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A gene that protects from kidney disease

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Researchers from the European Molecular Biology Laboratory (EMBL) and the University of Michigan have discovered a gene that protects us against a serious kidney disease. In the current online issue of *Nature Genetics* they report that mutations in the gene cause nephronopthisis (NPHP) in humans and mice.

NPHP is a disease marked by kidney degeneration during childhood that leads to kidney failure requiring organ transplantation. The insights might help develop effective, noninvasive therapies.

The kidneys are the organs that help our body dispose of potentially harmful waste. Diseases that affect this fundamental function are very serious but so far only poorly understood. NPHP is such a disease; it causes the kidneys to degenerate and shrink starting early on in childhood often leading to renal failure before the age of 30. So far, kidney transplantation in early age has been the only way to save patients suffering from NPHP. With a new mouse model Mathias Treier and his group at EMBL have shed new light on the molecular mechanisms underlying NPHP opening up novel ways to treat the disease.

“Our mice show striking similarities with NPHP patients,” says Mathias Treier, group leader at EMBL. “Very early on in their lives their kidney cells start to die and the mice develop all the characteristic disease symptoms. It is the first time that a mouse model reveals increased cell death as the mechanism underpinning kidney degeneration in NPHP. The genetic cause is a mutation in a gene called GLIS2.”

GLIS2 normally prevents cell death in the adult kidney. It does so by shutting down genes that initiate cell death and that are only required during the development of the organ. A mutation interfering with GLIS2 function reactivates these harmful genes the result being that large numbers of kidney cells die. The organ shrinks and changes in its architecture occur which affect normal kidney function.

To find out if GLIS2 has the same effect in humans Friedhelm Hildebrandt and his team at the University of Michigan carried out a genetic screen of patients suffering from NPHP. They found that like the mouse model some patients carried mutations in the same GLIS2 gene, confirming that GLIS2 is a crucial player in NPHP also in humans.

“This is an excellent example of how combining basic research with clinical studies can help uncovering mechanisms of human disease,” says Henriette Uhlenhaut who carried out the research in Treier’s lab. “The next step will be to translate the insights gained into new therapeutic approaches to develop alternatives to kidney transplantations. With GLIS2 we have already identified one promising candidate drug target and our mouse model will help us find many others.”

Source: European Molecular Biology Laboratory