Embryonic gene Nanog reverses aging in adult stem cells

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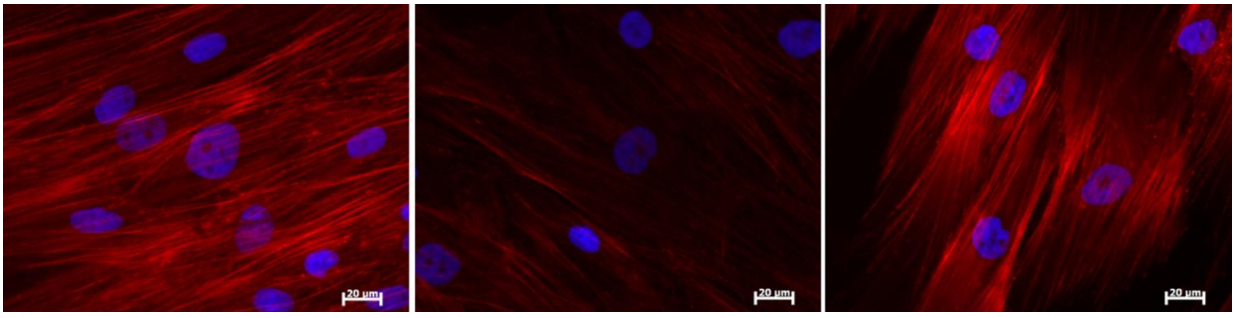

The images show, from left to right, functioning stem cells, stem cells no longer functioning due to Hutchinson-Gilford Progeria syndrome (HGPS), and stem cells previously not functioning due to HGPS that were rebooted by the embryonic stem cell gene Nanog. Credit: Stelios Andreadis.

The fountain of youth may reside in an embryonic stem cell gene named Nanog.

In a series of experiments at the University at Buffalo, the gene kicked into action dormant cellular processes that are key to preventing weak bones, clogged arteries and other telltale signs of growing old.

The findings, published June 29 in the journal *Stem Cells*, also show promise in counteracting premature aging disorders such as Hutchinson-Gilford progeria syndrome.

"Our research into Nanog is helping us to better understand the process of aging and ultimately how to reverse it," says Stelios T. Andreadis, PhD, professor and chair of the Department of Chemical and Biological Engineering at the UB School of Engineering and Applied Sciences, and the study's lead author.

Additional authors come from UB's Department of Biomedical Engineering, a joint program between UB's engineering school and the Jacobs School of Medicine and Biomedical Sciences at UB, and the Department of Biostatistics and Bioinformatics at Roswell Park Cancer Institute in Buffalo.

To battle aging, the human body holds a reservoir of nonspecialized cells that can regenerate organs. These cells are called adult stem cells, and they are located in every tissue of the body and respond rapidly when there is a need.

But as people age, fewer adult stem cells perform their job well, a scenario which leads to age-related disorders. Reversing the effects of aging on adult stem cells, essentially rebooting them, can help overcome this problem.

Andreadis previously showed that the capacity of adult stem cells to form muscle and generate force declines with aging. Specifically, he examined a subcategory of muscle cells called smooth muscle cells which reside in arteries, intestines and other tissues.

In the new study, Panagiotis Mistriotis, a graduate student in Andreadis' lab and first author of the study, introduced Nanog into aged stem cells. He found that Nanog opens two key cellular pathways: Rho-associated protein kinase (ROCK) and Transforming growth factor beta (TGF-β).

In turn, this jumpstarts dormant proteins (actin) into building

cytoskeletons that adult stem cells need to form muscle cells that contract. Force generated by these cells ultimately helps restore the regenerative properties that adult stem cells lose due to aging.

"Not only does Nanog have the capacity to delay aging, it has the potential in some cases to reverse it," says Andreadis, noting that the embryonic stem cell gene worked in three different models of aging: cells isolated from aged donors, cells aged in culture, and cells isolated from patients with Hutchinson-Gilford progeria syndrome.

Additionally, the researchers showed that Nanog activated the central regulator of muscle formation, serum response factor (SRF), suggesting that the same results may be applicable for skeletal, cardiac and other muscle types.

The researchers are now focusing on identifying drugs that can replace or mimic the effects of NANOG. This will allow them to study whether aspects of aging inside the body can also be reversed. This could have implications in an array of illnesses, everything from atherosclerosis and osteoporosis to Alzheimer's disease.

More information: Panagiotis Mistriotis et al, NANOG Reverses the Myogenic Differentiation Potential of Senescent Stem Cells by Restoring ACTIN Filamentous Organization and SRF-Dependent Gene Expression, *STEM CELLS* (2016). DOI: 10.1002/stem.2452

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