Stem cell scientists discover genetic switch to increase supply of stem cells from cord blood

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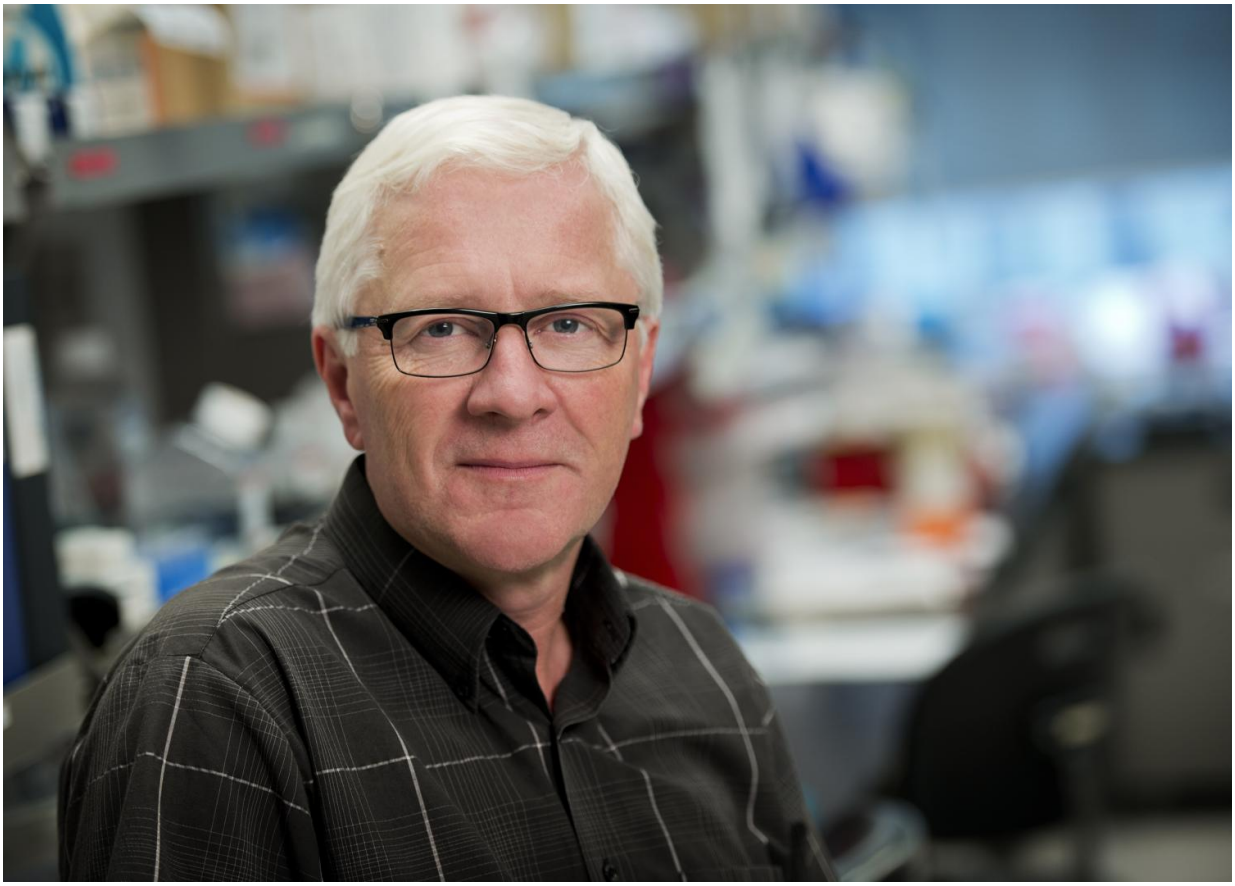

Dr. John Dick, Senior Scientist, Princess Margaret Cancer Centre. Credit: UHN

International stem cell scientists, co-led in Canada by Dr. John Dick and in the Netherlands by Dr. Gerald de Haan, have discovered the switch to

harness the power of cord blood and potentially increase the supply of stem cells for cancer patients needing transplantation therapy to fight their disease.

The proof-of-concept findings, published online today in *Cell Stem Cell* provide a viable new approach to making more stem cells from cord blood, which is available through public cord blood banking, says co-principal investigator John Dick, Senior Scientist, Princess Margaret Cancer Centre, University Health Network (UHN). Dr. Dick is also Professor, Department of Molecular Genetics, University of Toronto, and holds a Canada Research Chair in Stem Cell Biology. The co-principal investigator was stem cell scientist Gerald de Haan, Scientific Co-Director, European Institute for the Biology of Ageing, University Medical Centre Groningen, the Netherlands.

"Stem cells are rare in cord blood and often there are not enough present in a typical collection to be useful for human transplantation. The goal is to find ways to make more of them and enable more patients to make use of blood stem cell therapy," says Dr. Dick. "Our discovery shows a method that could be harnessed over the long term into a clinical therapy and we could take advantage of cord blood being collected in various public banks that are now growing across the country."

Currently, patients needing stem cell transplants are matched to an adult donor with a compatible immune system through international registry services. But worldwide, many thousands of patients are unable to get stem cell transplants needed to combat blood cancers such as leukemia because there is no donor match.

"About 40,000 people receive stem cell transplants each year, but that represents only about one-third of the patients who require this therapy," says Dr. Dick. "That's why there is a big push in research to explore cord blood as a source because it is readily available and increases the

opportunity to find tissue matches. The key is to expand stem cells from cord blood to make many more samples available to meet this need. And we're making progress."

Although there is much research into expanding the rare stem cells present in cord blood, the Dick-de Haan teams took a different approach. When a stem cell divides it makes a lot of progenitor cells immediately downstream that retain key properties of being able to develop into every one of the 10 mature blood cell types, but they have lost the critical ability to self-renew (keeping on replenishing the stem cell pool) that all true stem cells possess.

In the lab, analysing murine and human models of blood development, the teams discovered that microRNA (mirR-125a) is a genetic switch that is normally on in stem cells and controls self-renewal; this normally gets turned off in the progenitor cells.

"Our work shows that if we artificially throw the switch on in those downstream cells, we can endow them with stemness and they basically become stem cells and can be maintained over the long term," says Dr. Dick.

In 2011, Dr. Dick isolated a human blood stem cell in its purest form - as a single stem cell capable of regenerating the entire blood system, providing a more detailed road map of the human blood development system, and opening the door to capturing the power of these life-producing cells to treat cancer and other debilitating diseases more effectively.

Dr. Dick is also Senior Scientist at the McEwen Centre for Regenerative Medicine (UHN) and Director of the Cancer Stem Cell Program at the Ontario Institute for Cancer Research.

Stem cells were first discovered in Toronto in 1961 at the Princess Margaret by Drs. James Till and the late Ernest McCulloch - a discovery that launched a new field of science and formed the basis of all stem cell research that continues to this day.

More information: *Cell Stem Cell*, DOI: 10.1016/j.stem.2016.06.008

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