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THE ROLE OF THE Y CHROMOSOME IN CANCER OUTCOMES STUDIED

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Two studies have shed light on the role of the Y chromosome in cancer outcomes, in which males are often more adversely affected than females. The results of the studies were published in Nature. One paper identified an upregulated gene on the Y chromosome that contributes to colorectal cancer in mice by driving tumour invasion and aiding immune escape in males. The other study demonstrated how the loss of the Y chromosome in bladder cancer generates a more immunosuppressive tumour microenvironment and contributes to worse outcomes.

Sex is known to affect cancer incidence, clinical outcomes and tumour biology, with most cancers causing worse outcomes in males than in females. Some studies have suggested that the function of the Y chromosome may have a role.

Ronald DePinho from the University of Texas MD Anderson Cancer Center, Houston, Texas and colleagues assessed sex differences in colorectal cancer in a mouse model of the disease. Colorectal cancer is the second most common cause of cancer-related deaths, which is more frequent, aggressive and metastatic in males. The model is a specific form of the disease, driven by a known oncogene called KRAS. The researchers observed a higher frequency of metastasis and worse survival in male mice, mirroring the outcomes seen in humans. Analyses reveal upregulation of a gene for an enzyme which drives tumour invasion and immune escape. This gene is expressed on the Y chromosome, thereby providing a potential basis for sex-specific differences in the progression of KRAS-driven colorectal cancer.

In the other study, Dan Theodorescu from Cedars-Sinai Medical Center, Los Angeles and colleagues investigated how the loss of the Y chromosome might affect cancer outcomes. Loss of the Y chromosome is a feature observed in multiple cancer types. They first looked at clinical data from 300 male patients with bladder cancer to identify an association between Y chromosome loss and poor prognosis. Then they studied bladder cancer cell lines and found that tumours lacking the Y chromosome were more aggressive and had a dampened T cell-mediated immune response compared with tumours which had the Y chromosomes intact. They note that loss of the Y chromosome is associated with an increased response to a specific type of immunotherapy called anti-PD1 checkpoint blockade therapy in both mice and humans, suggesting a potential line of treatment for this subset of bladder cancers.

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