

Investigation of novel biochemical pathways responsible for kidney injuries in cystinosis patients

Renal Fanconi Syndrome (one specific form of kidney failure) is mostly caused by cystinosis. So far, it is not understood, why mutations in the cystinosis gene prevent kidney cells from functioning normally and ultimately cause kidney failure. To understand these processes in more detail, we compared the gene expression patterns

- from kidney cells derived from animals that do not have a functional cystinosis gene
- from kidney cells from control animals that do have a functional cystinosis gene
- from kidney cells from cystinosis patients

The differences between these gene expression patterns enabled us to identify several genes and biochemical pathways that could provide an explanation for the injuries that occur in the kidneys of cystinosis patients. The most significant candidates are involved in apoptosis, a controlled and programmed form of cell death, or in lysosomal pathways (lysosomes are little vesicles inside the cells that are involved in the chemical degradation of cellular waste products including proteins. The cystinosis protein is located in the membrane of these lysosomes and essential for their proper functioning).

Detailed follow-up investigations on one of these proteins confirm the findings from the large scale gene expression studies. We are conducting experiments that are aimed at understanding what one protein that is downregulated in cystinosis cells is doing in the healthy kidney and if its lack is important for disease progression in renal Fanconi syndrome. We postulate that monitoring the amounts of this protein will help at assessing the prognosis of cystinosis patients with progressive renal disease. We are hopeful that drugs could be used to increase the amounts of this protein and that these drugs could have beneficial effects in cystinosis.