

Surprising mechanism discovered in polycystic kidney disease

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A study by Yale researchers has uncovered a new and unexpected molecular mechanism in the development of polycystic kidney disease, or PKD. The study appears in *Nature Genetics*.

PKD is a life-threatening genetic disorder that causes multiple cysts to form on the kidneys—enlarging them, cutting off proper urine flow, and causing [kidney failure](#) in half of affected people by age 60. It affects more than 12 million people worldwide.

Cilia are the hair-like structures on the surface of many [human cells](#) that can either move things along – dirt out of the lungs, or an egg from the ovary to the uterus – or sense the environment, such as vision in the retina or smell in the nose. Recent research has implicated defects in the sensory cilia—often caused by [genetic mutations](#)—in many human diseases, including cancer, cardiac disease, blindness, and kidney disease. In the kidney, disruption of sensory cilia cause kidney cysts.

The polycystin-1 and -2 (also known as PC1 and PC2) proteins are key players in the normal functioning of the kidneys. Earlier research has shown that when they are lost or mutated, cysts grow in the kidneys and cause almost all cases of PKD in humans.

Working in mice, the Yale team found that cysts grew when the cilia were intact but lacked polycystin—but, surprisingly, cysts stopped growing despite the absence of polycystins when the cilia were disrupted or eliminated.

The activity of this pathway, and the timing of the loss of polycystin proteins and the cilia, determined the severity of both early- and adult-onset PKD, the researchers found.

"None of the other pathways discovered so far have proven as universal as the cilia dependent pathway in explaining polycystic [kidney disease](#)," said corresponding author Dr. Stefan Somlo, professor of internal medicine (nephrology) and genetics at Yale School of Medicine. "We found to our surprise that elimination of cilia suppresses cyst growth in all of the [genetic models](#) of human PKD."

Somlo believes that his team's research could lead to discovery of new targets for therapies to inhibit this cilia-dependent pathway of PKD, and slow cyst growth.

More information: *Nature Genetics* [DOI: 10.1038/ng.2715](https://doi.org/10.1038/ng.2715)

Provided by Yale University

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