Keeping stem cells from changing fates

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Johns Hopkins researchers have determined why certain stem cells are able to stay stem cells.

The report in the June 4 issue of *Cell Stem Cell* reveals that an enzyme that changes the way DNA is packaged in cells allows specific genes to be turned on and off, thereby preventing a stem cell from becoming another cell type.

Each cell has to fit in 6 feet of highly organized and carefully packaged DNA. Some regions of the DNA are more tightly compacted than others and this structure is dynamic. There are specific enzymes that change how condensed the DNA is to help turn genes on and off. The genes that are turned off generally are found in tightly condensed DNA. To turn genes on, the DNA around those genes is loosened so that activators and other proteins can interact with the DNA.

The Johns Hopkins researchers believed that restructuring the DNA by proteins that make up chromosomes could play a role in deciding if a stem cell was going to change into another cell or stay a stem cell, since change in the DNA packaging would allow for many genes to be turned off and other genes to be turned on.

By genetically engineering flies to lack several proteins involved in packaging DNA, in the stem cells of the testes in fruit flies, the research team found that if the enzyme NURF is removed from testis stem cells, the stem cells disappeared. A constant supply of stem cells in the testes is responsible for making cells that eventually become sperm. More

staining of the testes with colored markers showed that these cells hadn't gone away completely, but were becoming another cell type, sperm cells.

"This experiment was really hard to do," says Erika Matunis, Ph.D., professor of cell biology from the Johns Hopkins School of Medicine. "As soon as you remove NURF from these cells, they leave, so you have to take a lot of samples to see how the cells are moving, since we are not looking at living moving cells but rather individual flashes in time."

So how does NURF keep stem cells as stem cells? NURF can both turn on and turn off genes. "We still don't know what is happening in this case with how NURF regulates genes to keep stem cells from changing," says Matunis.

Matunis' group last year discovered proteins that were able to prevent stem cells from becoming other types of cells in the fruit fly testes. Now they showed that these same proteins also work with NURF to keep stem cells from changing. "By any means this isn't the only pathway though, it's just the one we know more about" says Matunis. "It's probably a tangled hair ball of all kinds of signals going on in these cells that prevent these stem cells from differentiating."

NURF keeps stem cells from changing in fruit fly testes, but whether NURF keeps other stem cells from changing still needs to be tested. Matunis believes that proteins similar to NURF will factor into whether a cell decides to change or not in other cell types.

More information: *Cell Stem Cell*: www.cell.com/cell-stem-cell/

Provided by Johns Hopkins Medical Institutions