ETHESDA, MD—New knowledge on prostate cancer risk genes and a virus linked to the disease is likely to lead to new ways of stratifying patients by risk group and basing treatment on the level of risk, said speakers here at the Society of Urologic Oncology (SUO) Annual Meeting. The meeting, cosponsored by the National Cancer Institute, was held on the grounds of the National Institutes of Health here.

In the future, if men are found to be at very high risk for prostate cancer, “we may need to do prophylactic prostatectomies,” said Adam S. Kibel, MD, Professor in the Division of Urological Surgery at the University of Washington Medical School, who moderated a session at the meeting on prostate cancer. He compared that possibility with some very high-risk women with BRCA1 and BRCA2 mutations, who today are electing to have prophylactic mastectomies. But, noted Dr. Kibel, prostate cancer patients would have to be very carefully selected, since not all those in a high-risk group will develop the disease.

To date, there are about 16 discovered genetic variants that confer a higher risk for prostate cancer, said William J. Catalona, MD, Medical Director of the Clinical Prostate Cancer Program at the Robert H. Lurie Comprehensive Cancer Center at Northwestern University’s Feinberg School of Medicine.

Chromosome 8q24

Noting that prostate cancer clusters in families but that it is highly unlikely that any one gene causes the disease, Dr. Catalona said there are four significant regions of chromosome 8q24 that have been associated with prostate cancer susceptibility genes. Two of these are more common in African Americans, and
There are many different risk alleles.

In addition to chromosome 8q24, said Dr. Catalona, chromosomes 17q12 and 17q26 have prostate cancer risk alleles. Not all the prostate cancer susceptibility alleles carry the same risk, and, as in breast cancer, high-risk variants appear to be rare.

These can be used for patient profiling to determine risk, and “the more of these risk alleles there are, the higher the risk of prostate cancer,” he said. “The total risk is the product of all the marker risks.

“If we could discover all the [risk] alleles, we could get a risk profile for a patient. We need better genotyping arrays to find the rare variants. What we haven’t yet identified are the genes involved in aggressive disease.”

Dr. Catalona cited a prostate cancer risk test recently made available to physicians by a biopharmaceutical company in Iceland, deCODE genetics, which identifies eight known variants, three on chromosome 8, two on chromosome 17, one on chromosome 2 (in the 2p15 region), one on chromosome 11, and one on the X-chromosome. The test is performed on patient DNA from a cheek swab sent to a CLIA-registered laboratory.

Information from the company notes that based on the assumption that these markers are independent of each other and that the individual risks multiply, the variants in furthering the science of urologic oncology’s highest honor, the M. Thompson 2004-2005 Annual Lecture in Clinical Urology, especially advancement, treatment, and prostate cancer outcomes. At the meeting, he was recognized for his 25 years as an active urologist, and the formation of the new international organization, the International Society of Urological Oncology (ISUO), which he founded in 1982.

“Dr. Catalona, who has performed thousands of prostatectomies, added, “Until we can prevent prostate cancer or cure patients at advanced stages of the disease, the only practical strategy for reducing death rates is early diagnosis and effective treatment.” (Dr. Catalona stated in his SUO faculty disclosure form that he receives research support and honoraria from Beckman Coulter, Inc., a manufacturer of PSA tests.)

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**Huggins Award to Ian Thompson**

Ian M. Thompson, Jr., MD, Professor and Chair of the Department of Urology at the University of Texas Health Science Center at San Antonio, was given the Society of Urologic Oncology’s highest honor, the Huggins Award, in recognition of his “outstanding contributions in furthering the science of urological oncology and furthering patient care for individuals with genitourinary cancer.”

In his award lecture he put in a strong plea for more randomized clinical trials in urologic oncology, especially advanced prostate cancer. Noting that he was a medical resident in 1982, he said, “The treatment today is far different from 1982, and I would contend far superior,” differences that are the result of clinical trial data.

“Make these trials a priority,” he urged his listeners. “Accrue to them.”

“Used to think that if you got one bad gene from your mother and one bad gene from your father, you had a high risk of disease. We now know there are many different risk alleles.”

Dr. Klein, who is studying the new retrovirus is a contributing factor in the development of prostate cancer, XMRV could be not only a biomarker to aid in diagnosis but also a new target for drug treatment or immunotherapy.

Dr. Kibel theorized that the results of such a genetic test might be used to determine when prostate cancer screening should start; men with a high-risk genetic profile might be advised to start screening earlier.

XMRV

In addition to genetic variants that confer a higher risk of prostate cancer, a newly discovered infectious retrovirus may also confer a higher risk of prostate cancer on a subset of males—perhaps 15%, said Eric A. Klein, MD, Vice-Chairman of the Glickman Urological and Kidney Institute at the Cleveland Clinic, who co-discovered XMRV (xenotropic murine leukemia-related virus) with Robert Silverman, PhD, a cancer biologist at Cleveland Clinic’s Lerner Research Institute.

The virus affects only primates and humans, and may possibly be oncogenic, Dr. Klein said. “XMRV very efficiently infects prostate epithelial cells,” and may live in the lower urinary tract.

Two men with prostate cancer have been found to harbor XMRV viral DNA, according to recently published work by Drs. Silverman and Klein—proving that XMRV has infected humans.

Dr. Klein, who is studying the new retrovirus in rhesus monkeys, emphasized that at this point “We are far away from proving that XMRV is oncogenic...Does XMRV cause prostate cancer? We simply can’t answer that.”

If continued research shows that the retrovirus is a contributing factor in the

**We used to think that if you got one bad gene from your mother and one bad gene from your father, you had a high risk of disease. We now know there are many different risk alleles.”**