MedicalXpress

deCODE discovers genetic markers that improve the power of PSA testing for detecting prostate cancer

December 15 2010

Scientists from deCODE genetics and academic colleagues from Iceland, the UK, US, Netherlands, Spain and Romania today report the discovery of a set of single-letter variations in the sequence of the human genome (SNPs) that impact individual baseline levels of prostate specific antigen, or PSA. Testing for PSA levels is the most commonly used screening tool for the detection of prostate cancer. A prostate biopsy is routinely recommended for men with PSA above a certain threshold. However, PSA levels can rise for reasons unrelated to prostate cancer and baseline healthy levels vary substantially between individuals, resulting in many men without cancer being biopsied while cancer in others is not detected. The paper published today demonstrates that analysis of four SNPs can be used to derive a personalized PSA threshold that more accurately identifies those men who are more likely to have a positive biopsy and for whom one should therefore be recommended.

"This is straighforward genetics with direct clinical utility. Detected early, prostate cancer can be treated with near total success. The challenge is to more effectively risk stratify the population, identifying and biopsying those at high risk and with aggressive disease while minimizing the number of negative biopsies we perform. And using the genetics we are improving the sensitivity and specificity of PSA testing. Like virtually every protein in the body, PSA levels vary between individuals according to SNPs that regulate gene expression. The SNPs

reported today enable us to personalize PSA thresholds, thereby changing the recommendation on whether to biopsy for a substantial proportion of men. Moreover, the discriminatory power of testing for these SNPs is highest when done in tandem with the SNPs associated directly with risk of the disease measured by our deCODE ProstateCancer™ test. We are working to swiftly incorporate these PSA markers into our testing portfolio," said Kari Stefansson, CEO of deCODE and senior author on the study.

The paper, entitled "Genetic correction of PSA values using sequence variants associated with PSA levels," is published today online in *Science Translational Medicine* at www.ScienceTranslationalMedicine.org and will appear in an upcoming print edition of the journal. The study was conducted in several stages and involved tens of thousands of men with and without prostate cancer. First, more than 300,000 SNPs were analyzed in 16,000 Icelandic men with PSA measurements but who had never been diagnosed with prostate cancer. SNPs that correlated with PSA levels were identified and then validated in a cohort from the UK. These SNPs were then studied in large case-control cohorts from Iceland, the Netherlands, Spain, Romania and the US to establish the association with PSA levels independent of risk of prostate cancer itself. The authors then demonstrated how measuring four SNPs correlated with PSA levels can be used to obtain a personalized threshold for when to biopsy, and that using such thresholds improves the ratio of positive to negative biopsies. The greatest improvement in prediction accuracy was seen when men are tested both for the PSA correction SNPs as well as a panel of prostate cancer risk SNPs detected by the deCODE ProstateCancer™ test.

Provided by deCODE genetics

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