GENETICS

mtDNA mutations key to prostate cancer development?

New research has found a link between mitochondrial (mt)DNA mutations and increased serum PSA levels in patients with prostate cancer. "To the best of our knowledge, our study was the first to detect a genetic association between somatic mtDNA mutations and a quantitative trait such as PSA levels," says first author Anita Kloss-Brandstätter from Innsbruck Medical University, Austria.

The genetics underlying prostate cancer are complex and incompletely understood. Previous studies have linked mitochondria to carcinogenesis, not least because of their key role in energy production and apoptosis, but also because the mitochondrial genome has a high mutation rate and different populations of mtDNA can exist within a cell or organism (termed heteroplasmy). Moreover, some studies have indicated a role for mtDNA in prostate tumorigenesis.

Kloss-Brandstätter and co-workers set out to clarify the role of mtDNA mutations in prostate cancer. They adopted a stringent sequencing approach that met 'forensic standards' and aimed to minimize sequencing artefacts (which had undermined results from previous studies on mtDNA mutations in tumors). The researchers collected benign and cancerous tissue samples from 30 patients with prostate cancer (all with varying Gleason scores) and sequenced the entire mitochondrial genome (16,569 bp). In 22 of the patients with prostate cancer, 41 somatic mutations (either point or length heteroplasmy) were detected in several genes including those encoding ribosomal RNAs and transfer RNAs; most of the mutations (55.8%) had not been previously detected in human phylogeny and 14% were known to be associated with mitochondrial diseases. Importantly, patients harboring somatic transfer RNA mutations had markedly increased serum levels of PSA (about a twofold increase in PSA level compared with men who did not harbor somatic transfer RNA mutations).

"We want to establish a set of biomarkers for prognosis of prostate cancers," says Kloss-Brandstätter. "We are trying to find a connection between the respiratory functionality and integrity of mitochondria in tumor cells and the occurrence of somatic mutations in the mitochondrial genome." The study authors are also testing the next generation in sequencing technology to increase the sensitivity of their approach and to detect low-level heteroplasmy in tumor cells.

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