Stem cell-based test predicts leukemia patients' response to therapy to tailor treatment

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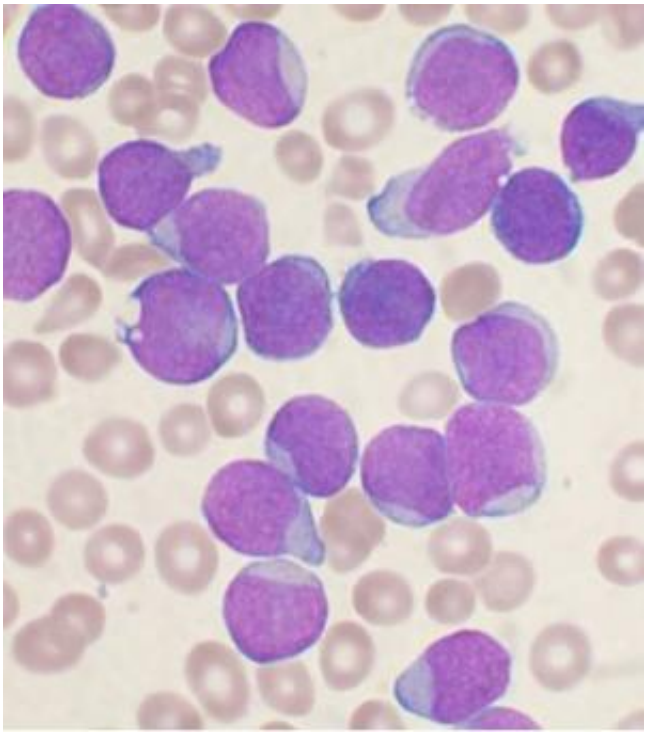

A Wright's stained bone marrow aspirate smear from a patient with precursor B-cell acute lymphoblastic leukemia. Credit: VashiDonsk/Wikipedia

Leukemia researchers at Princess Margaret Cancer Centre have developed a 17-gene signature derived from leukemia stem cells that can predict at diagnosis if patients with acute myeloid leukemia (AML) will respond to standard treatment.

The findings, published online today in *Nature*, could potentially transform patient care in AML by giving clinicians a risk scoring tool that within a day or two of diagnosis can predict individual response and help guide treatment decisions, says co-principal investigator Dr. Jean Wang, Affiliate Scientist at the Princess Margaret, University Health Network (UHN). Dr. Wang is also an Assistant Professor, Faculty of Medicine, University of Toronto and a Hematologist at Toronto General Hospital, UHN.

The new biomarker is named the LSC17 score as it comes from the leukemia stem cells that drive disease and relapse. These dormant stem cells have properties that allow them to resist standard chemotherapy, which is designed to defeat rapidly dividing cancer cells. The persistence of these stem cells is the reason the cancer comes back in patients despite being in remission following treatment. AML is one of the most deadly types of leukemia and the most common type of acute leukemia in adults; it increases in frequency as we age. In Canada, there are more than 1,200 new cases each year. The five-year survival ranges between 20% - 30% and is lower in older people.

The study authors write that using the LSC17 score to single out high-risk patients predicted to have resistant disease "provides clinicians with a rapid and powerful tool to identify AML patients who are less likely to be cured by standard therapy and who could be enrolled in trials evaluating novel upfront or post-remission strategies."

The researchers identified the LSC17 score by sampling the leukemia stem cell properties of blood or bone marrow samples from 78 AML patients from the cancer centre combined with molecular profiling technology that measures gene expression. Stanley W. K. Ng, a senior PhD candidate in the lab of Dr. Peter Zandstra at the Institute for Biomaterials and Biomedical Engineering, University of Toronto and co-lead author of the paper, used rigorous statistical approaches to develop

and test the new "stemness score", using AML patient data provided by the Princess Margaret leukemia clinic and collaborators in the United States and Europe.

"We identified the minimal set of genes that were most critical for predicting survival in these other groups of AML patients, regardless of where they were treated. With this core 17-gene score, we have shown we can rapidly measure risk in newly diagnosed AML patients," says Dr. Wang.

In the study, analysis of patient samples demonstrated that high LSC17 scores meant poor outcomes with current standard treatment, even for patients who had undergone allogeneic stem cell transplantation. A low score indicated a patient would respond well to standard treatment and have a long-term remission.

The test to measure the LSC17 score has been adapted to a technology platform called NanoString. As the research team and international collaborators continue to validate the stemness risk score, plans are under way to test the score in a clinical trial at the Princess Margaret, which now has the NanoString system in its molecular diagnostic laboratory.

Dr. Wang explains that the fast turnaround time to measure the LSC17 score on the NanoString system will be key to moving the test into the clinic.

"The LSC17 score is the most powerful predictive and prognostic biomarker currently available for AML, and is the first stem cell-based biomarker developed in this way for any human cancer," says Dr. Wang. "Clinicians will now have a tool that they can use upfront to tailor treatment to risk in AML."

More information: A 17-gene stemness score for rapid determination of risk in acute leukaemia, nature.com/articles/doi:10.1038/nature20598

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