Medical Xpress

Big data analysis identifies prognostic RNA markers in a common form of breast cancer

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A Big Data analysis that integrates three large sets of genomic data available through The Cancer Genome Atlas has identified 37 RNA molecules that might predict survival in patients with the most common form of breast cancer.

The study by researchers at the Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James) initially analyzed messenger RNA (mRNA) and microRNA expression, DNA methylation data and clinical findings for 466 patients with invasive ductal carcinoma, the most common type of breast cancer.

The analysis identified 30 mRNAs and seven microRNAs – short snippets of RNA – that were consistently associated with patient outcome across 44 clinical and molecular subclasses, including early-stage tumors. The researchers then validated the prognostic signature using genome-wide expression data from 2,399 breast-cancer patients in eight independent groups and found that it performed better than other RNA signatures currently used for breast-cancer risk stratification.

The findings are published in the *Proceedings of the National Academy of Sciences*.

"This is the first prognostic signature in breast cancer or other type of cancer that combines both mRNA and microRNA," says first author and researcher Dr. Stefan Volinia, associate professor of molecular virology,

immunology and medical genetics at the OSUCCC – James, "and we believe this concise RNA signature could prove useful for the clinical management of breast-cancer patients."

Principal investigator Dr. Carlo M. Croce, professor of [molecular virology](link), immunology and medical genetics, and director of [Human Cancer Genetics](link), notes that most of the genes involved in the RNA signature have not previously been linked to breast cancer and that unlike many other prognostic signatures, this one does not contain genes involved in the cell cycle or tumor grade.

"Most of these prognostic genes are newcomers, and therefore they might represent novel drug targets," says Croce, who is also the John W. Wolfe Chair in Human Cancer Genetics. "They also are novel genes with unknown function and need further study."

He noted that these genes could also be candidates for a blood test for early detection.

Key points related to the study's findings include:

- The identified RNA signature might predict response to treatment, as well as being prognostic;
- [DNA methylation](link) was used to confirm the association between mRNA expression and overall survival;
- The signature includes mutations in PIK3CA and its pathway, indicating that the PIK3CA/AKT2/PTEN axis is an important and independent cofactor in prognosis;
- The prognostic value of the integrated signature was highest in early stage I and II breast cancers, making this a potentially valuable biomarker signature in clinical practice.