Elucidating mechanisms of matrix protein secretion in podocytes to understand the role of the secretory pathway in kidney disease

The kidneys filtration barrier, the glomerular basement membrane, is essential for our health as it removes toxins and unwanted components form our blood. If this barrier breaks down, it results in kidney disease, often resulting in kidney failure.

The primary cells responsible for the production and maintenance of the glomerular filtration barrier are podocytes, a highly complex, arborised (branched) cell type. Despite their fundamental importance, we do not have a complete understanding of how these cells build or maintain the filtration barrier. We have identified an organelle, Golgi outposts, that appear to have a role in basic processes in podocyte function and filtration barrier maintenance. While these outposts are known to be important in brain cells, our work has identified them in podocytes for the first time. These organelles help to build the highly branched shape of podocytes, and have roles in protein transport; sending components of the glomerular filtration barrier to the correct destination. In addition to this, we have found that a Golgi outpost specific protein, TPPP, is strongly genetically linked to kidney disease through large genetic association studies.

We aim to uncover the role of Golgi outposts in podocyte function, and specifically understand the mechanisms and consequences of TPPP dysregulation in the context of kidney health. By understanding how Golgi outposts in the kidney function and how TPPP works, we can explain how a specific genetic fault leads to kidney disease. This is a crucial first step towards developing new therapies to treat the condition