

Group of Prof. Gert Mayer

Clinics and renal biopsies:

The research group of Gert Mayer at the Department of Internal Medicine IV (Nephrology and Hypertension) at Innsbruck Medical University focuses on transcriptional profiling of kidney tissue from patients with various renal disorders. The Department performs around 100 renal biopsies (native kidney and transplants) per year. After complete routine pathological workup cryosections are stored at -80 °C, and this surplus material serves as a valuable basis for several research projects including SysKid. As our institution is the tertiary nephrology care centre of the Western part of Austria, patients after biopsy are also usually being taken care of by us and hence detailed clinical follow up data are available making it possible to link transcriptomics with clinic.

Methodology:

In recent projects we have successfully established Laser-capture microdissection (LCM) for isolation of specific cells of interest - such as proximal renal tubule cells - from kidney cryosections. Due to the minute amount of material isolated by LCM we have generated and optimized protocols for T7-based linear RNA amplification, quality control (QC) and microarray hybridization of RNA isolated from tubule cells. Array based genome wide gene expression profiling is combined with state of the art methodologies such as quantitative real-time PCR, immunohistochemistry, immunofluorescence and western blotting of candidate genes and proteins. Furthermore, we test regulatory mechanisms of genes of interest *in vitro* in collaboration with the group of Prof. Herbert Schramek at our Department.

Genomics and biomarker research:

Transcriptional profiling of tubule cells from patients with proteinuric nephropathies and of tubule cells from control tissues revealed significant differential regulation of pro-fibrotic and tubulo-protective (e.g. BMP-7) mechanisms already at an early stage of kidney disease. We also compared renal gene expression patterns from patients with stable disease and progressive renal failure during follow-up. Interestingly, an attenuated tubular VEGF-A expression was noted despite a strong tubular hypoxia response and the activation of VEGF signalling pathways. These gene expression profiles serve also as a basis for further research on biomarkers in chronic kidney disease. For example, the expression levels of HIF-1a and VEGF-A were significantly superior in predicting clinical outcome as compared with proteinuria, renal function, and degree of tubular atrophy and interstitial fibrosis.

Further research interests:

Another area of interest of our laboratory is the influence of ageing on transcriptomics in the kidney. This area is of special importance in the field of renal transplantation as chronological donor age is one of the major determinants of long term outcome. A currently ongoing project tries to improve the predictive power by assessing biological donor age.

Cooperations:

We perform our projects in close collaboration with many institutions, amongst others emergentec biodevelopment GmbH (www.emergentec.com), the Medical University of Vienna (<http://www.meduniwien.ac.at/nephrogene/>) and the University of Katowice. Furthermore, we cooperate closely with the Department of Transplant Surgery at the Medical University in Innsbruck and the Department of General, Visceral and Transplant surgery at the University of Tübingen.

Our involvement in the large-scale integrating European research project “SysKid”:

Our goal for many years has been the identification of novel biomarkers to assess the risk to develop CKD and to predict the rate of progression. Syskid for us is the unique opportunity to find new collaborators, which will allow us to combine our transcriptomics data with state of the art bioinformatics as well as animal models and cell culture experiments. All –omics techniques are extremely valuable hypothesis generating tools, however the data obtained need confirmation and we are looking forward to be able to combine and share whatever is necessary to improve our understanding of CKD.

Reference Papers

Hypoxia response and VEGF-A expression in human proximal tubular epithelial cells in stable and progressive renal disease.

Rudnicki M, Perco P, Enrich J, Eder S, Heining D, Bernthaler A, Wiesinger M, Sarközi R, Noppert SJ, Schramek H, Mayer B, Oberbauer R, Mayer G.

Lab Invest. 2009 Mar; 89(3): 337 - 46. Epub 2009 Jan 12.

Gene expression profiles of human proximal tubular epithelial cells in proteinuric nephropathies.

Rudnicki M, Eder S, Perco P, Enrich J, Scheiber K, Koppelstätter C, Schratzberger G, Mayer B, Oberbauer R, Meyer TW, Mayer G.

Kidney Int. 2007 Feb; 71(4): 325 - 35. Epub 2006 Dec 20.

Reliability of t7-based mRNA linear amplification validated by gene expression analysis of human kidney cells using cDNA microarrays.

Rudnicki M, Eder S, Schratzberger G, Mayer B, Meyer TW, Tonko M, Mayer G.

Nephron Exp Nephrol. 2004; 97(3): e86 - 95.

Read more about this group and our cooperating partners at www.microarray.at and www.syskid.eu.



The research group of **Gert Mayer** (from left to right):
Michael Rudnicki, Hannes Neuwirt, Gert Mayer, Susie-Jane Noppert,
Christian Koppelstätter, Judith Sunzenauer, Susanne Eder, Georg Kern