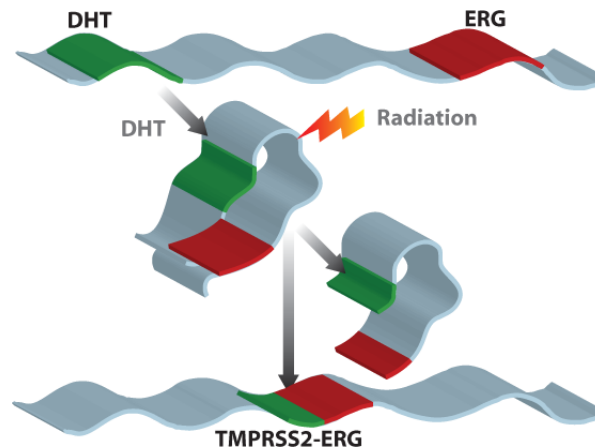


**TATRC Highlighted Research News Article:
“National Functional Genomics Center—A Center for Genetic Origins of Cancer”**

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New Studies Reveal Genetic Changes That Lead to Cancer



A proposed model for the androgen-induced gene movement that creates gene fusions leading to prostate cancer.

Image courtesy of Michigan Center for Translational Pathology

In 2005, University of Michigan medical researchers made the groundbreaking discovery that mutant fused genes play a role in many common cancers.

Fused genes form when chromosomes (the structures that carry a cell’s genetic information) rearrange and bring two genes into proximity that shouldn’t be together. The DNA in the genes merges and causes problems by activating certain proteins.

Finding recurrent gene fusions for a specific type of cancer brings researchers closer to making a specific test for that cancer and offering novel ways to treat it—perhaps even personalized drugs with fewer side effects.

The Michigan group recently identified an influential gene fusion in lung cancer. They also recreated gene fusions in the laboratory that explain how prostate cancer may be triggered.

Their work is part of the new National Functional Genomics Center established last year with DoD support at the University of Michigan Comprehensive Cancer Center. Dr. Max Wicha is the principal investigator. He leads research efforts along with Dr. Eric Fearon and Dr. Arul Chinnaiyan.

Military members may face increased risk of certain cancers due to occupational exposures. Says Fearon, “We hope our work will lead to greatly improved cancer prevention and therapy for members of the armed forces.”

The team reported in the journal *Nature Biotechnology* in November that their new analysis method identified a gene fusion that causes proliferation of certain types of lung cancer cells.

Cancer chromosomes contain many mutant gene fusions, but not all of these fusions actually drive the disease. The group developed a mathematical algorithm (the concept signature or “ConSig” score) that can be applied to high-throughput gene sequencing data to determine which fusions are important. They tested one of the identified fusions and found that “shutting off” that gene did, indeed, slow cancer growth.

Chinnaiyan says that several different fusions could be responsible for lung cancer, the leading cause of cancer deaths in the United States. “A gene fusion-based test might help define molecular subtypes that may be treated differently.”

The team reported their most recent prostate cancer findings October 29 in *Science Express* online. They demonstrated that environmental damage in the presence of the male hormone androgen can trigger a gene fusion that leads to prostate cancer.

The researchers examined a particular fusion that is present in half of human prostate cancers. They took cancer cells without this driving fusion, exposed them to androgen and found that two pieces of chromosome relocated near each other. When the group then applied radiation, the pieces fused. The team concluded that gene fusion is not a chance event, but a two-step process.

According to Chinnaiyan, the group could have a gene-fusion-based urine test for prostate cancer by late 2010. He notes that the test would be more specific than the one that is currently used. “It will tell us who has the more aggressive forms of prostate cancer.”

The Michigan NFGC is investigating breast, colon, lung, pancreas, prostate and ovarian cancer. Several projects are managed by the U.S. Army Medical Research and Materiel Command’s Telemedicine and Advanced Technology Research Center.

Says Chinnaiyan, “TATRC support has allowed us to pursue high-risk projects in new cancers and new technologies that are extremely costly but shed light on the origin of cancer.”

TATRC Director Col. Karl Friedl says, “These researchers have shifted the cancer paradigm with their discovery that gene fusion is not limited to blood cancers and that it can be related to androgen. Their science is outstanding and will help the military in our goal of moving to more effective, individualized medicine.”