Researchers from NewYork-Presbyterian Hospital/Weill Cornell Medical Center have discovered a new gene fusion that is highly expressed in a subset of prostate cancers. The results may lead to more accurate prostate cancer testing and new targets for potential treatments. Experts believe that gene fusions -- a hybrid gene formed from two previously separated genes -- may be at the root of what causes cancer cells to grow more quickly than normal cells.

The new findings, published in the August issue of the journal *Neoplasia*, are exciting, because unlike two previous fusions co-discovered by the same Weill Cornell Medical College laboratory group, this fusion, called NDRG1-ERG, produces a protein that may be a potential target for drug therapies.

"The prostate cancer gene fusions, and proteins they produce, are important because they serve as a cancer-specific marker," says Dr. Mark A. Rubin, the Homer T. Hirst Professor of Oncology in Pathology, professor of pathology and laboratory medicine, and vice chair for experimental pathology at Weill Cornell Medical College. "Currently, PSA testing is the standard of care, yet it is not accurate enough to predict prostate cancer, because many men may have an elevated PSA level, but have benign conditions such as inflammation of the prostate."

It is important to distinguish harmful cancer from non-lethal diseases, such as benign prostatic hyperplasia, or enlarged prostate disease that exhibits similar symptoms to prostate cancer, in order to provide
effective care, explains Dr. Rubin. Gen-Probe, a biotechnology
diagnostics company, has licensed this technology and is currently
working with Dr. Rubin, and his collaborator Dr. Arul Chinnaiyan at the
University of Michigan, to develop urine tests to screen for gene fusions
as a means of improving upon the current standard PSA test.

Dr. Rubin, working in collaboration with Dr. Chinnaiyan's group at the
University of Michigan, previously described the discovery of the
TMPRSS2-ERG fusion found in 45 percent of prostate cancers. The
new gene fusion, although only seen in 5 percent of prostate cancers, is
the only one of this fusion class that is predicted to produce a protein.

This fusion protein may be a target for drug therapy and could help
target the other more common gene fusions.

"In the future, these fusions, specific to certain types of prostate cancer,
may help physicians prescribe tailored therapies for their patients by
avoiding the trial and error that is often associated with cancer
treatments," says Dr. Rubin, who is also the associate director of
translational research and a pathologist at the Weill Cornell Cancer
Center at NewYork-Presbyterian Hospital/Weill Cornell Medical Center.

"We believe this is a first step toward providing patients with specific
therapies that target individual cancer variants, and hope these findings
will help doctors diagnose a patient's specific disease," explains Dr.
Rubin.

**Novel Gene Fusion Sheds Light on How Cancer Works**

Unlike most of the gene fusions previously found in prostate cancer, the
two genes, NDRG1 and ERG, likely produce a cancer-specific protein
through genetic rearrangements. This fusion and protein are only found in cancer cells, and not within normal cells. Ongoing work is exploring the potential biologic implications of this discovery. However, the diagnostic implications are more immediate because these types of genetic chimera occur only in cancer.

"We think this type of gene fusion might be a common mechanism in other cancers," Dr. Rubin says. "This expands our understanding of how prostate tumor cells can hijack androgen-regulated genes by using neighboring genes to effectively alter their regulation. This may be a way tumors gain a competitive advantage over normal tissue."

**Novel Technology Employed to Make Discovery**

Dr. Rubin's team used state-of-the-art gene sequencing tools to discover the new class of gene fusion. Using pair-end digital sequencing of messenger RNA -- the message that all cells produce -- the computational team, lead by Dr. Mark Gerstein from Yale University and Andrea Sboner from Weill Cornell Medical College, were able to identify messages that emanated from two separate genes. The approach led to the discovery of the new **gene fusion**. The team is actively working on identifying other novel fusions with this approach, which will be applicable to other tumors as well.

Source: New York- Presbyterian Hospital/Weill Cornell Medical Center/Weill Cornell Medical College
