

A New Explanation for Sex Differences in Cancer

Translocation renal cell carcinoma, a type of kidney cancer, occurs mainly in female individuals, though why this is the case has never been clear.

April 25, 2025 By [Damon Runyon Cancer Research Foundation](#)

Translocation renal cell carcinoma (tRCC) is a type of kidney cancer that arises when a gene called TFE3 on the X chromosome fuses with another gene on either the X chromosome or an autosome, as non-sex chromosomes are called. Unlike most kidney cancers, tRCC occurs mainly in female individuals, though why this is the case has never been clear. Now, a new study from Damon Runyon-Rachleff Innovator Srinivas R. Viswanathan, MD, PhD, and his colleagues at Dana-Farber Cancer Institute offers an explanation for this cancer's female bias—and, potentially, explains why people with two X chromosomes are at higher risk for other cancer types.

In cells with two X chromosomes, one X is active and one X is inactive, approximately equalizing the dosage of X-linked genes between males and females. Surprisingly, however, Dr. Viswanathan's team showed that a TFE3 gene from either the active or inactive X chromosome can fuse with an autosomal gene, leading to a 2:1 female-to-male ratio of these gene fusions. It makes sense, then, that the cancer arising from this fusion event is more often seen in females. Moreover, the team's RNA sequencing analysis indicated that fusions involving the inactive X chromosome can have a wide-ranging epigenetic impact, meaning they affect the expression of many other genes. This may underlie the female risk bias observed in other cancer types.

"While many cancer sex differences may be associated with non-genetic factors, this points to a genetic basis for sex bias in a specific cancer," tweeted Dr. Viswanathan upon the study's release. "There is much more to be done to further understand the plasticity of [the inactive X chromosome] in cancer, genetic determinants of cancer sex bias, and to move towards sex-specific precision oncology."

This study was published in [Cell](#).

This blog was published by [Damon Runyon Cancer Research Foundation](#) on April 10, 2025. It is republished with permission.
