

Study of 'sister' stem cells uncovers new cancer clue

September 26 2013

Scientists have used a brand new technique for examining individual stem cells to uncover dramatic differences in the gene expression levels – which genes are turned 'up' or 'down' – between apparently identical 'sister' pairs.

The research, published today in *Stem Cell Reports*, was conducted and funded by The Institute of Cancer Research, London. It provides the latest evidence that despite having identical DNA, sister stem cells can display considerable differences in their [molecular characteristics](#).

The study showed that DNA methylation, a process that controls which [genes](#) are expressed in cells, plays an important role in generating non-genetic (or 'epigenetic') differences between sister cells.

DNA methylation could therefore be one of the reasons for the major molecular variation between different [cancer](#) cells in the same [tumour](#) – and drugs to reduce methylation might help control variation and make cancers easier to treat.

In the new research, scientists at The Institute of Cancer Research (ICR) developed a novel micro-dissection technique to separate pairs of sister [embryonic stem cells](#) for single cell RNA analysis [1].

Using their new high-tech method, researchers separated and isolated mouse stem cells from their sister pairs and measured the behaviour of key genes known to be expressed in those cells. By comparing which of

these genes were up – or down – regulated, they determined the levels of similarity between sister cells at the molecular level for the first time.

They found that under normal conditions, pairs of sister stem cells displayed considerable differences to each other, showing nearly as much diversity as two cells from different sister pairs.

The researchers then looked at cells grown in the presence of a chemical cocktail called 2i, which reverts cells back to their most primitive stem cell state where they can make identical copies of themselves. They found that the cells had reduced levels of two enzymes critical for DNA methylation and they produced more similar sister cells.

The results suggest that DNA methylation is a major cause of the diversity between sister cells when they divide.

Dr Tomoyuki Sawado, leader of the Stem Cells and Chromatin Team at The Institute of Cancer Research, said: "Embryonic stem cell division is generally believed to be a symmetrical process, but what we found was that sister cells are actually often quite different from one another.

"We used a new technique to separate paired stem cells combined with assays that measure RNA in individual cells. Our research showed that sister stem cells display considerable differences in which genes are expressed. These differences are advantageous for normal stem cells in their constantly changing environment, and in cancer cells, the same characteristics can enable them to evade treatments. If we can control a process like DNA methylation that creates diversity in cell populations, we could create more efficient treatments for cancer."

Professor Mel Greaves, Professor of Cell Biology at The Institute of Cancer Research, said: "How [stem cells](#) regulate expression of their genes is crucial to many fundamental biological processes, such as

embryonic development, regeneration and turnover of blood, skin and other tissues in the body, but especially to cancer.

"One of the biggest challenges in cancer treatment is overcoming drug resistance. Research from the ICR has revealed that the cells of individual tumours are remarkably diverse and this new research highlights one way this might be achieved. The inherent variability of cancer cell populations provides them with the flexibility to adapt and survive even when confronted with innovative new drugs. If we could harness these new insights to restrict the diversity of [cancer cells](#) it would substantially increase the prospects for effective control or eradication of cancer."

More information: Sawado et al., Identifying division symmetry of mouse embryonic stem cells: negative impact of DNA methyltransferases on symmetric self-renewal. *Stem Cell Reports*, 2013, [dx.doi.org/10.1016/j.stemcr.2013.08.005](https://doi.org/10.1016/j.stemcr.2013.08.005)

[1] Single cell RNA analysis is the investigation of an individual cell's gene expression profile to determine which genes have been expressed.

Provided by Institute of Cancer Research

Citation: Study of 'sister' stem cells uncovers new cancer clue (2013, September 26) retrieved 20 March 2024 from

<https://medicalxpress.com/news/2013-09-sister-stem-cells-uncovers-cancer.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.
