Stem cells battle for space

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The body is a battle zone. Cells constantly compete with one another for space and dominance. Though the manner in which some cells win this competition is well known to be the survival of the fittest, how stem cells duke it out for space and survival is not as clear. A study on fruit flies published in the October 2 issue of *Science* by Johns Hopkins researchers describes how stem cells win this battle by literally sticking around.

"Our work exemplifies how one signal coordinately maintains two types of stem cells in a single niche, or microenvironment," says Erika Matunis, Ph.D., associate professor of cell biology at the Johns Hopkins School of Medicine. "What we found may emerge as common themes of mammalian stem cell niches as they become better characterized."

To tackle the stem cell competition quandary, the team looked at fruit fly testes where two different stem cells exist: germline stem cells which give rise to sperm, and somatic stem cells which develop into non-reproductive cell types.

Using genetics, the researchers grew flies lacking the SOCS protein, which controls other molecules that promote stem cell growth. SOCS normally ensures that the right numbers of stem cells are present in the stem cell niche, a region at the far end of the fly testis where new cells are born. In a normal testis, the germline stem cells are surrounded by somatic stem cells at a ratio of about one germline stem cell for every two somatic stem cells.

The researchers isolated testes from flies lacking SOCS and, under a microscope, counted the number of germline stem cells and somatic stem cells. They found that nearly half of the germline stem cells were gone and the somatic stem cells appeared to be occupying that space.

"The somatic stem cells almost look like they've invaded the niche area," says Melanie Issigonis, a graduate student in the Biochemistry, Cellular, and Molecular Biology graduate program at Johns Hopkins. "I saw that image and said, 'Wow, it's right there. Germline stem cell loss.'"

To figure out where the lost germline stem cells went and how they lost the battle for space, the team returned to the microscope. This time, they examined the cells for whether they contained integrin, a protein that helps cells stick to each other. They found that somatic stem cells from flies lacking SOCS seemed to contain more integrin than somatic stem cells from flies with functional SOCS. According to Matunis, it's the increase in integrin that allows somatic stem cells to gain the upper hand because they can stick to the niche better than neighboring germline stem cells can.

Though the somatic stem cells were invading the niche, germline stem cells were not dying. In the microscope images, the team found that all remaining germline stem cells still looked alive and healthy, but elbowed out of their niche by somatic stem cells. Says Matunis, no matter how healthy a germline stem cell is, if it cannot stick, it will eventually be outcompeted by the somatic cells and pushed all the way out of the niche. Issigonis found the discovery remarkable: "The germline stem cells are perfectly fine," she says. "They're just leaving the niche and differentiating."

The team believes this model can be applied to other stem cell niches such as cancer. Just like the somatic stem cells overrunning the fly testes, cancer stem cells in mammalian systems become a danger when they become the stickiest cell in the niche. In both cases, the important control protein, SOCS, is lost. Knowing what is necessary for some stem cells to thrive and others to dwindle could have great importance to understanding the roots of stem cell diseases.

Source: Johns Hopkins Medical Institutions