

Group of Prof. Herbert Schramek

The Department of Internal Medicine IV, Nephrology and Hypertension of Innsbruck Medical University (IMU) represents the tertiary referral centre for patients with renal disease and hypertension for the Western part of Austria and Southern Tyrol. The main infrastructural components include three dialysis facilities, an inpatient ward, an outpatient clinic, a clinical laboratory and research laboratories.

The **CELLULAR AND MOLECULAR NEPHROLOGY LAB** of Herbert Schramek is a basic research unit and has its focus on projects studying cellular and molecular mechanisms of tubulointerstitial fibrogenesis as well as of tubular protection and repair.

The respective specific research interests can be summarized as follows:

Regulation of tubular epithelial cell differentiation, survival, and proliferation; mechanisms of tubular epithelial cell protection; regulation of epithelial-mesenchymal-transition (EMT), mesenchymal-epithelial-transition (MET), and tubulointerstitial repair; role of oncostatin M for the differentiation and proliferation of renal tubular epithelial cells when compared with profibrotic mediators such as TGF- β 1 and IL-1 β ; the regulation of these processes by intracellular signaling molecules with a special emphasis on mitogen-activated protein kinases (MAPK), Akt/PKB, NF κ B, Smad and Stat signaling.

A second large field of research interest of this laboratory represents diagnosis, therapy and prevention of myeloma-associated kidney disease. In this context, the lab members are predominantly interested in tubular injury mechanisms induced by nephrotoxic monoclonal light chains and on tubular effects of the proteasomal inhibitor bortezomib.

Within WP5.1 of SysKid, the Cellular and Molecular Nephrology group uses advanced in vitro human epithelial renal cell culture models with the objectives of:

- i. mechanistic analysis of the effects of candidate biomarkers and mediators known or identified in WP 2, 4, and 5.2 on the progression of CKD;
- ii. the identification and functional characterization of candidate target genes in in vitro models,
- iii. the identification of signaling processes, interacting partners and regulation of selected candidate targets.

Real-time PCR and Western blot analyses are utilized to study intrinsic expression of genes of interest in distinct cell culture models in order to identify those cell types, which are most suitable for subsequent over-expression and knock-down experiments. As powerful research tools for assessing gene function as well as its regulation the group primarily uses gene knockdown and overexpression strategies utilizing RNA interference (RNAi) technology and transient/stable transfections, respectively. In addition, the Cellular and Molecular Nephrology Lab of P3-IMU is able to provide various well established assays in order to study functional endpoints such as cell phenotype, cell differentiation, EMT/MET, cell survival/protection, proliferation and apoptosis.

Selected references:

Neuropilin-1 and neuropilin-2 are differentially expressed in human proteinuric nephropathies and cytokine-stimulated proximal tubular cells.

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Oncostatin M-induced effects on EMT in human proximal tubular cells: Differential role of ERK signaling.

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Am J Physiol Renal Physiol 2007;293:F1714-1726.

ERK1/2-driven and MKP-mediated inhibition of EGF-induced ERK5 signaling in human proximal tubular cells.

Sarközi R, Miller B, Pollack V, Feifel E, Mayer G, Sorokin A, Schramek H.
J Cell Physiol 2007;211:88-100.

Loss of active MEK1-ERK1/2 restores epithelial phenotype and morphogenesis in transdifferentiated MDCK cells.

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Am J Physiol Cell Physiol 2003;285:C652-C661.



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