Experiments point to new treatments for PKD

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A family of small molecules called CFTR inhibitors show promising effects in slowing the progression of polycystic kidney disease (PKD), the most common genetic disease of the kidneys, according to preliminary research reported in the July 2008 issue of the *Journal of the American Society Nephrology*.

Although much more study is needed, CFTR inhibitors could provide a useful new approach for the treatment of PKD. "The CFTR inhibitors could be the basis of a lifelong treatment to slow renal cyst growth and decline in renal function, prolonging dialysis-free patient survival," comments Dr. Alan S. Verkman of University of California, San Francisco, School of Medicine.

Patients with PKD develop cysts on the kidneys, which progressively increase in size and number. The kidneys become enlarged, eventually leading to kidney failure. Previous research has suggested that the buildup of fluid in the cysts is related to chloride secretion, which is affected by the CFTR (cystic fibrosis transmembrane conductance regulator) gene. The researchers used automated "high-throughput" screening techniques to identify CFTR inhibitors that might affect cyst growth.

These screening studies identified two classes of small-molecule CFTR inhibitors that slowed the growth of renal cysts. The best inhibitor of each class was identified and shown to reduce the number and growth of cysts by more than 80 percent.

The inhibitors were then tested in mice that had been genetically altered to produce a condition similar to PKD. Animals treated with CFTR inhibitors for up to seven days had significantly slower cyst expansion and kidney enlargement, and better preservation of kidney function. There was no evidence of harmful effects on kidney function.

PKD is an incurable condition for which new treatments are urgently needed. If effective medications to reduce the rate of fluid buildup in cysts could be developed, they might provide an entirely new approach to treatment to slowing the progression of the disease.

The results show that CFTR plays a role in the growth of renal cysts, and suggest that CFTR inhibitors have potential as treatments to reduce cyst growth in PKD. However, much more research will be needed to see if drugs based on the CFTR blockers will be useful in human PKD.

"The mouse model of PKD is not the real human disease for many reasons, such as the more rapid progression of disease in mice," says Dr. Verkman. "Clinical trials will be needed to determine the efficacy of these compounds in human PKD."

Source: American Society of Nephrology