Convergent mechanism of aging discovered

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Several different causes of aging have been discovered, but the question remains whether there are common underlying mechanisms that determine aging and lifespan. Researchers from the Max Planck Institute for Biology of Ageing and the CECAD Cluster of Excellence in Ageing research at the University Cologne have now come across folate

metabolism in their search for such basic mechanisms. Its regulation underlies many known aging signaling pathways and leads to longevity. This may provide a new possibility to broadly improve human health during aging.

In recent decades, several cellular signaling pathways have been discovered that regulate the lifespan of an organism and are thus of enormous importance for aging research. When researchers altered these signaling pathways, this extended the lifespan of diverse organisms. However, the question arises whether these different signaling pathways converge on common metabolic pathways that are causal for longevity.

The search begins in the roundworm

The scientists started their search in the roundworm Caenorhabditis elegans, a well-known model organism for aging research. "We studied the metabolic products of several, long-lived worm lines. Our analyses revealed that, among other things, we observed clear changes in the metabolites and enzymes of the folate cycle in all worm lines. Since folate metabolism plays a major role in human health, we wanted to further pursue its role in longevity," explains Andrea Annibal, lead author of the study.

A common mechanism for longevity

Folates are essential vitamins important for the synthesis of amino acids and nucleotides—the building blocks of our proteins and DNA. "We tuned down the activity of specific enzymes of folate metabolism in the worms. Excitingly, the result was an increase in lifespan of up to 30 percent," says Annibal. "We also saw that in long-lived strains of mice, folate metabolism is similarly tuned down. Thus, the regulation of folate metabolism may underlie not only the various longevity signaling

pathways in worms, but also in mammals."

"We are very excited by these findings because they reveal the regulation of folate metabolism as a common shared mechanism that affects several different pathways of longevity and is conserved in evolution," adds Adam Antebi, director at the Max Planck Institute for Biology of Ageing. "Thus, the precise manipulation of folate metabolism may provide a new possibility to broadly improve human health during aging." In future experiments, the group aims to find out the mechanism by which the folate metabolism affects longevity.

More information: Andrea Annibal et al, Regulation of the one carbon folate cycle as a shared metabolic signature of longevity, *Nature Communications* (2021). DOI: 10.1038/s41467-021-23856-9

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