

Researchers crack genetic code of rare kidney cancer

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The genetic code of a rare form of kidney cancer, called reninoma, has been studied for the first time. In a paper, published in *Nature Communications*, researchers at the Wellcome Sanger Institute, Great Ormond Street Hospital and The Royal Free Hospital also revealed a new drug target that could serve as an alternative treatment if surgery is not recommended.



There are around 100 cases of reninoma <u>reported to date worldwide</u>, and it is among the rarest of tumors in humans. Although it can usually be cured with surgery, it can cause severe hypertension or it can spread and develop into metastases. There are no existing medical treatments for reninoma and management involves surgery alone. Until now, it had been unknown what genetic error causes reninoma.

In the new study, a collaboration between the Wellcome Sanger Institute and Great Ormond Street Hospital and The Royal Free Hospital, researchers found that there is a specific error in the genetic code of a known cancer gene, NOTCH1, that is behind the development of this rare cancer.

The team examined two cancer samples—from a young adult and a child—with advanced genomic techniques, known as whole genome and single nuclear sequencing. Their findings suggest that the use of existing drugs targeting this specific gene is a possible solution to treating reninoma for patients where surgery is not a viable option.

Taryn Treger, first author of the study and The Little Princess Trust Fellow at the Wellcome Sanger Institute, said, "Many <u>cancerous tumors</u> have already been deciphered with genomic technologies, however, this is not so true in rare cancers, particularly those affecting children. Our work aims to fill that gap. This is the first time that we have identified the drivers for reninoma and we hope that our work continues to pave the way towards new therapies for childhood cancers."

Dr. Tanzina Chowdhury, co-lead author of the study, at Great Ormond Street Hospital, said, "Rare kidney cancers known as reninomas do not respond to conventional anti-cancer therapies. The only known treatment at the moment is surgery. Our study shows that, actually, there is a specific and well-studied gene that drives this rare cancer. If we use already known drugs that affect this gene, we might be able to treat it



without the need for an invasive technique such as surgery."

Dr. Sam Behjati, co-lead author of the study, Wellcome Senior Research Fellow at the Wellcome Sanger Institute and Honorary Consultant Pediatric Oncologist at Addenbrooke's Hospital, said, "Rare cancers are exceedingly challenging to study, and patients with such tumors may therefore not benefit from <u>cancer</u> research. Here, we have a powerful example of cutting-edge science rewriting our understanding of an ultra rare <u>tumor</u> type, reninoma, while delivering a finding that potentially has immediate clinical benefits for patients."

More information: Treger, T.D., et al, Targetable NOTCH1 rearrangements in reninoma, *Nature Communications* (2023). DOI: 10.1038/s41467-023-41118-8

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