UNIL | Université de Lausanne
Faculté de biologie et de médecine

Cardiovascular and Metabolism PhD Program

Mini-Symposium

"Kidney Physiology and Pathophysiology: Challenges & New Concepts"

Organizer: Edith Hummler Beermann, Department of Biomedical Sciences, University of Lausanne (DSB-UNIL)

When: 20 September 2024 from 9:00 – 13:00
Where: CHUV Lausanne, main building BH08, Auditorium YERSIN

8:30 – 9:00	**COFFEE & CROISSANTS**
9:00 - 9:15	**WELCOME** EDITH HUMMLER BEERMANN, DEPARTMENT OF BIOMEDICAL SCIENCES, UNIVERSITY OF LAUSANNE (DSB-UNIL)
9:15 - 10:00	**THE RENAL CONTROL OF POTASSIUM HOMEOSTASIS** JOHANNES LOFFING, INSTITUTE OF ANATOMY, UNIVERSITY OF ZURICH, SWITZERLAND
10:00 - 10:45	**SERINE PROTEASES AND THEIR IMPLICATION IN PREECLAMPSIA** SARA DI CARLO, DEPARTMENT OF BIOMEDICAL SCIENCES, UNIVERSITY OF LAUSANNE (DSB-UNIL), SWITZERLAND
10:45 – 11:15	**COFFEE BREAK**
11.15 - 12:00	**NEPHROCARDIOLOGY: ROLE OF THE MINERALOCORTICOID RECEPTOR AND THERAPEUTIC OPPORTUNITIES** FRÉDÉRIC JAISSER, CORDELIERS RESEARCH CENTER, PHYSIOPATHOLOGY & METABOLISM DEPARTMENT INSERM U1138, PARIS, FRANCE
12:00- 12.45	**UNDERSTANDING THE BIOLOGICAL PROCESSES OF KIDNEY REPAIR** ANNA RINALDI, LABORATORIES FOR TRANSLATIONAL RESEARCH EOC, BELLINZONA, SWITZERLAND
14:00 – 16:00	**AFTERNOON WORKSHOPS FOR DOCTORAL CANDIDATES WITH SYMPOSIUM SPEAKERS**

The event will be submitted for accreditation to the Direction of veterinary affairs and their inspection (DAVI), section Lausanne, as a half day of continuing education.

The meeting is free of charge, but for organization purposes **please register HERE** prior to September 10, 2024. The UNIL-FBM doctoral school attributes max. 1 ECTS to doctoral candidates for participation (0.25 ECTS morning session, 0.75 ECTS afternoon paper discussion workshop with speakers). For questions, please contact Dr. Ulrike Toepel (Ulrike.toepel@unil.ch).

Co-organized by UNIL | Université de Lausanne Faculté de biologie et de médecine CHUV

TALK ABSTRACTS

THE RENAL CONTROL OF POTASSIUM HOMEOSTASIS

JOHANNES LOFFING, INSTITUTE OF ANATOMY, UNIVERSITY OF ZURICH, SWITZERLAND

The maintenance of potassium (K^+) homeostasis is crucial for the proper functioning of excitable cells. Even minor fluctuations in the low extracellular K^+ concentration can lead to life-threatening cardiac arrhythmias. The kidneys play a key role in K^+ homeostasis by adjusting urinary K^+ excretion in response to dietary K^+ intake. Renal adaptation to a dietary K^+ load involves both aldosterone-dependent and independent mechanisms. These mechanisms require the coordinated action of various nephron segments and ion transport systems, including the thiazide-sensitive NaCl cotransporter (NCC) in the renal distal convoluted tubule (DCT) and the epithelial sodium (Na^+) channel (ENaC), as well as the renal outer medullary K^+ channel (ROMK) in the connecting tubule (CNT) and collecting duct (CD). The activity of these ion transport systems is regulated by a complex network of kinases, including With-No-Lysine-(K) kinases (WNK1 and WNK4), serum- and glucocorticoid-regulated kinase (SGK1), and several protein phosphatases (PP1 and PP3). While aldosterone-dependent mechanisms primarily mediate the long-term adaptation of the kidneys, rapid and acute changes in urinary K^+ excretion are largely dependent on the direct sensing of altered extracellular K^+ concentrations by cells in the DCT, CNT, and CD. This talk will highlight these adaptive changes and place them in a broader physiological and pathophysiological context.

SERINE PROTEASES AND THEIR IMPLICATION IN PREECLAMPSIA

SARA DI CARLO, DEPARTMENT OF BIOMEDICAL SCIENCES, UNIVERSITY OF LAUSANNE (DSB-UNIL), SWITZERLAND

Preeclampsia is a hypertensive disorder that affects 3-5% of all pregnancies worldwide and leads to premature embryonic death and severe consequence for mother's health. It is characterized by defective placentation and impaired placenta vascular development. Although some molecular targets have been identified to be important for the onset of the disease, treatments are still not available. In human, dysregulation of prostasin expression and activity has been associated with severe pre-eclampsia, and with premature embryonic death in knockout mice. Prostasin is a member of the serine protease family and plays an important role in multiple biological processes in a tissue- specific regulatory mechanism of protease cascades. Here, we show that lack of mature red blood cells during embryogenesis in prostasin deficient embryos causes a defective vessel remodeling, possibly causing subsequent defect in vascular development of the placenta. This model opens up new possibilities to study the onset of preeclampsia as mouse model as for identifying therapeutic targets and treatment

NEPHROCARDIOLOGY: ROLE OF THE MINERALOCORTICOID RECEPTOR AND THERAPEUTIC OPPORTUNITIES

FRÉDÉRIC JAISSER, CORDELIERS RESEARCH CENTER, PHYSIOPATHOLOGY & METABOLISM DEPARTMENT INSERM U1138, PARIS, FRANCE

Frederic JAISSER, MD, PhD got a permanent position as Director of Research at the National Institute of Health and Medical Research (INSERM) in 1996. Dr. JAISSER received his medical training and degrees from the Reims Medical School France and was qualified as Nephrologist in 1990. In 2003, he joined the Collège de France in Paris as an independent INSERM team and since 2009 he managed a team of the INSERM Unit U1138, at the Cordeliers Research Centre, Paris (http://www.crc.jussieu.fr/frederic_jaisser2.html). He is Deputy Director of the Cordeliers Research Centre and Head of the "Pathophysiology, Metabolism" Department http://www.crc.jussieu.fr/crc/index.php .

The aim of his studies is to improve the understanding of the pathophysiological roles and signaling pathways whereby the hormone aldosterone promotes pathologies in various organs including the kidney and the cardiovascular system but also eye skin and liver. His work combines cellular and molecular approaches, animal physiology, pharmacological studies and has implications in human diseases. His interest includes translational research aimed to identify and validate biomarkers of Mineralocorticoid Receptor activation in cardiovascular and kidney diseases and novel therapeutic use of MR antagonists.
In the past years he focused his research on the impact of various MR antagonists, including the non-steroidal MRAs finerenone on the cardiovascular impact of chronic kidney disease and/or progression of renal failure. He uncovered in collaboration with experts of skin or eye diseases a major benefit of topical or systemic MR antagonism in skin wound healing delay associated to dermocorticoids and diabetes or in age-related macular degeneration or diabetic retinopathy. He identified novel signaling pathways such as the Neutrophil Gelatinase-Associated Lipocalin as a major underlying mechanism in fibrotic and inflammatory consequences of MR activation in renal and cardiovascular diseases.

During the symposium we will discuss the following points

- deleterious mechanisms of mineralocorticoid receptor (MR) activation in renal pathologies
- specificity of steroidal/non-steroidal MR antagonists
- position of MR antagonists in the therapeutic arsenal of chronic renal failure and its cardiovascular comorbidities
- future opportunities of this therapeutic class

UNDERSTANDING THE BIOLOGICAL PROCESSES OF KIDNEY REPAIR

ANNA RINALDI, LABORATORIES FOR TRANSLATIONAL RESEARCH EOC, BELLINZONA, SWITZERLAND

Renal physiology relies on the interaction of multiple cell types within complex structures. Following injury, renal tissue activates a coordinated process to replace damaged cells and restore function. Fibrosis remains a major barrier in regenerative medicine, and the mechanisms of kidney repair with or without fibrosis are not fully understood. We employed a multimodal approach and lineage tracing models to investigate these mechanisms. Our findings highlight the transcription factor SOX9 as a key regulator. Upon acute kidney injury, injured cells express SOX9. Lineages that regenerate epithelium and silence SOX9 (SOX9on-off) heal without fibrosis, while those that maintain SOX9 activity (SOX9on-on) and fail to restore apicobasal polarity drive chronic kidney disease (CKD) through WNT-induced fibroproliferation. Transplanted human kidneys exhibited similar SOX9/CDH6/WNT2B responses. Thus, we identify a sensor of epithelial repair status that determines whether regeneration occurs with or without fibrosis.