Team develops prognostic test for E2F4 in breast cancer

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By looking at the expression levels of downstream genes of the regulators in breast cancer, investigators at Dartmouth Hitchcock's Norris Cotton Cancer Center (NCCC), led by Chao Cheng, PhD, have identified a gene signature in E2F4 that is predictive of estrogen receptor positive (ER+) breast cancer. The findings, published in *Breast Cancer Research*, define a new opportunity for personalizing medicine for women whose Oncotype DX assay results classify them as of "intermediate-risk for recurrence." Until now, there has been no standard of care for those with intermediate risk. Results at NCCC support reclassifying 20-30% of those patients as "high-risk for recurrence," indicating they should receive aggressive follow-up treatment.

"Our data-driven approach to designing an effective prognostic genomic signature for E2F4 activity in ER+ breast cancer patients gave us the essential information to develop what will be a simple clinical test to aid physicians in selecting the most effective treatment regimens for each patient," reported Cheng. "Furthermore, our approach is highly flexible, and because of the widespread essentiality of E2F4 in many types of cancer, it will be of great utility in solving many biomedical questions."

With the goal to design an accurate and quick genomic test to measure the activity levels of the regulators associated with E2F4, Cheng's team looked to the aberrant behavior of transcription factors as a way to track and predict the root cause of all cancers - dysregulated gene expression that leads to uncontrollable cell proliferation, tumor genesis, and

ultimately metastases.

The target genes were identified by chromatin immunoprecipitation sequencing (ChIP-seq) and researchers compared the regulatory activity score (RAS) of E2F4 in cancer tissues to determine the correlation with activity and patient survival. The prognostic signature for E2F4 was significantly predictive of patient outcome in breast cancer regardless of treatment status and the states of many other clinical and pathological variables.

Cheng explained the translational use of the E2F4 signature, "By developing a flexible, reproducible, and predictive test, we are providing physicians working in many areas of cancer with the information they need to tailor treatment regimens to specific individual patients. This is the essence of personalized medicine: the right treatment for the right patient at the right time."

The team's next steps include evaluating the prognostic potential of E2F4 in additional breast cancer datasets to validate its broad effectiveness, and improving the signature by reducing it to its core component genes.

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