

New Cell Labeling Technique May Help Detect and Treat Prostate Cancer

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Prostate cancer is the most common non-skin cancer in America, affecting 1 in 6 men (for more information visit the [Prostate Cancer Foundation](#) website). As with any illness, early detection of the disease is important for disease control by therapeutic intervention. A common chromosomal rearrangement in prostate cancers involves the fusion of the *TMPRSS2* gene to the *ERG* oncogene, both genes located in close proximity on chromosome 21. This genomic alteration results in the deletion of intervening genomic sequences and leads to increased ERG expression, disrupting androgen receptor signaling to promote disease progression.

Several fluorescence *in situ* hybridization (FISH) techniques have been previously developed to investigate *TRMPRSS2/ERG* rearrangements with relatively low resolution. For instance, a dual-color FISH assay can detect chromosome changes at the *ERG* gene but cannot ascertain whether a fusion event of *ERG* to *TRMPRSS2* or any other gene has occurred. To overcome this weakness in identifying *ERG* or *TRMPRSS2* rearrangements, the Fang Lab at Seattle Cancer Care Alliance and Nelson Lab in the Division of Human Biology at the Hutchinson Center developed a FISH assay that can detect a variety of *TRMPRSS2/ERG* rearrangements in prostate cancer cells.

The researchers developed four color-distinct probes, two of which label the 5' and 3' ends of the *TMPRSS2* gene and the other two label the 5' and 3' region of the *ERG* gene. They used these probes to stain normal and prostate cancer cells to analyze the different genomic rearrangements that occurred with the *TMPRSS2* and *ERG* genes. In normal cells, all four probes recognize the intact chromosome and produce a cluster of four-colored signals. In prostate tumors, a common gene fusion event involves the fusion of the 5' region of *TMPRSS2* with the 3' region of *ERG*. The intervening chromosomal sequences can become deleted or translocated to a different chromosome. Indeed, 50% of the scored prostate tumors showed this common *TRMPRSS2/ERG* fusion, as indicated by the loss of hybridization of two of the probes due to chromosomal deletion. The four-colored FISH assay also efficiently detected other less common *TRMPRSS2/ERG* fusions including dual and multiple-deletion fusions (see figure).

To prove the applicability of their novel FISH assay to detect gene fusions in a variety of cells, the researchers stained prostate cell lines, and also primary and metastatic prostate cancer samples.

Indeed, the four-color FISH assay revealed the presence of the *TRMPRSS2/ERG* fusion in ~50% of primary and metastatic prostate cancer samples. More importantly, additional and alternative genetic rearrangements at the *TRMPRSS2* and *ERG* loci were apparent. These alternative rearrangements would have been missed by other FISH-based approaches, highlighting the ability of the FISH approach devised by Qu *et al.* to detect novel genomic alterations within genes that promote prostate cancer progression. The researchers also showed that the *TRMPRSS2/ERG* fusion status identified by their novel FISH assay was consistent with the fusion status defined by two complementary approaches: RT-PCR and Gen-Probe.

In summary, Qu *et al.* have generated a robust, analytically sensitive and highly specific assay to identify typical and atypical *TRMPRSS2/ERG* fusions in prostate cancer cells. This assay will aid in the elucidation of the complex genomic alterations that are involved in prostate cancer pathogenesis and prognosis.

[Qu X, Randhawa G, Friedman C, O'Hara-Larrivee S, Kroeger K, Dumpit R, True L, Vakar-Lopez F, Porter C, Vessella R, Nelson P, Fang M.](#) 2013. A novel four-color fluorescence *in situ* hybridization assay for the detection of *TRMPRSS2* and *ERG* rearrangements in prostate cancer. *Cancer Genet.* Epub ahead of print, doi: 10.1016/j.cancergen.2012.12.004

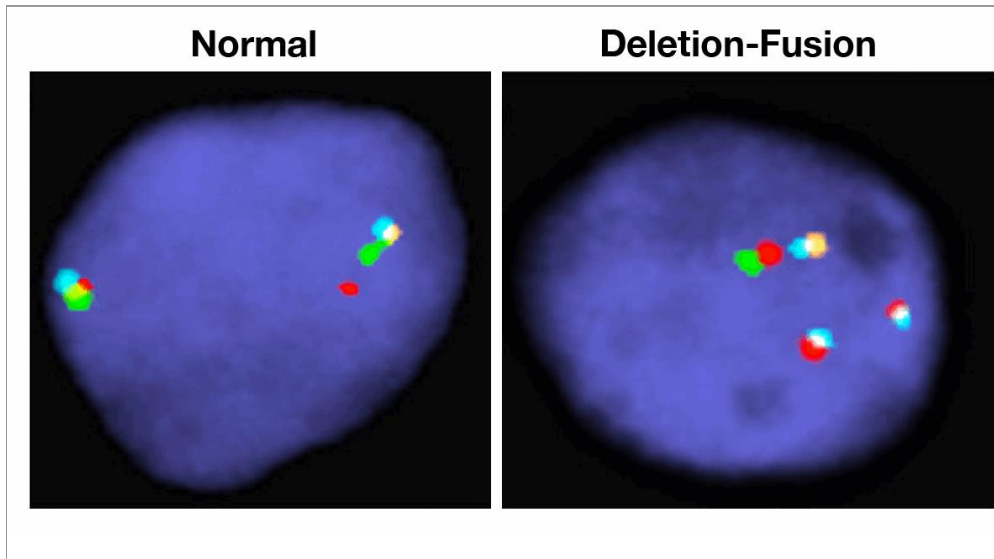


Image modified from the manuscript

An example of the four-color FISH assay after probe hybridization in a normal (left) and prostate tumor cell (right). In the normal cell, all four of the probes (red, yellow, green, and blue) exist within close proximity to one another (in two four-colored foci corresponding to a diploid nucleus) since the probes recognize a distinct chromosomal locus containing two adjacent genes, TRMPRSS2 and ERG. The tumor cell on the right has had two deletion-fusion events at the TRMPRSS2 and ERG loci, as evidenced by two blue/red dimeric probe signals and the loss of the other two-colored signals (lower right side of nucleus).