Genetic mutations associated with increased PSA and prostate cancer

December 2 2010

Austrian researchers have uncovered mutations throughout the mitochondrial genome that are associated with prostate cancer. An exciting aspect of the study, published by Cell Press on December 2 in the *American Journal of Human Genetics*, is the association of tRNA mutations with elevated levels of prostate-specific antigen (PSA) in Austrian men diagnosed with various stages of prostate cancer.

Prostate cancer is among the most prevalent cancers diagnosed in the United States and Europe. The most common and noninvasive way to detect prostate cancer is to check PSA levels. This is a routine part of men's health checks starting around the age of 50. Elevated PSA levels indicate the possibility of prostate cancer. Prostate biopsies are used for verification of PSA results and cancer diagnosis. Treatment may include surgery, radiation, or chemotherapy. "Identifying genetic variants associated with prostate cancer and its primary biomarker is an exciting accomplishment," says Dr. Anita Kloss-Brandstätter, the lead author of this study.

Recognizing the important role mtDNA mutations have been found to play in development and progression of many types of cancer, Dr. Kloss-Brandstätter and colleagues set out to sequence the entire mitochondrial genome in 30 prostate cancer patients. "The influence of mtDNA on the origin and progression of prostate cancer is still not understood, leaving much to be discovered," says Dr. Kloss-Brandstätter. The group used a high-quality sequencing approach to detect differences in mtDNA sequence between cancerous and noncancerous tissue from the same 30

men. "It is the first study targeting the entire mitochondrial genome in prostate cancer and benign tissue from the same patient with a superior sequencing strategy," notes Dr. Kloss-Brandstätter.

By examining both the frequency and types of somatic mtDNA mutations in prostate cancer patients, Dr. Kloss-Brandstätter and colleagues were able to identify several genetic changes having clinical significance. They suggest that, "sequencing of selected mitochondrial regions will likely result in a mutation spectrum useful for prognosis." Perhaps the most striking finding of the study is the association between somatic tRNA mutations and PSA levels at diagnosis. "Patients with a somatic tRNA mutation had a significantly higher PSA value at diagnosis than did patients without a somatic tRNA mutation," explains Dr. Kloss-Brandstätter. "These findings will potentially help others monitor malignant transformation, tumor progression, and metastasis," she says.

Provided by Cell Press