Study uncovers key to how 'triggering event' in cancer occurs

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This is Arul Chinnaiyan, M.D., Ph.D., from the University of Michigan Comprehensive Cancer Center. Credit: University of Michigan Health System

Researchers at the University of Michigan Comprehensive Cancer Center have discovered what leads to two genes fusing together, a phenomenon that has been shown to cause prostate cancer to develop.

The study found that pieces of chromosome relocate near each other after exposure to the hormone androgen. This sets the scene for the gene fusion to occur. The finding is reported online Oct. 29 in *Science Express*.

"This work shows the origin of how the gene fusion is actually created and perhaps the origin of prostate cancer itself. This is a triggering event for the genesis of prostate cancer," says study author Arul Chinnaiyan, M.D., Ph.D., director of the Michigan Center for Translational Pathology and S.P. Hicks Professor of Pathology at the U-M Medical School. Chinnaiyan is also a Howard Hughes Medical Institute investigator.

Chinnaiyan and his team identified in 2005 a prostate-specific gene called TMPRSS2 that fuses with the gene ERG, which is known to play a role in prostate cancer. Their earlier research has shown that this gene fusion acts as an "on switch" to trigger prostate cancer. In the current study, the researchers focused on what causes the gene fusion to occur.

The researchers took prostate cancer cells that did not reflect the gene fusion but that were sensitive to androgen, a male hormone known to play a role in some prostate cancers. They exposed the cells to androgen and found that two pieces of chromosome that are normally far apart are relocated near each other.

Next, the researchers applied radiation to the androgen-stimulated cells. This stress or insult to the cells - designed to induce chromosomal breaks - led to the gene fusion occurring.

"We thought the gene fusions occurred as a chance event, but it's not. Chromosomes can actually be induced in three-dimensional space to be close to each other. Then when an insult to the DNA occurs, the fusion happens," says lead study author Ram-Shankar Mani, Ph.D., a research fellow in pathology at the U-M Medical School.

The researchers believe the findings could have implications for gene fusions that occur in other cancer types. By understanding how gene fusions occur, the researchers suggest that screening tools or prevention strategies could potentially be developed.

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