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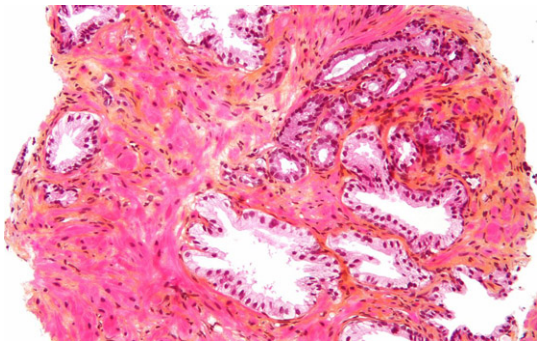
Prostate Cancer and Blood Lipids Share Genetic Links

Based on analyses of genome-wide association studies using novel analytical methods

Numerous studies have suggested a relationship between cardiovascular disease risk factors and prostate cancer. A new study by researchers at the University of California, San Diego School of Medicine, with colleagues in Norway, significantly refines the association, highlighting genetic risk factors associated with low density lipoprotein (LDL) cholesterol and triglycerides as key players and identifying 17 related gene loci that make risk contributions to levels of these blood lipids and to prostate cancer.



Micrograph of normal prostatic glands and those with prostate adenocarcinoma (upper right portion of image).

The findings, published in the April 30, 2014 online issue of the *International Journal of Epidemiology*, provide new insights into the pathobiology of prostate cancer and may point to novel therapies to lower blood lipid levels that might help prevent prostate cancer – the second most common cause of cancer death among American men.

The research team, headed by senior authors Anders M. Dale, PhD, professor in the departments of radiology, neurosciences and psychiatry at the UC San Diego School of Medicine, and Ole Andreassen, professor of psychiatry at Oslo University, applied a genetic epidemiology method to assess statistics from multiple genome-wide association studies, looking for genetic overlap between the phenotypes for prostate cancer and cardiovascular disease (CVD) risk factors. In the case of the latter, they specifically investigated triglycerides, LDL and high density lipoprotein cholesterol, systolic blood pressure, body mass index, waist-hip ratio and type 2 diabetes.

The researchers also examined enrichment of single nucleotide polymorphisms – bits of DNA that vary among individuals – associated with prostate cancer and CVD risk.

LDL cholesterol and triglycerides displayed a strong association with prostate cancer.

“It’s fair to say that risk relationships of various sorts have been proposed between prostate cancer and cardiovascular disease, although not comorbidity per se,” said co-author Ian G. Mills, PhD, of the University of Oslo and Oslo University Hospital in Norway. “There is a lack of consistency across cohorts, however, in size and direction of effects, depending on cardiovascular risk factor considered. The significant risk association with LDL cholesterol and triglycerides versus the other traits at a genetic level was novel and unexpected.”

Mills said the identification of 17 pleiotropic loci – specific sites in the genome which may affect the expression of a number of genes and influence a range of biological pathways, in this case affecting both prostate cancer and cardiovascular disease risk – was a key finding. He said the loci provide clues to the common regulatory elements that affect expression of disease-related genes. They may be incorporated into future disease risk test panels. And they might, ultimately, help shape “genetically stratified dietary or chemoprevention studies repurposing clinically approved drugs that regulate blood lipid levels” to alter the risk of developing prostate cancer, he said.

The current findings were made possible through use of a novel analytical approach developed by researchers at UC San Diego and University of Oslo, which previously had been shown to increase the statistical power for gene discovery in other diseases, including hypertension, neurological diseases, psychiatric disorders and immune-mediated diseases.

Co-authors include Francesco Bettella and Srdjan Djurovic, NORMENT - KG Jebsen Centre for Psychosis Research, Institute of Clinical Medicine, University of Oslo and Oslo University Hospital; Verena Zuber, Centre for Molecular Medicine and NORMENT, University of Oslo; Wesley K. Thompson, UCSD Department of Psychiatry; Andrew J. Schork, UCSD Cognitive Sciences Graduate Program and Center for Human Development; Rahul S. Desikan, UCSD Department of Radiology; the PRACTICAL Consortium and the CRUK GWAS.

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MEDIA CONTACT

Scott LaFee, 858-249-0456, slafee@ucsd.edu

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