Focal segmental glomerulosclerosis (FSGS) and IgA nephropathy (IgAN, Berger's disease) are the predominant subtypes of primary glomerular diseases (primary glomerulopathies, PGs) and the commonest cause of chronic renal failure (CRF, chronic kidney disease) worldwide in adults. The precise diagnosis of these disease entities is based entirely on kidney biopsy that is an aggressive procedure with the 3% risk of minor and major complications (including massive bleeding, nephrectomy and death). Presently there are no molecular diagnostic strategies available that could serve as non-invasive alternative to renal biopsy (so-called "liquid biopsy"). There is an urgent need to discover specific and sensitive biomarkers / biomarker panels for non-invasive diagnosis of the primary glomerulopathies (FSGS and IgAN) and for evaluation of their severity (sub-nephrotic vs. nephrotic range proteinuria). Nano-sized (~ 20-180 nm) urinary exosome vesicles (exosomes, EVs) comprise a potent, valuable source of kidney-disease specific biomarkers as they are secreted constantly into the urine by kidney cells (both normal and pathologic) and possess mRNA and protein profiles that is cell-off-origin-specific.

Within the framework of the proposed project we would like to study the global molecular pattern of exosomes isolated from the urine of FSGS and IgAN patients as well as healthy-disease controls in order to define specific mRNA and protein signatures indicative of the variant of primary glomerulopathy and its severity. We also plan to perform functional analysis of the defined transcriptomic and proteomic signatures in order to get insight into the molecular pathomechanisms of these diseases.

So far no studies have attempted to characterize the coding transcriptome (mRNA content) and proteome of urinary exosomes in primary glomerulopathies, specifically FSGS and IgA nephropathy. The proposed project will be the first to explore globally the mRNA and protein content of urinary exosomes in FSGS and IgAN conditions with varying degrees of severity (sub-nephrotic and nephrotic range proteinuria).

In order to perform the global transcriptomic analysis we will employ the high-throughput mRNA-seq protocol and for the purpose of proteomic analysis we will take advantage of TRAQ LC-MS/MS strategy.