Long-term low-calorie diet prevents age-related molecular changes

May 25 2018

Scientists from Russia and the United States have looked at how the gene methylation process changes its behavior with age and how the amount of calories consumed affects these molecular changes. They found that the age-related changes affect multiple genes associated with the molecular pathways involved in the aging process at the cellular level, while long-term low-calorie dieting prevents the changes from progressing further. The results of their study were published in *Aging Cell* journal.

Aging triggers multiple molecular changes, including epigenetic changes, in the human body. Epigenetic changes are the DNA and protein modifications that do not alter the genetic code sequence, but strongly influence the way the genes operate. Currently, DNA methylation (attachment of additional methyl groups to the DNA) is one of the most intensively studied epigenetic processes. Methylation in the living organisms, humans included, is known to become more intensive with age in some parts of the genome and less intensive in its other parts. Better understanding of the changes provoked by aging can help to reverse them and, possibly, increase the life expectancy.

The scientists from Skoltech and Harvard Medical School (Boston, USA) studied the methylation process behavior in mouse blood in the course of aging, using 16 different age groups for this purpose. It was found that the changes become more evident at an older age, manifesting themselves as an increase in the methylation system's entropy (i.e., the low-methylation genes tend to increase the degree of methylation, while

the high-methylation genes lose their methylation ability). Also, the researchers identified specific cellular mechanisms affected by the change and discovered that many of them are well-known for their role in the aging process and are the targets for animal life-extension drugs. Finally, the researchers traced the effects of the life-extending low-calorie diet on the changes they identified. Interestingly, the mice put on a long-term low-calorie diet displayed slower age-related changes, whereas short-term cuts in calories did not only fail to slow down the age-related changes but instead made them even faster.

"The experiment has clearly demonstrated that a life-extending action can produce different effects depending on its duration. In the case at hand, we see that a low-calorie diet has a cumulative effect, so the longer the diet, the slower the age-related changes. Short-term actions, on the contrary, speed up the aging, although this increase in the aging rate is soon eliminated as the dieting continues," says one of the authors, Skoltech Ph.D. student Alexander Tyshkovskiy.

More information: Sziráki A, Tyshkovskiy A, Gladyshev VN. Global remodeling of the mouse DNA methylome during aging and in response to calorie restriction. *Aging Cell*. 2018;17:e12738. doi.org/10.1111/acel.12738

Provided by Skolkovo Institute of Science and Technology