

Mini-Symposium
"Renal metabolism in health and disease"

Organizer: Dmitri Firsov (Department of Biomedical Sciences, UNIL)

When: November 26, 2021 from 9:30 – 13:00

Where: Auditorium Mathias MAYOR, CHUV main building, Rue Bugnon 46, Lausanne

On-site participants:

- Please respect sanitary measures and wear a mask at all times
- Please favour the CHUV back entrance close to the parking and auditoria instead of the CHUV main entrance. Please present your CHUV/UNIL card (if applicable), your sanitary pass, and the invitation e-mail that will be sent to you just before the symposium.

Remote participants please connect via:

<https://chuv.webex.com/chuv-en/j.php?MTID=m502bc06a978a8952b9bf950f9c8579c8>

PROGRAM

9:30 - 9:45	Welcome Dmitri Firsov (Department of Biomedical Sciences, University of Lausanne, Switzerland)
9:45 - 10:30	Fabienne Rajas (INSERM U1213, Université Claude Bernard Lyon1, France) <i>Links between metabolism and chronic kidney disease</i>
10:30 - 11:15	Andrew Hall (University of Zurich, Switzerland) <i>4D imaging of protein metabolism in the functioning kidney</i>
11:15 – 11:30	Coffee break
11.30 – 12:15	David Legouis (University of Geneva, Switzerland) <i>Renal Gluconeogenesis in the Acute Kidney Injury</i>
12:15- 13.00	Dmitri Firsov (Department of Biomedical Sciences, University of Lausanne, Switzerland) <i>Role of the circadian clock in renal function and metabolism</i>
13:00 – 14.30	Lunch break
14:30 – 16:30	Afternoon workshops for MD and PhD students with symposium speakers

The mini-symposium has been accredited by 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 registration necessary [here](#) prior to November 1, 2021. The UNIL-FBM doctoral school attributes 1.0 ECTS to PhD students who present a signed participation form for the mini-symposium (0.25 ECTS morning session, 0.75 ECTS afternoon session). For additional information, please contact Dr. Ulrike Toepel (Ulrike.toepel@unil.ch).

Talk abstracts



Fabienne Rajas (INSERM U1213, Université Claude Bernard Lyon1, France)

Links between metabolism and chronic kidney disease

Chronic kidney disease (CKD) has been recognized as a leading public health problem worldwide. Renal dysfunction generally remains silent for a long period of time, with glomerular hyperfiltration being the only demonstrable renal abnormality. Then, when the glomerular filtration rate decreases below a critical level, CKD continues to progress toward kidney failure. Diabetes might account for more than half of CKD burden. Unfortunately, almost all adult patients with Glycogen Storage Disease type 1 (GSD1) develop CKD.

While diabetes (DT) is characterized by chronic hyperglycemia and increased endogenous glucose production (EGP), GSD1 leads to a loss of EGP and severe hypoglycemia during short fasts. GSD1 is a rare metabolic disease due to mutations in glucose-6 phosphatase, the key enzyme of EGP that allows the release of glucose into the bloodstream after dephosphorylation of glucose-6 phosphate (G6P). For several years, we have used contrasting diabetes and GSD1 as a strategy to reciprocally unravel these two mirror diseases. This strategy has allowed us to emphasize the striking similarities between renal metabolism in GSD1 and diabetes. In both, impaired glucose homeostasis is responsible for an increase in metabolic pathways downstream of G6P that leads to an activation in de novo lipogenesis and a decrease in lipid oxidation. Undoubtedly, renal ectopic lipids play a crucial deleterious role by activating inflammation and fibrosis that is responsible for the progressive loss of the renal filtration function. In mice, the pharmacological activation of PPAR α by fenofibrate treatment strongly stimulates the expression of genes involved in lipid catabolism in the kidneys that entails a decrease in renal triglyceride content and prevention of CKD by inhibiting RAS and TGF β 1 pathways. Thus, in diabetes and GSD1, lowering renal lipids is probably the best approach to preventing CKD.

In this regard, comparing diabetes and GSD1 is a fruitful approach to better understand the key role of G6P in renal metabolism in health and disease. This has allowed us to highlight the link between glucose/lipid metabolism and CKD progression.



Andrew Hall (University of Zurich, Switzerland)

4D imaging of protein metabolism in the functioning kidney

The glomerulus filters plasma proteins smaller than albumin, which have to then be reabsorbed in the proximal tubule (PT) to prevent loss in the urine (proteinuria). Proteins enter cells in the PT via receptor mediated endocytosis, but their subsequent fate was unclear. We have developed new methods using custom-designed probes, intravital microscopy and computational analysis, to follow the progression and metabolism of filtered proteins through the mouse kidney in real-time, and how this changes in diseases. We have discovered that protein processing within PTs is highly conserved and spatiotemporally organized, and involves coordinated activity of different specialized segments. Moreover, we have found that compensatory remodeling along the PT limits urinary protein wasting in pathological states, suggesting that measurement of proteinuria underestimates the severity of tubular defects in patients.



David Legouis (University of Geneva, Switzerland)

Renal Gluconeogenesis in the Acute Kidney Injury

Acute Kidney Injury (AKI), defined as a sudden drop in renal function, is a very common condition in the critical care setting. Occurring in one over two patients admitted to an intensive care unit, AKI is associated with both mortality and morbidity, while therapeutic option is only suppletive (i.e., dialysis). Normal renal function involves massive solute reabsorption and requires large amount of ATP. Kidneys are the second organ after the heart in terms of mitochondrial abundance, making it a highly metabolic organ. However, renal gluconeogenesis, the synthesis of glucose from non-hexose precursors has long been underrated because of technical limitations. In the past decades, several groups have highlighted the major role played by the kidneys in the systemic glucose homeostasis. We found experimentally that AKI alters this process, further confirmed in patients admitted to the intensive care unit in which renal catheterization showed that AKI decreases renal glucose release and lactate uptake. The renal gluconeogenic decline was accompanied by a systemic metabolic pattern including high lactate and low glucose levels, which was predictive of an increase mortality.



Dmitri Firsov (Department of Biomedical Sciences, University of Lausanne, Switzerland)

Role of the circadian clock in renal function and metabolism

Most, if not all, specific renal functions exhibit significant circadian fluctuations. These functional rhythms are driven, at least in part, by the circadian clock, a self-sustained molecular oscillator based on a network of interlocked transcriptional/translational feedback loops. Numerous studies have shown that the circadian clock plays a key role in the maintenance of homeostasis. Previous work from our group has shown that *intrinsic* renal circadian clocks are critically involved in blood pressure (BP) control, in circadian oscillations of glomerular filtration rate (GFR) and, in renal handling of water and major ions. At the molecular level we demonstrated that intrinsic tubular circadian clocks control expression levels of a great number of renal transcripts, including those encoding enzymes of essential metabolic pathways. Our recent data reveals that dysfunction of the intrinsic renal tubule circadian clock can aggravate diabetic hyperglycemia via enhancement of gluconeogenesis in the renal proximal tubule. These results further highlight the importance of circadian behavior in diabetic patients.