

Gene variations that alter key enzyme linked to prostate cancer

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Researchers at the National Institutes of Health have found that variations in a gene for an enzyme involved in cell energy metabolism appear to increase the risk for prostate cancer.

The genetic variations all impair the enzyme phosphodiesterase 11A (PDE11A), which helps regulate a cell's responses to hormones and other signals. Previous studies by NIH researchers have linked genetic variations that inactivate PDE11A with increased susceptibility to testicular cancer and adrenal tumors

The researchers found that a group of men with <u>prostate cancer</u> were nearly four times more likely to have variations affecting the activity of PDE11A than did men who did not have prostate cancer. In 2010, it is estimated that there will be 217,730 new cases of <u>prostate cancer</u>, and 32,050 deaths.

"Our study indicates that PDE11A one day may have a place in <u>genetic</u> <u>screening</u> for predisposition to prostate cancer," said the senior author of the study, Constantine Stratakis, M.D., D.Sc., acting director of the Intramural Research program at NIH's Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD).

Dr. Stratakis's research team included colleagues at the NICHD, first author Fabio Rueda Faucz and colleagues from the Pontifical Catholic University of Parana, Brazil; the Cochin Institute in Paris; and A.C. Camargo Hospital in Sao Paulo. The investigators also received support



from the Parana State Secretariat of Science, Technology and Higher Education.

The findings were published online in the <u>Journal of Clinical</u> <u>Endocrinology and Metabolism</u>.

The researchers examined tissue from 50 men with prostate cancer and 287 men who did not have prostate cancer. The researchers analyzed the DNA of the men and found 8 variations in the PDE11A gene that decreased the production or activity of PDE11A. Of the men with prostate cancer, 30 percent had one or more of these variations, compared with 10 percent of the men who did not have prostate cancer. Of the variations the researchers detected, 5 had been detected in previous studies and 3 were previously unknown.

Dr. Stratakis explained that phosphodiesterase enzymes, of which there are nearly a dozen, regulate cellular activity in hormone producing organs such as the testes, prostate gland, adrenal gland and ovaries. PDE11A regulates cyclic adenosine monophosphate, a compound involved in supplying cells with energy.

Tadalafil, a drug used to treat erectile dysfunction, also inhibits PDE11A. The researchers called for future studies to determine if tadalafil or other drugs that inhibit PDE11A might affect the prostate in men who have a variant gene for PDE11A.

There is no current clinical evidence to date linking tadalafil to prostate cancer or to other cancers.

Provided by National Institutes of Health

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