Polycystic Kidney Disease

Polycystic Kidney Diseases (PKD) are among the most common and severe diseases in Pediatric Nephrology and represent one of the most frequent causes of dialysis-requiring end stage renal failure both in children and adults. In polycystic kidney disease, fluid-filled cysts and fibrotic tissue accumulate in the kidney leading to a progressive loss of renal function.

While the autosomal dominant ADPKD usually presents clinically in adults, the more severe autosomal recessive PKD (ARPKD) is usually seen in children. ADPKD is caused by mutations in the genes PKD1, PKD2, GANAB and DNAJB11. ARPKD is mainly caused by mutations in the PKHD1 gene, encoding the protein fibrocystin. Fibrocystin is a large transmembrane protein of poorly understood function. Recently, mutations in DZIP1L and PMM2 have been described as causes of ARPKD.

The overarching aim of our group is to understand the molecular mechanisms underlying cystogenesis and renal fibrosis in PKD as well as to deeply characterize clinical courses and the effect of current therapeutic approaches in pediatric patients with PKD.

A special focus of our cell biological work is on the role of FC and FC-associated ciliary proteins. Like other gene products affected in cystic kidney disease, fibrocystin localizes to the so-called primary cilia of cells. Cilia are small hairlike membrane protuberances projecting from nearly every cell of the human body. Cilia seem to act as little antennae sensing the cellular environment and are crucial regulators of multiple intracellular signaling pathways. Using multiple screening approaches we recently identified various novel candidates for members of the FC protein complex and are currently characterizing these proteins functionally both in vitro and in vivo. In close collaboration with the Nephrology Research Laboratory of the Department II of Internal Medicine this work examines two main aspects of protein dysfunction in PKD and other ciliopathies: impaired trafficking to cilia and defective signal transduction from cilia to the cell resulting e.g. in altered expression of transcriptional cell programs.

In addition to our molecular work a second main project is a deep clinical and phenotypic characterization of pediatric PKD patients. ARPKD shows major phenotypic variability. The underlying mechanisms remain unclear. Detailed data on long-term courses are rare and current treatment approaches are symptomatic and mainly based on the opinion of experts. To improve clinical characterization of ARPKD patients, to gather long-term data and to assess current therapeutic approaches, we recently set up an international ARPKD registry study (www.aregpkd.org). With the support of the German
Pediatric Nephrology Association (GPN) and the ESCAPE Network (European Study Consortium for Chronic Kidney Disorders Affecting Pediatric Patients) this registry study pro- and retrospectively collects pseudonimyzed clinical data of ARPKD patients in a web-based data base. This registry study may lay the foundation for first clinical trials on ARPKD. With the associated biobank ARegPKD may also open novel options for translational research.

Following a similar approach and in a close collaboration with Prof. D. Mekahli from Leuven, we have also established the pediatric ADPKD registry ADPedKD (www.adpedkd.org). ADPedKD aims to identify early markers for rapid progression in ADPKD as a basis for a potential therapeutic intervention in ADPKD during childhood and adolescence.

The Team

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Publications

**Selected Publications Max Christoph Liebau**


8. Ebner K, Liebau MC. “No general treatment recommendation for nephrectomy in prenatal suspicion of ARPKD”; Der Urologe, 2017 Nov;56,(11), 1465-1466


1. Center for Pediatric Research Cologne

1. Basic-Translational Research

1. Autosomal Recessive Polycystic Kidney Disease (ARPKD)(AG Liebau)

   1. Team
   2. Publications
   3. Open Positions

- Experimental Neonatology (Brachvogel)