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Estrogen May Explain the Higher PCa Risk in Blacks

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WASHINGTON, D.C.—African-American men are at higher risk for prostate cancer than [white men](#), a disparity that may be due at least in part to a [gene](#) that is reprogrammed by excessive exposure to estrogen, according to researchers at the [University of Cincinnati](#).

Recent data suggest that estrogen plays a major role in about 50% of all cases of [prostate cancer](#). Although men do not normally produce much estrogen, the levels of this hormone rise as men age. Studies also suggest that [African-American men](#) have higher blood levels of estrogen than do Caucasians men at all ages.

A research team led by Shuk-mei Ho, PhD, Chair of the university's Department of Environmental Health, now have evidence that this lifelong exposure to higher levels of estrogen may be responsible for a 60% greater risk of prostate cancer in African-American men compared with white men. African Americans also may be exposed to higher levels of maternal estrogen in the womb than whites, and this could contribute to the greater risk of prostate cancer, she said.

“We know very little about how estrogen during early development and adult life could affect prostate cancer risk,” said co-investigator Winnie Wan-ye Tang, PhD, a research scientist. “Now we have found that estrogen can sometimes reprogram the epigenome and cause prostate cancer later on in life.”

Dr. Tang reported study findings here at the Endocrine Society's Annual Meeting. The research team also included Patricia Revelo, MD, and Linda Levin, PhD.

In a prior study, Dr. Tang and collaborators found that if they gave newborn male rats estrogen for only five days, the animals in adulthood still had a gene, PDE4D4, which could be reprogrammed to have abnormal overexpression. They believe that this gene is “reprogrammed” by estrogen. This “estrogen reprogramming” is caused by DNA demethylation in the promoter region of the PDE4D4.

In their new study, Dr. Tang and her team compared the methylation status of the human PDE4D4 promoter in normal and cancerous prostate cancer cells obtained from black men and white men. The PDE4D4 promoter in white men had DNA demethylation in prostate cancer cells but not in normal prostate cells. In black men, even normal prostate cells had substantial demethylation in the PDE4D4 promoter, perhaps setting a stage for earlier neoplastic transformation.

“Our finding suggests that the apparently normal prostate cells in African-American men already show signs of PDE4D4 demethylation, a change observed only in prostate cancer cells in white and black men,” Dr. Tang said. “Therefore, this change in methylation may be an early predictor 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 DNA sequence and thus is potentially reversible. “It may be possible to prevent prostate cancer by reversing PDE4D4 expression with countermeasures and life style changes that can modulate epigenetic changes on its promoter,” Dr. Tang explained.

As a result of the new findings, Dr. Tang said, urologists can tell their African-American patients why their risk for the disease is higher and how these findings may lead to important new therapies.

- By John Schieszer | renalandurologynews.com