Clinical importance of leukemia stem cells validated

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Cancer scientists have long debated whether all cells within a tumour are equal or whether some cancer cells are more potent - a question that has been highly investigated in experimental models in the last decade. Research published today in *Nature Medicine* focuses on patients and shows that acute myeloid leukemia (AML) contains rare cells with stem cell properties, called leukemia stem cells (LSC), that are better at predicting clinical outcome than the majority of AML cells, showing for the first time that LSCs are significant not just in experimental models but also in patients.

"Even though LSCs are like a needle in a haystack, their unique properties influence whether AML will respond to therapy or whether the disease comes back. This means that future efforts to prevent the disease from recurring and improving overall patient survival must consider ways to target LSCs to ensure they are killed," says principal investigator John Dick, who holds a Canada Research Chair in Stem Cell Biology and is a Senior Scientist at the McEwen Centre for Regenerative Medicine and the Ontario Cancer Institute, Princess Margaret Hospital. Dr. Dick pioneered the cancer stem cell field by identifying leukemia stem cells in 1994 and colon cancer stem cells in 2007.

By sorting, analyzing and comparing healthy stem cells, leukemia stem cells and clinical data, Dr. Dick's international research team uncovered a set of genes, or signature, that was common to both normal and LSCs and showed that the set could accurately predict the course of disease in the patients studied. Patients that strongly expressed the stem cell

signature had much shorter survival than those patients that had low expression of the signature. The research team included post-doctoral fellows Kolja Eppert, Eric Lechman and Katsuto Takenaka and PhD student Peter van Galen.

The genes within the stem cell signature provide new drug targets that could be used to eliminate LSCs. These genes also represent potential AML biomarkers that could be used to identify those patients that might benefit from more aggressive therapy. In the long term, this information could be used to personalize cancer therapy and get the right drug to the right patient, as opposed to a "one-size-fits-all" approach of treating groups of patients identically.

"Although our research was on AML, our findings that LSCs are real and relevant in patients set the entire cancer stem cell field on a firmer footing. Our approach could be used as a template to test the clinical importance of cancer stem cells from solid tumors and other forms of leukemia," says Dr. Dick, who works out of UHN's Ontario Cancer Institute - where stem-cell science began 50 years ago - and alongside this generation's other leading stem-cell scientists at the McEwen Centre for Regenerative Medicine.

Dr. Dick recently isolated normal human blood stem cells and developed the first means to collect them in large quantities. As well as being a Senior Scientist at UHN's Princess Margaret and Toronto General Hospitals, he is a Professor in the Department of Molecular Genetics, University of Toronto, and Director of the Cancer Stem Cell Program at the Ontario Institute for Cancer Research.

More information: Paper: DOI:10.1038/nm.2415

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