MedicalXpress

New type of biomarker shows promise in improving prostate cancer care

March 5 2015

Many men experience prostate cancer as a curable disease. But in those who recur in the form of metastasis death is inevitable. Pinpointing patients at high risk of relapse is imperative to giving them early treatment options when it's more likely to be effective. Dr. Andrew Hsieh has identified two biomarkers that may improve oncologists' ability to predict which patients' prostate cancer will recur after surgery, long before the development of visible cancer elsewhere in the body. According to Hsieh, "once clinically verified, biomarkers like these have the potential to help clinicians identify patients who are more likely to relapse and therefore may benefit from additional therapy after surgery."

In an upcoming paper in *Oncotarget*, Dr. Hsieh's team showed that the levels of two proteins are closely linked to prostate cancer outcomes. In collaboration with groups at the University of California, San Francisco, and the University of California, Los Angeles, Dr. Hsieh found that patients with higher levels of these two proteins, called YB-1 and MTA1, were much more likely to suffer prostate cancer recurrence and three times as likely to require treatment such as hormone therapy or radiation therapy.

Moreover, adding YB-1 and MTA1 levels to clinical factors currently used to predict prostate cancer recurrence improved their predictive potential.

The search for prognostic biomarkers have primarily focused on changes in DNA and messenger RNA, the intermediate molecule that enables the

genetic message encoded in DNA to be translated into proteins. But Dr. Hsieh suspects that a whole field of potential biomarkers remains little studied: proteins whose levels are altered in the absence of gene mutations or changes in messenger RNA expression. In pursuing this hypothesis as a physician-scientist, Dr. Hsieh is navigating uncharted waters.

Proteins are cells' "work horses," said Dr. Hsieh. They underpin how cells live, behave and die. But the process of producing proteins from RNA messenger molecules "is not static," Dr. Hsieh said. "It's not like a factory that does the same thing every time. There are levels of regulation," and changes in how key proteins are produced, independent of alterations to the proteins' genes or messenger RNA, have been shown to drive cancer. YB-1 and MTA1 are just two of potentially hundreds of such proteins, and would never have been discovered if Dr. Hsieh had not ventured beyond traditional DNA and RNA biomarker discovery techniques.

Dr. Hsieh previously identified YB-1 and MTA1 as potential protein biomarkers in a groundbreaking study conducted at UCSF with Dr. Davide Ruggero, using new technology that measure changes in protein production that occur independently of any changes in mRNA. "This work is the clinical application of that finding," he said.

Hsieh aims to uncover how differences in the levels of specific proteins—without accompanying DNA or RNA changes—can give clues to how cancers develop and potentially recur. Such mechanisms which control these phenomena could also be the target of drugs, currently in development, that block the key steps in which RNA messages are translated into proteins.

The findings not only have the potential to improve care for prostate cancer patients, but strengthen the hypothesis that the control of protein

abundance produces a potentially rich source of biomarkers for many types of cancer. "We have the opportunity to revisit the topic of biomarker discovery in a completely new way," said Dr. Hsieh. "It's great to be working at the forefront of basic research and clinical medicine here at the Hutch."

More information: "YB-1 and MTA1 protein levels and not DNA or mRNA alterations predict for prostate cancer recurrence." *Oncotarget.* January 27, 2015 Accepted: February 03, 2015 Published: March 03, 2015. www.impactjournals.com/oncotar … article&op=view&path%5B%5D=3477

Provided by Fred Hutchinson Cancer Research Center