Unlocking a key to kidney cancer: Study advances understanding of tumor growth

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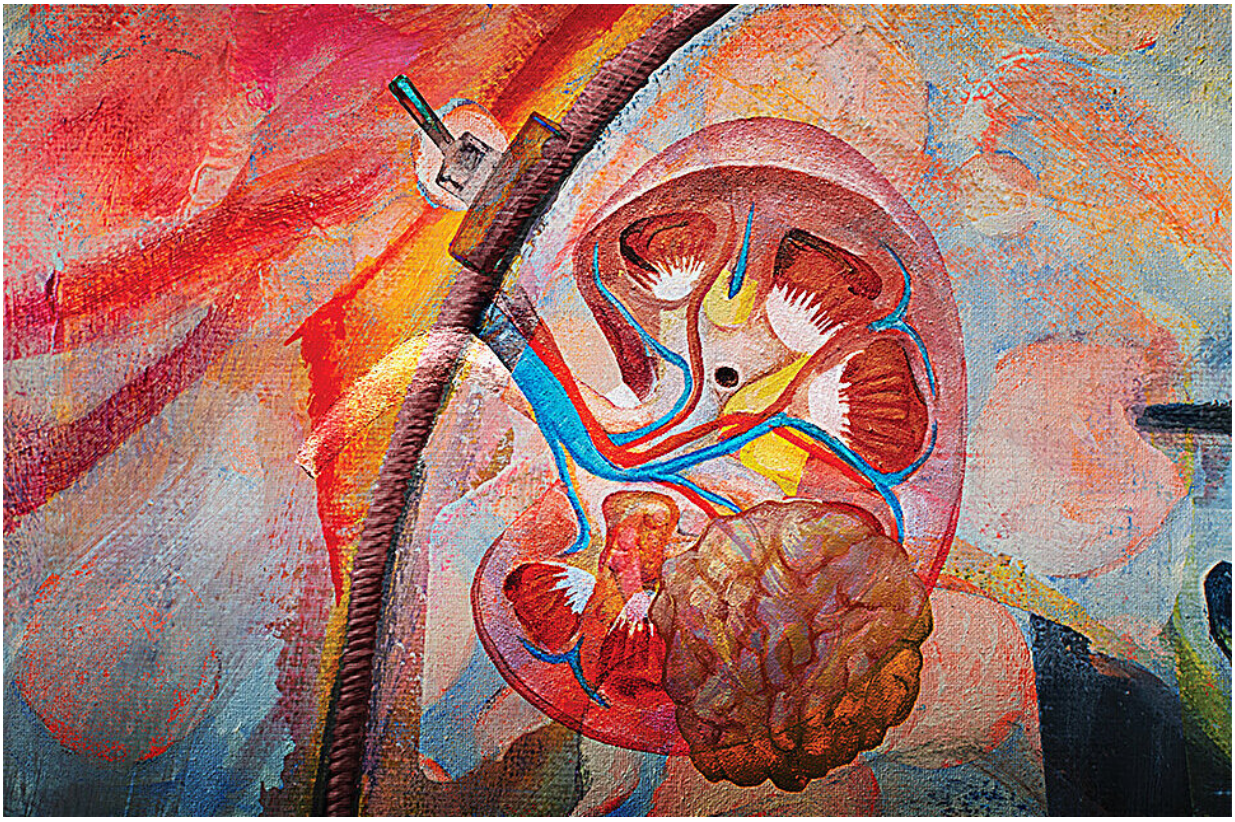

Artistic rendition of kidney cancer being 'switched on' or activated by the loss of the gene PBRM1. Credit: Gregoire Vion

Researchers from A*STAR's Institute of Molecular and Cell Biology (IMCB) and National Cancer Centre Singapore (NCCS) have discovered how the loss of a gene, PBRM1, can lead to the development of kidney

cancer. The work is published in the journal *Nature Cell Biology*.

When the gene PBRM1 is inactive, it results in the formation of abnormal protein complexes that activate a cancer-causing pathway called NF-κB. These complexes redistribute proteins throughout the genome, leading to heightened NF-κB activity and the expression of genes that promote cancer cell growth.

The PBRM1 gene is the second most frequently mutated gene in kidney cancer, but there are limited studies as to how it affects the formation of kidney cancer. This study provides new insight into the development of kidney cancer and could lead to new potential treatments for the disease.

Led by Professor Teh Bin Tean, Joint Research Director at IMCB's Chromatin Therapeutics Laboratory and Deputy Chief Executive Officer (Research) at NCCS, the research team compared normal and diseased proteins to understand their impact on cancer development.

The findings highlight that PBRM1 serves as a protective mechanism, preventing the abnormal activation of NF-κB and maintaining the integrity of healthy proteins. Additionally, the researchers discovered that treating kidney cancer with a drug called bortezomib can suppress NF-κB activation and delay tumor growth.

"In better understanding how the gene PBRM1 activates cancer-causing pathways, we have unlocked potential new ways to target kidney cancer. These findings provide scientists and clinicians a new therapeutic target that can be used to develop improved treatments for all cancers linked to the NF-κB pathway," said senior author of the study, Professor Teh Bin Tean.

"The inactivation of PBRM1 is a type of genetic change that is caused by altering the structure of DNA in the cell. Scientists have been finding

ways to target and treat these changes to prevent cancer. Our study has proven that it is possible to control and target this kind of genetic change, thus paving the way for emerging therapeutic methods to develop suitable treatments for cancer," said Dr. Yao Xiaosai, lead author of the study and principal scientist from the Department of Oncology Bioinformatics and Discovery Oncology, Genentech.

More information: Xiaosai Yao et al, PBRM1-deficient PBAF complexes target aberrant genomic loci to activate the NF-κB pathway in clear cell renal cell carcinoma, *Nature Cell Biology* (2023). DOI: 10.1038/s41556-023-01122-y

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