PANS2019 New Orleans
laissez la bonne science rouler

New Orleans
Louisiana, USA

March 21 & 22, 2019

Marriott New Orleans Downtown
at the Convention Center
Welcome Message from PANS President Denise Belsham

As President of the Pan American Neuroendocrine Society, I am delighted to extend a warm welcome to everyone participating in the inaugural PANS2019 Meeting in New Orleans. Thank you for attending our satellite meeting with ENDO2019, and we wish you an exceptional experience.

Dr. Deborah Kurrasch, Chair of the program organizing committee, and her committee have put together an integrated scientific program addressing the full spectrum of neuroendocrine research and covering cutting edge developments within four sessions. The flavor is truly international with expert speakers from across the western hemisphere and it promises to be a celebration of scientific excellence in an iconic setting.

The keynote presentation is by Dr. Margaret McCarthy, who is a preeminent leader in the integration of molecular mechanisms, physiology, and behavior when dissecting the complex nature of sexual dimorphism. She is an outstanding choice and we thank her for accepting our invitation.

Dr. Andy Babwah, Chair of the local organizing committee, and his team have been instrumental in planning the meeting to be both intellectually stimulating, but with ample opportunities for networking (and fun – we are in New Orleans after all). There is a special emphasis on trainees and young scientists, and we encourage everyone to attend the poster sessions, professional development breakfast, as well as the opening reception to network with the next generation of neuroendocrinologists.

I would be remiss if I did not mention all that came before us to rejuvenate the neuroendocrine community in the Americas. We are indebted to the first Chairperson of the Executive Council of PANS, Dr. Robert Handa, who poured his energy and enthusiasm into bringing this group back together, and expanded our reach across all of North and Latin America. Also, thanks to the entire Executive Council of PANS for their invaluable input towards the direction of our society. We encourage everyone to become members of PANS, and spread the message to their friends and colleagues.

I wish you a very successful meeting professionally and personally. Please engage in all of the planned activities that are centered on research excellence, collaborative interactions, and professional networking opportunities. We also encourage you to meet our sponsors, and support their endeavors. We truly hope that you will enjoy your time in New Orleans at this marvelous meeting. It’s time to celebrate neuroendocrinology!

Professor Denise Belsham,
President of the Pan American Neuroendocrine Society
PROGRAM ORGANIZING COMMITTEE

Deborah Kurrasch, Chair
Associate Professor
University of Calgary

Andy Babwah
Associate Professor
Rutgers University

Daniel Bernard
Professor
McGill University

Carol Elias
Professor
University of Michigan

Michael Lehman
Professor
Kent State University

Jon Levine
Professor
University of Wisconsin-Madison

Jessica Rosin, Trainee Member
Postdoctoral Fellow, Kurrasch Lab
University of Calgary

Deborah Suchecki
Professor
Universidade Federal de Sao Paulo

Dominique Walker
Professor
McGill University

John Wu
Professor
Uniformed Services University

LOCAL ORGANIZING COMMITTEE

Andy Babwah, Chair
Associate Professor
Rutgers University

Dan Bernard
Professor
McGill University

Bruno Carabelli
Post-Doctoral Fellow, Suchecki Lab
Universidade Federal de Sao Paulo

Carol Elias
Professor
University of Michigan

Alexander Sasha Kauffman
Professor
University of California San Diego

Debbie Kurrasch
Associate Professor
University of Calgary

Mike Lehman
Professor
Kent State University

Aleisha Moore
Post-Doctoral Fellow, Lehman Lab
Kent State University

Victoria Lux Lantos
Principal Investigator
Instituto de Biologia y Medicina Experimental, Buenos Aires

Shannon Stephens
Post-Doctoral Fellow, Kauffman Lab
University of California San Diego

Deborah Suchecki
Professor
Universidade Federal de Sao Paulo

Jeffrey Tasker
Professor
Tulane University
TRAVEL AWARD RECIPIENTS

Arvand Asghari
PhD student
University of Houston, USA

Emma McIlwraith
PhD student
University of Toronto, Canada

James Garcia
Post-Doctoral Fellow
University of Wisconsin, USA

Marianne Bizzozzero Hiriart
Post-Doctoral Fellow
University of Buenos Aires, Argentina

Richard McCosh
Post-Doctoral Fellow
University of California San Diego, USA

Dinu Nesan
Post-Doctoral Fellow
University of Calgary, Canada

Karen Jill Tonsfeldt
Post-Doctoral Fellow
University of California San Diego, USA

Rajae Talbi
Post-Doctoral Fellow
Harvard, USA

Jennifer Yang
Post-Doctoral Fellow
University of California San Diego, USA
THURSDAY, MARCH 21 – registration begins at 7 am

POSTER SET UP  Blaine Kern Ballroom D  8:00 – 9:00 am
BREAKFAST  River Bend Ballroom  8:00 – 9:00 am

9:00-9:15 am
Welcome
Denise Belsham, PhD, President of PANS
Andy Babwah, PhD & Deborah Kurrasch, PhD, Chairs Local Organizing & Program Organizing Committees
Robert Millar, PhD, President International Neuroendocrine Federation

MORNING SESSION  Blaine Kern Ballroom A  9:15 – 12:00 noon
SYMPOSIUM 1: Epigenetic regulation of endocrine signaling
Session Chair: Deborah Suchecki & Jeffrey Tasker

9:15-9:45 am
Methyl CpG binding protein-2 (Mecp2): a molecular bridge connecting environmental factors and energy homeostasis
Bredford Kerr, PhD, Centro de Estudios Cientificos, Chile

9:45-10:15 am
Maternal and paternal epigenetic influences on neuroendocrine development
Frances Champagne, PhD, University of Texas, USA

10:15-10:45 am
Epigenetics of social bonding in prairie voles
Mohamed Kabbaj, PhD, Florida State University, USA

BREAK  Blaine Kern Ballroom Foyer  10:45 – 11:00 am

11:00-11:30 am - Trainee talks
EDC mixture disrupts maternal behavior and the hypothalamic control of puberty through epigenetic mechanisms
David Lopez Rodriguez, University of Liege, Belgium

Specific microRNAs are regulated in hypothalamic neurons after exposure to the saturated fatty acid palmitate or endocrine-disrupting chemical bisphenol A
Emma McIllwraith, University of Toronto, Canada

11:30-12:00 noon
Bones and behavior mediated by sex-dependent neurocircuits
Holly Ingraham, PhD, University of California, San Francisco, USA
### LUNCH & POSTERS #1  
**Blaine Kern Ballroom D**  
**12:00 – 2:00 pm**

12:00-2:00 pm  
**Networking + Thursday Posters**  
Presenters stand with their poster starting at 12:30pm

### KEYNOTE  
**Blaine Kern Ballroom A**  
**2:00 – 3:00 pm**

2:00-3:00 pm  
**Surprising origins of sex differences in the brain**  
Margaret McCarthy, PhD, University of Maryland, USA

### AFTERNOON SESSION  
**Blaine Kern Ballroom A**  
**3:00 – 6:00 pm**

SYMPOSIUM 2: Functional investigation of neuroendocrine circuits  
**Session Chair: Sasha Kaufmann & Vicky Lux-Lantos**

3:00-3:30 pm  
**Central regulation of energy and glucose metabolism by growth hormone**  
Jose Donato, PhD, University of Sao Paulo, Brazil

3:30-4:00 pm  
**Central circuits for water homeostasis**  
Charles Bourque, PhD, McGill University, Canada

### BREAK  
**Blaine Kern Ballroom Foyer**  
**4:00 – 4:15 pm**

4:15-4:45 pm  
**Kisspeptin neurons in the arcuate hypothalamus are at the heart of converging networks**  
Stephanie Padilla, PhD, University of Massachusetts, USA

4:45-5:15 pm  
**Trainee talks**  
**Melanocortins act on Kiss1 neurons to regulate reproduction in females**  
Rajae Talbi, PhD, Harvard Medical School, USA

**Prepubertal tonic gamma-aminobutyric acid (GABA) inhibition is upstream of the neurokinin b (NKB), kisspeptin and gonadotropin releasing hormone (GnRH) neuronal network in male rhesus monkeys**  
James Garcia, PhD, University of Wisconsin, USA

5:15-5:45 pm  
**New anatomical approaches to identifying neuroendocrine circuits: KNDy neurons and their role in reproduction**  
Aleisha Moore, PhD, Kent State University, USA

5:45-6:00 pm - **Short talk**  
**Pharmacological chaperone rescue of function in human HPG axis GPCRs with inactivating mutations**  
Robert Millar, PhD, University of Pretoria, South Africa

### SOCIAL  
**River Bend Ballroom**  
**6:00 – 7:30 pm**

6:00-7:30 pm - **Wine & Cheese Social**
**FRIDAY, MARCH 22**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
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<tr>
<td>8:00-9:00 am</td>
<td><strong>Let’s talk science</strong> breakfast – all are welcome</td>
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<td>Delegates have the opportunity to discuss relevant topics (one of six) with two experienced faculty members.</td>
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<td>9:15-12:00 noon</td>
<td><strong>MORNING SESSION</strong></td>
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<td><strong>SYMPOSIUM 3:</strong> Circadian and metabolic control of neuroendocrine function</td>
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<td>Session Chair: Michael Lehman &amp; Jennifer Hill</td>
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<td>9:15-9:45 am</td>
<td>The garden of the forking paths: Forced circadian desynchronization and metabolic alterations</td>
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<td>Diego Golombek, PhD, National University of Quilmes, Argentina</td>
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<td>9:45-10:15 am</td>
<td>Animal models of shift work and metabolic health</td>
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<td>Carolina Escobar, PhD, National Autonomous University, Mexico</td>
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<td>10:15-10:45 am</td>
<td>Circadian disruption by bisphenol A and saturated fat: A view from the NPY neuron</td>
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<td>Denise Belsham, PhD, University of Toronto, Canada</td>
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<td>11:00-11:30 am</td>
<td>Trainee talks</td>
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<td><strong>The contribution of Bmal1 expression in the suprachiasmatic nucleus on female fertility</strong></td>
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<td>Karen Tonsfeldt, PhD, University of California, San Diego, USA</td>
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<td>Differential effects of saturated and unsaturated fatty acids on neuronal autophagy</td>
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<td>Andressa Reginato, University of Campinas, Brazil</td>
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<td>11:30-12:00 noon</td>
<td><strong>Metabolic regulation of kisspeptin and GnRH release</strong></td>
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<td>Victor Navarro, PhD, Harvard Medical School, USA</td>
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<td>12:00-2:00 pm</td>
<td><strong>LUNCH &amp; POSTERS #2</strong></td>
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<td>Blain Kern Ballroom D</td>
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**POSTER SET UP** Blaine Kern Ballroom D 8:00 – 9:00 am

**BREAK** Blaine Kern Ballroom Foyer 10:45 – 11:00 am

**LUNCH & POSTERS #2** Blain Kern Ballroom D 12:00 – 2:00 pm

12:00-2:00 pm

**Networking + Friday Posters**

Presenters stand with their poster starting at 12:30 pm
Microglial inflammation in obesity pathogenesis: Protective role of sex hormones  
Mauricio Dorfman, PhD, University of Washington, USA

Hot baby: How early life inflammation programs the brain  
Quentin Pittman, PhD, University of Calgary, Canada

Glucocorticoid signaling and neuroinflammation  
Carolina Munhoz, PhD, University of Sao Paulo, Brazil

Microglia interact with hypothalamic progenitors during development and are required for proper energy balance  
Jessica Rosin, PhD, University of Calgary, Canada

Estradiol enhances the inhibitory effect of the cytokine interleukin 1B on pulsatile LH secretion in female mice  
Katherine Makowski, DVM, University of California, San Diego, USA

Neuroinflammation and aging: Focus on experimental Alzheimer’s disease  
Flavia Saravia, PhD, University of Buenos Aires, Argentina

Closing remarks  
Andy Babwah, PhD & Deborah Kurrasch, PhD, Chairs Local Organizing & Program Organizing Committees  
Denise Belsham, PhD, President of PANS

Thanks for joining us at PANS2019!  

See you next year in Buenos Aires, Argentina  
at our PANS2020 “Meeting-within-a-Meeting” at ICE2020  
October 4-7, 2020
Let's Talk Science

PROFESSIONAL DEVELOPMENT  River Bend Ballroom  8:00 – 9:00 am

FRIDAY, MARCH 22 – ALL ARE WELCOME TO JOIN US FOR THE DISCUSSIONS
Please sign up at the registration desk

Table #1 - Grant writing: Where to start and how to be clear
Michael Lehman, Victor Navarro and Ravi Ravindranath

Table #2 - Interdisciplinary careers: Communicating science
Deboleena Roy and Margaret McCarthy

Table #3 - Alternative careers: Working in industry
Richard Mills and Lisa Burnett

Table #4 - An opportunity to meet women in neuroendocrinology
Susan Wray and Pamela Mellon

Table #5 - Commercialization: So you think you have a great idea, what to do next
Robert Millar and Denise Belsham

Table #6 - Networking: How to grab peoples’ attention and have them remember you
Deborah Kurrasch and Holly Ingraham
THURSDAY, MARCH 21

1. Distinct Changes in Gut Microbiota Are Associated with Estradiol-Mediated Protection from Diet-Induced Obesity in Female Mice

2. Retroperitoneal Paraganglioma in a Patient Post-Fontan: The Association
   S. Agarwal, I. Jindal, A.E. Balazs, D.L. Paul, Baylor College of Medicine, USA

3. Unusual Case of Plurihormonal Pituitary Macroadenoma
   E.S. Allehaibi, M.H. Almalki, I. Brema, King Fahad Medical City, Saudi Arabia

4. Galanin-Like Peptide Neurons Are Required for Correctly-Timed Puberty Onset in Mice
   C. Decourt, G.M. Anderson, University of Otago, New Zealand

5. 27-Hydroxycholesterol a Selective Estrogen Receptor Modulator: Profiling 27-Hydroxycholesterol Effects on Estrogen Receptor Activity in Mice
   A. Asghari, S. Hiramitsu, K. Dao, M. Umetani, University of Houston, USA

6. Brain Derived Neurotrophic Factor in the Regulation of Supraoptic Vasopressin Neurons in Development of Hyponatremia
   K. Balapattabi, J.T. Little, J. Cunningham, UNT Health Science Center, USA

7. IGSF1 Does Not Regulate FSH Synthesis or Secretion
   E. Brûlé, Y. Li, G. Schang, Y. Wang, X. Zhou, D.J. Bernard, McGill University, Canada

8. Taste Sensitivity is Related to Incretin Response to Oral Glucose Challenge, Dietary Habits and Body Composition: A Novel Link with Energy Metabolism

9. Pituitary Microadenoma and Cerebral Venous Thrombosis in a Patient with Transient Adipsic Diabetes Insipidus after Treatment for Craniopharyngioma
   L.V. Evangelista, J.B. Aragon, Makati Medical Center, Philippines

10. A Case of Pseudo-Apoplexy: An Unexplored Mechanism of Acute Pituitary Failure
    J.M. Francisco, D.C. Francisco, M.C. Agcaoili, The Medical City, Philippines

11. Severe Iron-Deficiency Anemia Leading to Hypothyroidism
    R.D. Ghiya, S.R. Ahmad, Baylor Scott & White Medical Center, USA
12. Estradiol Protects Against High-Fat Diet-Induced Obesity and Anxiety in Female Mice
   M.E. Graham, K. Acharya, A. Parakoyi, A. Corcoran, S. Gottipati, M.J. Tetel, Wellesley College, USA

13. The Effects of Selective Serotonin Reuptake Inhibitors on Urinary Free Cortisol in Patients with Carney Complex and Primary Pigmented Nodular Adrenocortical Disease
   C.D. Kamilaris, N. Sinaii, C.A. Stratakis, Eunice Kennedy Shriver National Institute of Child Health & Human Development, NIH, USA

14. Ectopic ACTH Syndrome with a Pituitary Mass
   J.C. Lake, A.R. Crawford, R.J. Comi, K.S. Kuyilan, Dartmouth Hitchcock Medical Center, USA

15. Vitamin B₆ and N-Acetylcysteine Protect Hypothalamic Neurons from Bisphenol A-Mediated Induction of Neuropeptide Y Gene Expression
   N. Loganathan, E.K. McIlwraith, D.D. Belsham, University of Toronto, Canada

16. Complete Recovery of Central Diabetes Insipidus Associated with Isolated Stalk Thickening in a Neurosarcoidosis Patient
   A. Madan Paramasivan, K. Buddhdev, A.T. Drincic, University of Nebraska, USA

17. Evidence for Impaired Kisspeptin Signaling During Metabolic Stress in Female Mice
   R.B. McCosh, K.J. Michael, K. Tian, K.M. Breen, University of California, San Diego, USA

18. Estrogen-Responsiveness of Female Mouse Hypothalamic Astrocytes: A Developmental Study
   M.A. Mohr, B.A. Falcy, B.J. Laham, P.E. Micevych, University of California, Los Angeles, USA

19. Conversion of a Non-Secreting to a Growth Hormone-Secreting Pituitary Adenoma: A Case of Rapid Development of Acromegaly
   K. Motwani, E.S. Siraj, EVMS, USA

20. High-Fat Diet Suppresses Basal Lh Pulsatile Levels in Female Mice at Estrus
    A.L. Negron, S. Radovick, Rutgers-Robert Wood Johnson Medical Center, USA

21. An Unusual Presentation of Delayed Onset Panhypopituitarism after Cardiac Surgery
    L.T. O'Murchadha, M. Healy, N.A. Phelan, A. Pazderska, St James’ Hospital, Ireland

22. Cell-Specific Ablation of GnRH Neurons Using Kisspeptin-Saporin in the Preoptic Area of Sheep, but Not Mice
    D.T. Porter, A.M. Moore, R.L. Goodman, S.M. Hileman, L.M. Coolen, M.N. Lehman, University of Mississippi Medical Center, USA

23. The Placenta as a Potential Target of Neuroendocrine Disruption: Effects of Brominated and Organophosphate Flame Retardants
    K. Rock, B. Horman, A. Phillips, H. Stapleton, M. Ruis, H.B. Patisaul, North Carolina State University, USA

24. Hypothalamic-Pituitary-Gonadal (HPG) and Hypothalamic-Pituitary-Thyroid (HPT) Axes in Cushing Syndrome (CS): A Retrospective Study
    S. Shekhar, S. Gubbi, R. McGlotten, L.K. Nieman, National Institutes of Health, USA

25. Discovering the Function of IGSF1 and Its Role in the Hypothalamic-Pituitary-Thyroid Axis
    C.L. Smith, D.J. Bernard, McGill University, Canada

26. Vaginal Microbial Diversity Changes across the Menstrual Cycle in Healthy Young Women
27. A Novel Population of Kisspeptin Neurons in the Medial Tuberal Nucleus of the Hypothalamus in Mice
   S.B. Stephens, R.B. Liaw, N.P. Di Giorgio, V.A. Lux-Lantos, A.S. Kauffman, University of California, San Diego, USA

28. Mechanisms Underlying Glucocorticoid-Induced Suppression of Pulsatile LH: Insights from Immortalized Kisspeptin Cells
   K. Tian, M.J. Kreisman, R.B. McCosh, K.M. Breen, University of California, San Diego, USA

29. Familial X-Linked Acrogigantism: Postnatal Outcomes and Tumor Pathology in a Prenatally Diagnosed Infant and His Affected Mother
   B.K. Wise-Oringer, G.J. Zanazzi, R.J. Gordon, S.L. Wardlaw, C. William, B. Kohn, J.H. Wisoff, S.E. Oberfield, Columbia University Medical Center, USA

30. Corticosterone-Mediated Suppression of the Reproductive Neuroendocrine Axis in Male Mice
   J.A. Yang, A.S. Kauffman, University of California, San Diego, USA

31. Functional Role of Arcuate Nucleus NPY/AgRP Neurons in the GnRH Circuit Regulating LH Secretion
   E.A. Coutinho, M. Prescott, C.J. Marshall, S. Hessler, A.E. Herbison, R.E. Campbell, University of Otago, New Zealand

32. Tachykinins Are Essential for the Induction of the Preovulatory LH Surge in Mice
   S. Leon, C. Fergani, R. Talbi, S. Serap, C. Maguire, A. Gerutshang, S.B. Seminara, V.M. Navarro, Brigham and Women’s Hospital/Harvard Medical School, USA

POSTER SESSION

FRIDAY, MARCH 22

1. Systemic and Hypothalamic Hyperandrogenism Emerges Following Elimination of Ovarian and Extra-Ovarian Sources of Estradiol in Female Marmoset Monkeys
   M. Kraynak, R.W. Goy, A. Kapoor, J.E. Levine, D.H. Abbott, University of Wisconsin, USA

2. Evidence of a Role for Kisspeptin in Regulation of LH and Testosterone Secretion in the Ovine Fetus
   R. Amodei, K. Gribbin, I. Lindgren, K. Corder, S. Louey, F. Stormshak, C. Estill, C.E. Roselli, Oregon Health Science University, USA

3. Blocking GABAB Receptors (GABABR) from Birth to Weaning in Mice Induces Profound Changes in the Gonadotropic Axis
   M. Bizzozzero Hiriart, N.P. Di Giorgio, C. Libertun, V.A. Lux-Lantos, IBYME-CONICET, Argentina

4. Hot Flashes, Flushing, and Sweating in a Middle-Aged Man with Pituitary Macroadenoma
   S. Boddhula, S. Boddhula, J. Hughes, Mary Imogene Bassett Hospital, USA

5. Investigating the Metabolic and Reproductive Role of AR in Leptin Receptor Expressing Cells
   A. Cara, C. Elias, University of Michigan, USA

6. Aberrant DNA Methylation in Regulatory Genomic Elements Are Associated with Invasive Behavior of Pituitary Macroadenomas: An Integrative Analysis of Epigenome-Wide Studies
7. Thyrotropin-Releasing Hormone-Degrading Ectoenzyme Controls Thyrotropin Secretion and Body Weight in Male Rodents
   J. Charli, A. Cote-Velez, R. Adair, K. Hernández-Ortega, R. Uribe, M. Anaya-Vergara, J. Pérez-Estrada, M. Matziari, P.I. Joseph-Bravo, Universidad Nacional Autonoma de Mexico, Mexico

8. Labile Ca-Permeable AMPA Receptors Comprise New Synapses Following Salt Loading-Induced Plasticity in Hypothalamic Magnocellular Neurons
   S. Di, L. Harrison, Z. Jiang, J.G. Tasker, Tulane University, USA

9. NKB Signaling in the Posterodorsal Medial Amygdala Stimulates Gonadotropin Release in a Kisspeptin-Independent Manner in Female Mic
   C. Fergani, S. Leon, E. McCarthy, V.M. Navarro, Brigham and Women’s Hospital, Harvard Medical School, USA

10. In Vitro Exposure to Bisphenol A, Benzophenones 2 or 3, Have Different Effects on GnRH Gene Expression and Secretion in Mature and Immature GnRH Neurons

11. Is There a Cut-Off of Ki-67 Indicative of Pituitary Carcinoma?

12. Low Chloride Transporter Expression in Vasopressin Neurons
    M.O. Fisher, J.G. Tasker, Tulane University, USA

13. Gestational Diabetes Alters Hypothalamic Development, Microglial Activation, and Insulin Signaling in Offspring
    R.V. Gonzalez, K.E. Weis, L.T. Raetzman, University of Illinois, Urbana-Champaign, USA

14. Leuprolide Injection Induced Pituitary Apoplexy

15. Optogenetic Activation of Mu Opioid Receptors in the Medial Preoptic Nucleus Attenuates Lordosis Behavior
    C. Johnson, P.E. Micevych, University of California, Los Angeles, USA

16. Prospective Study of the Association between Early Adrenarche and Cognitive Function in Children with Cushing Disease
    M.F. Keil, J. Kang, E.A. Wiggs, D.P. Merke, C.A. Stratakis, National Institutes of Health, USA

17. The Effects of the Menstrual Cycle and Caloric Restriction on Sleep in Young Women
    A.E. Kim, B.P. Purse, K.R. Hirsch, A.B. Rice, J.A. McGrath, A.E. Smith-Ryan, J.E. Hall, Cleveland Clinic Lerner College of Medicine, USA

18. Selective Inhibition of Epigenetic Pathways Has Anti-Proliferative and Pro-Apoptotic Effects on the Mouse Corticotroph Tumor Cells, AtT20

19. The Case of a Dual-Secreting Pituitary Macroadenoma
    N. Malkani, D.M. Vodopivec Kuri, A. Restrepo, Lahey Clinic, USA
20. Activation of Kiss1 Neurons in the Posterodorsal Medial Amygdala Stimulates Gonadotropin Release via the Release of Kisspeptin in Female Mice
C. Fergani, E. McCarthy, S. Leon, V.M. Navarro, Brigham and Women’s Hospital, Harvard Medical School, USA

21. A Case of Metastatic Paraganglioma
M. Mohammadi, S.A. Sovran, McMaster University, Canada

22. Low-Dose Gestational BPA Exposure Alters Circadian Rhythms in Mice
D. Nesan, M. Antle, D.M. Kurrasch, University of Calgary, Canada

23. Chronic Variable Stress Worsens Effects of Mild Blast Traumatic Brain Injury on the Stress Response
M.G. Oyola, A.L. Russell, L.A. Miller, R.J. Handa, T.J. Wu, Uniformed Services University of the Health Sciences, USA

24. Combination of Octreotide and Dexamphetamine to Control Weight Gain in Pediatric Patients with Hypothalamic Obesity
F. Reschke, R. Knoefler, M. Smitka, A. Huebner, Children’s University Hospital Dresden, Germany

25. Nitric Oxide Induces Spexin (Spx), Galanin Receptor 2 (GalR2), and Galanin Receptor 3 (GalR3) mRNA Independently of the cGMP/PKG Pathway and Enhances C/EBP-β Binding to the Spx 5’ Regulatory Region
A. Tran, D.D. Belsham, University of Toronto, Canada

26. Tumor Control after Radiotherapy and Temozolomide in a Cushing’s Disease Patient with Giant Aggressive Pituitary Tumor

27. Synthetic Progestin, Neural Development, and Cognitive Behavior: A Rodent Model Investigation of a Drug Used in Human Pregnancy
C.K. Wagner, R.I. Wood, M. Lolier, A. Phillips, University at Albany, USA

28. Rapid Glucocorticoid Regulation of Adrenoreceptor Trafficking Desensitizes CRH Neurons to Noradrenergic Activation
G.L. Weiss, J.G. Tasker, A.M. Neilsen, Tulane University, USA

29. Chronic Psychosocial Stress during Pregnancy Affects Maternal Behavior and Neuroendocrine Function and Modulates Hypothalamic CRH Signaling Pathway and Nuclear Steroid Hormone Receptor Expression
S. Zoubovsky, L. Muglia, University of Cincinnati, USA

30. Differential Regulation of Hypothalamic and Hepatic Reproductive Signals by Leptin and Sex Steroids in the Mozambique Tilapia Oreochromis mossambicus
E. Cheung, North Carolina State University, USA

31. Role of BMAL1 in Western Diet-Induced Disruption of Circadian Hypothalamic Feeding Neuropeptides
M.N. Clemenzi, A. Martchenko, D.D. Belsham, P.L. Brubaker, University of Toronto, Canada

32. Panhypopituitarism Causing a Life Threatening Prolonged QT Interval Which Can Be Reversible with Treatment of Underlying Endocrine Disorders
R.D. Sittol, J.H. Jang, R. Chaudhary, C. Bryan, A. Chokshi, M. Adrian, C. Kim, Englewood Hosp & Med Ctr, USA

33. Cryptolepine Action on Insulin Resistance in High-Glucose Diet-Fed Caenorhabditis Elegans
R.C. Young, K. Jones, R. Gibson, J. Del Ponte, P.S. Dalvi, Gannon University, USA
Speaker Bios and Abstracts
Dr. Bredford Kerr, Centro de Estudios Científicos, Chile

**Title:** Methyl CpG binding protein-2 (Mecp2): a molecular bridge connecting environmental factors and energy homeostasis

**Biography:** Bredford Kerr is Researcher in the Centro de Estudios Científicos-CECs in Valdivia, Chile. Dr. Kerr’s research is focused on characterizing the gene-environment interaction in the control of body weight and how the exposure to diet components alters the expression of genes associated with body weight balance in both hypothalamus and adipose tissue, using wild-type and transgenic mice as models. His lab group is also involved in unveiling the mechanism through which the exposure to an experience-dependent plasticity paradigm changes the methylation of DNA in highly plastic brain areas to modulate energy homeostasis, and learning and memory process. Dr. Kerr received his Ph.D. in Physiological Science from Pontifical Catholic University of Chile and conducted two postdoctoral fellowships, one at the Oregon National Primate Research Center in Portland and the second back in Chile at the Centro de Estudios Científicos-CECs in Valdivia; the institution in which he subsequently formed his working group.

**Abstract:** The impact of epigenetics on body weight control has only been recently addressed. Body weight balance in commanded by the melanocortin system (MS). This neuronal circuit maintains high levels of plasticity even during adulthood and one of the mechanisms underlying its high plasticity is the permanent control of gene expression, a process in which cytosine methylation plays a pivotal role. The DNA methylation reader MECP2 is a transcription factor with a dual role on gene expression that is able to activate or repress its target genes by binding to methylated CpG dinucleotides. Some patients carrying MECP2 mutations exhibit alterations in body weight and evidence from our lab has shown that mice lacking a fully functional Mecp2 allele exhibit a defective body weight regulation and an altered hypothalamic response to metabolic signals. Our goal during the last years has been to elucidate the mechanisms through which environmental factors impact on the epigenetic control of gene expression and its consequence on hypothalamic function. To that, we use both null-mutant mice lacking the expression of Mecp2 and conditional KO mice, in which the expression of Mecp2 has been deleted in a subset of neurons comprising the MS. Our results show that hypothalamic neurons express the methylation reader Mecp2 and its absence disrupts body weight balance by increasing adiposity. In addition, Mecp2 absence alters post-translational modifications in leptin-signaling components that regulate the expression of genes commanding feeding behavior and energy expenditure. Moreover, environmental factors related to changes in energy demands alter the expression of proteins commanding chromatin remodeling, modifying the hypothalamic expression of neuronal plasticity genes, which impacts on cytoarchitecture of melanocortin system neurons, feeding behavior and energy expenditure. Our results highlight the role of chromatin remodeling for the proper hypothalamic function required for an adequate control of feeding behavior, energy expenditure, and body weight. (Fondecyt 1140162, PFB01/2007)

**NOTES:**
Dr. Frances Champagne, University of Texas, USA

Title: Maternal and Paternal Epigenetic Influences on Neuroendocrine Development

Biography: Frances A. Champagne is a Professor in the Department of Psychology at University of Texas, Austin and an Adjunct Associate Professor in the Department of Psychology at Columbia University. She received a M.Sc. in Psychiatry and Ph.D. in Neuroscience from McGill University. Dr. Champagne is a world leader within the evolving field of behavioral epigenetics – the study of how life experiences lead to behavioral and neurobiological variation through epigenetic factors. Though mechanistic studies in this field are addressed primarily in animal models, Dr. Champagne has also established collaborations to explore epigenetics within humans to determine the contribution of these molecular marks to neurobiological outcomes. In addition to her multidisciplinary research program funded by NIH, NICHD, NIA, NIEHS, EPA and NIMH, Dr. Champagne teaches several courses, including The Developing Brain, Ethics, Genetics and the Brain and Behavioral Epigenetics.

Abstract: Development is shaped by environmental influences occurring at various life stages and there is increasing evidence for the role of epigenetic mechanisms in this process. The experience of parents can likewise shape the development of offspring leading to environmental impacts that persist across generations. Though maternal and paternal epigenetic influences are often explored separately, there is increasing evidence for the interplay between paternal experiences and characteristics of the maternal prenatal and postnatal environment that shapes developmental outcomes in offspring. In this talk, I will highlight research investigating the epigenetic impact of prenatal maternal exposure to stress/toxins, variation in the quality of postnatal mother-infant interactions shaped by maternal exposure to adversity and the impact on offspring development of paternal exposure to stress. Using embryo transfer, these studies highlight the interactive influence of mothers and fathers and the dynamic routes through which the environment can lead to behavioral and neurobiological effects across generations.

NOTES:
Dr. Mohamed Kabbaj, Florida State University, USA

Title: Epigenetics of social bonding in prairie voles

Biography: Dr. Kabbaj earned his Ph.D. at Bordeaux II University (France), under the supervision of Dr. Michelle LeMoaal, and then he completed five years of postdoctoral studies at the Mental Health Research Institute at the University of Michigan (Ann Arbor) under the supervision of Dr. Huda Akil. Dr. Kabbaj joined the Biomedical Sciences Department of the Florida State University College of Medicine in August 2002, where he went through the academic ranks and he is now Professor of Biomedical Sciences & Neurosciences at the same institution. Research interests: Dr. Kabbaj uses animal models (rats, mice and voles) to examine the neurobiology of sex and individual differences in stress and drug addiction. He is also examining epigenetic mechanisms underlying social behaviors in the social monogamous prairie voles. Recently, he has been working on the mechanisms of sex differences in the antidepressant and addictive properties of ketamine. Funding: Dr. Kabbaj is funded by NIDA and NIMH.

Abstract: Social attachments are a vital part of healthy human behavior and an inability to form such attachments is regarded as a symptom of mental disorders such as anti-social disorders, schizophrenia and autism. Studying the mechanisms underlying social attachment requires an animal model that displays behaviors similar to that of human social attachment. Prairie voles (Microtus ochrogaster) have become an important model for the study of the neurobiology of social attachment. In the field, male and female prairie voles form long-term, monogamous bonds and share a nest throughout the breeding season. Such a breeding pair typically remains together until one animal dies. Given that mating in prairie voles induces neuroadaptations that eventually lead to bonding, we will share in this talk some of the underlying epigenetic bases of social bonding in this unique animal model.

NOTES:
Dr. Holly Ingraham, University of California, San Francisco, USA

**Title:** Bones and Behavior Mediated by Sex-Dependent Neurocircuits

**Biography:** Dr. Holly Ingraham is a Professor and Vice Chair in the Department of Cellular and Molecular Pharmacology at the University of California, San Francisco (UCSF). Dr. Ingraham’s lab seeks to define the pathways that contribute to endocrine and hypothalamic tissue function. To do so, they use diverse approaches such as structural biology, biochemistry, and genetic mouse models to mechanistic study central and peripheral physiological systems relevant to energy homeostasis. Recently, the Ingraham lab has focused on understanding how estrogen responsive modules in the medial basal hypothalamus (MBH) mediate sex-dependent metabolic responses in females. The lab has employed stereotaxic and chemogenetic approaches to manipulate these estrogen responsive neurons in the hypothalamus, with an ultimate goal to understanding how neural circuits control sex-dependent energy and bone metabolism in females.

**Abstract:** We seek to discover sex-differences in the central control of female physiology across the lifespan. In the course of these studies we found that central estrogen signaling is linked to sex-dependent anabolic bone responses in female mice. In our recently published work, a stunning increase in bone mass occurs after deleting estrogen hormone signaling in the female arcuate nucleus of the hypothalamus (ARC). In female mice, the robust increase in new bone formation stems from loss rather than gain of estrogen signaling in the ARC and is uncoupled from high circulating peripheral 17β-estradiol (E2), which can promote bone formation in female mice. Three independent and intersectional models confirmed that ablating estrogen receptor alpha (ERα) signaling in ARC neurons leads to a robust increase in bone density and bone strength only in female mice. We identified ARC Kiss1 neurons (ARC^{Kiss1}) in the medial basal hypothalamus (MBH) as the critical node for this powerful neuroskeletal circuit. These findings established that a sex-dependent brain-to-bone pathway normally restrains bone metabolism to divert energy resources elsewhere. When disrupted, a robust sex-dependent anabolic bone response is permanently triggered in young and old mutant female mice. Newer studies have asked if this is mediated by a humoral or neuronal mechanism. In parallel studies we find that a small cluster of estrogen-responsive neurons in the ventrolateral subregion of the ventromedial hypothalamus (VMHvl) acts form part of an ancillary female-specific circuit to integrate melanocortin and estrogen signaling, promoting activity and obsessive-like behaviors. Food intake was unaffected in all of our models. Collectively, our new findings show that estrogen signaling in the MBH controls sex-dependent circuits that are dispensable for energy consumption but essential for energy allocation and utilization in females.

**NOTES:**
**Title:** Surprising origins of sex differences in the brain

**Biography:** Dr. McCarthy is a leading neuroscientist who has made significant discoveries related to gender differences and the brain. Her seminal research focuses on the influence of steroid hormones on the developing brain with a special emphasis on understanding the cellular mechanisms that establish sex differences—that is, the numerous, novel mechanisms (including roles for prostaglandins, endocannabinoids, amino acid transmitters, and multiple enzymes) by which steroids permanently organize the developing brain differently in males and females. Dr. McCarthy conducted some of the first studies on how steroid hormones can imprint epigenetically on the developing brain to organize differences between males and females in adult physiology and behavior.

More recently, her laboratory generated a paradigm shift in understanding of sexual differentiation of sexual behavior with the discovery that the feminization program of development requires suppression of the masculinization program via DNA methylation, and that steroid hormones emancipate the male gene expression profile by reducing activity of DNA methylating enzymes. Her laboratory has also studied inflammatory and immune-mediated sex differences in the brain, sensitive periods in brain development, neurogenesis in the postnatal brain, and the role of GABA in brain differences. By increasing understanding of how the brain develops differently in males and females, Dr. McCarthy has revealed both naturally occurring variation as well as highlight points of vulnerability and nodes for intervention in treatment of developmental neuropsychiatric disorders with a gender bias.

**Abstract:** Elucidating the cellular and molecular mechanisms by which sex differences are developmentally programmed into the brain has been a central goal of neuroendocrinology since the discipline was formed half a century ago. Neuroanatomical sex differences range from cell number, to phenotype to dendritic morphology and synaptic patterning. Research emphasis has largely been on the intersection of steroids, neurotransmitters and growth/survival factors. Our laboratory has found a central role for a different source of neuromodulation, the neuroimmune system, and has discovered that at least two immune cells, microglia and mast cells, are critical partners in the process of brain masculinization. We further find that membrane derived signaling molecules, in particular the prostaglandins and endocannabinoids, are also essential drivers of the sexual differentiation process by modulating the activity of immune cells in the brain. Why males have higher levels of all of these is a mystery but may have its origins in the maternal immune system and its response to male fetuses during mammalian gestation. Combined, these surprising findings compel us to rethink our long-established views of how steroids establish and maintain sex differences in brain and behavior.
Dr. Jose Donato, University of Sao Paulo, Brazil

Title: Central regulation of energy and glucose metabolism by growth hormone

Biography: Jose Donato Jr. is associate professor at the Department of Physiology and Biophysics, Institute of Biomedical Sciences, University of Sao Paulo. He holds a Master's degree in Food Science and PhD in Morphofunctional Sciences from the University of Sao Paulo, and was a postdoctoral fellow at the University of Texas Southwestern Medical Center. He has experience in the following areas: leptin physiology, obesity, neuroendocrinology and central regulation of energy and glucose homeostasis. He uses neuroanatomical, histological, molecular and mouse genetic methods to investigate how neural circuits that regulate energy and glucose homeostasis are affected by the action of several hormones.

Abstract: Growth hormone (GH) responsive cells are extensively distributed in the central nervous system, including in neurons of the arcuate nucleus (ARH) and ventromedial nucleus (VMH) of the hypothalamus, areas that control food intake, energy expenditure and blood glucose levels. However, the functional role of central GH signaling for energy and glucose homeostasis has not been unveiled yet. We generated mice lacking GH receptor (GHR) specifically in AgRP neurons or in steroidogenic factor-1 (SF1) cells, which include VMH neurons. Our objective was to evaluate whether GH signaling in these neuronal populations modulates energy and glucose homeostasis during normal conditions or during metabolic stress. AgRP GHR KO mice exhibited similar body weight, food intake, energy expenditure, glucose tolerance and leptin sensitivity, compared to control animals. However, fasting induced a lower c-Fos expression, a marker of neuronal activation, in the ARH of AgRP GHR KO, suggesting that AgRP neurons are unable to appropriately sense food deprivation without GH signaling. Remarkably, GHR ablation in AgRP cells mitigated highly characteristic hypothalamic and neuroendocrine adaptations induced by weight loss. Thus, while control mice adapted to a 60% food deprivation by progressively saving energy, AgRP GHR KO mice exhibited a higher T4 and testosterone concentrations as well as an increased energy expenditure and UCP-1 mRNA expression in the brown adipose tissue, compared to control animals. These effects led to a higher rate of weight loss, which was predominantly due to fat. In contrast, SF1 GHR KO mice exhibited similar responses to food restriction in comparison with control group. However, a blunted counter-regulatory response to hypoglycemia was observed in SF1 GHR KO mice, indicating that GH signaling in VMH neurons helps the organism to recover from hypoglycemia. In summary, GH signaling in AgRP neurons regulates the metabolic adaptations to starvation, while GH signaling in the VMH controls the counter-regulatory responses to hypoglycemia. These findings indicate a previously unidentified function of GH to induce appropriate metabolic responses that ensure survival via its action on specific neuronal populations.

NOTES:
Dr. Charles Bourque, McGill University, Canada

Title: Central circuits for water homeostasis

Biography: Charles Bourque is a Professor in the Department of Neurology-Neurosurgery at McGill University. He holds a Distinguished James McGill Chair and his laboratory is part of the Centre for Research in Neuroscience at the Montreal General Hospital. Bourque and his team are characterizing the molecular and cellular mechanisms by which the brain monitors and regulates body hydration. His lab uses multidisciplinary techniques ranging from single channel electrophysiology to behavioral analysis, and from super-resolution microscopy to in vivo optogenetics. Bourque has published over 140 scientific papers and delivered over 170 invited oral presentations on his work. He has received numerous awards from the Canadian Institutes of Health Research (Scholarship, Scientist and Senior Investigator), as well as prestigious awards from Organizations such as the Société de Neuroendocrinologie (prix Jacques Benoit) and the American Physiological Society (Joseph Erlanger Award). He was inducted as a Fellow to the Royal Society of Canada in September 2016.

Abstract: Mammals have evolved behavioral and physiological mechanisms that oppose perturbations in extracellular fluid (ECF) osmolality via positive (anticipatory) and negative (homeostatic) feedback. For example, ECF hyperosmolality increases water intake and causes release of vasopressin (VP, antidiuretic hormone) from the neurohypophysis. Conversely, ECF hypotonicity suppresses thirst and VP secretion to reduce body water and restore isotonicity. These negative feedback responses are triggered by the effects of ECF osmolality on osmoreceptor neurons in the organum vasculosum lamina terminalis (OVLT) which project to thirst promoting centers and VP-releasing neurons in the hypothalamus. Osmoreceptor neurons show changes in firing rate that vary in proportion with fluid osmolality and cause similar changes in electrical activity in homeostatic effector neurons via the release of glutamate. Studies in our laboratory showed that neurons in the suprachiasmatic nucleus (SCN) can promote feed forward changes in thirst and VP release that anticipate physiological requirements for fluid conservation associated with the absence of fluid intake during sleep. Notably, clock neurons mediate such effects via postsynaptic modulation of firing by Thirst-promoting neurons, and via circadian modulation of synaptic transmission between osmoreceptor and baroreceptor inputs to VP neurons. In both cases, the effects are mediated by activity dependent release of VP from the axon terminals of SCN neurons. Here, Dr. Bourque will discuss recent findings which clarify how the electrical activity of SCN clock neurons generates adaptive changes in thirst or VP release.
Dr. Stephanie Padilla, University of Massachusetts, USA

Title: Kisspeptin Neurons in the Arcuate Hypothalamus are at the Heart of Converging Networks

Biography: Fluctuations in sex hormones can influence behavior and physiology. My lab is interested in resolving the neural circuits and signaling molecules that orchestrate these dynamic state changes. We believe that there may be a ‘hub’ in the neuroendocrine reproductive axis that is not only instrumental for fertility, but converges with thermoregulatory, circadian and metabolic circuits. Resolving the molecular details of such converging networks will help to determine how gonadal hormone status can regulate body weight, sleep and temperature.

I trained in the laboratory of Dr. Richard Palmiter as a postdoctoral fellow of the Howard Hughes Medical Institute where I established a means to dissect the functional and molecular signaling components of complex neural circuits. I received a PhD from Columbia University, under the mentorship Dr. Lori Zeltser. My thesis work investigated the ontogeny of neurons that regulate food intake and body weight.

Abstract: Successful reproduction in female mammals is precisely timed and must be able to withstand the metabolic demand of pregnancy and lactation. We show that kisspeptin-expressing neurons in the arcuate hypothalamus (Kiss1^{ARH}) of female mice control the daily timing of food intake, along with the circadian regulation of locomotor activity, sleep, and core body temperature. Toxin-induced silencing of Kiss1^{ARH} neurons shifts wakefulness and food consumption to the light phase and induces weight gain. Toxin-silenced mice are less physically active and have attenuated temperature rhythms. Because the rhythm of the master clock in the suprachiasmatic nucleus (SCN) appears to be intact, we hypothesize that Kiss1^{ARH} neurons signal to neurons downstream of the master clock to modulate the output of the SCN. We conclude that, in addition to their well-established role in regulating fertility, Kiss1^{ARH} neurons are a critical component of the hypothalamic circadian oscillator network that times overt rhythms of physiology and behavior.
Title: New anatomical approaches to identifying neuroendocrine circuits: KNDy neurons and their role in reproduction

Biography: Dr. Aleisha Moore received her PhD in the laboratory of Dr. Rebecca Campbell at the University of Otago and is currently a postdoctoral fellow under the supervision of Dr. Michael Lehman at Kent State University. Her research uses a range of cutting-edge neuroanatomical techniques in multiple mammalian models to study the structure and connectivity of neuroendocrine circuits controlling fertility, including Kisspeptin/Neurokinin B/Dynorphin (KNDy) neurons. Recently, her research has focused on identifying alterations within the KNDy neuronal network that may underlie the development of neuroendocrine disorder in a mouse model of polycystic ovarian syndrome, the most common cause of infertility in women worldwide.

Abstract: Reproduction in mammals is dependent on the pulsatile secretion of gonadotropin-releasing hormone (GnRH) from GnRH neurons in the hypothalamus, which elicits the pulsatile secretion of luteinizing hormone (LH) from the pituitary gland. Although multiple upstream circuits have been associated with pulsatile GnRH/LH release, a unique population of cells in the arcuate nucleus that express kisspeptin, neurokinin B and dynorphin, termed KNDy cells, are strongly implicated as the GnRH pulse generator. The identification of upstream cells that regulate KNDy neuron activity is therefore a critical next step to understand the neurocircuitry regulating fertility; however, the anatomical dissection of neuronal networks can be difficult using conventional techniques within the hypothalamus given the heterogeneity of cell types in individual regions and nuclei. This lecture will describe a series of studies using transgenic mice and viral-mediated tract tracing to define the network of afferent neurons regulating KNDy neuron populations. In particular, we will highlight recent work using rabies-mediated tract-tracing to map the brain-wide distribution of cells providing monosynaptic input to KNDy neurons. Further, we will discuss the use of whole tissue optical clearing and light sheet microscopic imaging of the intact mouse brain in order to study the complex three-dimensional structure of the KNDy neuronal population and upstream circuits. The use of these cutting-edge tools is expanding our understanding of the multilayered neurocircuitry required for GnRH pulse generation. Future studies can use these tools and others to identify and manipulate upstream neuron populations that relay critical peripheral signals controlling fertility, and, identify changes in synaptic connectivity that are either required for normal changes in reproductive states or lead to infertility through driving abnormal pulsatile LH release, such as in polycystic ovarian syndrome.

NOTES:
Dr Robert Millar, University of Pretoria, South Africa

**Title:** Pharmacological chaperone rescue of function in human HPG axis GPCRs with inactivating mutations

**Biography:** Professor and Director, Centre for Neuroendocrinology, University of Pretoria; Research Fellow, Centre of Integrative Physiology, University of Edinburgh, UK. President of the International Neuroendocrine Federation (INF). Bob Millar’s research focuses on peptide regulators of reproductive hormones. He pioneered the discovery of the GnRH prohormone, novel GnRH structures, and the first cloning of the GnRH I and GnRH II receptors. His laboratory delineated GnRH binding sites and the molecular mechanisms underlying receptor activation and coupling. He has participated in, and led, a number of programmes developing GnRH analogues for use in a wide range of clinical pathologies. His group’s research on direct antiproliferative effects of selective GnRH analogues on tumour cells has revealed the novel concept of ligand-induced-selective-signaling by GnRH analogues, which has implications for improved selectivity in the development of new GnRH therapeutics and other GPCR targets. Most recently he has focused on novel GPCRs regulating reproduction, appetite, inflammation, cell invasion and angiogenesis with a particular focus on the RFamides such as metastin/kisspeptin and gonadotropin-inhibitory-hormone, and NKB and prokineticins. He developed kisspeptin antagonists as potential therapeutics in hormone-dependent diseases.

**Abstract:** Inactivating mutations in G-protein coupled receptors (GPCRs) at all levels of the HPG axis give rise to incomplete reproductive development and adult infertility. The majority of the mutations in GPCRs cause misfolding of the receptor and a failure to traffic to the cell surface. We have identified cell permeant small molecule agonists and antagonists which can bind orthostERICALLY or allosterically to stabilize the nascent GPCR in the endoplasmic reticulum and chaperone the mutant GPCR to the cell membrane. We have successfully ‘rescued’ many GnRH mutant receptors using small molecule antagonists which bind orthostERICALLY. After removal of the antagonists the mutant GnRH receptors demonstrate good cell surface expression. Michael Conn’s laboratory has demonstrated that such receptor rescue can restore reproductive competence in mice harboring an inactivating GnRH receptor mutation. We have also demonstrated rescue of cell surface expression and signaling in a substantial number of LH receptor mutations causing infertility in humans using a cell permeant allosteric agonist. This molecule is also able to rescue function in LHR binding and signalling deficient human mutations. Similarly, we have rescued cell surface expression and signalling in human neurokinin B receptor mutations with an NKB antagonist and are exploring rescue of GPR54 utilising cell penetrating peptides. These discoveries represent an advance towards personalized medicine for GPCR deficiencies in the human HPG axis.

**NOTES:**
Dr. Diego Golombek, National University of Quilmes, Argentina

Title: The garden of the forking paths: forced circadian desynchronization and metabolic alterations

Biography: Dr. Diego Golombek received his Ph.D. in Biology at the University of Buenos Aires. Professor and director of the Chronobiology Lab at the National University of Quilmes, Investigator at the National Research Council (Argentina). About 140 international publications (h index 33), as well as some 20 science books. National Science Prize (Argentina), Kalinga Prize (UNESCO), TWAS award, among others.

Abstract: Metabolic functions are synchronized by the circadian clock setting daily patterns of food intake, nutrient delivery and behavioral activity. Daily interactions between the hypothalamic clock at the suprachiasmatic nuclei (SCN) and peripheral circadian oscillators regulate physiology and metabolism to set temporal variations in homeostatic regulation. The SCN coordinate activity and feeding rhythms, thus setting the timing of food intake, energy expenditure, thermogenesis, and active and basal metabolism. We have developed a murine model of chronic circadian desynchronization (6-h advances – ChrA - or delays – ChrdD - of the light-dark cycle every 2 days) and tested behavioral, metabolic and pathological effects. Body weight was rapidly increased under ChrA, with animals tripling the mean weight gain observed in controls by day 10. Weight gain was accompanied by changes in glucose metabolism, increases in adipose tissue masses, and alterations in circulating triglycerides and liver weight. Daily patterns of food and water intake were abolished under ChrA. In contrast, ChrdD had no effect on body weight. Wheel-running, the housing of animals in groups, and the restriction of food availability to the hours of darkness prevented the abnormal increase in body weight under ChrA. In addition, animals under constant desynchronization developed a significantly higher susceptibility to experimental tumorigenesis or to an immune challenge. A profound knowledge of the photic and metabolic inputs to the clock, as well as its endocrine and autonomic outputs to peripheral oscillators driving energy metabolism, will help us to understand and alleviate circadian health alterations including cardiometabolic diseases, diabetes, and obesity.

NOTES:
Dr. Carolina Escobar, National Autonomous University, Mexico

**Title:** Animal models of shift work and metabolic health

**Biography:** Carolina Escobar is a Senior Professor in the Department of Anatomy, at the Faculty of Medicine, National Autonomous University in Mexico and directs a laboratory for basic research on Circadian Rhythms, Food intake and Metabolism.

She studied Physiological Psychology followed by a masters and PhD in Physiological Sciences. The main contributions of her laboratory have been 1. on the behavioral, metabolic and brain mechanisms associated with food entrainment and 2. the development of experimental models of shift work in order to better understand the adverse effects of circadian disruption. Her group described mechanisms of circadian entrainment by palatable food, which now can partly explain addictive behavior. Her data on circadian disruption have provided evidence of the negative effects of food and activity during the rest phase, which has provided a new insight of the circadian system as a key process for homeostasis and for metabolic health.

In this field she has published more than 90 scientific articles, 2 books and more than 25 book chapters. Since 2010 she is chief of the Research section in the Anatomy department. She is member of the Mexican Academy of Sciences and of the Mexican Academy of Medicine.

**Abstract:** Shift-work is a risk factor to develop overweight and metabolic disturbance. Shift-workers are exposed to shifted sleep schedules, to light at night and to irregular eating patterns. Such activities contradict the temporal signals elicited by the biological clock leading to a loss of behavioral and physiological circadian rhythms.

We have developed experimental models with rodents trying to mimic such disruptive conditions of modern life style in order to better understand the mechanisms that lead to the loss of metabolic balance and in order to elaborate possible strategies to prevent or to reverse circadian and metabolic disruption. We have observed that a main risk factor of shift-work is the conflict established between shifted feeding schedules and the light-dark cycle. Food ingestion out of phase from the normal light-dark cycle showed to have deleterious effects on metabolism and body weight, while eating synchronized to the light-dark cycle had beneficial effects for the circadian system and for metabolism.

In this symposium I will discuss the organization of the circadian system and the contribution of food elicited signals as internal synchronizing factors. Using our experimental models of circadian disruption, I will present experimental evidence of the relevance of the timing of food intake using regular and palatable food. I will further discuss the benefits and limitations of feeding schedules to ameliorate the metabolic burden in shift workers and other individuals affected by circadian disruption. The group is supported by grants PAPIIT IG-200417 and CONACyT 239403.

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**NOTES:**
Title: Circadian disruption by bisphenol A and saturated fat: A view from the NPY neuron

Biography: Denise is a Professor of Physiology, Medicine, and Ob/Gyn at the University of Toronto, Canada. She has over 25 years of neuroendocrine research in obesity, circadian rhythms, and reproduction. She developed an array of over 250 clonal neuronal cell models from the hypothalamus, now in over 600 labs worldwide. She was the Chairperson for the ICN2018 held July 2018 in Toronto, and currently is the President of the Pan American Neuroendocrine Society. Recently, she was awarded the “Sustained Excellence in Graduate Teaching and Excellence” for her contributions towards the careers of the over 125 trainees from her laboratory.

Abstract: Research indicates that common dietary components, such as high fat and high sugar diets, as well as chemicals in plastics, food contaminants, and other prevalent household items, may be major contributors to the rise in the rates of obesity around the world. Diets high in fat or sugar have been shown to alter circadian clock function. Bisphenol A (BPA), a ubiquitous, environmental endocrine disruptor, is considered an obesogen. Its role in the hypothalamic control of energy balance, however, remains largely unexplored. As disruption of the circadian clock is tightly associated with metabolic consequences, we explore how BPA and the saturated fatty acid palmitate affects the components of the molecular circadian clock in the feeding-related neurons of the hypothalamus. These changes can be related to the development of metabolic disorders, including obesity and Type 2 diabetes. This presentation discusses our recent findings concerning the influence of nutrients and endocrine disrupting chemicals, in particular the fatty acid palmitate and bisphenol A, on molecular circadian rhythms in neuropeptide Y-expressing hypothalamic cell models. We explore the molecular events that control the expression of NPY and whether the central clock components have a direct impact on gene expression in hypothalamic neurons. Understanding the impact of the circadian clock in neurons will allow for guidance toward the composition of meals optimal for physiological health, as well as putative therapeutic targets to regulate the molecular clock.

NOTES:
**Dr. Victor Navarro, Harvard Medical School, USA**

**Title:** Metabolic regulation of Kisspeptin and GnRH release

**Biography:** Dr. Navarro is an Assistant Professor of Medicine at Harvard Medical School and Brigham and Women’s Hospital. He received his PhD from the University of Córdoba, Spain, in 2006 under the mentorship of Dr. Manuel Tena-Sempere, followed by a postdoctoral period at the University of Washington, Seattle (WA) in Dr. Robert Steiner’s group (2007 – 2011). In 2012, Dr. Navarro joined the faculty of the Division of Endocrinology, Diabetes and Hypertension at Harvard Medical School and Brigham and Women’s Hospital, Boston (MA). Dr. Navarro is also a faculty of the Harvard-MIT Health Sciences and Technology and the Harvard Program in Neuroscience. The Navarro lab focuses on the characterization of the neuroendocrine mechanisms that control pulsatile and surge-like GnRH release, with special interest in the role of tachykinins and metabolic cues in the regulation of Kiss1 neurons, the main drivers of sexual maturation and fertility.

**Abstract:** Reproduction is a very energy costly function for the organism and, therefore, very tightly regulated by central and peripheral cues that ultimately determine the proper pattern of kisspeptin and GnRH release. Among these, metabolic cues play a critical role in the control of reproductive function, through the interplay of satiety and hunger signals. Further, the interaction between reproductive and metabolic functions is bidirectional, as kisspeptin has also emerged as a novel satiety factor. However, despite the critical role of these neuronal networks for the survival of the individual, the precise mechanisms underlying the control of reproduction and food intake remain incompletely understood. Recent studies from our lab have extended the characterization of this bidirectional regulatory process and identified, on one hand, a novel leptin-responsive population of PACAP neurons in the ventral premammillary nucleus that targets Kiss1 neurons to regulate reproduction—as part of the metabolic control of reproduction. On the other hand, we have documented an active role of Kiss1 neurons in the metabolic (anorexigenic) action of melanocortins through MC4R—as part of the reproductive control of metabolism. Overall, understanding the neuronal pathways and mechanisms underlying this bidirectional interaction of metabolism and reproduction is critical for the development of new approaches to treat metabolic and reproductive disorders with a central origin.

**NOTES:**
**Dr. Mauricio Dorfman**, University of Washington, USA

**Title:** Microglial inflammation in obesity pathogenesis: protective role of sex hormones

**Biography:** Dr. Dorfman obtained a B.S. degree in Biochemistry and a Ph.D. in Pharmacology from University of Chile in 2001 and 2008, respectively. His early work in Dr. Hernan Lara’s laboratory focused on investigating the role of ovarian sympathetic nerve activity in the pathogenesis of polycystic ovary syndrome. He further pursued the study of ovarian pathophysiology as a postdoctoral fellow in Dr. Sergio Ojeda’s laboratory at the Oregon National Primate Research Center/Oregon Health and Science University. Following his interest in the field of obesity and diabetes, Dr. Dorfman moved to Seattle in 2012 to complete his postdoctoral training under the mentorship of Drs. Michael W. Schwartz and Joshua P. Thaler at the University of Washington. He was appointed as a Research Assistant Professor in the Division of Metabolism, Endocrinology and Nutrition in 2016, where he is investigating the intersection of reproductive and metabolic science. Currently, Dr. Dorfman is focused on studying the role of hypothalamic cells (neurons, astrocytes and microglia) in the regulation of energy balance and glucose homeostasis. Dr. Dorfman has special interest in the identification of metabolically-relevant sexual dimorphisms in non-neuronal and neuronal cells to improve the management of gender-specific metabolic disease risk factors. Dr. Dorfman has obtained several awards including a Scientist Development Award by the American Heart Association (AHA), two Pilot and Feasibility Awards (UW), and an institutional Royalty Research Fund. Recently, he was honored with the Early Investigator Award by the Endocrine Society.

**Abstract:** Obesity is a significant health problem with few effective treatments available. One potential avenue stems from the finding that diet-induced obesity (DIO) is associated with activation of the primary brain immune cells (microglia) in the hypothalamus, a brain region that controls appetite and metabolism. Rodent studies have demonstrated that reducing hypothalamic inflammation and microglial activation limits weight gain and the metabolic complications of obesity. Moreover, sensitivity to hypothalamic microglial activation and DIO in male mice and resistance in female mice reflect differential regulation of the neuronally-expressed chemokine CX3CL1 and its inhibitory receptor CX3CR1 on the surface of microglia (endogenous pathway to maintain microglial quiescence). Unlike female mice, males showed reductions in both ligand and receptor expression after HFD exposure, suggesting that CX3CR1 signaling might be a potential therapeutic target for obesity in males. Indeed, restoring hypothalamic CX3CL1-CX3CR1 signaling in male mice promotes a “female-like” response to HFD feeding characterized by both reduced microglial activation and DIO susceptibility. Based in this sexual dimorphism and the fact that sex steroids (estrogens and androgens) are involved in whole-body energy homeostasis and central immunological modulation we are now testing the hypothesis that sex hormones reduce DIO susceptibility through central anti-inflammatory action. Our observations show that estrogens protect from diet-induced hypothalamic inflammation through estrogen receptor beta (ERb) and reduces susceptibility to DIO in male mice. Together, these studies implicate neuron-microglia crosstalk in modulation of energy homeostasis, elucidate a relationship between microglial ERs and CNS inflammatory signaling, and identify microglial CX3CR1 and ERb signaling as a potential obesity therapeutic target. This work was supported by the AHA (Scientist Development Grant), the NIH (DRC P&F) and UW Royalty Research Fund.
Dr. Quentin Pittman, University of Calgary, Canada

Title: Hot baby: how early life inflammation programs the brain

Biography: Quentin J. Pittman is Professor of Physiology and Pharmacology at the University of Calgary, the Hotchkiss Brain Institute and the Snyder Institute for Chronic Disease. He has published over 300 scientific articles and has been the recipient of many awards and recognitions, including Fellowship in the Royal Society of Canada and in the Canadian Academy of Health Sciences. Most recently, his research, using animal models, has focused in two areas: 1. upon the long term, sexually dimorphic influence of early life inflammation and events such as febrile seizures on the mature brain 2. The mechanisms underlying the behavioral co-morbidity that occurs with chronic inflammatory disease.

Abstract: A peripheral inflammation is accompanied by a parallel, mirror inflammation in the brain, wherein cytokines and other neuroactive molecules are generated to affect neurally-mediated behavior and physiology. To determine how such molecules may affect the brain at an early, developmentally plastic stage, we have explored the effects of a mild peripheral inflammation produced by low doses of lipopolysaccharide (LPS) in neonatal rodents (<2 weeks age) on juvenile and adult physiology. While the effects of the inflammation are transient, mimicking the well described sequelae in adults, there are long lasting change in behavior and neuronal properties seen only if the inflammation is given early in life. Of particular note is that the brain is more excitable in adults, revealed by increased susceptibility to convulsants and emergence of epilepsy in a susceptible mouse model. Electrophysiological recordings from hippocampal pyramidal neurons indicate that there are changes in many electrophysiological and synaptic properties; some are altered only in adult, post-pubertal males, but not in females or in juveniles of either sex; other changes in synaptic function are seen in both males and females. While there are also sexually dimorphic changes in brought about by early life LPS in conditioned fear extinction, adolescent social interactions and anxiety-like behaviors, the relationship of these to altered electrophysiological properties is still unknown. The changes brought about by mild early life inflammation are most likely a normal developmental process, as all human babies get sick (colds, ear infections, etc.) frequently throughout early life. However, these findings raise questions as to the appropriateness of the specified pathogen free rodent as a model of normal human physiology and patho-physiology.

NOTES:
**Abstract:** Stressful situations can predispose the organism to some disabling psychiatric conditions, including depression and anxiety. Stress, also, can aggravate neuron loss in such situations via adrenal glucocorticoid (GC) hormones and glucocorticoid receptor (GR) activation. It is becoming evident a role for neuroinflammation in those settings, since, for some injuries, the neuronal GC endangerment is accompanied by greater immune cell infiltration and glial cells activation. This is a conundrum since GCs are anti-inflammatory and protective agents due to their ability to blunt gene expression of pro-inflammatory mediators and other possible harmful molecules. However, several studies have revealed situations in which these hormones act as pro-inflammatory agents depending on the dose, chronicity of exposure, and the structure/organ studied. Here, we will provide an overview of the conditions under which these phenomena occur, a discussion that will explore the mechanistic foundation of glucocorticoids endangering effects in the brain and their role in neuroinflammation and behavior.

**NOTES:**
**Dr. Flavia Saravia**, University of Buenos Aires, Argentina

**Title:** Neuroinflammation and aging: Focus on experimental Alzheimer’s disease

**Biography:** Dr. Flavia Saravia received her Bachelor in Biological Sciences at the University of Buenos Aires (UBA) (1984-1990) and her Ph.D. in Sciences, Faculty of Pharmacy and Biochemistry University of Buenos Aires (1993). At present, Dr. Flavia Saravia is an independent Researcher National Research Council, Lab of Neurobiology of Aging, Institute of Biology and Experimental Medicine and Faculty of Exact and Natural Sciences, University of Buenos Aires, Argentina.

**Abstract:** The incidence of metabolic disorders including obesity, diabetes and metabolic syndrome have seriously increased in the last decades. These diseases - with growing impact in modern societies - constitute major risk factors for neurodegenerative disorders such as Alzheimer’s disease (AD), sharing insulin resistance, inflammation and associated cognitive impairment. The dentate gyrus of the hippocampus - a neurogenic area associated with memory and learning processes - is a recognized target for diabetic alterations and neurodegeneration. We explored the hippocampal neurogenesis and its microenvironment (microglia, astrocytes, vascularisation and glucocorticoid influence) in different dysmetabolic scenarios provided by spontaneous or induced experimental models. We found astrogliosis, reactive microglia, and reduced vascular arborization in association with cognitive impairment and lower or disturbed neurogenic ability, even in young animals. These phenomena were accompanied by a insulin-resistant state in the hippocampus, an impaired response to insulin. In the context of Alzheimer’s disease (AD), hippocampal alterations have been well described in advanced stages of the pathology, when amyloid deposition, inflammation and glial activation occur, but less attention has been directed to studying early stages. The neurogenic capability, measured as DCX+ cells, was strongly diminished and associated to alterations in cell maturity in a transgenic mouse model of AD, at early stages, when no amyloid deposits are present. Microglia already exhibited mostly intermediate and ameboid morphology-suggestive of activated state-and less corresponding to the ramified phenotype. Microglia, is able to sense pathogens and but also react against metabolic insults through phagocytosis and the release of cytokines. A chronic microglia stimulation may contribute to a persistent inflammation that can precede the neurodegenerative process.

**NOTES:**
**Trainee Oral Abstracts**

**David Lopez Rodriguez.** *EDC mixture disrupts maternal behavior and the hypothalamic control of puberty through epigenetic mechanisms*

**Abstract.** Endocrine disrupting chemicals (EDCs) are a rising concern for public health due to their ubiquitous presence as complex mixtures affecting development throughout generations. Our goal was to study the effect of a mixture of EDCs on female sexual development during 3 generations. Female rats (F0 generation) were orally exposed to a mixture of 14 anti-androgenic and estrogenic EDCs or corn oil for 2 weeks before and throughout gestation and until weaning. The mixture was composed of plasticizers (BPA, DBP, DEHP), fungicides/pesticides (Vinclozolin, Procymidon, Prochloraz, Epoxynazole, Linurone, p-p’-DDT), UV filters (4-MBC, OMC), Butyl Paraben and the analgesic Acetaminophen. The doses were in the micrograms/kg range in order to represent human exposure. Sexual development (vaginal opening, GnRH interpulse interval and estrous cyclicity) as well as maternal behavior were studied from F1 to F3 generations. At PND21 the mediobasal hypothalamus of the F1 and F3 were removed for gene expression analysis by RNAseq and RT-qPCR as well as for Chromatin Immunoprecipitation of histone modifications at regulatory regions of target genes. While F2 and F3 females showed delayed vaginal opening, decreased percentage of regular estrous cycles and decreased GnRH interpulse interval, no such changes were detected in F1 animals. These reproductive phenotypes were associated with alterations in both transcriptional and histone posttranslational modifications of hypothalamic genes involved in reproductive competence and behavior like kisspeptin (Kiss1), oxytocin (Oxt), estrogen (Esr1), glutamate (Grin2d), dopamine signaling (Th and Drd1) as well as glucocorticoid activity (Nr3c1 and Crh). Concomitant with a decrease in transcriptional activity, we have observed either a decrease of active histone marks (H3K4me3, H3K9ac) for Esr1 and Oxt promoter regions, an increase of repressive histone modifications (H3K27me3, H3K9me3) for Grin2D, Th and Nr3c1 promoter regions or both for the Kiss1 promoter. Up-regulated genes (Pomc, and CRH) showed decreased H3K9me3 and increased H3K9ac at their 5’ regulatory regions. F1 females that were exposed in utero to the EDC mixture, showed a reduction in Th mRNA expression and decreased grooming/licking behavior while spending more time resting alone. These alterations on maternal behavior are known to cause transgenerational alterations of the development of the corticotrophic and gonadotrophic axis. Overall, our data shows that gestational and lactational exposure to an environmentally relevant EDC mixture transgenerationally affects sexual development throughout epigenetic reprogramming of the hypothalamus. Such effects could be mediated by alterations of maternal behavior caused by exposure of the first generation to the EDC mixture.

**NOTES:**
**Emma McIllwraith.** *Specific microRNAs are regulated in hypothalamic neurons after exposure to the saturated fatty acid palmitate or endocrine-disrupting chemical bisphenol A*

**Abstract.** Phoenixin (PNX) is a recently identified peptide that forms part of the hypothalamic-pituitary-gonadal axis. It is a highly conserved, 14 or 20 amino acid peptide expressed at high levels in the hypothalamus. Within hypothalamic neurons, PNX increases gene expression of gonadotropin-releasing hormone (GnRH) and kisspeptin, two critical reproductive peptides. In relation to reproductive function, knockdown of either PNX or its receptor, GPR173, extends the estrous cycle. As PNX and GPR173 are relatively understudied, delineating how this peptide and its putative receptor are regulated at the gene level is essential for further definition of functional significance. We have previously reported that palmitate, a saturated fatty acid, increases \(<i>Pnx</i>\) and reduces \(<i>Gpr173</i>\) mRNA levels over 24 hours in immortalized hypothalamic clonal cell lines. We have also found that bisphenol A (BPA), an endocrine disrupting chemical widely thought to inhibit reproductive function, reduces Pnx and Gpr173 gene expression. The mechanism by which these compounds alter gene expression is the subject of current investigation. One layer of gene regulation is microRNAs (miRNAs), short segments of RNA that decrease mRNA expression levels. Palmitate and BPA are known to alter microRNA (miRNA) levels in tissues outside of the hypothalamus; therefore, we hypothesized that levels of miRNAs that target Pn and pr173 in the hypothalamus may be contributing to the observed palmitate- and BPA-mediated changes in mRNA levels. Using the predictive online resources, miRwalk 3.0, TargetScan and miRanda, we have identified 112 miRNAs with putative binding sites in the Pnx 3’UTR, as well as 300 miRNAs that can bind the Gpr173 3’UTR. To identify miRNAs affected by palmitate or BPA exposure, the mHypoE-46 and the mHypoA-59 cell lines were treated with 50 μM palmitate or 100 μM BPA, respectively, for 4 and 24 hours. The miRNA profiles after these treatments are being assessed on the Affymetrix GeneChip miRNA 4.0 array, which includes over 30,000 probe sets for mature miRNAs. Whether the miRNAs mediate the alterations in Pnx and Gpr173 gene expression will be assessed through the use of antagonirs and mimics. Knowledge of miRNAs controlling Pnx and Gpr173 expression contributes to our understanding of how nutrients and environmental chemicals affect the hypothalamus, potentially representing new targets for therapeutics.

NOTES:
Rajae Talbi. *Melanocortins act on Kiss1 neurons to regulate reproduction in females*

**Abstract.** Reproduction, controlled by the excitatory action of the neuropeptide kisspeptin, is an energy costly function for the organism and, therefore, it is tightly regulated by metabolic factors. Among those, hypothalamic melanocortins are essential in the control of metabolism. Inactivating mutations in the proopiomelanocortin (Pomc) gene or melanocortin receptor 4 (Mc4r) cause severe obesity and subfertility in humans and mice. However, whether the reproductive impairment is a direct consequence of the lack of melanocortin signaling, or indirect resulting from the obesity phenotype, remains unknown. α-MSH (derived from Pomc) stimulates LH release and this action has been shown to be mediated by Kiss1 neurons. We evaluated the expression of Mc4r in Kiss1 neurons, and using dual fluorescence in situ hybridization (RNAscope), we showed that Kiss1 neurons of the arcuate nucleus (Kiss1-ARC) and the anteroventral periventricular/periventricular nucleus (Kiss1-AVPV/PeN) express Mc4r. Mc4r colocalized with 84% of Kiss1-ARC and with 74% of Kiss1-AVPV/PeN, suggesting that Kiss1 neurons are a direct target of melanocortins. In order to evaluate the involvement of Kiss1 neurons in the reproductive role of melanocortins, we ablated Mc4r specifically from Kiss1 neurons by generating a specific Kiss1-Mc4rKO (Kiss1-cre/Mc4r-lox+/+) mouse line. We found that Kiss1-Mc4rKO females exhibit disrupted estrous cycles with prolonged diestrous phases and delayed puberty onset compared to their control littermates, without developing obesity during the time of the study. The reproductive phenotype of Kiss1-Mc4rKO males was not affected. When central injections of an Mc4r selective agonist were performed on Kiss1-Mc4rKO intact males and their control littermates, LH levels were significantly increased to the same extend in both groups at 15 min post-injections, suggesting that, in the male, α-MSH controls LH levels through a Kiss1 neuron independent mechanism. Taken together, these results support a direct role of melanocortins on Kiss1 neurons in the control of GnRH release in female mice. Overall, understanding the neuroendocrine mechanisms underlying the metabolic regulation of reproduction will help improve the fertility rates in patients affected by metabolic disturbances.

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**NOTES:**
James Garcia. Prepubertal tonic gamma-aminobutyric acid (GABA) inhibition is upstream of the neurokinin b (NKB), kisspeptin and gonadotropin releasing hormone (GnRH) neuronal network in male rhesus monkeys

Abstract. The concept that GnRH release during the prepubertal period is under tonic central inhibition is well established in primates. Although it has been reported that the makorin RING finger protein 3 (MKRN3) gene plays a role in this process (1), neuronal substrates responsible for prepubertal tonic inhibition remain unclear. A series of studies in this lab have shown that GABA neurons are consistently inhibitory to GnRH and kisspeptin neurons in female prepubertal rhesus monkeys (2, 3, 4). Because we recently found that release of GnRH, kisspeptin and NKB in prepubertal male monkeys is significantly lower than those in pubertal monkeys and the pubertal increase in release of these neuropeptides is gonadal steroid independent, in the present study, we ask the question of whether GABA neurons play a role in central inhibition of GnRH release before puberty onset in male monkeys. As described previously, a microdialysis probe was inserted into the median eminence of the hypothalamus in 4 gonadally intact prepubertal male monkeys (15.1 ± 1.9 months of age) and the effects of GABA-A receptor antagonist, bicuculline, on release of GnRH, kisspeptin and NKB were examined. The results indicate that bicuculline at 1 µM, but not vehicle, dramatically stimulated release of GnRH, kisspeptin, and NKB in prepubertal male monkeys. Subsequently, we examined whether the bicuculline-induced release of GnRH and kisspeptin was affected by the presence of NKB antagonist, SB222200, as previously we found that NKB signaling is upstream of kisspeptin and GnRH neurons in male monkeys (5). We found that inhibition of NKB signaling attenuated the bicuculline-induced release of GnRH and kisspeptin, suggesting that NKB neurons, in part, relay inhibitory GABA signals to GnRH and kisspeptin neurons. These results are interpreted to mean that in male monkeys, inhibitory GABA signaling plays a role in central inhibition during the prepubertal period and that inhibitory GABA signaling is upstream of the NKB, kisspeptin, and GnRH neuronal pathway. How “Central GABA Inhibition” is regulated by genes involved in this process, such as <i>MKRN3</i>, remains to be investigated. Reference: (1) Abreu et al., N Engl J Med. 2013;368:2467-2475. (2) Mitsushima et al., Proc Natl Acad Sci USA. 1994;91:395-399. (3) Keen et al., Endocrinology. 1999;140:5257-5266. (4) Kurian et al., Endocrinology. 2012;153:3331-3336. (5) Garcia et al., Endocrinology. 2018;159:3048-3060. Sources of Research Support: NIH R01 and T32 Grants

NOTES:
Karen Tonsfeldt. The contribution of Bmal1 expression in the suprachiasmatic nucleus on female fertility

Abstract. The preovulatory gonadotropin-releasing hormone (GnRH) and resulting luteinizing hormone (LH) surge is gated to the onset of the active period in mice by a circadian and steroid signal. The temporal signal that initiates this process is believed to arrive from the suprachiasmatic nucleus (SCN), the hypothalamic circadian pacemaker. The SCN may contribute to reproduction through two discrete projections: vasoactive inhibitory peptide (VIP) neurons in the SCN project to gonadotropin-releasing hormone (GnRH) neurons in the preoptic area, and arginine vasopressin (AVP) neurons in the SCN project to kisspeptin (Kiss1) neurons in the anteroventral periventricular (AVPV). Genomic deletion of the critical circadian clock component, Bmal1, results in infertility in females. We sought to determine whether Bmal1 was critical in the SCN VIP and AVP neurons by using cre/lox technology to create three lines of mutant mice: AVP-Bmal1-/-, VIP-Bmal1-/-, and AVP-VIP-Bmal1-/-.. We found no significant difference in LH levels following a kisspeptin challenge (2 mg/kg) between AVP-Bmal1-/- and Bmal1flox/flox (617.4 ± 216.9 vs 629.6 ± 110.6 pg/mL) or GnRH challenge (10 μg/kg) (1029.0 ± 246.2 vs 712.7 ± 142.6 pg/mL). Preliminary findings of an induced LH surge found AVP-Bmal1-/- and VIP-Bmal1-/- mice are able to mount a surge at the time of lights off (Bmal1flox/flox: 3 of 5; AVP-Bmal1-/-: 1 of 2, VIP-Bmal1-/-: 4 of 4; AVP-VIP-Bmal1-/-: 0 of 2). Additionally, we were able to detect an endogenous surge at the time of lights off in both AVP-Bmal1-/-, VIP-Bmal1-/- mice, but not AVP-VIP-Bmal1-/-.. However, AVP-Bmal1-/-, VIP-Bmal1-/- and AVP-VIP-Bmal1-/- females carried litters to term and show no differences in the time to first litter compared to Bmal1flox/flox control (AVP-Bmal1-/-: 48 ± 4.8 vs 44.3 ± 0.3 days; VIP-Bmal1-/-: 29.6 ± 7.7 vs 31.0 ± 4.2 days; AVP-VIP-Bmal1-/-: 27.7 ± 7 vs 23 ± 0 days); number of litters in 100 days (AVP-Bmal1-/-: 3.7 ± 0.6 vs 4 ± 0.6; VIP-Bmal1-/-: 3.0 ± 1.0 vs 3.0 ± 0.0; AVP-VIP-Bmal1-/-: 3.5 ± 0.7 vs 3.5 ± 0.7 days); or pups per litter (AVP-Bmal1-/-: 7.2 ± 0.7 vs 7.3 ± 0.7; VIP-Bmal1-/-: 6.2 ± 1.6 vs 7.6 ± 2.9; AVP-VIP-Bmal1-/-: 8.1 ± 0.9 vs 9 ± 1.4 pups). Overall, these findings suggest that Bmal1 expression in the SCN AVP or VIP neurons is not required for fertility in a 12:12 light:dark cycle.

NOTES:
Andressa Reginato. *Differential effects of saturated and unsaturated fatty acids on neuronal autophagy*

**Abstracts:** Autophagy is a well-known process that regulates cellular homeostasis by degrading malformed organelles and dysfunctional proteins. Normal autophagy is crucial to maintain the functionality of hypothalamic neurons, which are important in regulating energy balance. Fatty acids can be sensed by hypothalamic neurons and affect cell viability, inflammation and metabolic pathways. We recently found that the most prevalent dietary saturated fatty acid palmitate (PA) was able to induce hypothalamic autophagy by as yet undefined mechanisms. We are currently investigating if an unsaturated fatty acid palmitoleate (PO) has any effect on autophagy modulation. Given that unsaturated fatty acids protect other cells from palmitate-mediated dysfunction, we hypothesized that palmitoleate could protect neurons from palmitate-induced autophagy. We used the clonal, embryonic male, mHypoE-46, and adult-derived male, mHypoA-2/29, neuronal cell lines to evaluate autophagy modulation in response to palmitoleate (PO) treatment. Neurons were first treated with 25, 50 or 250 µM of PO alone. In the mHypoE-46 cells, the highest 250 µM concentration of PO was extremely toxic to the cells, as determined by cell death. In order to measure autophagy vacuoles (autophagosomes and autolysosomes) flow cytometry technique was performed. Partial data suggested that 25 and 50 µM PO was able to reduce overall autophagy. When we performed a co-treatment using PA (25 µM) and PO (25 µM), we observed that PA-mediated autophagy induction was blocked. In the mHypoA-2/29 cells, all concentrations of PO alone, including 250 µM, were able to reduce autophagy modulation, as detected by flow cytometry. We also tested the effect of a mixture of multiple saturated and unsaturated fatty acids (palmitate, stearic, oleic, linoleic and arachidonic) in the mHypoE-46 cells and found that this mixture did not affect autophagy. Thus, the saturated fatty acid PA increases autophagy, and we present evidence that an unsaturated fatty acid PO may rescue this induction, contributing to an overall protective response in neurons. We are now investigating the molecular mechanisms by which specific fatty acids control neuronal autophagy and predict that these will be unique to saturated versus unsaturated fatty acids. Understanding how fatty acids affect autophagy in neurons that control food intake could potentially represent a promising therapeutic target against obesity.

**NOTES:**
Jessica Rosin. Microglia interact with hypothalamic progenitors during development and are required for proper energy balance

Abstract. Microglia are the resident mononuclear phagocytic immune cells of the central nervous system (CNS), and are primarily responsible for responding to neural insults and disposing of cellular debris. However, over the last decade studies are showing that microglia are highly dynamic cells involved in various critical neurodevelopmental processes. We set out to study microglia dynamics in the embryonic hypothalamus given that the hypothalamus is responsive to external stressors and critical for maintaining homeostatic processes such as energy balance, thirst, food intake, reproduction, and circadian rhythms. Using slice culture and time-lapse imaging we showed that hypothalamic microglia are highly dynamic during embryogenesis, constantly surveying their environment and often interacting with radial glia precursor cells that line the third ventricle and are responsible for generating hypothalamic neurons, oligodendrocytes, astrocytes, and tanycytes. Moreover, given that microglia colonize the embryonic brain alongside key steps of hypothalamic development, we wanted to test whether microglia are required for the proper establishment of this brain region. To eliminate microglia from the fetal brain, we treated pregnant dams with the Colony-stimulating factor-1 (Csf1r) inhibitor PLX5622, as Csf1r is expressed by microglia and is required for their proliferation, differentiation, and survival. Embryonic microglia depletion resulted in a decreased litter size, as well as an increase in the number of pups that died within the first two postnatal days of life. In pups that survived, the elimination of microglia in the fetal brain resulted in a decrease in the number of Pro-opiomelanocortin (POMC) neurons and a concomitant accelerated weight gain, suggesting that microglia could be important for the development of hypothalamic satiety centers. Depletion of microglia during embryogenesis also had long-term sex-specific effects on behaviour. Furthermore, hypothalamic microglia appear to be sensitive to the endocrine disruptor Bisphenol A during embryogenesis. Taken together, these data demonstrate an important role for microglia during the development of the embryonic hypothalamus.

NOTES:
**Katherine Makowski. Estradiol enhances the inhibitory effect of the cytokine interleukin 1B on pulsatile LH secretion in female mice**

**Abstracts.** Inflammatory and infectious processes can disrupt reproduction function and fertility in a wide range of species including humans, domesticated species and laboratory animals. Immune cells produce cytokines in response to systemic stressors such as lipopolysaccharide and these cytokines have the potential to disrupt the central mechanisms controlling gonadotropin secretion and ovulatory cyclicity in females. When administered peripherally, interleukin (IL)1B, a member of the interleukin-1 family of cytokines, has been shown to inhibit the proestrus luteinizing hormone (LH) surge in intact female rats. However, in male gonadectomized rats, IL1B delivered via intraperitoneal (i.p.) injection does not alter LH secretion, so the effect of IL1B may depend on the presence of gonadal steroids. Here, we began by investigating whether peripheral IL1B can inhibit mean LH secretion in female mice and if estradiol is necessary for this inhibition. Female C57bl6 mice (10 wk) were ovariectomized and implanted with a silastic capsule containing oil or 100ng estradiol, which approximates a diestrus level. LH was measured prior to and 60, 120 and 180 min following i.p. administration of 2ng/g IL1B or saline (control) from tail-tip blood samples. In oil treated females, mean LH did not significantly change following saline, compared to pretreatment levels. Treatment with IL1B elicited a 39% reduction in LH at 120 min; LH was not significantly different 60 or 180 min following IL1B. In animals treated with estradiol, IL1B elicited a more rapid and robust reduction in LH at all three time points. LH was reduced by 50%, 71% and 68%, at 60, 120 and 180 min, respectively. These data indicate that estradiol enhances the LH response to peripheral IL1B. Based on these findings, we have conducted two experiments. First, we performed a study (N=13) to measure pulsatile LH prior to and following i.p. administration of 2ng/g IL1B or saline (control) in ovariectomized C57bl6 mice pretreated with estradiol. Second, we are investigating the neural pathways whereby IL1B may access the kisspeptin and GnRH circuit to influence LH pulsatility using c-Fos as a marker. These data suggest that estradiol affects neural pathways by which stress hormones influence reproduction and may indicate why women are differentially responsive to inflammatory signals depending on their ovarian cycle stage.

**NOTES:**
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**Why ANY-maze Behavioral Tracking Software?**

ANY-maze is today’s most advanced video tracking system. Trusted by thousands of researchers around the world, ANY-maze couples an unrivalled depth of features with a simple, familiar design, to provide automated testing in virtually any behavioral test.

Easy to use - As a scientist you want to run tests, not spend time learning software and with ANY-maze you’ll be up and running in no time.

Fully featured - Despite its ease of use, ANY-maze is no lightweight with features like moveable zones, three-point tracking, and freezing detection.

Unlimited Support and Upgrades - Unlimited technical support is available to all users of ANY-maze, forever - we'll even support you if you've just downloaded the system to try it out.

Value for money - Unlike other video tracking systems, ANY-maze has no modules or add-ons - for just US$ 7,995.00 (10% discount if you mention this ad) for the software, computer, camera, and accessories.

At Stoelting, we have a strong commitment to support scientific research. We seek to offer only high quality, reliable instruments, including prompt, educated customer service from our staff of science professionals.

**Please stop by the table to speak to the Stoelting representative, Richard Mills.**