

### SCIENTIFIC PROGRAM

Thursday, March 30th, 2017: "BRAIN..."

7:30 - 9:00 am: Buffet breakfast (Grand Ballroom DE)

8:30 – 9:00 am: Welcome and overview (Grand Ballroom DE)

9:00 – 11:00 am: **Poster session** (odd numbered posters) with coffee service at 10 am (Salons 5/6, 7/8, 9/10)

11:30 – 1 pm: Lunch Table Discussions: Tables with assigned topics and discussion leaders (L1-L13) (Grand Ballroom DE)

1:00 – 6:00 pm: Facilitated group discussion sessions (all in Grand Ballroom DE)

**S-1:** 1:00-1:45 pm: <u>How do kisspeptin neurons participate in the gating of puberty?</u> Are sex differences in the tempo of puberty, and pubertal disorders, due to kisspeptin sex differences? What is the relative importance—if any—of each specific kisspeptin population (ARC, AVPV, amygdala) in regulating puberty? What turns on kisspeptin at puberty (epigenetic factors, upstream afferent neural signals, hormonal factors, etc.)? Can puberty or reproduction happen (under the right circumstances/models) without kisspeptin?

Facilitator: Suzanne Moenter (Univ. Michigan, USA)

<u>Lead Speakers</u>: Alexander Kauffman (UCSD, USA), Ei Terasawa (Univ. Wisconsin, USA), Victor Navarro (Harvard Medical School, USA), Yoshihisa Uenoyama (Nagoya University, Japan)

Additional presenter: Ming Chan (Harvard Medical School, USA)

1:45-2:00 pm: **BREAK** 

**S-2:** 2:00-2:45 pm: <u>What is the mechanistic basis of pulse generation?</u> What are the molecular/cellular mechanisms in kisspeptin and other neurons responsible for GnRH pulse generation? Are KNDy cells really the pulse generator? If KNDy neurons don't have Kiss1r, how can kisspeptin reset the GnRH pulse generator in some human cases?

Facilitator: Robert Goodman (West Virginia Univ., USA)

<u>Lead Speakers</u>: Jenny Clarkson (Univ. Otago, New Zealand), Michael Lehman (Univ. Mississippi Med. Ctr., USA), Pasha Grachev (Oregon Health Sciences Univ., USA), Jian Qiu (Oregon Health Sciences U., USA)

Additional presenter: Katalin Skrapits (Hungarian Academy of Sciences, Hungary)

2:45-3:00 pm: BREAK with coffee service

**S-3:** 3:00 -3:45 pm: <u>Negative feedback and hormone regulation of ARC kisspeptin cells</u>. Do ARC kisspeptin cells (KNDy neurons) mediate E2, P4, or androgen negative feedback? If not, what other cells mediate negative feedback and how does the KNDy population fit into that model? How do sex steroids regulate KNDY neurons?

<u>Facilitator</u>: Michael Lehman (Univ. Mississippi Med. Ctr., USA) <u>Lead Speakers</u>: Jon Levine (Univ. Wisconsin, USA), Kei-ichiro Maeda (Univ. Tokyo, Japan), Robert Goodman (West Virginia Univ., USA), Suzanne Moenter (Univ. Michigan, USA)

# 3:45-4:00 pm: BREAK

**S-4:** 4:00-4:45 pm: <u>Positive feedback and hormone control of preoptic kisspeptin neurons</u>. How do steroid hormones and other factors (circadian, etc) activate preoptic/AVPV kisspeptin neurons during the LH surge? Do AVPV kisspeptin cells participate in other functions? Do KNDy neurons project to and regulate AVPV kisspeptin neurons for positive feedback modulation?

Facilitator: Alexander Kauffman (UCSD, USA)

<u>Lead Speakers</u>: Richard Piet (Univ. Otago, New Zealand), Oline Rønnekleiv (Oregon Health and Science Univ., USA), David Grattan (Univ. Otago, New Zealand); Paul Micevych (UCLA, USA)

4:45-5:00 pm: BREAK with coffee service

**S-5:** 5:00-5:45 pm: <u>How do kisspeptin neurons participate in regulation of body temperature,</u> <u>stress and other non-reproductive functions?</u> Role in thermoregulation and hot flashes? Role in prolactin secretion and ARC TH/dopamine neurons? Role in oxytocin/PVN/SON biology? Which kisspeptin populations are involved in mediating the effects of stress on reproduction? Where do hypothalamic kisspeptin neurons project to besides GnRH neurons, and what is the function of those non-GnRH projections?

Facilitator: Martin Kelly (Oregon Health Sciences Univ., USA)

<u>Lead Speakers</u>: Naomi Rance (Univ. Arizona, USA), Stephanie Padilla (Univ. Washington, USA), Raphael Szawka (Univ. Sao Paolo, Brazil), Colin Brown (Univ. Otago, New Zealand), Yoshitaka Oka (University of Tokyo, Japan)

<u>Additional presenters</u>: Joanna Sliwowska (Poznan University, Poland), Kellie Breen Church (UCSD, USA)

7pm-9:00 pm Social mixer reception and buffet dinner (Harry's bar at Rosen Centre)

### Friday, March 31<sup>st</sup>, 2017: "...AND BEYOND"

8:00 – 9:00 am: Continental Breakfast (Grand Ballroom DE and Salons 5/6, 7/8, 9/10)

# 8:00 – 9:00 am: Career Development Workshop for trainees (Grand Ballroom DE) <u>Moderator</u>: Lique Coolen (Univ. Mississippi Med. Ctr., USA) <u>Speakers</u>: Andy Spencer (Millendo, USA), Mike Trower (NeRRe Therapeutics Ltd, UK), Janet Hall (NIH/NIEHS), Genevieve Neal-Perry (University of Washington), Maricedes Acosta-Martinez (Stony Brook University, USA), Casey Nestor (North Carolina State, USA)

9:00 – 11:00 am: **Poster session** (even numbered posters) with coffee service at 10 am (Salons 5/6, 7/8, 9/10)

11:30 – 1 pm: Lunch Table Discussions: Tables with assigned topics (L13-L25) (Grand Ballroom DE)

1:00 – 6:00 pm: Facilitated large group discussion sessions (all in Grand Ballroom DE)

**S-6:** 1:00-1:45 pm: What are the reproductive functions of kisspeptin/GPR54 systems in the periphery? Endometrial function, placentation, and pregnancy? Local actions to control ovarian and testicular function?

Facilitator: Sally Radovick (Rutgers Medical School, USA)

<u>Lead Speakers</u>: Manuel Tena-Sempere (Univ. Cordoba, Spain), Andy Babwah (Western University, Canada), Nicolas De Roux (INSERM, Paris, France), William Colledge (Cambridge Univ., UK)

1:45-2:00 pm: BREAK

S-7: 2:00-2:45 pm: Metabolic functions of kisspeptin in the periphery? In the liver? Pancreas effect on insulin? Role in adipose tissue and related metabolic cell types?
 <u>Facilitator</u>: Manuel Tena-Sempere (Univ. Cordoba, Spain)
 <u>Lead Speakers</u>: Andrew Wolfe (Johns Hopkins Univ., USA), Joseph Kurian (Southern Illinois Univ., USA), Jeremy Smith (Univ. West. Australia, Australia)

2:45-3:00 pm: **BREAK** with coffee service

**S-8:** 3:00 -3:45 pm: What are the challenges and likely outcomes of drug development in the field? Clinical applicability of kisspeptin biology to fertility clinic - why has take-up been so poor? What about NKB? What are the future non-reproductive uses of drugs which mimic or block kisspeptin and related peptides? How does an understanding of the phenotypic spectrum of human disease contribute to our understanding (or not) of kisspeptin biology? What are the biggest impediments in the clinical domain to progress?

Facilitator: Stephanie Seminara (Harvard Medical School, USA)

<u>Lead Speakers</u>: Waljit Dhillo (Imperial College, London, UK), Robert Millar (Univ. Pretoria, South Africa), Genevieve Neal-Perry (Univ. Washington, USA), Toshiya Matsuzaki (Tokushima Univ, Japan), Pharis Mohideen (Millendo Therapeutics) <u>Additional presenter</u>: Graeme Fraser (Ogeda SA)

#### 3:45-4:00 pm: **BREAK**

**S-9:** 4:00-4:45 pm: What are the biggest technical and conceptual impediments or concerns to progress in the field? What have you struggled with? Lack and/or limitations of current tools? Lack of appropriate, well-validated cellular and animal models? Variability in experimental protocols used in different labs? Lack of robust and reliable critical reagents? Relating reductionist measurements to whole animal physiology?

<u>Facilitators/speakers</u>: Allan Herbison (Univ. Otago, New Zealand); Andy Babwah (Western University, Canada); Stephanie Padilla (Univ. Washington, USA); Andrew Wolfe (Johns Hopkins Univ., USA)

4:45-5:00 pm: BREAK with coffee service

**S-10:** 5:00-5:45 pm: **Recap of highlights/consensus items/closing remarks**. Open questions, remaining controversies, challenges? Opportunities? Frontiers? Resources? Where to from here?

6:30 pm: Buses depart for Disney Epcot

7pm-9:30 pm Social event/dinner at Disney Epcot

# Lunch Table Discussion topics (Day 1 and Day 2)

- 1. <u>Development/Sex Differences of Kiss1 neurons</u>
  - What are the origins and lineages of the different neuronal kisspeptin populations? How does the kisspeptin network form? How do kisspeptin neuron fibers target/find GnRH cells? What mechanisms (hormonal, epigenetic) lead to the sexual differentiation of kisspeptin neurons what are the functional consequences? Is the ARC kisspeptin system actually sexually dimorphic in rodents? Is there a functional role for kisspeptin before birth? <u>Discussion leaders</u> Manuel Tena-Sempere (Univ. Cordoba, Spain), Alexander Kauffman (UCSD, USA), Hiroko Tsukamura (Nagoya Univ., Japan), Stephanie Seminara (Harvard Medical School, USA)
- <u>Plasticity of Kisspeptin neurons</u>. Is there synaptic plasticity of Kiss1 neurons under different physiological conditions? Is there selective silencing of kisspeptin populations during development and/or disease, and is it reversible?
  <u>Discussion leaders</u>: William Colledge (Cambridge Univ., UK), Martin Kelly (Oregon Health Sciences Univ., USA), Michael Lehman (Univ. Mississippi Med. Ctr., USA)
- 3. <u>What are the roles of Kisspeptin co-transmitters in each population</u>? DYN and NKB in the ARC? Mechanistic roles? Glutamate or GABA in ARC cells? Dopamine (TH) in AVPV cells? Other co-expressed neuropeptides/neurotransmitters? Functional importance and role of each?

<u>Discussion leaders</u>: Allan Herbison (Univ. Otago, New Zealand), Victor Navarro (Harvard Medical School, USA), Bob Goodman (West Virginia Univ., USA), Martin Kelly (Oregon Health Sciences Univ., USA),

- What are the neurons and circuitry upstream of kisspeptin neurons responsible for their regulation and downstream responsible for their actions? Where do kisspeptin neurons project to, other than GnRH neurons, and what is the function of those non-GnRH projections?
  <u>Discussion leaders</u>: Aleisha Moore (Univ. Mississippi Med. Ctr., USA), Shel-Hwa Yeo (Cambridge Univ., UK), Jon Levine (Univ. Wisconsin, USA), Lique Coolen (Univ. Mississippi Med. Ctr., USA)
- 5. What are the roles of amygdala and BNST kisspeptin neurons fertility or other functions? Where do they project? How are they regulated? Functional roles? Does kisspeptin act in the amygdala as well as being made and signaling elsewhere from there? <u>Discussion leaders</u>: Shannon Stephens (Univ. Calif. San Diego, USA), Kevin O'Byrne (King's College, London, UK), Alex Comninos (Imperial College, London, UK)
- 6. <u>What are the common threads among mammals in the functional organization of the</u> <u>kisspeptin system?</u> What are the evolutionary aspects of kisspeptin function in the brain and placenta? Are kisspeptin/GPR54 systems involved in the neuroendocrine control of

reproduction in non-mammals, and if not, how are GnRH neurons in those species regulated? <u>Discussion leader</u>: Yoshitaka Oka (University of Tokyo, Japan)

- What role does kisspeptin play as a mediator or downstream target in the prenatal origin of adult diseases? Are reproductive and metabolic effects of prenatal exposure to androgens and environmental toxicants mediated by kisspeptin and related peptides? <u>Discussion leaders</u>: Rebecca Campbell (Univ. Otago, New Zealand), Heather Patisaul (North Carolina State University, USA), Andy Babwah (Western University, Canada)
- Aging and kisspeptin. What are the effects of age on the kisspeptin system? How do agerelated changes in kisspeptin affect reproductive and other functions? <u>Co- Discussion leader</u>: Kinuyo Iwata (Nagoya University, Japan), Margaret Lippincott (Harvard Medical School, USA)