Washington, DC, May 16, 2010 — Clinicians treating bladder and prostate cancers face significant challenges not only in treating, but also diagnosing these diseases. Diagnostic tests are limited, and, in some cases, the tests’ ability to distinguish indolent vs. aggressive disease is questionable. New research on genetic tests and biomarkers for disease, being presented during the 2011 Annual Meeting of the American Urological Association (AUA), holds the promise for newer, better tests for these cancers. The studies will be presented to the press during a special session on Monday, May 16, 2011 at 1:00 p.m. in the AUA Press Suite. The session will be moderated by AUA Public Media Committee Chair Anthony Y. Smith, MD.

Studies being presented include:

Genetic Risk Variants On 8q24 Associated with Prostate Cancer Aggressiveness (#715): Certain genetic alleles associated with prostate cancer risk may also be connected to aggressive pathology features and may predict higher Gleason-grade disease in some men, according to researchers at Northwestern University. Genotypes for certain previously reported risk alleles were determined for more than 900 men with Gleason 6 prostate cancers who had undergone radical prostatectomy, and authors compared allele frequency for men whose tumors were ultimately upgraded to a pathologic Gleason 7 and those whose final pathologic Gleason was 6. Those with risk alleles on chromosomes 8q24 and 19q13 were 1.7 and 2.7 times more likely to be upgraded in the final pathology tumor specimen, suggesting that certain genotypes may be a strong predictor of aggressive pathology features.

Rational Basis for the Combination of PCA3 and TMPRSS2:ERG Gene Fusion in Prostate Cancer Diagnosis (#1616): According to new data from Radboud University Nijmegen Medical Center in the Netherlands, measuring TMPRSS2:ERG expression in addition to PCA3 may improve the sensitivity and accuracy of the PCA3 test for prostate cancer. Using tissue samples for benign prostatic hyperplasia (48 samples) and prostate cancer (48 samples), as well as normal prostate tissue (32 samples), authors measured PCA3 and TMPRSS2:ERG expression. The PCA3 test had a sensitivity of 84.4 for prostate cancer, but included one false-positive and seven false-negative samples. The TMPRSS2:ERG gene fusion test was positive in 8.3 percent of the BPH samples, 15.6 percent of the normal tissue samples and half the prostate cancer samples. However, combining both tests resulted in the highest sensitivity and diagnostic accuracy. Using TMPRSS2:ERG in addition to PCA3 added only one false positive, and eliminated four of the seven false negatives seen with PCA3 alone.

Genetic Polymorphisms of CYP17A1 May Predict Early Progression after Primary Androgen Deprivation Therapy in Japanese Men with Prostate Cancer (#2289): Certain genetic polymorphic variations may allow physicians to predict a patient’s sensitivity to hormonal therapy to treat prostate cancer, according to new researchers in Japan, who examined a possible correlation between certain single nucleotide polymorphisms (SNPs) from eight genes involved in androgen synthesis and metabolism and a man’s progression to castration-resistant disease. The period from diagnosis to data collection was 43 months. In this study, which included 214 patients, researchers compared the association of genotypes to the efficacy of androgen deprivation therapy, and found that patients with SNP rs6162 on the CYP17A1 gene were more likely to experience cancer progression following androgen deprivation therapy.

A TMPRSS2:ERG Gene Fusion Molecular Urine Assay Correlates with Pathologic Stage and Prostatectomy Gleason Score and is Associated with Biopsy-to-Prostatectomy Gleason Upgrading (#2319): Researchers in Germany and the United States will present data on a new quantitative
TMPRSS2:ERG gene fusion urine assay to predict outcomes in men with prostate cancer scheduled for radical prostatectomy. Researchers obtained urine specimens from men to assess TMPRSS2:ERG levels prior to surgery, and compared these levels with post-surgery pathologic findings. Of the 74 men, 28 had non-organ confined disease, and 69 had a Gleason score of 7 or greater. 21 patients with biopsy Gleason 6 disease were upgraded to a pathologic Gleason grade of 7 or greater. Median TMPRSS2:ERG score was significantly higher in men with non-organ confined disease compared to those who had organ-confined disease (80 vs. 9). Median TMPRSS2:ERG scores for patients with pathological upgrading was 32, compared to 2 for those whose Gleason scores were not upgraded.

Autoantibody Signatures as Biomarkers to Distinguish Prostate Cancer from Benign Prostatic Hyperplasia using a Native Antigen Capture Microarray Platform (#2325): A common criticism of the prostate-specific antigen (PSA) test is its lack of specificity in differentiating between benign prostatic hyperplasia (BPH) and prostate cancer. Through the use of a customized array platform, researchers at Brigham and Women’s Hospital and Northeastern University have identified five autoantibody signatures to specific cancer targets that, when the antigens were combined, were more effective than the PSA test in distinguishing between benign and malignant disease.

Detection and Identification of a miRNA Expression Profile from Cell-Free Urine: Potential Utility in Bladder Cancer (#1362): Micro ribonucleic acid (miRNA) molecules, previously shown to play a key role in tumorigenesis, can play a promising role in diagnosing and treating cancers. Researchers from the Lahey Clinic in Boston examined the role that miRNA might play in diagnosing bladder cancer. Using urine from patients with confirmed bladder cancer and control patients with no history of cancer, authors isolated cell-free RNA from 35 healthy control patients and 142 patients with bladder cancer, and profiled 730 miRNAs. Disease progression correlated with the number of miRNAs expressed, with healthy controls expressing 8 miRNAs and patients with >T2 carcinoma expressing 228 miRNAs. Individual samples revealed an increase with some miRNA as disease progressed, suggesting that miRNA profiling could be of future clinical value in the treatment of bladder cancer.

Pre-Operative Urinary Prostate Cancer Gene 3 (PCA3) is Predicting Pathologically Confirmed Small Volume and Insignificant Prostate Cancer (#187): PCA3 has demonstrated success in identifying patients with prostate cancer; however, new data from the Medical University of Graz in Austria suggests that the test may be a valuable predictor of low-volume disease and may have a future role in managing patients on active surveillance protocols. Using pre-operative PCA3 scores and tumor volume data from 160 patients, authors used logistic regression models to identify endpoints for low-volume disease (less than 0.5 ml) and insignificant disease (using Epstein criteria). Low tumor volume and pathologically insignificant prostate cancer were present in 21.2 percent (n=34) and 10 percent (n=16) of patients. In those patients with low-volume and/or insignificant disease, PCA3 scores were significantly lower.

“The critical piece of the puzzle that is missing right now for treatment of a number of urologic cancers, but particularly for prostate cancer, are biomarkers that can be used to tell us prior to treatment which patients harbor slow growing indolent cancers, which harbor cancers that we might have a shot at curing and which harbor cancers that are so aggressive that they require a systemic approach,” Dr. Smith said.

NOTE TO REPORTERS: Experts are available to discuss this study outside normal briefing times. To arrange an interview with an expert, please contact the AUA Communications Office at the number above or e-mail wisett@AUAnet.org.

About the American Urological Association: Founded in 1902 and headquartered near Baltimore, Maryland, the American Urological Association is the pre-eminent professional organization for urologists, with more than 17,000 members throughout the world. An educational nonprofit organization, the AUA
pursues its mission of fostering the highest standards of urologic care by carrying out a wide variety of programs for members and their patients.

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