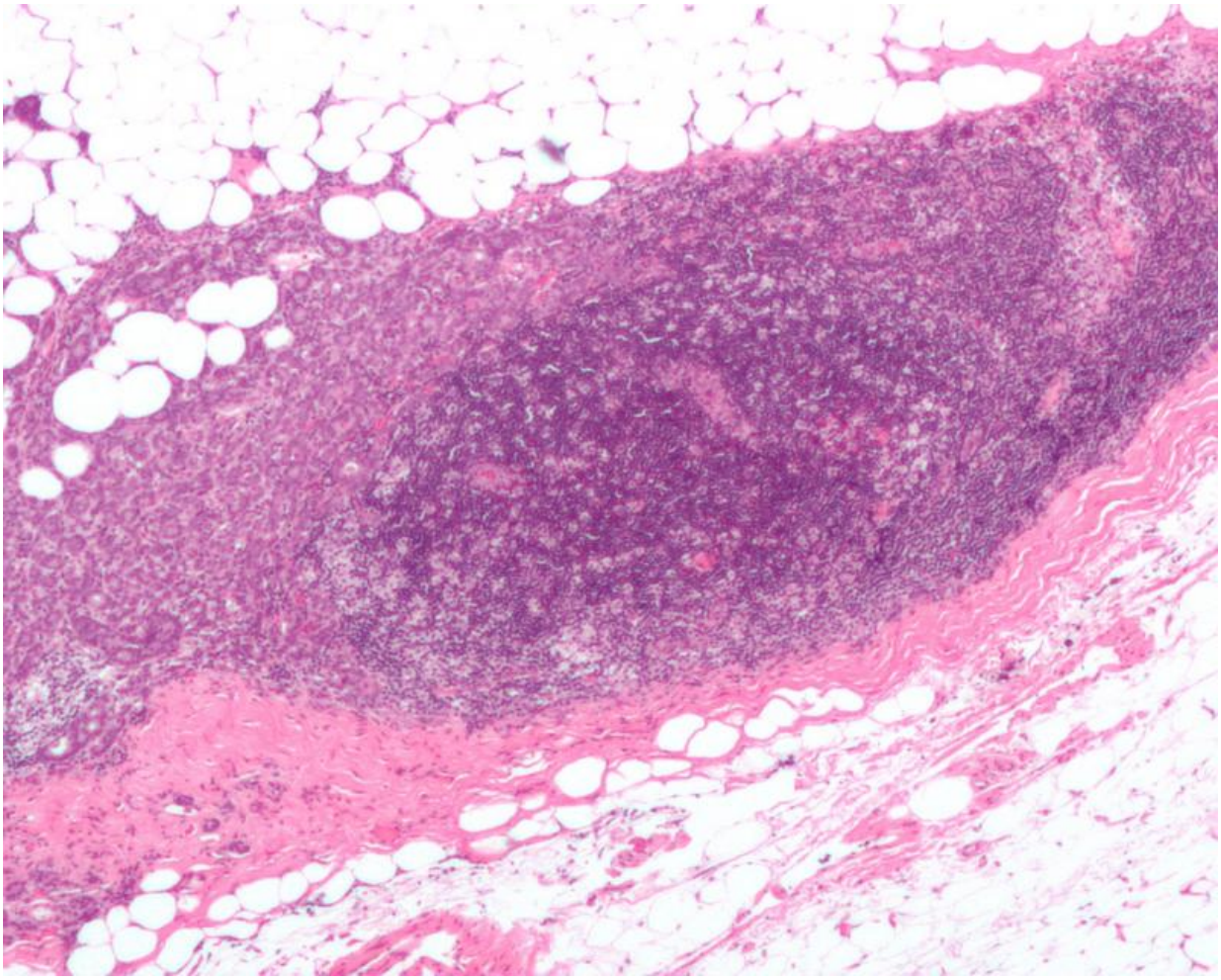
DNA methylation test might predict breast cancer relapse

September 17 2015



Micrograph showing a lymph node invaded by ductal breast carcinoma, with extension of the tumour beyond the lymph node. Credit: Nephron/Wikipedia

Every woman successfully treated for breast cancer lives with the knowledge that it could come back. New research published today in the journal Clinical Epigenetics may lead to a simple blood test to determine the risk of such recurrence, or the cancer invading other organs such as the lungs, bone or brain. Such a test would have profound implications for improving the future treatment of women with all types of breast cancer, a disease that will impact one-in-eight women.

Through the study, researchers at the Translational Genomics Research Institute (TGen) identified 21 DNA hypermethylation hotspots - gene locations along the 3 billion chemical bases of DNA - with increased levels of methylation that could indicate the existence of metastatic breast cancer.

"These findings could lead to a highly sensitive blood-based test panel - a type of liquid biopsy - which could help improve the care of women with breast cancer," said Dr. Bodour Salhia, an Assistant Professor in TGen's Integrated Cancer Genomics Division, and the study's senior author.

"This 21-gene signature is a potential biomarker that could indicate patients who are at high risk of cancer recurrence, either in the breast or elsewhere in the body, and who might benefit from additional therapy to eliminate the potential of recurrence," Dr. Salhia said. "This would be critically important information for oncologists as they consider ongoing treatments post surgery and/or the completion of each round of chemotherapy."

Biomarkers are indicator molecules, such as proteins or DNA, that are measurable in blood, body fluids or tissue samples and can be used to diagnose or measure a particular disease or the effects of a given treatment.

Using whole-genome sequencing, researchers looked for biomarkers in

the cell-free strands of DNA (cfDNA) circulating in pooled samples of blood from 40 metastatic breast cancer patients, and compared them to samples from 40 healthy individuals and 40 disease-free breast cancer survivors.

The findings offered insights that suggest despite the huge quantity of information gleaned from other gene signatures currently available, none can precisely predict the clinical course of an individual, and they rely on the presence of tissue at a single time point. There are patients deemed high-risk who do very well with standard therapy and never experience a recurrence, and patients with low-risk profiles who succumb to the disease.

In contrast, the TGen study identified 21 genes that were "differentially methylated" - meaning they could have altered levels of methylation - all of which were consistently higher in patients with metastatic breast cancer when compared to the levels in healthy individuals and cancer-free survivors.

"This study is one of the first whole-genome descriptions of methylation in blood, and the first unbiased study reporting on the circulating methylome of metastatic breast cancer," said Dr. Salhia. "There is likely a predictive clinical window of opportunity to detect microscopic disease before the cancer spreads throughout the body."

The next step would be to further validate the results using individual samples.

More information: "Whole-genome bisulfite sequencing of cell-free DNA identifies signature associated with metastatic breast cancer." *Clinical Epigenetics* 2015, 7:100 DOI: 10.1186/s13148-015-0135-8