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miRNAs in the kidney and their role in podocyte (dys) function

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iRNAs are short non-coding RNAs which posttranscriptionally regulate the intracellular level of mRNAs. It is known since 2008 that miRNAs are important for the development and maintenance of podocyte structure. Deletion of the two key enzymes of miRNA biogenesis, Drosha or Dicer, leads to proteinuria and glomerular injury in podocytes, e.g. podocyte foot process effacement, in mice. Although many podocyte miRNAs are meanwhile known, their potential target mRNAs are still mostly unknown. In the present work a mouse model with inducible podocyte-specific deletion of Dicer was generated. Using SDS-Page and protein-creatinine-ratio, proteinuria was determined. In addition, H&E and PAS staining as well as electron microscopy were used to investigate histological and ultrastructural abnormalities. We were able show that the inducible deletion of Dicer leads to an onset of proteinuria after 3 weeks with further progression. Proteinuria was accompanied by podocyte foot process effacement and endothelial changes. We also observed mesangial matrix expansion and protein casts in the tubule system. Using freshly isolated podocytes of double-fluorescent Cre reporter mice, we identified miRNAs and putative target mRNAs by different approaches. Through in silico predictions putative miRNA-mRNA pairs were generated and validated using a luciferase reporter assay. We were able to identify specific miRNA-mRNA interactions which are currently investigated using the Dicer knock-out mouse model.

Biography

Sandra Elisabeth Meisinger completed her Master of Science in Biology at the University of Salzburg in 2016. Since 2017, she is pursuing her PhD at the University of Regensburg in analysing the role of miRNAs in the kidney.

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