At the molecular level, aging is not always a matter of 'pay later'

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A new USC Dornsife study indicates that aging may have originated at the very beginning of the evolution of life, at the same time as the evolution of the first genes.

"This could be a game changer for research on longevity and aging. It may also be relevant to the scientific discussions surrounding CRISPR9 gene editing," said John Tower, biologist at the USC Dornsife College of Letters, Arts and Sciences. "We found that when it comes to genes, aging may not always be a negative trait. It may help an organism survive."

The findings, published on Sept. 11 in the journal *Origins of Life and Evolution and Biospheres*, may reshape scientific conversations about a long-held hypothesis of aging first proposed by the biologist George C. Williams.

Williams had suggested in a 1957 paper that as part of natural selection, biology favors genes that will optimize functions and characteristics necessary for reproduction within a specific period of time. But later in life, those genes that enhance reproduction actually contribute to aging. Williams' hypothesis was known as "antagonistic pleiotropy."

There are several examples of this biological tradeoff. The gene p53, for example, suppresses cancer, but it is known to accelerate aging in cells.

Tower, an expert on the biology of aging, said that under this hypothesis, aging of the organism is a consequence of natural selection for optimal reproduction. He wondered, though: Is aging is always a negative trait at the level of individual genes?

To test this, Tower and a team of researchers developed a scenario with molecules can replicate themselves. Such molecules are believed to be the evolutionary origin of modern genes.

Using computer modeling, the researchers paired an unstable short-lived gene, B, and its interactions with a longer-living gene, A, to create a new replicator, AB. In some simulations, the fact that B was short-lived

enhanced beneficial aspects of A that would maximize the proliferation of the AB replicator.

"The results suggest that evolution can favor the limited stability of genes as a way to increase complexity and the reproductive fitness of the organism," Tower said. "Interventions designed to stabilize genes might help combat aging."

More information: Zewei Li et al, Models of Replicator Proliferation Involving Differential Replicator Subunit Stability, *Origins of Life and Evolution of Biospheres* (2018). DOI: 10.1007/s11084-018-9561-x

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