Game changing diagnostic and prognostic prostate cancer genetic tests revealed

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Researchers at the Kimmel Cancer Center at Jefferson (KCC) have developed potentially game-changing diagnostic and prognostic genetic tests shown to better predict prostate cancer survival outcomes and distinguish clinically-relevant cancers.

The team, led by Richard G. Pestell, M.D., Ph.D., Director of the KCC and the Chair of the Department of Cancer Biology at Thomas Jefferson University, report their preclinical findings from a blinded, retrospective analysis of over 350 patients and mouse study in a recent issue of the journal of Cancer Research.

Using an oncogene-specific prostate cancer molecular signature, the researchers were able to separate out men who died of prostate cancer versus those who lived, and more specifically, identifying men who died on average after 30 months (recurrence free survival). The diagnostic test distinguished patients with clinically relevant prostate cancer from normal prostate in men with elevated prostate-specific antigen (PSA) levels.

The researchers worked with three oncogenes previously associated with poorer outcomes in prostate cancer: c-Myc , Ha-Ras, and v-Src.

The test, the researchers say, is superior to several previously published gene tests and to the Gleason scale, which is a rating given to prostate cancer based upon its microscopic appearance and currently used to help evaluate the prognosis of men with the disease.

Given the diversity of prostate cancer outcomes—some men live two years after diagnosis, others live for more than 20 more years— a new oncogene-specific signature like this could not only help better identify prostate cancer risk but also test targeted therapies—by way of a new prostate cancer cell line.

These studies describe the first isogenic prostate cancer cell lines that metastasize reliably in immune competent mice. Previous studies were in immune deficient mice.

"This oncogene signature shows further value over current biomarkers of prediction and outcomes," said Dr. Pestell. "Such a signature and cell line may also enable the identification of targets for therapies to better treat prostate cancer, which takes the lives of over 27,000 men a year."

In breast cancer, the identification of tumor subsets with various gene signatures has improved clinical care for patients because of targeted therapies.

The work here by the KCC aims to identify gene patterns and subsequent tests in prostate cancer that could serve similar purposes. But to help develop such therapies, model systems that closely resemble human disease are required. To date, there have been several limitations with currently available cell lines.

Although important transplantation experiments have been conducted using human prostate cancer cell lines in immune deficient animals, the immune system plays an important role in prostate cancer onset and progression making it imperative to develop prostate cancer cell lines that can be studied in immune competent animals.

Also, although the transgenic mouse has been an effective model to study the molecular basis of human cancers, the prostate cancer mouse

models have long latency and often unpredictable metastasis.

Here, the researchers succeeded in overcoming these issues.

The oncogene-specific prostate cancer molecular signatures were recapitulated in human prostate cancer and validated in distinct populations of patients as a prognostic and diagnostic test.

What's more, the researchers demonstrated how the isogenic prostate cancer cell lines metastasized in immune-competent mice.

"Identification of gene signatures in breast cancer has allowed for a deeper understanding of the disease, and this paper moves us steps closer to being able to follow a similar trajectory with prostate cancer. Today, such an understanding and a formidable testing ground for new therapies is lacking for this disease," Dr. Pestell said. "With this new oncogene-specific prostate cancer molecular signature, we have a valuable prognostic and diagnostic resource that could help change the way we manage and treat prostate cancer."

More information: cancerres.aacrjournals.org/con … 472.CAN-12-2133.long

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