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Breaking News on Drug Discovery

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'Theory of Everything' for stem cells

By Mike Nagle

20/06/2007- **A team of Canadian scientists have identified which genes help decide a stem cell's fate; a discovery that one day could lead to drugs that invoke their regenerative power.**

Oct4 is a POU transcription factor protein; it promotes the transcription of a gene's DNA into messenger RNA. This particular protein is considered to be the master regulator of the stem cell state: it is thought to control what stem cells become, adult stem cell identity and has also been implicated in diseases such as cancer. However, until now, the molecular mechanism of how it does this was poorly understood.

The researchers at the Sprott Centre for Stem Cell Research in Ottawa and Ottawa University found that 1,155 genes are under the control of Oct4. Currently stem cells are commonly defined based on what they will become. However, this research adds to the emerging molecular definition of stem cells; knowledge that will enable scientists to begin designing therapies to control these cells and their ability to regenerate tissue.

"You could call this a 'theory-of-everything' for stem cells," said one of the team, Dr Michael Rudnicki, referring to the often-cited unifying theory of everything for physics.

The study, outlined in today's online issue of the journal PloS One, took a unique approach to identifying the genes. Typically, scientists have measured which genes are switched on in one type of stem cell and then compared this with gene expression in another type of stem cell. In this way, they can see which genes decide the fate of a particular type of stem cell.

However, rather than simply searching for any genes expressed by stem cells, the Canadian scientists decided to look for genes whose expression was also correlated with Oct4. They did this using gene expression profiling coupled with statistical analysis.

The analysis used 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.

The team detected several new ways that Oct4 may regulate stem cell identity: these include regulating chromatin structure (the complex of DNA and proteins that make up chromosomes) to enable stem cells to self-renew and turn into other cell types; and helping activate genes that keep the stem cell ready to respond to signals and differentiate into other cell types.

According to this research, stem cells can be defined as 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.

"These findings may help us to understand how the key genes which control cell fate are regulated, and how, when regulated improperly, they can lead to disease," said another of the scientists, Pearl Campbell.

"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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