I SEMINARI DI biogem

12 ottobre 2023 ore:12.00

Dr. Alessandro Luciani

Institute of Physiology, University of Zurich

Unlocking mechanisms and therapeutic paradigms in rare diseases

Biografia

Alessandro pursued his education in the field of medical biotechnology at the University of Naples Federico II in Italy. During his undergraduate studies, he successfully completed his thesis, which focused on understanding molecular pathways responsible for epithelial cell plasticity and their impact on tissue damage.

Subsequently, he embarked on a PhD program in Cell Biology at San Raffaele Scientific Institute in Milan, Italy. Working in Maiuri's and Kroemer's labs, he employed advanced microscopy and chemical genetic techniques to investigate the proteostasis network in both normal physiological conditions and diseases characterized by protein misfolding, such as Cystic Fibrosis.

In 2012, Alessandro joined the laboratory of Olivier Devuyst at the University of Zurich (UZH) in Switzerland. Here, his research approach involved using model organisms, biochemical assays, and microscopy to explore the impact of lysosomes on cell-fate decisions within kidney tubule epithelium and their role in the development of various kidney diseases.

Early in 2018, Alessandro assumed the role of a Lecturer and Team Leader at the Institute of Physiology, UZH, and was subsequently promoted to the position of Principal Investigator within the University Research Priority Program ITINERARE – Innovative Therapies in Rare Diseases in 2021. His research team is dedicated to investigating autophagy- and lysosome-related pathways in the context of homeostasis, kidney diseases, and the discovery of therapeutic interventions.

Abstract

The epithelial cells that line the kidney proximal tubule (PT) play a critical role in homeostasis by efficiently reabsorbing small proteins and solutes through receptor-mediated, clathrin-dependent endocytosis and lysosome-related pathways. Defects in these fundamental processes disrupt the reabsorptive activities of the tubular cells, resulting in the appearance of low molecular weight proteins (LMWPs) and solutes in the urine. This condition known as renal Fanconi syndrome, RFS can eventually progress towards chronic kidney disease (CKD) and life-threatening complications. Functional studies of rare inherited disorders affecting the proximal tubule have gleaned actionable insights into fundamental mechanisms of homeostasis while revealing drug targets for therapeutic innovation.

Using cystinosis as a paradigm of lysosome dysfunction causing RFS and kidney disease, I will discuss how lysosome-directed signaling circuits govern the homeostasis of tubular epithelial cells, and how these mechanisms can become disrupted in disease states. Furthermore, I will highlight latest advances in preclinical models and introduce a conceptual framework for the utilization of cell- and lysosome-based function assays, disease-relevant screening technologies, and digital tools in drug discovery and development. These innovative approaches may ultimately lead to new treatment options, not only for cystinosis but also for other currently intractable kidney diseases, and transform our ability to regulate homeostasis and health.

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