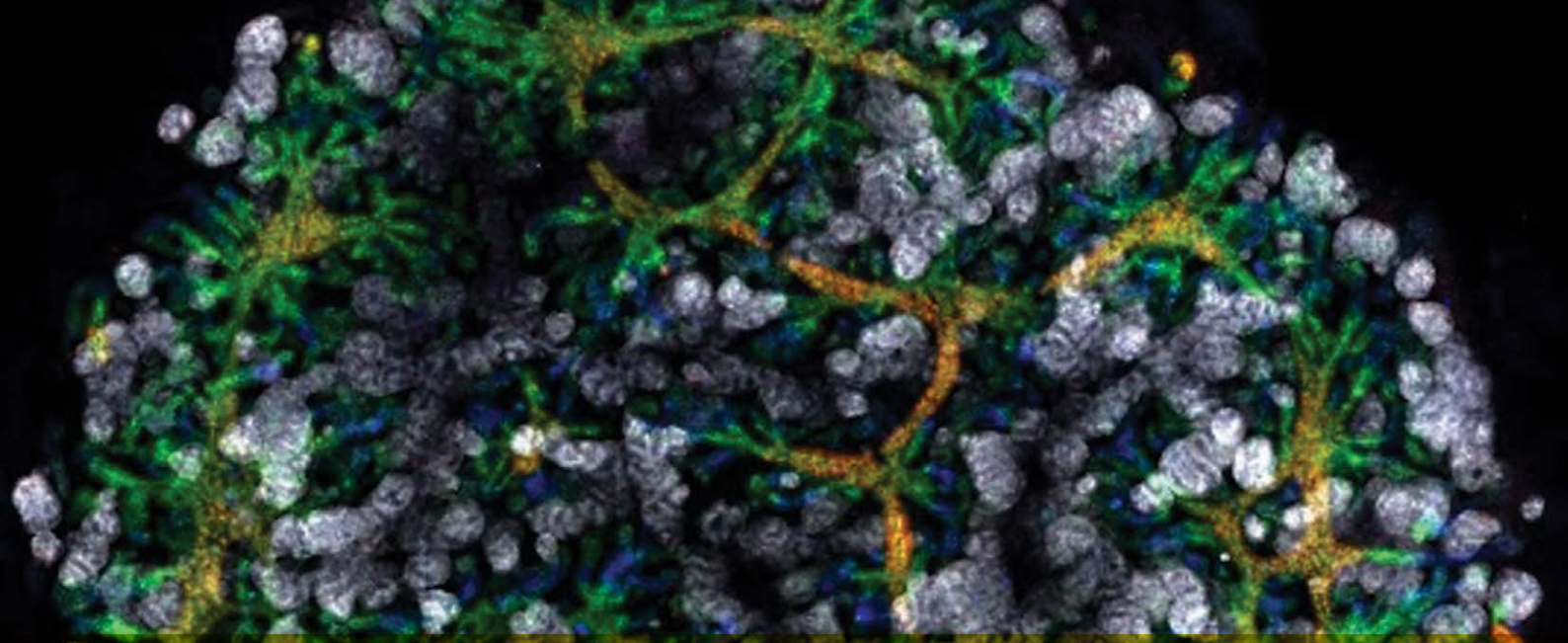

# Mini-kidneys tell two sides of a genetic story

## Gene-editing technology combined with stem cells provides a powerful new way to study genetic kidney diseases and their treatments.

Melbourne researchers have used mini-kidney 'organoids' grown in the lab to unravel the mystery of why Mainzer-Saldino syndrome, a rare disease involving a single defective gene, causes life-threatening kidney damage. In doing so, they've proven an approach that can be used to study a whole range of other genetic kidney diseases.

**Chronic kidney disease costs Australia's economy $4.1 billion each year and is one of our biggest killers. In many cases the cause is genetic. It is estimated that one in ten Australians will show evidence of chronic kidney disease by 2020, but only one in four patients will receive a transplant.**

The researchers took skin cells from a child with the disease, turned them into stem cells, and used CRISPR gene-editing technology to correct the mutation that causes the condition. This multidisciplinary effort was led by organoid pioneer Professor Melissa Little and her Kidney Regeneration group at Murdoch Children's Research Institute, located on the grounds of the Royal Children's Hospital in Melbourne.

"When you create reprogrammed stem cells from a patient's own skin cells you carry across the patient's whole genetic fingerprint," explains paediatric nephrologist and PhD candidate Dr Tom Forbes. "A kidney organoid made from those stem cells behaves under the influence of that patient's genes."

They grew mini-kidneys from both diseased and gene-corrected stem cells, providing the perfect experimental control for studying the condition.

The defective gene, they found, caused malformation of cilia—finger-like cell projections that detect movement of liquid past the surface of the cell—which are vital for the normal function of kidney cells.

Group member Dr Sara Howden used a new method she invented to reprogram patients' cells to stem cells and gene-edit to correct mutations at the same time.

"Making kidney tissue from human stem cells and then correcting any genetic mutations to study the way the disease develops is an important step towards developing personalised future treatment," says Sara, who heads MCRI's Gene Editing Facility.

Project leader Melissa Little previously produced the world's first mini-kidneys in a dish, grown from stem cells that were able to produce several different cell types and self-organise into the complex tissues of a functioning kidney.

Ultimately, Melissa's group wants to make organs for transplantation from stem cells. Along the way, they expect their regenerated kidney tissues will improve the understanding, diagnosis and treatment of kidney diseases, and help identify life-extending drug treatments.

This gives Tom great hope for his patients who are facing a daunting future of dialysis or a kidney transplant.

"If these diseases can be detected through genetic testing and addressed before symptoms appear, it can save patients a lot of suffering and reduce the costs to our healthcare system."