Study finds that one third of children with a kidney tumor have hereditary predisposition

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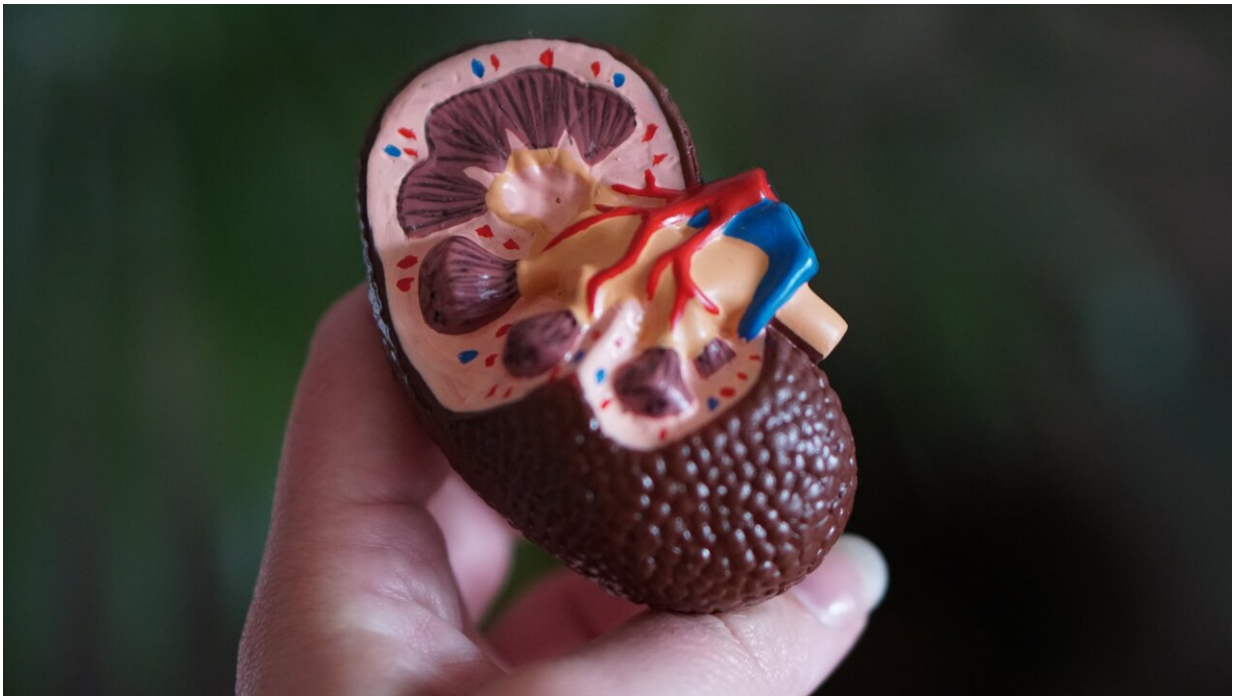

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In cancer, there's a mistake in the hereditary material, the DNA, which causes uncontrollable growth of cells in the body. One in ten children with cancer has hereditary predisposition: a combination of DNA changes, spontaneous or inherited from a parent, that increases the risk of developing a tumor. How often and how strongly hereditary predisposition plays a role in the development of childhood cancer

differs per tumor type.

In a new study, researchers at the Princess Máxima Center for pediatric oncology in Utrecht, the Netherlands, mapped out hereditary information from all children diagnosed with a Wilms' tumor between 2015-2020. It's the first time that information on hereditary predisposition was collected together with clinical data in all children with a Wilms' tumor in a national cohort. The study was published today in the *Journal of Clinical Oncology*.

More than expected

Janna Hol, Ph.D. candidate in the Van den Heuvel-Eibrink and Kuiper groups at the Princess Máxima Center, worked on the study. She says, "All children with a Wilms' tumor were examined by a clinical geneticist. They looked at a number of clinical features that could point to hereditary predisposition. Those children for whom standard diagnostics did not indicate hereditary factors were offered a broader genetic test to map out their full DNA. Where possible, we examined DNA from blood as well as DNA from healthy kidney tissue that had been removed during the operation."

The researchers collected information about the hereditary predisposition of 126 children with a Wilms' tumor who had been treated in the Netherlands between 2015-2020. Hol explains, "We found hereditary factors in 42 of 126 children, so one third of the patients. That was much more than we expected."

Reassuring

"For many children with a hereditary predisposition, we can reassure the family," continues Hol. "We see, for example, that the predisposition in

the child arose shortly after fertilization. Sometimes the predisposition is only found in kidney tissue, and not in blood. Then we know that siblings do not have an increased risk of developing a Wilms' tumor. If the hereditary predisposition does come from one or both parents, siblings can get a genetic test. They are then screened extra carefully."

Gene fault

One of the hereditary factors that the researchers found was the so-called DIS3L2 gene. That gene was already known—children who inherit a faulty copy from both parents have a rare syndrome that can lead to a Wilms' tumor. Janna Hol notes, "Our study showed that five children had only one faulty copy of this gene, inherited from a healthy parent. We found the second gene fault in the tumor itself, where it had arisen spontaneously." The researchers believe this makes the DIS3L2 gene less important for early detection of tumors, but scientifically very interesting for understanding how Wilms' tumors arise.

Dr. Marjolijn Jongmans, clinical geneticist at UMC Utrecht and co-principal investigator of the Kuipers group, led the study. She explains, "On the basis of our research, all children with a Wilms' tumor in the Netherlands are now offered extensive genetic diagnostics. Children are tested for changes in the most important genes that are currently known, including the genes that emerged from our study."

More information: Prevalence of (epi)genetic predisposing factors in a 5-year unselected national Wilms tumor cohort: a comprehensive clinical and genomic characterization, *Journal of Clinical Oncology*, DOI: 10.1200/JCO.21.02510

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