

## HOW THE Y CHROMOSOME MAKES SOME CANCERS MORE DEADLY FOR MEN

Two recent studies published in Nature suggest that the Y chromosome plays a role in the aggressiveness of colorectal and bladder cancers: the first study reports that the loss of Y chromosome plays a detrimental role; in the second, a specific Y-chromosome gene, in mice, increases the likelihood of certain colorectal cancers to metastasize.

Researchers at Cedars-Sinai Medical Center ([Abdel et al. 2023<sup>1</sup>](#)) removed the Y chromosome from human bladder cancer cells using CRISPR-Cas9 genome editing. They found that these cells were more aggressive when transplanted into mice and that immune cells surrounding tumors without the Y chromosome were dysfunctional. However, treating these Y-less tumors with a therapeutic antibody restored immune cell activity and made them more susceptible to treatment. This discovery may lead to new approaches for treating bladder cancer.

Another team ([Li et al. 2023<sup>2</sup>](#)), studying colorectal cancer in mice, discovered that a gene called KDM5D, on the Y chromosome, weakened connections between tumor cells, allowing them to spread. Removing the gene made tumor cells less invasive and easier for immune cells to recognize, suggesting that this could be a potential target for anti-cancer therapies.

These studies suggest that genetics may explain the male bias observed in many cancers. However, the contrast between a defensive function for the Y chromosome in bladder cancer and a detrimental function for a specific Y-chromosome gene in colorectal cancer, highlights the importance of context in cancer. This context depends on the affected organ, the position of the tumor within the organ, and the presence of other genetic mutations

1- <https://www.nature.com/articles/s41586-023-06234-x>

2-<https://www.nature.com/articles/s41586-023-06254-7>