Researchers find genetic predictors of fatigue for some prostate cancer patients

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Researchers at Moffitt Cancer Center and the University of South Florida have found that men with prostate cancer who receive androgen deprivation therapy may predictably suffer from fatigue if they have single nucleotide polymorphisms in three pro-inflammatory genes. The discovery highlights the importance of personalized medicine, in which therapies are tailored to a patient's genetic profile.

The study appears in the October issue of *Brain, Behavior, and Immunity*.

"Few studies have examined the role of genes in cancer-related fatigue and none, to our knowledge, have examined genetic variation related to androgen deprivation therapy," said study co-principal investigator Heather S.L. Jim, Ph.D., assistant member of the Health Outcomes and Behavior Program. "We found that prostate cancer patients who carry the variants of the IL6 and TNFA genes and are treated with androgen deprivation therapy are susceptible to heightened fatigue."

Evidence from prostate cancer studies suggests that pro-inflammatory cytokines, which have been linked to fatigue in cancer patients, are influenced by testosterone. At the same time, testosterone inhibits IL6 gene expression. Androgen deprivation therapy restricts testosterone.

"The goal of our study was to examine whether single nucleotide polymorphisms in genes that regulate pro-inflammatory cytokines can predict changes in fatigue in men receiving androgen deprivation

therapy," said co-principal investigator Paul B. Jacobsen, Ph.D., associate center director for Cancer Prevention & Control at Moffitt. "We hypothesized that patients displaying variants at these sites would display greater increases in fatigue following initiation of androgen deprivation therapy."

The researchers found that patients with a greater number of variants reported greater increases in fatigue and of longer duration.

"It is still unclear why IL6 and TNFA genotypes affected some aspects of fatigue but not others," Jim said. "While the single nucleotide polymorphisms found in our study were located in predicted transcription factor binding sites that regulate gene expression, a single gene can have many regulatory sites scattered across the genome."

The authors speculated that new single nucleotide polymorphisms may be uncovered that will help to clarify the mechanisms of inflammatory gene transcription as they relate to fatigue in cancer patients. Preliminary findings from this study "represent an important first step in identifying genetic variation as a predictor of fatigue secondary to androgen deprivation therapy," the researchers concluded.

"Early identification of patients with genetic risk factors can enable clinicians to provide timely interventions, behavioral or pharmacologic, to prevent or reduce fatigue," Jacobsen said. "This goal is consistent with personalized cancer treatment tailored to individual gene profiles to maximize benefit and minimize side effects."

More information: *Brain, Behavior, and Immunity*
www.sciencedirect.com/science/ … ii/S0889159112000657

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