SOUTHWESTERN NEWS

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EMBARGOED UNTIL 4 P.M. CST MONDAY, MARCH 31, 2003

DEFECT OF CILIA-ASSEMBLY PROTEIN COULD CAUSE MOST COMMON GENETIC CAUSE OF KIDNEY FAILURE

DALLAS – March 31, 2003 – A protein responsible for the assembly of cell cilia – the hair-like projections from cells – may cause polycystic kidney disease, the most common genetic cause of kidney failure, according to a new study at UT Southwestern Medical Center at Dallas.

The study, which will be published online this week and will appear in a future edition of the *Proceedings of the National Academy of Sciences*, is the first to directly test the role of cilia in polycystic kidney disease. Previous studies have hinted at a possible link, said Dr. Peter Igarashi, chief of nephrology at UT Southwestern and senior author of the study.

"For a long time, renal cilia have been thought to be unimportant organelles," said Igarashi. "This study and others before it have renewed the interest in what cilia are doing normally and also how abnormalities in cilia cause disease."

Polycystic kidney disease (PKD) afflicts about one in every 500 people and causes fluid-filled cysts to accumulate in the kidney, liver and other organs. Formation of the cysts causes progressive renal failure, which requires dialysis or kidney transplantation. No other effective treatment is available.

To test whether stopping cilia formation causes PKD, researchers created knockout mice missing the gene *Kif3,* specifically in the kidneys. That gene codes for a motor protein that's critical in cilia formation and maintenance. Researchers created kidney-specific knockouts because cilia are essential for embryonic development.

The knockout mice had normal kidneys at birth, but researchers found that kidney cysts began to develop about five days later and caused renal failure after about three weeks. Dissection by day 35 showed enlarged kidneys with multiple, fluid-filled cysts that had characteristics similar to cysts found in PKD.

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"We are trying to understand the mechanism of cyst formation," said Dr. Fangming Lin, assistant professor of pediatrics and lead author of the study. "Once you understand the mechanism we will have the target to prevent or slow the cyst formation.

"That could eventually lead to a treatment of human polycystic disease."

Other UT Southwestern researchers who worked on the study were Dr. Thomas Hiesberger, assistant professor of internal medicine, and Kimberly Cordes, research assistant. Researchers from Yale University School of Medicine and the University of California, San Diego, School of Medicine also contributed to the study, which was funded by the National Institute of Diabetes and Digestive and Kidney Diseases.

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