Scientists demonstrate dual intrinsic and extrinsic control of stem cell aging

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The Stowers Institute's Xie Lab has published recent findings that reveal some of the factors underlying the aging of stem cells.

The paper, "Stem Cell Aging is Controlled both Intrinsically and Extrinsically in the Drosophila Ovary," was published in the Oct. 11 issue of *Cell Stem Cell*. Lei Pan, Predoctoral Researcher, and Ting Xie, Ph.D., Associate Investigator, are the paper's first and last authors, respectively.

It is widely postulated that a decrease in the number and activity of stem cells contributes to the aging of human tissue. These changes could be fundamental to many symptoms of aging such as wrinkling of skin and decreased organ function.

The control of stem cell aging has, until now, been poorly understood, but the Xie Lab has demonstrated that specific factors are associated with an age-dependent decline in the function of stem cells and their microenvironment, called a niche.

"In this study, we used Drosophila (fruit fly) ovarian germline stem cells (GSCs) as a model to demonstrate that age-dependent decline in the functions of stem cells and their niche contributes to overall aging of stem cells," said Mr. Pan. "We examined three factors in the control of stem cell aging and found evidence that it is controlled both extrinsically and intrinsically."

First, the team examined a family of proteins called bone morphogenic proteins (BMPs), which plays an important role in the development of many tissues. They found that as BMP signaling activity from the niche decreases with age, the stem cell's ability to proliferate is compromised, and the stem cell population declines. Conversely, they established that an increase in BMP signaling can prolong the lifespan of stem cells and promote proliferation.

Second, the team established that time also takes a toll on the adhesion between stem cells and their niche. Strong adhesion can prolong a stem cell's lifespan, and weakened adhesion can enhance stem cell aging.

Finally, the paper highlights how over-expression of an enzyme that helps eliminate free oxygen species, either in GSCs or in their niche, can prolong the lifespan of stem cells and increase proliferation.

"Inefficient replacement of worn-out cells in adult tissues due to the declining function of stem cells over time may be a primary cause of human aging," says Dr. Xie. "If we learn how to slow down stem cell aging by manipulating functions of stem cells and/or their niche, we may be able to slow down human aging and the progression of age-related degenerative diseases."

Source: Stowers Institute for Medical Research