Regenerating Kidney Tissue to Combat Nephropathic Cystinosis

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The kidneys are highly sensitive to the effects of cystinosis, resulting in renal Fanconi syndrome and eventually kidney failure. Pluripotent stem cells are powerful cells that give rise to all of the body's cell types and organs, including the kidneys. These stem cells exist naturally only in the womb, but it is now possible to generate them after birth by 'reprogramming' other types of cells into stem cells. Using these stem cells, we have devised a plan to combat cystinosis.

In the first step of this plan, we are creating a biobank of human pluripotent stem cells derived from patients with cystinosis. This starts from a humble urine sample, from which we purify urinary cells. We subsequently reprogram those urinary cells into pluripotent stem cells. By using a gene editing technique called CRISPR, we are able to supply cystinosis stem cells with a healthy copy of the CTNS gene. This brings cystine levels in these cells back down to their normal levels.

The final step is to change these stem cells into kidney. To do this, we have coaxed cystinosis stem cells to change into kidney organoids – tiny structures that resemble kidney tissue. We are implanting the organoids into the kidneys of mice, to practice transplant. There, the organoids become more mature, forming filter units that integrate beautifully with the host's blood supply. Taking this one step further, we have recently generated mice with cystinosis in which human stem cells can form grafts. These studies will establish a framework for more advanced studies in human patients.