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Study finds four genes linked to cystic diseases of the liver and kidney

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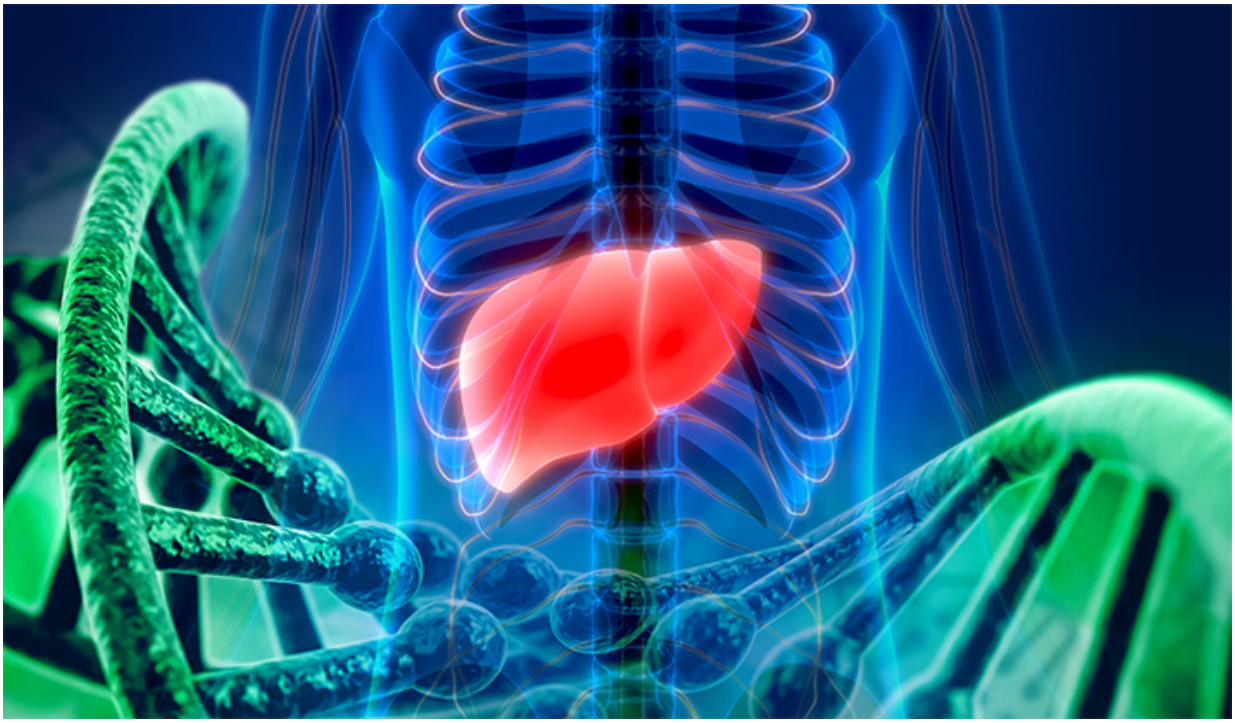

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Yale researchers are studying kidney and liver diseases to determine which genes are involved in the formation of cysts.

In order to diagnose and find treatments for a genetic disorder, scientists need to identify which gene mutations cause the disease. A common and

often devastating genetic disease known as polycystic kidney disease (PKD) results in cysts in both the kidney and liver. Cysts are pockets of fluid in an organ that develop over time and crowd out the normal functioning parts. The more common form of PKD that affects adults and approximately half of their children, typically leads to kidney failure by the sixth decade of life. It is caused by mutations in the genes PKD1 or PKD2. The more rare juvenile form is caused by mutations inherited from both parents in a gene called PKHD1.

Researchers in the lab of Yale nephrologist Dr. Stefan Somlo have found that some patients have only liver cysts, not kidney cysts, and thus don't get kidney failure. This disease, known as isolated polycystic liver disease (PCLD), is typically benign but can lead to symptoms in rare cases where the liver becomes very large. Nonetheless cysts form due to a dysregulation of the same disease process as those in the kidney, the details of which are an important area of investigation. To deepen understanding of why liver and kidney cysts form, a Yale-led research team examined the genes of patients with liver cysts.

Through sequencing of patient genomes and computer analyses, the researchers identified four additional genes associated with PLCD. This discovery demonstrated that many different genes are involved in the process of cyst formation. Interestingly, one of the identified genes was PKHD1, suggesting that a subset of carriers of PKHD1 mutations (parents of children with the juvenile form of PKD) can present with PCLD.

This finding supports a common mechanism of disease between both the adult and juvenile PKD and PCLD. Researchers, such as first author Whitney Besse, a clinical fellow in medicine, hope that through improving understanding of the genes involved in cyst formation, an effective treatment can be developed. It could be hypothesized now that blocking a single pathway could cure all of these diseases, said Besse.

She and her colleagues plan to further study the underlying mechanisms of these diseases and how they might interact.

The study published is in the *Journal of Clinical Investigation*.

More information: Whitney Besse et al. Isolated polycystic liver disease genes define effectors of polycystin-1 function, *Journal of Clinical Investigation* (2017). DOI: 10.1172/JCI90129

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