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7 in 1 blow: Scientists discover DNA regions influencing prostate cancer risk

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Scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) are taking part in an international research consortium studying the genetic risks for prostate cancer. The consortium, a collaboration of 48 institutes worldwide, has now published its latest results. The researchers have discovered seven DNA regions for which an association with an increased prostate cancer risk has now been established for the first time.

Doctors have known for a long time that prostate cancer "runs in the family". Men with relatives who have been diagnosed with prostate cancer have an elevated risk of also developing this type of cancer. It was only last year that DKFZ scientists calculated that this risk rises with the number of affected direct family members and also depends on the relatives' age at outbreak of the disease.

The exact DNA variants that contribute to prostate cancer risk have now been published by an international research consortium with participation of scientists from the German Cancer Research Center. In a multi-stage study, the collaborators systematically searched the whole genome of cancer patients and healthy controls for specific gene variants. Then they calculated whether specific variants are found more often in patients than in healthy people.

Professor Dr. Hermann Brenner, one of the DKFZ researchers participating in the consortium, explains: "Each of these gene variants taken on its own is associated with only a slight increase in prostate

cancer risk by a few percent. However, by taking account of the different variants at the same time it becomes possible to identify groups of persons who have a significantly elevated risk. Examining the genetic material for such risk variants might therefore improve medical consultation on the prevention and early detection of prostate cancer in the future."

Such DNA variants are scientifically called single nucleotide polymorphisms (SNPs). They are defined as a single variation of a nucleotide which occurs with varying frequency in the whole population. If a relationship in numbers is found between a particular SNP and cancer incidence, researchers conclude that a gene within the affected DNA region plays a role in cancer.

The first two study stages conducted by the consortium had already identified 16 SNPs in 16 different DNA regions to be associated with an elevated prostate cancer risk. Together with the results of prior association studies, about 30 risk genes for prostate cancer were known then. In the third and last round the research consortium searched in 4,574 cancer patients and 4,164 controls for another 1,536 SNPs. The emerging associations with cancer risk were then verified once more using 51,311 DNA samples of cancer patients and healthy men.

Alongside a number of already identified variants, the investigators found seven SNPs that emerged for the first time in association with an elevation in prostate cancer risk. The variants are all located in DNA regions that also contain genes for which the scientists consider it plausible that they play a role in carcinogenesis. However, an association with the malignancy of cancer could not be established for any of these variants. With the seven newly discovered DNA regions, scientists are now able to explain about 25 percent of familial cancer risk.

More information: Zsofia Kote-Jarai et al.: Seven prostate cancer

Susceptibility loci identified by a multi-stage genome-wide association study. *Nature Genetics* 2011, DOI: 10.1038/ng.882