

News Summary

P3-59: A gene reprogrammed by the hormone estrogen may explain why black men have higher prostate cancer risk than whites

Black men have an increased risk of prostate cancer, and scientists now believe it may be due at least in part to the genes that are epigenetically reprogrammed by excessive exposure to estrogen in the body, possibly occurring early in life. The results of the new study will be presented Friday at The Endocrine Society's 91st Annual Meeting in Washington, D.C.

Estrogen is a key player in about 50 percent of the cases of prostate cancer, according to recent research. Men do not normally produce much of this primarily female hormone, but estrogen levels rise when men age. Also, black men have higher blood levels of estrogen than do white or Mexican-American men at all ages, past research shows.

This lifelong exposure to higher levels of estrogen may be responsible for black men having a 60 percent higher risk of prostate cancer than white men, said the new study's lead author, Wan-ye Tang, PhD, a research scientist in the University of Cincinnati's Department of Environmental Health. Blacks' exposure in the womb to higher levels of maternal estrogen, compared with whites, also may play a role, she said.

"We know very little about how estrogen during early development and adult life could affect prostate cancer risk," Tang said.

In a prior study, Tang and her co-workers found that if they gave newborn male rats estrogen for only 5 days, the animals in adulthood still had a gene called phosphodiesterase type IV variant (PDE4D4) that could be reprogrammed to have abnormal overexpression. They believe that this gene is "imprinted" by estrogen. The cause of this phenomenon, the researchers found in their rodent study, is that the promoter region of the PDE4D4 gene undergoes DNA demethylation. DNA de- or methylation of genes is maintained as a balance for normal development, however, aberrant loss or gain of gene methylation, can cause cancer.

Tang and colleagues, in their new study, compared the methylation status of the human PDE4D4 promoter in normal and cancerous prostate cells in samples obtained from black men and white men. They found that the PDE4D4 promoter in white men had DNA demethylation in prostate cancer cells, compared with normal cells. In black men, however, even normal prostate cells had substantial loss of methylation in the PDE4D4 promoter, the authors reported.

"Our finding suggests that the apparently normal prostate cells in African-American men already show signs of PDE4D4 deregulation, a change observed only in prostate cancer cells in white men," Tang said. "Therefore, this change in methylation may be a biomarker signifying a higher risk of prostate cancer."

Unlike gene mutations, which are permanent changes in DNA sequence, the estrogen reprogramming of the PDE4D4 gene via DNA methylation is epigenetic, meaning it is heritable but does not change the entire DNA sequence and thus is potentially reversible, according to Tang. "It may be possible to prevent prostate cancer by reversing PDE4D4 expression with gene therapy," she said.

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