**WORKSHOP**

**“The neurohumoral control of body fluid and cardiovascular homeostasis in males and females - vive la difference!**

**Córdoba, Argentina, 2-4 December 2019**

**Local Organizer:** Dr. Laura Vivas, Dr. Ximena Caeiro and Dr. Andrea Godino (Instituto de Investigación Médica Mercedes y Martin Ferreyra, Fac. cs Ex. Fis. y Nat. UNC, Córdoba, Argentina.)

**Foreign Organizer**: Dr. Professor David Murphy (University of Bristol, Faculty of Medicine, Bristol, United Kingdom.

**Location:** Auditory of the Instituto de Investigación Médica M. y M. Ferreyra, Friuli 2434 (o Friuli esquina Finochietto), Barrio Parque Vélez Sarsfield. 5016 - Córdoba, Córdoba, Argentina

Link event (<https://andigodino.wixsite.com/workshopcba2019> )

**Support:** BBSRC, Mincyt-Cba, SECyT, INIMEC-CONICET-UNC.

**Description of Event:**

The Workshop, which will take place over 3 days in early December in Cordoba, Argentina, will be organised by The Instituto de Investigación Médica Mercedes y Martin Ferreyra, a non-profit organization dedicated to scientific research and the development of scientific and technical human resources in medical science <http://www.institutoferreyra.org/>

Prof David Murphy (UK main Lead) and Prof Laura Vivas (local main Lead), proposed a Workshop that will cement the formation of a collaborative network that will apply state-of-the art molecular genetic and genomic technologies to study sex differences in cardiovascular diseases.

The Workshop will include a combination of lectures given by experts, followed by posters sessions, and round tables, giving the opportunity to the participants to design a new approach addressing their individual/collaborative research projects. The estimated number of attendees is approximately 80 among researchers, posdoctoral students and young researchers. The goal of these discussions is not only to provide understanding of how to design and use modern molecular tools, but also provide novel insight into integrative physiology of the cardiovascular sexual differences during health and disease. Our collaborative network will advance understanding of the mechanisms underlying normal physiology and their homeostatic control or the genesis of pathophysiology with a view to improving human health and wellbeing across the life-course.

Men and women are different, not only in rates of cardiovascular disease, but also in terms of symptoms and risk factors, but studies on females have lagged behind those on males. We will address the sources of physiological disparity between sexes, in particular the contribution of the genetic and sex chromosome factors, with a view to designing sex-tailored therapeutic strategies.

Cardiovascular diseases are the leading cause of death in both men and women, but there are significant differences in the incidence, etiology, and outcomes of the disease between the genders. Whilst awareness of the importance of sex differences in cardiovascular disease has increased of late, much of what we know about cardiovascular regulation has been derived from studies in males, and lessons learnt in males do not necessarily apply to females. In addition, the impact of uniquely female characteristics and physiological activities (oestrous cycle, pregnancy, lactation, menopause) on cardiovascular health are not well understood. For example, hypertension is less prevalent in young women compared with young men, but menopausal women are at greater risk for hypertension compared with men of similar age. Despite these risks, women do not consistently receive first line treatment for the early stages of hypertension, and the greater morbidity in menopause reflects this neglect.

But why are male and female different? For a long time, it was assumed that male female differences were completely determined by gonadal hormonal actions. In most of the cases, XX females developed a masculine phenotype when they were treated with testosterone whilst XY males showed a feminine phenotype when the effects of testosterone were blocked. However in the late 80's, it was shown that some dimorphic phenotypes appeared before gonadal differentiation and thus could not be explained as the solely result of sex hormones actions. Rather, it was recognised that sex chromosome complement itself is important. Some X and Y genes act in a sex-specific manner on the gonads and other tissues to cause sex differences in XX and XY cells. Thus, the genetic and/or hormone pathways could, thus, act independently or interact (synergistically/ antagonistically) in modulating sexual dimorphic development.

The renin angiotensin system (RAS) and the vasopressinergic systems are involved in blood pressure and hydroelectrolyte balance control with clear sex differences in cardiovascular parameters in males and females. Clinical and basic findings demonstrate major sex differences in the way males and females respond to stimulation and inhibition of the RAS under physiological and pathophysiological circumstances. Although sex hormones (activational effects) are known to directly interact with RAS, the potential contribution of organizational hormonal and SCC effects on physiological sex-based differences in the regulation of the RAS and vasopressin remains undefined. It is, however, tempting to speculate that genes residing in the sex chromosomes may serve as regulators of sexually dimorphic cardiovascular phenotypes. We will thus assess whether sex-related genetic and transcriptomic differences may differentially modulate sexually dimorphic cardiovascular outcomes.

**Participant Professors**

**United Kingdom**

**Prof David Murphy and Dr Alex Paterson**

*The Dorothy Hodgkin Building, University of Bristol, Bristol, England*

Functional genomics of the CNS circuits regulating cardiovascular homeostasis.

a. transcriptome analysis (Affymetrix hardware and GeneSpring Software).

b. gene transfer (germline and somatic) in mice and rats.

c. stereotaxic surgery.

d. gene expression analysis.

**Canada**

**Prof Charles Hindmarch** (http://chipboy.wixsite.com/research)

*Genomics, Transcriptomics and Molecular Medicine, Queen’s Cardiopulmonary Unit*

*(QCPU), Translational Institute of Medicine (TIME)Queen's University, Kingston, Canada*

Transcriptomic analysis of autonomic brain centres controlling the cardiovascular system.

\*RNAseq.

\*bioinformatics.

\*testosterone and cardiovascular health.

**Serbia**

**Prof Dr Nina Japundzic-Zigon** (https://www.researchgate.net/profile/Nina\_Japundzic-Zigon)

*Institute of Clinical Pharmacology, Medical Faculty University of Belgrade, Belgrade, Serbia*

Neurohumoral regulation of cardiovascular short-term variability in female rats – effects of ageing, pregnancy and lactation.

\*real-time acquisition of cardiovascular data.

\*computerised analysis of long-term and short-term cardiovascular signals, including

software development.

\*stereotaxic surgery.

**United States**

**Dr Rebecca Cunningham** (https://www.unthsc.edu/bios/cunningham-2/)

*Health Sciences Centre, University of North Texas, Fort Worth, Texas, USA*

Androgen signaling mechanisms and the effects of androgens on central nervous system

function.

\*sleep apnea.

\*chronic intermittent hypoxia

\*ageing.\*oxidative stress and neurodegeneration.

**Dr Thomas Cunningham** ( <https://www.unthsc.edu/bios/cunningham-3/>)

Health Sciences Centre, University of North Texas, Fort Worth, Texas, USA

Role of the central nervous system in the regulation of the cardiovascular system, and water and electrolyte balance. Chronic diseases like hypertension and water or salt retention that can be associated with heart disease or liver failure.

**Dr Gina Yosten** (https://www.slu.edu/medicine/medical-education/graduateprograms/

pharmacology-physiology/faculty/yosten-gina.php)

*School of Medicine, St Louis University, St Louis, USA*

Sexual dimorphism, plasticity and genomic diversity of the hypothalamic paraventricular

nucleus.

\*neuropeptides.

\*integrative physiology.

\*G protein coupled receptors.

\*Receptor “de-orphanisation”.

**Brasil**

**Prof José Antunes-Rodrigues** (<http://ppgfisiologia.fmrp.usp.br/en/jose-antunes-rodrigues/>), *Department of Physiology in the Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, Brazil*

**Prof. Dr. André de Souza Mecawi** ( http://lattes.cnpq.br/7081349017203771)

UNIFESP, University in São Paulo.

Neuroendocrine control of hydroelectrolytic equilibrium and reproductive physiology.

\*cardiovascular and hydromineral balance in ageing female rats.

\*integrative physiology.

**Prof Lucila Elias** (http://ppgfisiologia.fmrp.usp.br/en/lucila-leico-k-elias/)

Department of Physiology in the Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, Brazil

The neuroendocrine regulation of energy homeostasis.

\*cell-specific knockout mice.

\*leptin signaling.

\*integrative physiology.

Neuroendocrine control of hydroelectrolytic equilibrium and reproductive physiology.

\*cardiovascular and hydromineral balance in ageing female rats.

\*integrative physiology.

**Argentina**

**Profesoras Dras: Laura Vivas, Ximena Caeiro, Julia Cambiasso y Carla Cisternas** (https://inimec.conicet.gov.ar/Vivas/)

*Instituto de Investigación Médica Mercedes y Martín Ferreyra, Unidad Ejecutora del Consejo Nacional de Investigaciones Científicas y Técnicas - Universidad Nacional de Córdoba,Córdoba, Argentina*

**Profesora Dra. Analia Tomat** *Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica. Cátedra de Fisiología, Buenos Aires, Argentina; CONICET, Universidad de Buenos Aires, Instituto de la Química y Metabolismo del Fármaco, Buenos Aires, Argentina*

Areas de interés:

Sexual dimorphism of cardiovascular and hydromineral homeostasis in health and disease.

\*impact of sex chromosomes on cardiovascular and hydromineral balance.

\*integrative physiology.

**Workshop Program:**

**Day 1 December 2 Monday**

09:00 Registration

10:00 Official Welcome and ceremony in honour to Dr. José Antunes Rodrigues and Dr. Samuel Taleisnik.

Dr. David Murphy, Dr Alfredo Cáceres and Dr Laura Vivas

11:00-12:00 Lecture 1: “Aging and gender differences on hydromineral balance”.

 Dr. José Antunes-Rodrigues.

12:00 Cocktail

14:00-15:00 Lecture 2: "Sex differences in gene expression in neural structures regulating hydromineral and cardiovascular homeostasis.”

Dr David Murphy

15:00 Coffee Break

15:30-16:30 Lecture 3: “Pregnancy-induced changes of cardiovascular variability and baroreflex sensitivity in SHR”.

Dr. Nina Zigon.

16:30-17:30 Lecture 4: “Investigating the Biologic Link Between Sex Hormone Status and Fluid Homeostasis: Role of Phoenixin and GPR173”.

Dr. Gina L.C. Yosten

**Day 2 December 3**

09:00 -10:00 Lecture 5: “Sex differences in blood pressure regulation and body fluid homeostasis:  angiotensinergic and vasopressinergic sexual dimorphisms”.

​Dr Ximena Caeiro.

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10:00 -11:00  Lecture 6: “Sex differences in the developmental programming of cardiovascular and metabolic diseases induced by  zinc deficiency during fetal and postnatal life in rats”

 Dr. Analia Tomat

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​11:00 Coffee Break

11:15 -12:15  Lectura 7: “The role of astrocytes in the control of energy homeostasis and sex differences”.

Dr. Lucila Leico K. Elias.

12.15- 13.00 Lectura 8: “Dam environmental changes influence offspring hydroelectrolyte balance regulation”.

 Dr. Andrea Godino

13:00 Lunch Break

14:00-16:00 Poster Sesions

15:30 Coffee Break

16:00-17:00 Lecture 9: “Angiotensin and oxidative stress: what’s sex got to do with it?”.

 Dr. Rebecca Cunningham

17:00-18:00 Lecture 10: “Transcriptomics: the state-of-the-art”.

 Dr. Charles Hindmarch

**Day 3 December 4**

09:00-10:00 Lecture11: “Gender and hypertension: physiological and transcriptomic responses to sex hormone manipulation in the hypertensive rat”.

Dr. Alex Paterson

10:00-11:00 Lecture 12: “Interaction of hormonal and genetic factors on the sexual differentiation of developing brain”.

​Dr Julia Cambiasso.

​11:00 Coffee Break

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11:15-12:15 Lecture 13: “Developmental changes and sex differences in the expression of DNA methylation and demethylation enzymes in hypothalamic regions of the mouse brain”.

 Dr. Carla Cisternas

12:15-13:15 Lecture 14:"Sex differences in a model of hyponatremia.”

 ​Dr. Thomas Cunningham

13:15 Lunch Break

15:00-16:00 Lecture 15: Sexual dimorphism on behavioral and neuroendocrine effects of neonatal serotonin depletion

​Dr. André de Souza Mecawi

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​16:00-18:00 Young Investigators Talks

18:00 Roundtable and Concluding remarks

19:00 Conference dinner