Researchers replicate human kidney gene changes in mouse model

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University of Louisville researchers have replicated the inflammatory gene changes of a human kidney as it progresses from mild to severe diabetic nephropathy, using a mouse model developed by a UofL researcher, according to an article published today in the journal *Experimental Nephrology*. Diabetic nephropathy is the foremost cause of kidney failure.

"In 2004 we published an article that showed that our diabetic mouse model, OVE26, excreted high levels of protein in the urine, as humans with diabetes do. We continue to see resemblance to human diabetes as we test different aspects of the disease using this mouse model," said Paul Epstein, Ph.D., acting director of the Kosair Children's Hospital Research Institute.

The processes leading to advanced diabetic nephropathy are poorly understood. Researchers have not been able to observe kidney failure through its full cycle of development, because of the natural lifespan and other limitations of available diabetic animal models.

Because of these limitations, changes in renal gene expression can be used to evaluate the progression of diabetic nephropathy. Gene expression studies, which measure the gene's synthesis of messenger RNA, identify individual genes or major signaling pathways activated as diabetic nephropathy progresses.

This is the first study of gene expression changes of whole kidney during

the progression from mild to very severe albuminuria, a condition common to patients with longstanding diabetes.

Researchers found that some gene expression differences between control and diabetic mice increased 10-fold. The change was most obvious for inflammatory genes.

This suggests that this strain of diabetic mice could be used to look for new insights into human diabetic nephropathy and raises questions about the role of inflammation in kidney failure.

"They provide an excellent model of diabetic nephropathy to assess the effect of inflammatory proteins," Epstein said. "In future studies, we can use this mouse model to explore whether inflammation causes disease progression or if the progression of the disease causes further inflammation. If it turns out that inflammation is causal, the next step would be to test the effectiveness of anti-inflammatory drugs."

Provided by University of Louisville