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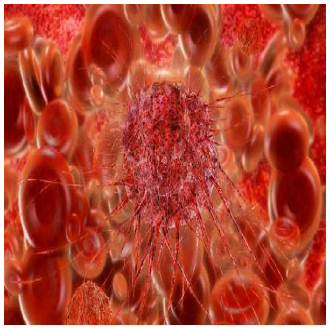
Innovative Prognostic Test for E2F4 in Breast Cancer



Researchers at Dartmouth Hitchcock's Norris Cotton Cancer Center (NCCC) have identified a gene signature in E2F4 that is predictive of oestrogen receptor positive (ER+) breast cancer. With the aim to design an accurate and simple genomic test to measure the activity levels of the regulators associated with E2F4, the investigators looked to the aberrant behaviour 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, tumour 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, the NCCC researchers explained.

The results, published in *Breast Cancer Research*, could help with personalising medicine for women whose Oncotype DX assay results classify them as of "intermediate-risk for recurrence." To date, there has been no standard of care for those with intermediate risk. The new findings support reclassifying 20-30 percent 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," said the study's lead author Chao Cheng, PhD. "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."

Cheng also 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 personalised medicine: the right treatment for the right patient at the right time," said Cheng.

Cheng's team plans to evaluate the prognostic potential of E2F4 in additional breast cancer datasets to validate its broad effectiveness. They hope to improve the signature by reducing it to its core component genes.

The other members of the research team are all from the Geisel School of Medicine at Dartmouth College and affiliated with Dartmouth's Norris Cotton Cancer Center in Lebanon, New Hampshire, USA. The study was supported by the American Cancer Society Research grant IRG-82-003-270, the Centers of Biomedical Research Excellence (COBRE) grant GM103534, and the Geisel School of Medicine at Dartmouth College.

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