MicroRNA variations associated with earlier prostate cancer diagnosis in African-American men

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Prostate cancer is the second leading cause of cancer-related death among American men. Yet population-wide screening programs have not reduced the number of deaths from the disease. By focusing screening programs on the men who are at greatest risk for aggressive disease or diagnosis at a young age, researchers think they could improve mortality rates and personalize the screening approach. For that reason, scientists have been looking for genetic markers to help them identify exactly which men are at high risk and require regular screening. Now, Fox Chase Cancer Center researchers have found that two novel genetic markers are associated with earlier time to prostate cancer diagnosis among African American men—and the markers are in a part of the genome that has only recently come under scientific study.

Veda Giri, MD, medical oncologist and director of Prostate Cancer Risk Assessment at Fox Chase, will present the findings at the AACR 102nd Annual Meeting 2011 on Monday, April 4.

Small RNAs, called microRNAs (miRNAs), help regulate gene activity. And expression of these miRNAs can influence an individual's risk of cancer. Knowing this, Giri and her colleagues have been researching genetic variations in miRNA binding sites. In two genes, IL-16 and IL-18, they have now found variations associated with a two-fold or greater increased risk of early prostate cancer diagnosis in African American men who are undergoing screening.

"We have found some preliminary data supporting the idea that genetic variation in miRNA target sites can influence prostate cancer risk," says Giri. "If we confirm these data, then we might be able to use these sites, along with other known genetic variants, to help individualize prostate screening in the future."

Giri notes that although miRNAs were only discovered recently, their role in cancer susceptibility is being rapidly uncovered, probably because they control expression of genes involved in tumor formation, progression, and metastasis. "miRNAs regulate gene expression. If miRNA binding sites are altered then there is a possibility that gene expression would change and could potentially contribute to the cancer process" Giri says.

Giri's team analyzed single nucleotide polymorphisms (SNPs) in miRNA binding sites in four genes of potential importance to prostate cancer risk– ALOX15, IL-16, 1L-18, and RAF1– in approximately 750 men enrolled in the Prostate Cancer Risk Assessment Program at Fox Chase. None of the SNPs were associated with prostate cancer risk in Caucasian men. However, African American men who carried a genetic variant in the miRNA binding site in the IL-16 gene had a 2.27-fold increased risk of early diagnosis, compared with African American men who did not carry the variant. The association was statistically significant (p=0.013).

Additionally, African American men who carried a variant in the miRNA binding site in the IL-18 gene had a 4.44-fold increased risk of early diagnosis, compared with men who did not. Giri cautions, though, that this association had a relatively weak statistical association (p=0.042) and needs to be followed up in a larger study.

"Our goal is to develop individualized prostate cancer screening approaches, particularly for high-risk men," Giri says. "Therefore, our research is focused on identifying which men may develop lethal or

clinically meaningful prostate cancer in order to screen these men for benefit, while sparing other men unnecessary tests and procedures. Down the road, these new markers may help us do that."

Provided by Fox Chase Cancer Center