expression and decreasing ROS during inflammation or hypoxia in human VSM. TLR4 expression was decreased via immunochemistry and Western blot, and ROS production was measured via the indicator dye carboxy-H2DCFDA in human VSM cells. TLR4 was detected in the cytosol and nucleus. Endothoxin, hypoxia, and HGD all increased TLR4 expression compared to controls. DHT inhibited endothox (LPS) and HGD-induced TLR4 expression. Furthermore, DHT’s effect during OGD was androgen receptor independent. Cyto-kine (IL-1β) induced basophilic granule degranulation in human VSM. These findings demonstrate that androgens may provide protection against inflammation in VSM under a variety of pathophysiological conditions in part by decreasing TLR4 expression and ROS production. 

10.6 Withdrawn.

10.7 TESTOSTERONE INDUCES LEUCOCYTE MIGRATION BY COX2 AND NADPH OXIDASE-DEPENDENT PATHWAYS
Andresia Changslia1, M Oliveira2, V Debbas2,1, F Laurindo3,1, MH Carvalho2, R Touyz4, Z Fortes2, R Tostes2

1Vascular Biology, Heart Inst., Av Dr. Enes de Carvalho Aguiar 44, Sao Paulo, 05058-904, Brazil, 2Pharmacology, Inst. of Biomed. Sci., Av. Lineu Prestes 1252, Sao Paulo, 05058000, Brazil, 3KRC, Univ. of Ottawa, 451 Smyth Rd., Ottawa, ON, K1H 8M5, Canada, 4Pharmacology, Med. Sch. of Ribeirao Preto, Univ. of Sao Paulo, Av Bandeirantes 3900, Ribeirao Preto, 14094900, Brazil.

Mechanisms whereby Testosterone (T) exerts vascular effects remain unclear but inflammatory processes (IP) and reactive oxygen species (ROS) may be crucial. We investigated whether T induces leucocyte migration (LM) via NADPH oxidase (NADPHox) or COX2 activation. Wistar rats were treated with vehicle, sodium salicylate (SS, COX inhibitor, 0.2%Kg, 1%), flutamide (Flu, androgen receptor blocker, 10mG, 4h), apocynin (Apo, NADPHox non-specific inhibitor, 30mM, 4h) or NS398 (NS, COX inhibitor, 1mM, 4h) and then received T (10mG, 24h, i.p.). T plasma levels were assessed by ELISA, LM and ROS formation [diidothiophosphate (DHP-E-F) by immunofluorescence] in the peripheral immune system in both sexes using an embolic stroke model that closely mimics ischemic stroke in humans. Minocycline was given intravenously at stroke onset. At 24 hours, the animal brains, spleens and blood hematology were analyzed. Results: sex-dependent immune-protection with minocycline after experimental embolic stroke

Irina Sazonova1, Md Nasrul Hoda2, David Hess3, Jody Levasseur2, Rayna Gonzalez1


The acute neuroprotective effects of minocycline in an embolic stroke model have been well documented. However, the sex-dependent immune-protection with minocycline after experimental embolic stroke is still unclear. We tested the effects of minocycline on brain injury and the peripheral immune system in both sexes using an embolic stroke model that closely mimics ischemic stroke in humans. Minocycline was given intravenously at stroke onset. At 24 hours, the animal brains, spleens and blood hematology were analyzed. Results: sex-dependent immune-protection with minocycline after experimental embolic stroke
investigate the role of hearts. Flow cytometry data revealed that CSC expressed Sca-1, CD29 and CD44 (all cardioprotection. However, there is no information regarding estrogen in modulation thus further promoted myocyte survival in response to hypoxia.

SDF-1 receptor blocker. Conclusion: E2-treated CSC enhanced SDF-1 production and CSC-mediated paracrine protection. To study this, CSC were isolated from mouse following toxic stimuli. In addition, estrogen has been shown to improve SC-mediated firming that estrogen-specific modulation of vascular Hcy synthesis via the intra-cellular regulation of Hcy signaling potentiates endothelial NO synthesis and vascular estrogen-dependent mechanism, female rats were ovariectomized (OV) and given with 2-mercaptoethanol for two minutes, followed by collecting endothelial (EC) lysates for the isolation of EC protein. Western blotting shows that vessels of OV rats cannulated and then continuously perfused with 30 µl of 1X Laemmli sample buffer (HET0016) for 14 days. Media-to-lumen ratio of renal interlobar arteries from DHT-treated rats was higher than vehicle-treated rats (0.21±0.01 vs 0.15±0.02). This was determined. In a separate cohort, F2 male and female offspring were aged to 6mo for whether growth restriction, nephron deficits, hypertension and renal dysfunction are transmitted to the next generation. Late gestation uteroplacental insufficiency was in-duced by bilateral uterine vessel ligation (Restricted, R) or sham surgery (Control, C) determined. In a separate cohort, F2 male and female offspring were aged to 6mo for whether growth restriction, nephron deficits, hypertension and renal dysfunction are transmitted to the next generation. Late gestation uteroplacental insufficiency was induced by bilateral uterine vessel ligation (Restricted, R) or sham surgery (Control, C) compared.

<table>
<thead>
<tr>
<th></th>
<th>M</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>M'SBP</td>
<td>183±4</td>
<td>171±4*</td>
</tr>
<tr>
<td>F'SBP</td>
<td>170±3*</td>
<td>3.2±0.2</td>
</tr>
<tr>
<td>M'NOS</td>
<td>6.0±3.9</td>
<td>33±6*</td>
</tr>
<tr>
<td>F'NOS</td>
<td>5.6±3.9</td>
<td>30±1.4*</td>
</tr>
<tr>
<td>M'AMF</td>
<td>65.6±2.5</td>
<td>65.6±2.5</td>
</tr>
<tr>
<td>F'AMF</td>
<td>2.7±0.4*</td>
<td>1.5±0.3*</td>
</tr>
</tbody>
</table>

<0.01 vs M; *p<0.01 vs F. Two-way ANOVA, Bonferroni's post-hoc test. ANP treatment decreased SBP in rats of both sexes. Vascular early fibrosis was higher in M than F SHRs. ANP treatment induced an increase in NO system activity and modified aorta remodeling only in males rats, probably improving aortic wall properties. Funding source: CONICET-UBA, Argentina.

**SEX DIFFERENCES IN DOWNTREAM TGF-BETA SIGNALING IN THE ARTERIES OF SPONTANEOUSLY HYPERTENSIVE RATS**

Ashle Tipton1, Jennifer Sullivan1


Recent evidence suggests that the protein, TGF-β has a role in the pathogenesis of vascular damage often associated with hypertension. TGF-β is known to exert inflammatory affects by signaling through the Smads and MAPK pathway. Our lab recently showed that female SHR have higher urinary secretion of TGF-β compared to male SHR, therefore the goal of this study was to determine if there were sex differences in the downstream TGF-β signaling molecules within the vasculature. To test this hypothesis, arteries were isolated from 12-14 week old female and male SHR. TGF-β protein expression was measured in arteries by immunoblotting and expression was significantly higher in arteries from female SHR compared to the male SHR (0.92±0.35 vs 0.19±0.04 relative densitometry units (RDU), p<0.05). Next, we investigated whether sex differences in TGF-β signaling proteins were present in the vasculature of SHR. TGF-β receptor type II protein expression was significantly less in arteries from female SHR compared to male SHR (3.4±0.9 vs 9.6±1.8 RDU, p<0.05). We also found that phospho-Erk1/2 expression was less in arteries from female SHR in comparison to male SHR (10.2±1.9 vs 29.7±5.0 RDU, p<0.05), while phospho-Smad3/2 tended to be more highly expressed in arteries from female SHR (1.1±0.3 vs 0.4±0.1 RDU). These findings might implicate a sex difference in the contribution of inflammation to the maintenance of hypertension in SHR.

**SEX DIFFERENCES IN THE INTERGENERATIONAL TRANS-MISSION OF HYPERTENSION ASSOCIATED WITH UTERO-PLACENTAL INSUFFICIENCY IN RATS**

Linda Gallas1, Karen Montez2, Melanie Tran1, Luise Cullen-McEwen1, Kate Denton1, Mark Wisor6

1Physiology, Univ. of Melbourne, Grattan St., Parkville, 3010, Australia, 2Biomed. Sci., Univ. of Queensland, Sir Fred Schonell Dr., St. Lucia, 4072, Australia, 3Anatomy and Developmental Biology, Monash Univ., Wellington Rd., Clayton, 3800, Australia, 4Physiology, Monash Univ., Wellington Rd., Clayton, 3800, Australia.

Intrauterine growth restriction increases risk of disease, particularly in male offspring, with recent evidence to transmission to subsequent generations. We determined whether growth restriction, nephron deficits, hypertension and renal dysfunction are transmitted to the next generation. Late gestation uteroplacental insufficiency was induced by bilateral uterine vessel ligation (Restricted, R) or sham surgery (Control, C) in SHR rats. At 4mo, Restricted and Control female offspring (F1) were mated with normal males. Second generation (F2) fetal weight and nephron number (E20) were determined. In a separate cohort, F2 male and female offspring were aged to 6mo for blood pressure (tail-cuff) and 24h renal excretion. A cohort of F2 males were aged to 12mo for renal function (Hbam and GFR clearance) measurements. F2 male and female fetuses were smaller than F2 (P<0.05). F2 male fetuses had fewer nephrons (P<0.05); female analysis ongoing. At 6mo, F2R males had increased systolic blood pressure compared with F2 (<15mmHg; P<0.05), while different amongst females. Renal excretions and function were not different between F2 and F2R, but renal and greater protein excretion than females (P=0.05, ∼3-fold). We provide novel evidence for intergenerational transmission of fetal growth restriction (males and females).
females) and nephron deficits (confirmed in males), with elevated blood pressure developing only in males. Funded: Heart Foundation of Australia and March of Dimes.

10.15 EXPRESSION OF NEONATAL FEMALE, BUT NOT MALE MICE TO TESTOSTERONE PROMOTES ANGIOTENSIN II-INDUCED ABDOMINAL AORTIC ANEURYSMS
Xuan Zhang1, Sean Thatcher1, Debra Rateri1, Alan Daugherty2, Lisa Cassis1

Objective: We previously demonstrated that administration of testosterone to adult female mice increased the development of an abdominal aortic aneurysm (AAA) only when administered during pregnancy. In this study, we advanced our knowledge to determine the presence of sex differences in the development of an AAA in neonatal female mice. Methods: Pregnant mice were administered KO or WT fetal serum (at 16.5 weeks of gestation) to neonatal female mice. Results: KO fetal serum increased the percentage of female mice developing an AAA to 74% compared to 4% in WT fetal serum treated females (p<0.001). There were no differences in KO or WT fetal serum treated males. Following female neonatal exposure to fetal KO serum, KO fetal serum was required to significantly increase AAA development in the female offspring, whereas WT fetal serum had no effect. Conclusions: The development of aortic aneurysms is dependent upon sex. Thus, sex differences in development of AAA exists both during pregnancy and in the neonatal period.

10.16 ACE2 DEFICIENCY IS ASSOCIATED WITH IMPAIRED GESTATIONAL WEIGHT Gain AND FETAL GROWTH RESTRICTION
Yuqi Yang1, Xingyi Zhao1, William Snee2, Mark Chappell2, Leanne Grodan1, Katie Atkins1, Carina Horta1, Luciana Fierro1, Liviu Farah1, Susan Garly2, K. Bridget Brossmann1

Angiotensin converting enzyme 2 (ACE2) is a key enzyme of the renin-angiotensin system that influences the relative expression of angiotensin (Ang) II and Ang-(1-7). Although ACE2 expression increases in normal pregnancy, the impact of ACE2 deficiency in pregnancy is unknown. Gestational body weight gain was lower in the ACE2 knockout (KO) mice compared to Wild type (C57Bl/6) (WT) mice (30.3 ± 4.7 vs 38.2 ± 1.0 g, p=0.001) at day 18 of gestation. Fetal weight (0.94 ± 0.1 vs 1.24 ± 0.1 g, p=0.01) and length (19.6 ± 0.2 vs 22.2 ± 0.2 mm, p<0.01) were less in KO. Serum testosterone concentrations in adult females were not significantly influenced by neonatal testosterone administration. In contrast, administration of testosterone to neonatal males had no effect on Ang-II induced AAs (vehicle: 50%; testosterone: 62%). Conclusions: These results demonstrate that female mice respond to neonatal testosterone administration to markedly promote increased adult susceptibility to AAs. This effect was independent of elevated serum testosterone concentrations in adult females. Future studies will define mechanisms for differing sensitivity of neonatal females compared to males in promotion of Ang-II induced AAs. Funding: NIH P01 HL080100.

10.17 HYPERTENSION IN MICE WITH THE CHRONIC INFLAMMATORY DISEASE SYSTEMIC LUPUS ERYTHEMATOSUS IS NOT SALT-SENSITIVE
Kesa Mathis1, Marcia Venegas-Pont1, Chester Masterson1, Katie Wasson1, Michael Fleming2
1Physiology, Univ. of Mississippi Med. Ctr., 2500 N. State St., Jackson, MS, 39216. 2Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disorder that primarily affects women during reproductive years. The prevalence of hypertension in patients with SLE is very high, reaching up to 74% depending on the cohort. Previous work of others shows a strong immune/inflammatory component to the development of salt-sensitive hypertension. Therefore, we tested whether blood pressure is salt-sensitive using an established mouse model of SLE (female NZBW/F1 mice) with hypertension. Thirty-week old SLE and control mice (NZW) were fed 8% high salt (HS) diet or normal diet (0.4% salt) for 4 weeks. Plasma levels of dDA EN auto-antibody, a hallmark of SLE (measured by ELISA), was increased in SLE mice compared to controls (1e5±3e4 vs. 5e4±3e4 U/ml; all p<0.05). HS did not alter dDA EN auto-antibody in SLE (1e5±3e4) or control mice (6e4±2e4). Blood pressure (measured by arterial catheter in conscious mice) was increased in SLE mice compared to controls (130±1 vs. 117±1 mmHg). HS did not significantly alter blood pressure in SLE (136±1 vs. control mice (119±2). At 34 weeks, 43% of SLE mice fed HS diet showed positive albuminuria (>100 mg/dL measured by dipstick) compared with 33% of SLE mice fed normal salt diet. No control mice developed albuminuria throughout the study. In conclusion, these data suggest that in SLE blood pressure is not salt-sensitive. Supported by AHA Postdoctoral Fellowships 4350019 (KWM) and 2260874 (MVP), as well as NIH grants HL059970 (MIR), HL092284 (MIR), HL085978 (MIR), and HL051971 (UMMC-Physiology).

10.18 A NOVEL REPRODUCTIVE HORMONE, COSPEPTIN
Gina Yosten1, Chloe Bryan1, Willis Samson1
1Pharmaceutical and Physiological Sci., St. Louis Univ., 1402 S. Grand Blvd., St. Louis, MO, 63104.

A bioinformatic search of the human genome for mRNAs encoding previously unidentified peptide sequences that are evolutionarily conserved and contain both a signal peptide for secretion and dibasic cleavage sites for liberation of small peptides, identified a previously undescribed peptide we name cospeptin. Mass spectrometry analysis revealed that endogenous cospeptin, isolated from rat hypothalami, was likely a 20 amino acid, C-terminally amidated peptide. Immunoreactive cospeptin was detected in several tissues, most abundantly in hypothalamus. Labeled cospeptin exhibited high specific binding to pituitary and ovary, and i.p. injection of cospeptin led to the induction of early gene expression in pituitary gonadotrophs. In dispersed rat pituitary cells, cospeptin potently activated the action of GnRH and induced LH, PRL, and FSH release, and upregulated LH and FSH Beta, and GnRH receptor messages. Cycling female rats injected i.c.v. with siRNA directed against cospeptin on diestrus days 1 and 2, had reduced levels of cospeptin message in the hypothalamus, a delay in the appearance of the subsequent estrus, and a decrease in GnRH receptor message in the pituitary, suggesting that endogenous cospeptin “sensitizes” pituitary gonadotrophs by up-regulating the transcription of the GnRH receptor gene. We have discovered a novel reproductive hormone, cospeptin, which acts in the pituitary to regulate expression of the GnRH receptor, and therefore reproductive hormone secretion.

10.19 AT THE HEART OF THE MATTER
Christine Carter1, Nanette Wenneker1
1Vice President for Scientific Affairs, Soc. for Women's Hlth. Res., 10253 Austin St., NE, Ste. 701, Washington, DC, 20036, 2Cardiology, Emory Univ. Sch. of Med., Atlanta, GA, 30322.

On June 21st, 2011 the Society of Women’s Health Research (SWHR) and Women Heart in collaboration with leading experts in women’s heart health released the 10Q Report on Capitol Hill. The 10Q Report contains 10 unanswered questions to guide future research to improve detection, diagnosis and treatment for women at risk of or with cardiovascular disease (CVD). The 10 questions and subsequent recommendations for initiatives related to science, policy and education, were created by clinical and basic scientists, policymakers and women health advocates. In addition to these challenges, there is a growing urgency for women and minorities to participate in clinical trials. Increasing women and minority participation in clinical studies will allow for valid analyses of sex differences in the presentation of and treatment effects of cardiovascular disease.

10.20 HYPERTENSION IN MICE WITH THE CHRONIC INFLAMMATORY DISEASE SYSTEMIC LUPUS ERYTHEMATOSUS IS NOT SALT-SENSITIVE
Kesa Mathis1, Marcia Venegas-Pont1, Chester Masterson1, Katie Wasson1, Michael Fleming2
1Physiology, Univ. of Mississippi Med. Ctr., 2500 N. State St., Jackson, MS, 39216. 2Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disorder that primarily affects women during reproductive years. The prevalence of hypertension in patients with SLE is very high, reaching up to 74% depending on the cohort. Previous work of others shows a strong immune/inflammatory component to the development of salt-sensitive hypertension. Therefore, we tested whether blood pressure is salt-sensitive using an established mouse model of SLE (female NZBW/F1 mice) with hypertension. Thirty-week old SLE and control mice (NZW) were fed 8% high salt (HS) diet or normal diet (0.4% salt) for 4 weeks. Plasma levels of dDA EN auto-antibody, a hallmark of SLE (measured by ELISA), was increased in SLE mice compared to controls (1e5±3e4 vs. 5e4±3e4 U/ml; all p<0.05). HS did not alter dDA EN auto-antibody in SLE (1e5±3e4) or control mice (6e4±2e4). Blood pressure (measured by arterial catheter in conscious mice) was increased in SLE mice compared to controls (130±1 vs. 117±1 mmHg). HS did not significantly alter blood pressure in SLE (136±1 vs. control mice (119±2). At 34 weeks, 43% of SLE mice fed HS diet showed positive albuminuria (>100 mg/dL measured by dipstick) compared with 33% of SLE mice fed normal salt diet. No control mice developed albuminuria throughout the study. In conclusion, these data suggest that in SLE blood pressure is not salt-sensitive. Supported by AHA Postdoctoral Fellowships 4350019 (KWM) and 2260874 (MVP), as well as NIH grants HL059970 (MIR), HL092284 (MIR), HL085978 (MIR), and HL051971 (UMMC-Physiology).
While many studies have focused on circulating systemic levels of sex steroids, there has been less appreciation for the local production and action of these hormones in the cardiovascular system during normal physiology and pathophysiology. Since sex steroids have been implicated in the outcome of cardiovascular disease, we investigated whether aromatase or androgen receptor (AR) expression was modified in human coronary vascular smooth muscle cells (HCVSM) and rat cardiac myofibroblasts (RCM) following stimulation with angiotensin II (AngII). Primary HCVSM (passage 8) and RCM (passage 0) were grown to 80% confluence and treated with AngII (24 hr; 10-7M). We demonstrated that AngII increased expression of both aromatase (77%) and androgen receptor (AR; 60%) in HCVSM, but not in RCMs. It has been shown that androgens may work in concert with AngII for some cardiovascular parameters, therefore additional experiments were performed in RCM with co-administration of testosterone (10nM). Testosterone did not have any impact on the effect of AngII on aromatase or AR expression in RCM. In conclusion, the presence of aromatase and AR in these two cell types suggests a possibility for circulating testosterone to act locally in an androgenic and/or estrogenic fashion. However, the functional consequence of upregulation of both estrogenic (aromatase) and androgenic (AR) systems in HCVSM following AngII stimulation remains to be determined. The following research was supported by NIH grants (HL116502, HL128835, K08HL137894, HL131212, and HL131217).
10.27 ESTROGEN PROTECTS AGAINST THE DEVELOPMENT OF HYPERTENSION DURING SYSTEMIC LUPUS ERYTHEMATOSUS

Emily Gilbert1, Marcia Venegas-Pont1, Michael Ryan1

1Physiology and Biophysics, Univ. of Mississippi Med. Ctr., 2500 N. State St., Jackson, MS, 35216.

Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease of unknown etiology. Due to SLE’s predilection for women during their childbearing years, estrogen is implicated as a contributor to SLE disease progression. Cardiovascular disease is a leading cause of mortality in women with SLE and the prevalence of hypertension, a major cardiovascular risk factor, is very high in these patients. Based on the presumed role for estrogens to promote SLE and the prevalent hypertension, we hypothesized that estrogens may promote hypertension during SLE. In the present study, we tested whether removal of estrogen ameliorates hypertension in a female mouse model of SLE (NZBWF1). An ovariectomy or sham control procedure was performed in 30 week old SLE and control (NZW/LacZ) mice. Four weeks after the surgery, mean arterial pressure (MAP in mmHg) was higher in SLE sham mice compared to control sham mice (132±2 vs. 118±3, n=9, p<0.05). Removal of estrogen by ovariectomy exacerbated the hypertension in SLE mice (152±5, n=5, p<0.05). We also found no effect on MAP in OVX control (118±3, n=2). 33% of the SLE mice developed albuminuria during this time. As expected, the characteristic anti-dsDNA antibodies were increased in SLE mice compared to controls. Ovariectomy did not significantly alter the production of autoantibodies. In conclusion, these data suggest estrogens play an important protective role against the development of hyper-tension and renal injury during SLE.

10.28 SEX REPORTING IS LACKING IN CARDIOVASCULAR STUDIES USING CELL CULTURES

K. Eflu Taylor1, Catalina Vallego-Giraldo1, Nicole Schalibel1, Rosita Zakeri1, Virginia M. Miller1

1Physiology and Biomed. Engineering, Grad. Sch. of Med., Mayo Clinic, 200 1st St. SW, Rochester, MN.

In 2009 between 22-42% of articles published in neuroscience and physiology journals failed to report the sex of the animals used in the study. Since every cell has a sex and sex chromosomes influence expression of proteins and molecular signaling, a survey was undertaken to ascertain sex reporting in cardiovascular studies utilizing cultured cells. Ten cardiovascular journals with high impact factors were selected (Circ Res, Cardiovasc Res, Circulation, JACC, Eur Heart J, J Mol Cell Cardiol, Am J Physiology, and Circ Cardiovasc Pharmacol) and the first ten articles published in 2010 found using search terms “cultural” and “cells” in any order were reviewed. Studies using established cell lines were excluded. Of 90 articles meeting inclusion criteria, only 25 (28%) reported the sex of cells; none used only female cells, 7 used male and female cells and 18 used only male cells. Sex was reported in 7 of the 10 articles reviewed from Am J Physiol Heart Circ Physiol and sex was not reported in any of 10 articles reviewed from Cardiovasc Res. Given that expression of proteins and molecular signaling are influenced by the sex chromosomes, sex is a critical experimental variable which should be reported in published studies to uphold scientific excellence. (Supported in part by the Mayo Clinic Graduate School of Medicine).

10.29 ESTROGEN RECEPTOR (ERα) MODULATES HEME OXYGENASE (HO-1) IN RESPONSE TO HYPERTENSION (HTN) AND RENAL INJURY IN FEMALES

Kirat Chandrashekar1, Armando Lopez Ruiz1, Ruisheng Liu2, Jane Reckelhoff1, Luis Garcia2

1Medicine, Univ. of Mississippi Med. Ctr., 2500 N. State St., Jackson, MS, 35216.
2Physiology, Univ. of Mississippi Med. Ctr., 2500 N. State St., Jackson, MS, 35216.

Gender specific protection in females may be mediated through ERα. We have shown, females had higher baseline HO-1 (a cytoprotective enzyme) levels than males and that ERα induced HO. We hypothesized that; ERα may induce HO-1 apropos to the magnitude of HTN and renal injury. To test this, female Sprague-Dawley rats were grouped into Control (CT), FVT (silvestran-ERα antagonist), CoPP (corticosteroid), and Sprague-Dawley rats that received silvestran, CoPP, or Sprague-Dawley rats that received silvestran, CoPP, or Sprague-Dawley rats that received silvestran, CoPP, or Sprague-Dawley rats that received silvestran, CoPP, or Sprague-Dawley rats that received silvestran, CoPP. We also investigated whether silvestran treatment in female Sprague-Dawley rats produced an increase in BBB permeability. We found that silvestran treatment in female Sprague-Dawley rats produced an increase in BBB permeability, which may be due to the blood-brain barrier remodeling during pregnancy.

10.30 HIGHER PDE-5 EXPRESSION IN PREGNANT RATS WITH REDUCED URINARY PRESSURE TRANSPORT

Anna Pala1, Erica George1, Kathy Cockrell1, Maritte Armany1, Joey Granger1

1Pharmacy, 2500 N. State St., Jackson, MS, 35216.

Objective: Cyclic nucleotide phosphodiesterases (PDEs) are a family of enzymes with multiple regulatory properties and wide tissue distribution. Such activity includes cyclic guanosine monophosphate (cGMP) breakdown. The goals of this study were to investigate whether urinary and placental expressions of PDE-5 enzyme are increased in an animal model of preeclampsia, possibly causing decreases in cGMP. Methods: On day 19 of pregnancy, placental villous explants and uterine vessels were collected from Sprague-Dawley normal pregnant rats (NP, n=5) and pregnant rats that underwent reduction in uterine perfusion pressure surgeries (RUPP, n=5). Uterine and placenta PDE-5 levels were measured by Western Blotting, and cGMP concentrations by Enzyme Immunoassay. Results: PDE-5 immunoreactivity was present in NP and RUPP placental villous explants and uterine vessels. A dominant antibody-specific band was identified around 100 kd in both tissue samples, the same weight found in nonpregnant rats. Although PDE-5 expression in uterine tissues was similar in NP and RUPP groups (P=0.05), its levels were higher (~ 1.5 fold) in placental tissues of RUPP compared with NP (P<0.05). We found no significant differences in cGMP concentrations between NP and RUPP groups (P=0.05). Conclusion: Our results suggest that PDE-5 play a role in the pathophysiology of preeclampsia, and its inhibition may be a potential therapeutic for the treatment of this disease. Funding source: NIH.

11.0 GENDER DIFFERENCES IN VASCULAR FUNCTION

11.1 CEREBRAL VASCULAR FUNCTION IN PREGNANCY AND PRE-ECLAMPSIA

Marlenne Cipolla1

1Neurology, OB/GYN and Pharmacology, Univ. of Vermont, 89 Beaumont Ave., Burlington, VT, 05405.

Pregnancy has a profound effect on the cerebral circulation, including selective outward remodeling of brain parenchymal arteries that decreases cerebral vascular resistance and promotes edema during acute hypertension. The mechanism by which brain arterioles undergo remodeling during pregnancy appears to be due to activation of PPARγ via relaxin. In addition, cerebral arteries appear to be in a state of inflammation during normal pregnancy, including increased expression of pro-inflammatory cytokines that promotes greater sensitivity to the inflammatory effects of endotoxin. Hypertension also has a profound effect on the cerebral circulation that is altered by pregnancy. Pregnancy prevents and reverses hyperensive inward remodeling of cerebral arteries, an effect that leaves the brain vulnerable to high hydrostatic pressure during hypertension. Lastly, circulating factors produced during pregnancy and pre-eclampsia affect the brain and cerebral circulation. Serum from normal pregnant, but not nonpregnant rats, is hyperxecetable to neuronal tissue, causing evoked seizure potentials that are blocked by inhibition of TNF-α signaling. Because pregnant rats do not normally display seizure activity, these results suggest that the blood-brain barrier (BBB) adapts to high levels of seizure-provoking factors produced during pregnancy to limit their effects. During preeclampsia, however, circulating factors increase BBB permeability that could expose the brain to these damaging factors. Plasma from pre-eclamptic women increases BBB permeability through activation of VEGF receptors and increasing sensitivity to VEGF. (Supported by: RO1 NS045940, RO1 NS043316, PO1 HL095488, The NINDS Neural Environment Cluster NS045940-06S1, ARRA Supplement NS045940-05S1, The Preeclampsia Foundation, and The Georgio Pardi Foundation).

11.2 SEX HORMONES AND ENDOTHELIAL FUNCTION IN HUMANS

Christopher Minson1

1Human Physiology, Univ. of Oregon, 1240 Univ. of Oregon, Eugene, OR, 97403-1158.

The vascular endothelium is at the intersection of the blood and the blood vessel, and that ERα may induce HO-1 apropos to the magnitude of HTN and renal injury. To test this, female Sprague-Dawley rats were grouped into Control (CT), FVT (silvestran-ERα antagonist), CoPP (corticosteroid), and Sprague-Dawley rats that received silvestran, CoPP, or Sprague-Dawley rats that received silvestran, CoPP, or Sprague-Dawley rats that received silvestran, CoPP. We also investigated whether silvestran treatment in female Sprague-Dawley rats produced an increase in BBB permeability. We found that silvestran treatment in female Sprague-Dawley rats produced an increase in BBB permeability, which may be due to the blood-brain barrier remodeling during pregnancy.
Neuronal Nitric Oxide Synthase in the Endothelium is a Novel Regulator of Estrogen Signaling

Sandra Davidge1, Olga Lekontseva1, Subhadeep Chakrabarti1

1Obstetrics/Gynecology and Physiology, Univ. of Alberta, 232 HMRC, Univ. of Alberta, Edmonton, AB, T6G 2S2, Canada.

Estrogen is a vasorelaxant, which increases nitric oxide (NO) generation. Traditionally, endothelial NO synthase (eNOS) was believed to be the primary source of NO. However, recent data suggest an important role for neuronal NOS (nNOS) on both groups appear to be at increased risk for CVD. Physicians caring for women need to help women retain the menopausal transition with as healthy a vasculature as possible. Support: NIH Grant HL 081671. References: Torgrimson, B.N., Meen- dering, J.R., Kaplan, P.F., and Minson, C.T. 2011. Depot-Medroxyprogesterone Acetate and Endothelial Function. Hypertension 57, 819-824.

11.3

Neuronal Nitric Oxide Synthase in the Endothelium is a Novel Regulator of Estrogen Signaling

Sandra Davidge1, Olga Lekontseva1, Subhadeep Chakrabarti1

1Obstetrics/Gynecology and Physiology, Univ. of Alberta, 232 HMRC, Univ. of Alberta, Edmonton, AB, T6G 2S2, Canada.

Estrogen is a vasorelaxant, which increases nitric oxide (NO) generation. Traditionally, endothelial NO synthase (eNOS) was believed to be the primary source of NO. However, recent data suggest an important role for neuronal NOS (nNOS) on both groups appear to be at increased risk for CVD. Physicians caring for women need to help women retain the menopausal transition with as healthy a vasculature as possible. Support: NIH Grant HL 081671. References: Torgrimson, B.N., Meen- dering, J.R., Kaplan, P.F., and Minson, C.T. 2011. Depot-Medroxyprogesterone Acetate and Endothelial Function. Hypertension 57, 819-824.

11.3

Neuronal Nitric Oxide Synthase in the Endothelium is a Novel Regulator of Estrogen Signaling

Sandra Davidge1, Olga Lekontseva1, Subhadeep Chakrabarti1

1Obstetrics/Gynecology and Physiology, Univ. of Alberta, 232 HMRC, Univ. of Alberta, Edmonton, AB, T6G 2S2, Canada.

Estrogen is a vasorelaxant, which increases nitric oxide (NO) generation. Traditionally, endothelial NO synthase (eNOS) was believed to be the primary source of NO. However, recent data suggest an important role for neuronal NOS (nNOS) on both groups appear to be at increased risk for CVD. Physicians caring for women need to help women retain the menopausal transition with as healthy a vasculature as possible. Support: NIH Grant HL 081671. References: Torgrimson, B.N., Meen- dering, J.R., Kaplan, P.F., and Minson, C.T. 2011. Depot-Medroxyprogesterone Acetate and Endothelial Function. Hypertension 57, 819-824.

11.3

Neuronal Nitric Oxide Synthase in the Endothelium is a Novel Regulator of Estrogen Signaling

Sandra Davidge1, Olga Lekontseva1, Subhadeep Chakrabarti1

1Obstetrics/Gynecology and Physiology, Univ. of Alberta, 232 HMRC, Univ. of Alberta, Edmonton, AB, T6G 2S2, Canada.

Estrogen is a vasorelaxant, which increases nitric oxide (NO) generation. Traditionally, endothelial NO synthase (eNOS) was believed to be the primary source of NO. However, recent data suggest an important role for neuronal NOS (nNOS) on both groups appear to be at increased risk for CVD. Physicians caring for women need to help women retain the menopausal transition with as healthy a vasculature as possible. Support: NIH Grant HL 081671. References: Torgrimson, B.N., Meen- dering, J.R., Kaplan, P.F., and Minson, C.T. 2011. Depot-Medroxyprogesterone Acetate and Endothelial Function. Hypertension 57, 819-824.
SCOPE OF JOURNAL
The *American Journal of Physiology-Heart and Circulatory Physiology* publishes original investigations on the physiology of the heart, blood vessels, and lymphatics, including experimental and theoretical studies of cardiovascular function at all levels of organization ranging from the intact animal to the cellular, subcellular, and molecular levels. It embraces new descriptions of these functions and of their control systems, as well as their bases in biochemistry, biophysics, genetics, and cell biology. Preference is given to research that provides significant new insights into the mechanisms that determine the performance of the normal and abnormal heart and circulation.

Authors are required to submit papers online at [www.apscentral.org](http://www.apscentral.org).

EDITORS' SELECTED ARTICLES
- **Discovery of shear- and side-specific mRNAs and miRNAs in human aortic valvular endothelial cells**
  Casey J. Holliday, Randall F. Ankeny, Hanjoong Jo, and Robert M. Nerem

- **The rate of oxygen loss from mesenteric arterioles is not unusually high**
  Aleksander S. Golub, Bjorn K. Song, and Roland N. Pittman

- **Understanding Guyton's venous return curves**
  Daniel A. Beard and Eric O. Feigl

- **Biochemical and myofilament responses of the right ventricle to severe pulmonary hypertension**
  Lori A. Walker, John S. Walker, Amelia Glazier, Dale Brown, Kurt R. Stemmerk, and Peter M. Buttrick

- **Catalase overexpression in aortic smooth muscle prevents pathological mechanical changes underlying abdominal aortic aneurysm formation**

IMPORTANT INFORMATION FOR READERS, AUTHORS, AND LIBRARIANS
- **NEW!** Editorial Podcast Series: Listen to the new Editorial Podcast Series that highlights the latest original research in cardiovascular physiology. Subscribe today to be alerted to new content via your preferred digital media player at [http://ajpheart.podbean.com](http://ajpheart.podbean.com).

- **NEW!** Article Collections: In January 2011 the Editors began subdividing the Table of Contents of each journal issue, resulting in collections of content organized by research topic. New content is added on a monthly basis. Web: [ajpheart.physiology.org/cgi/collection/](http://ajpheart.physiology.org/cgi/collection/)

- **Google search engine:** All online content searchable through the Google search engine.

- **Index Medicus, Biosis Previews, and ISI Web of Science** index APS journals. APS journal content indexed on MEDLINE and accessible through PubMed.

- **RSS Feeds:** A mechanism to subscribe to “headlines” from a web site.

- **eTOCs:** Free e-mail notification of new tables of content as they become available.

- **CiteTrack:** Receive e-mail alerts when new content matches criteria based on the topics, authors, and articles you want to track.

- **Manuscripts published online** within days of acceptance.

- **LOCKSS and CLOCKSS:** Perpetual/Electronic archiving of the LOCKSS and CLOCKSS systems preserves the electronic content of all APS journals.

- **CrossRef:** APS participates in CrossRef initiative, which links to over 5,600 journals worldwide.

- **Legacy Content** is an online package of over 100 years of historical scientific research from 13 APS research journals.

- **AuthorChoice:** Authors can choose to pay a fee on top of regular author fees and have their articles publicly available upon publication.

FURTHER INFORMATION: E-mail: subscriptions@the-aps.org, Call: 301-634-7180, Fax: 301-634-7418 or Mail to: The American Physiological Society, 9650 Rockville Pike, Bethesda, MD 20814-3991 (USA)
Call for Abstracts
and Program Information

SPONSORS:
American Association of Anatomists (AAA)
The American Physiological Society (APS)
American Society for Biochemistry and Molecular Biology (ASBMB)
American Society for Investigative Pathology (ASIP)
American Society for Nutrition (ASN)
American Society for Pharmacology and Experimental Therapeutics (ASPET)

Abstract Deadline: Tuesday, November 8, 2011

www.experimentalbiology.org