DBMR Research Conference

Seminar room EG050
Murtenstrasse 24, 3008 Bern

Date: **Monday, October 6, 2025, 5pm – 6pm**

Title: **MAGE-D2: A novel protector against ER stress and hypoxia**

Speaker: **Dr. Kamel Laghmani, Ph.D., Directeur de Recherche CNRS, Centre de Recherche des Cordeliers, Sorbonne Université, Paris, France**

Bio: Dr. Kamel Laghmani is a CNRS Research Director and group leader at the Cordeliers Research Center (CRC) in Paris, France, specializing in molecular renal physiology. With a Ph.D. in Molecular and Cellular Biology, Dr. Laghmani's research focuses on the regulation of kidney ion transporters, particularly the Na-Cl cotransporter, which is crucial for electrolyte balance and blood pressure control. His research has elucidated how hypoxia and endoplasmic reticulum (ER) stress contribute to kidney dysfunction and stress-related diseases, opening new avenues for therapeutic development. His work has further significantly advanced the genetic and molecular understanding of Bartter and Gitelman syndromes - rare inherited kidney disorders - and salt-sensitive hypertension. Dr. Laghmani has authored numerous high-impact publications, notably a landmark study published in the New England Journal of Medicine in 2016, which provided critical insights into the genetic basis and pathophysiology of Bartter syndrome. In recognition of his outstanding contributions, he received the prestigious PEDR Excellence Prize in 2016. Currently, Dr. Laghmani leads a collaborative research project funded by the French and Swiss National Science Foundations, working alongside Prof. Uyen Huynh-Do and Dr. Stefan Rudloff. This project investigates how MAGE-D2 protects the kidney, especially the Na-Cl cotransporters, from hypoxic and ER stress, offering transformative insights into kidney health and disease mechanisms.

Abstract: Bartter syndrome (BS) is a rare inherited kidney disorder that impairs the reabsorption of sodium, potassium, and chloride, leading to excessive salt and water loss in urine, dehydration, low potassium levels, and metabolic alkalosis. Several genetic forms have been identified, yet for decades more than 20% of patients remained without a genetic diagnosis. In 2016, Dr. Laghmani and collaborators discovered that mutations in the MAGE-D2 gene cause a very severe but transient form, known as BS type 5. This condition presents before birth with massive renal salt loss and fetal polyuria, leading to severe polyhydramnios, extreme prematurity, and high mortality. The disease's severity is due to disrupted cell surface expression of the NKCC2 and NCC salt transporters. The transient nature of BS type 5 appears linked to the hypoxic environment of early pregnancy, which induces endoplasmic reticulum (ER) stress and misfolding of these transporters. MAGE-D2 plays a critical role in counteracting this stress: it is required for proper induction of the hypoxia-response factor HIF1-alpha and for protecting NKCC2 and NCC from degradation under low-oxygen conditions. Consistent with this protective role, MAGE-D2 expression increases in kidney tubular cells during ER stress in various in vivo models, such as chronic metabolic acidosis or high salt diet. Understanding how MAGE-D2 protects against hypoxia and ER stress is key to clarifying its role in health and disease and could open avenues for new therapeutic strategies.

Host: Dr. Stefan Rudloff, Experimental Nephrology, Department for BioMedical Research and Department of Nephrology and Hypertension, Inselspital, University Hospital, University of Bern

Next DBMR Research Conference: Monday, November 3, 2025, 5pm-6pm
Speaker: Dr. Andrea Felser, Department of Pediatrics, Inselspital
Title: Mitochondrial dysfunction rewires adrenal steroidogenesis: from cortisol deficiency to androgen excess

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