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NEWS

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Multiple, distinct Y chromosomes associated with significant excess risk of prostate cancer, scientists report at ASHG 2013

An analysis of the genealogical and medical records of males in Utah's multi-generational families strongly supports the case that inherited variations in the Y chromosome, the male sex chromosome, play a role in the development of prostate cancer, according to a study presented today (Friday, Oct. 25) at the American Society of Human Genetics 2013 meeting in Boston.

The study identified multiple, distinct Y chromosomes associated with a significant excess risk of prostate cancer, said Lisa Cannon-Albright, Ph.D., Professor and Chief of the Division of Genetic Epidemiology at the University of Utah School of Medicine.

Dr. Cannon-Albright, who headed the study and presented the results today, said that her lab plans to search these Y chromosomes for the genetic mutations that can predispose a man to develop prostate cancer, the second most frequently diagnosed cancer in the U.S.

Because most of the Y chromosome does not recombine during cell division, it is passed virtually unchanged from father to son. "As a result, each male resident of Utah shares the Y chromosome of his father and his father's father and so on," she said. "This provided the ability to estimate the risk for prostate cancer in independent Y chromosomes represented in Utah."

The study relied upon the Utah Population Data Base (UPDB), which identifies over 6.5 million individuals, including many of the Utah pioneers in the 1800s. The pioneer genealogies in the UPDB are typically large, spanning 15 generations. The Utah population represented in the UPDB is genetically representative of Northern Europe. The database was created in the 1970s to define familial clustering and identify evidence for heritable contribution to cancer.

The Y-chromosomes associated with prostate cancer risk were detected through an analysis of male lineage in the computerized genealogical UPDB. Because UPDB is linked to the Utah Cancer Registry, an NCI Surveillance, Epidemiology and End Results (SEER) registry, the researchers were able to identify the men who developed prostate cancer.

The researchers began the study with 1.25 million living and deceased males who had at least 2 parents, 4 grandparents and 6 of 8 great grandparents in the database. All males whose fathers were not identified in the database were labeled as founders. Each founder was then assigned a unique, sequential Y chromosome identification (YID). The founder's sons, his son's sons and so on also were assigned this same YID.

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The YID groups with at least two males sharing the same Y chromosome totaled 257,252. “We effectively identified each independent Y chromosome in the UPDB,” Dr. Cannon-Albright said. Each group of males with the same YID was theorized to share the same Y chromosome since they descended from the same male founder.

The researchers used the Utah cancer registry to estimate specific rates of prostate cancer in the UPDB, by birth year and birth state. To estimate the number of prostate cancer cases expected to occur in each YID group, the researchers applied the results to all males in each group. The researchers compared the observed number of prostate cancers to the expected number of cases.

Dr. Cannon-Albright and her team focused on the 1,000 YID groups that included the most men. These groups ranged from 167 to 2,264 men. In 73 Y chromosome groups, the prostate cancer incidence was significantly higher ($p<0.05$) than expected, she said.

In one YID group of 9,750 men, the researchers had predicted that 45.6 prostate cancers cases would have occurred. According to the state’s cancer registry, 65 males in the group had been diagnosed with prostate cancer. In another group of 498 men, 26 had prostate cancer. However, 9.5 cases had been predicted for this group, said Dr. Cannon-Albright.

Among the male descendants who did not share the Y chromosome of this founder, 39 men had prostate cancer. The scientists had predicted 36.1, which was not statistically different from the actual rate. These results indicate that grouping males by their Y chromosomes reveals a Y chromosome-linked prostate cancer risk, while no such association was observed among males that do not share a common Y chromosome.

The research of Dr. Cannon-Albright and her colleagues may lead to the identification of specific Y-chromosome variants associated with prostate cancer. These and other variants associated with prostate cancer perhaps will provide the basis of a genetic test that will help to determine a man’s genetic predisposition to the disease. Understanding the genes that increase a male’s genetic risk for prostate cancer also may fuel research to improve the treatment of the cancer.

The scientists’ ASHG abstract is titled, "Identification of Y chromosomes associated with risk for prostate cancer.”

About ASHG
The American Society of Human Genetics is the primary professional membership organization for nearly 8,000 human genetics specialists worldwide. The ASHG Annual Meeting is the world's largest gathering of human genetics professionals and a forum for renowned experts in the field. For more information about ASHG, visit: http://www.ashg.org.