MedicalXpress

Scientists uncover cellular process behind premature aging

December 21 2016

In a new study, scientists from the Florida campus of The Scripps Research Institute (TSRI) have shown how two genes "balance" each other to maintain normal cell function. A disruption in one of the genes, called spns1, can induce degradation and premature "senescence"—or aging—while the other gene, called atp6v0ca, can jump in to suppress that degradation.

Their experiments in zebrafish suggest that these combined genetic disruptions can counteract premature aging and extend developmental lifespan.

"We found that the dual defects did indeed counteract senescence during development and extended the animal's survival and life span," said TSRI Associate Professor Shuji Kishi.

The findings, published recently in the journal *Autophagy*, could also guide future treatments for diseases that involve the body's inability to degrade unwanted or harmful compounds.

A Closer Look at Lifespan

Cellular senescence is when cells stop dividing and is a normal part of aging. Interestingly, senescence is not only observed in later aging stages but is also detectable during embryonic development in vertebrates.

In the new study, the researchers took a closer look at the gene spns1. In vertebrates, such as zebrafish and humans, the protein encoded by spns1 is important in a cellular process called autophagy, when the cell moves unwanted material to a cellular structure called the lysosome. Previous research had shown that defects in this gene can also cause senescence in the embryonic stage and premature aging symptoms in adulthood.

However, Kishi and his colleagues found that a concurrent disruption of another gene— atp6v0ca, whose sole defect still causes senescence—led to suppression of the process induced by the defective spns1 gene.

"Our findings suggest that these two defects actually function at a balance point that is critically involved in the regulation of developmental senescence—and that balance allows for normal cell function," said Kishi.

Restoring the Balance

The scientists are now considering ways to influence the balance between these genes as a strategy to treat lysosomal storage diseases such as Pompe disease, where the excessive buildup of a substance called glycogen results in severe muscle weakness. They believe there may also be applications in treating age-associated degenerative diseases linked to late-stage autophagy disruption.

"The use of appropriate inhibitors, selective for key steps in the biosynthesis of cellular macromolecules in general, may restore normal dynamics in the autolysosomal compartment and correct the pathological storage that is the ultimate cause of these types of disease," said TSRI Research Associate Shanshan Lian, the co-first author of the study.

The findings may also lead to the development of tools to help identify new genes that affect the aging process without the need for performing

lengthy adult lifespan analyses. This approach could be applied to the high-throughput identification of pharmacological agents that control aging and lifespan through enhanced resistance to various stressors, including oxygen radicals.

Provided by The Scripps Research Institute