MedicalXpress

New study suggests stem cells sabotage their own DNA to produce new tissues

February 15 2010

A new study from the Ottawa Hospital Research Institute (OHRI) and the University of Ottawa suggests that stem cells intentionally break their own DNA as a way of regulating tissue development. The study, published in *Proceedings of the National Academy of Science (PNAS),* could dramatically change how researchers think about tissue development, stem cells and cancer.

Human cells contain 46 strands of DNA that code for all our genes. Certain chemicals and UV light can break these strands into pieces, a process that has traditionally been considered a bad thing, leading to cell death or diseases such as cancer if the damage is not repaired quickly. The new research, led by Dr. Lynn Megeney, shows for the first time that stem cells will intentionally cut and then repair their own DNA as a mechanism of activating genes that promote the development of new tissues.

The project started as an attempt to understand how stem cells give rise to new muscle fibres. In 2002, Dr. Megeney and his team discovered that this process of producing new muscle was somehow connected to another important process called programmed cell death, which the body uses to get rid of unwanted cells. When they blocked or removed a key death-promoting protein called caspase 3, they found that stem cells stopped producing new muscle fibres.

"This discovery was very controversial at the time, but dozens of research groups have now reported that cell death proteins control the

maturation process of most stem cell types," says Dr. Megeney. "In the last few years, the big mystery has been how cell death proteins manage this complex process."

Now in the 2010 study Dr. Megeney and his team believe they have solved the mystery. They have discovered that the novel effect of caspase 3 in stem cells is related to its ability to activate another protein that cuts up the cell's DNA (called caspase-activated DNase) and has also traditionally been associated with programmed cell death. When they blocked this DNA-cutting protein, they also blocked muscle development. They also showed that when the DNA cutting occurs at a key gene known to promote muscle development, it activates that gene and induces the development of new muscle.

"Our research suggests that when a gene is damaged, it can actually increase the expression of that gene, as long as the damage is repaired quickly. This is a novel way for a gene to become activated," says Dr. Megeney. "We've shown that this process is crucial for the development of new muscle tissue, but we believe it may be important for the development of most other tissues as well."

The discovery has important implications for a number of areas. It could help researchers develop better ways to activate stem cells, so that they can produce new tissues for therapeutic purposes. It also suggests that DNA mutations, which can contribute to a variety of diseases, may initially occur as a result of a normal cellular process. And it has implications for researchers developing therapies that inhibit programmed cell death, suggesting that such therapies may also inhibit normal tissue development.

Provided by Ottawa Hospital Research Institute