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New research identifies five genetic themes crucial to keeping stem cells in a primitive, flexible state

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For more than 25 years, stem cells have been defined based on what they can become: more of themselves, as well as multiple different specialized cell types. But as genetic techniques have become increasingly powerful, many scientists have sought a more molecular definition of stem cells, based on the genes they express.

Now, a team of Canadian scientists has identified 1,155 genes under the control of a gene called Oct4, considered to be the master regulator of the stem cell state. A comprehensive molecular definition of stem cells is emerging: according to this research, stem cells are cells that keep their DNA packaged in a flexible format, keep cell division tightly controlled, prevent signals that might trigger death, repair DNA very effectively, and reinforce all of these characteristics by tightly controlling how molecules can move within the nucleus. The study will be published in the June 20, 2007 edition of *PLoS ONE*.

"You could call this a 'theory-of-everything' for stem cells," said senior author Dr. Michael Rudnicki, referring to the often-cited theory of everything for physics. Dr. Rudnicki is a Senior Scientist and Professor at the Ottawa Health Research Institute and the University of Ottawa. He also leads the Sprott Centre for Stem Cell Research in Ottawa and Canada's Stem Cell Network.

While previous studies have tried to compare gene expression in different types of stem cells, the strategy used in this study was unique. Rather than simply searching for any genes expressed by stem cells, the researchers looked for genes whose expression was also correlated with the master stem cell regulator gene Oct4. They also applied very rigorous analysis methods, using data from StemBase, the largest stem cell gene expression database in the world. Designed by bioinformaticist Dr. Miguel Andrade, the database includes data from thousands of DNA microarrays submitted mainly by scientists in Canada's Stem Cell Network. All data is freely available at www.stembase.ca.

Lead author Ms. Pearl Campbell noted that understanding how stem cells maintain their identity is key to the emerging field of regenerative medicine. "These findings may help us to understand how the key genes which control cell fate are regulated, and how, when dysregulated, they can lead to disease. This may ultimately allow us to develop targeted therapies to stimulate adult stem cells within our own bodies to repair damaged tissues, and may provide further areas of exploration for the treatment of cancer."

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