

DBMR Research Conference

Date **October 4, 2021, 5 pm – 6 pm**

Title **The arc of discovery: from genes to mechanisms to therapies for kidney diseases and beyond**

Speaker **Prof. Dr. Anna Greka, Center for Kidney Disease and Novel Experimental Therapeutics, Harvard Institutes of Medicine, Brigham and Women's Hospital, Boston MA, USA**

Bio: Anna Greka is a physician-scientist leading the translation of scientific discoveries from the laboratory to clinical trials. She is an Associate Professor at Harvard Medical School (HMS); an Associate Physician in the Renal Division in the Department of Medicine at Brigham and Women's Hospital (BWH); and the founding director of Kidney-NExT, a Center for Kidney Disease and Novel Experimental Therapeutics at BWH. Dr. Greka is also an Institute Member of the Broad Institute of MIT and Harvard, where she directs the institute's Kidney Disease Initiative (KDI) and the ion channel therapeutics interest group (CHannel Therapeutics, CHaRT).

The Greka laboratory specializes in the development of precision therapies for difficult-to-treat diseases with a special interest in genetically defined disorders. Specifically, her lab studies mechanisms of cell survival and metabolic regulation, including calcium signaling and transient receptor potential (TRP) ion channel biology.

Abstract: Intracellular accumulation of misfolded proteins causes toxic proteinopathies, diseases without targeted therapies. Mucin 1 kidney disease (MKD) results from a frameshift mutation in the MUC1 gene (MUC1-fs). Here, we show that MKD is a toxic proteinopathy. Intracellular MUC1-fs accumulation activated the ATF6 unfolded protein response (UPR) branch. We identified BRD4780, a small molecule that clears MUC1-fs from patient cells, from kidneys of knockin mice and from patient kidney organoids. MUC1-fs is trapped in TMED9 cargo receptor-containing vesicles of the early secretory pathway. BRD4780 binds TMED9, releases MUC1-fs, and re-routes it for lysosomal degradation, an effect phenocopied by TMED9 deletion. Our findings reveal BRD4780 as a promising lead for the treatment of MKD and other toxic proteinopathies. Generally, we elucidate a novel mechanism for the entrapment of misfolded proteins by cargo receptors and a strategy for their release and anterograde trafficking to the lysosome.

Prof. Dr. Anna Greka has been invited by Prof. Dr. Bruno Vogt

The DBMR Research Conference will take place as a webinar via Zoom.

For those wishing to attend, please use this link

<https://unibe-ch.zoom.us/j/62521337135?pwd=RjNXcTkzWTYrSE93YWJtMDBBMjFVZz09>

Meeting ID: 625 2133 7135

Password : 497260

or scan the QR code for the details



Next DBMR Research Conference

December 6, 2021

Prof. Dr. Anna Köttgen, Institut für Genetische Epidemiologie, Albert-Ludwigs-Universität Freiburg, DE

Title «Understanding Kidney Function through Population-based Genetic Studies»



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