Scientists identify, isolate adult mammary stem cells in mice

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For the first time, researchers at Fred Hutchinson Cancer Research Center have identified and isolated adult mammary stem cells in mice. Long-term implications of this research may include the use of such cells to regenerate breast tissue, provide a better understanding of the role of adult stem cells in breast cancer development, and develop potential new targets for anti-cancer drugs.

The findings, by Larry Rohrschneider, Ph.D., a member of the Basic Sciences Division at the Hutchinson Center, and Lixia Bai, M.D., Ph.D., a research associate in his lab, are published in the Sept. 1 issue of Genes *& Development*.

Using a genetically modified mouse model, the researchers tagged stem cells with green fluorescent protein (GFP), which exhibits bright green fluorescence during gene expression and can be easily seen under a microscope. GFP expression is controlled by the promoter of a newly identified gene, specifically expressed in stem cells, called s-SHIP.

“Until now, we have not been able to identify stem cells in mammary tissue. They have never been detected before with such specificity. It is extraordinary. You can see these green stem cells under the microscope in their pure, natural state,” said Rohrschneider, who has filed a patent on the s-SHIP promoter-GFP-labeling technology.

Previous systems for isolating stem cells have relied on a variety of biomarkers, none of which have yielded a pure stem cell population.

This limitation has prohibited accurate gene-expression analysis of such cells.

The researchers demonstrated the presence of active green stem cells at crucial stages of mammary development, such as puberty and pregnancy. During quiescent stages of development, however, the cells did not "light up."

Such stem cells represent a new alternative to induced pluripotent stem cells, or genetically altered stem cells, for various medical applications.

For example, by isolating the pure green mammary cells from donor female transgenic mice, the researchers have demonstrated the regenerative ability of these cells by transplanting them into the mammary fat tissue of recipient mice whose own mammary epithelium has been removed.

"We have found that those transplanted green stem cells can generate new mammary tissue and this tissue can produce milk, just like normal mammary epithelial cells," said co-author Bai. "Identification of the exact stem cell and its location is the first critical and fundamental step toward understanding the regulatory mechanisms of these important cells."

In addition to potential clinical applications regarding tissue regeneration, the researchers see these isolated stem cells as a window to better understanding how normal stem cells can become cancer stem cells, which are hypothesized to exist in tumors.

"Our belief right now is that perhaps the most aggressive tumors may be coming from the malignant transformation of stem cells in healthy tissue," Rohrschneider said. "This new technology offers a unified model for identifying normal and cancer stem cells."

Cancer stem cells are thought to be responsible for tumor initiation, growth, metastasis, therapy resistance and disease relapse.

"Because stem cells are critical for both normal tissue development and cancer development, exploring how they are regulated in normal development will help us to better understand how they are transformed into breast cancer cells," Bai said. "By searching for new methods to effectively and specifically target cancer stem cells, we hope we can cure breast cancer someday." she said.

Provided by Fred Hutchinson Cancer Research Center