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Leibniz-Institut für Altersforschung
Fritz-Lipmann-Institut e.V. (FLI)

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Glucose substitution prolongs lifespan of old mice with short telomeres

Glucose is one of the basic components of our nutrition representing an important source of energy production for cells and tissues. Glucose-rich diets have been implemented to contribute to the development of metabolic diseases such as diabetes, cardiovascular disease, obesity, and cancer. A new study from the Leibniz Institute for Age Research in Jena now revealed the first experimental evidence that aged mice with short telomeres require increased amounts of glucose for the maintenance of energy homeostasis. In this context, glucose substitution prolongs the maintenance of aging cells and tissues thus prolonging health and overall lifespan of the mice.

Clinical studies have proven that a reduction in body weight improves health parameters and prevents disease development in young and middle aged adults. Basic research studies on yeast cells, worms, flies and mice indicated that calorie restriction in the diet can increase the lifespan across different species. In monkeys, however, results were more ambiguous: calorie restriction improved health parameters (such as blood pressure and blood lipids) but did not lead to an elongation of the survival. “These outcomes appear to be contradictory – a possible explanation was that calorie restriction has beneficial effects on health parameters at middle age but exerts adverse effects during advanced aging”, indicate Pavlos Missios, Medical Doctor of the University of Tübingen and first author of the study.

The new data from the Leibniz Institute for Age Research – Fritz-Lipmann-Institute (FLI) in Jena point to a possible explanation. During aging, cells lose the ends of their chromosome – the telomeres. Telomeres shorten as a consequence of cell divisions and it is known that this mechanism limits the proliferative capacity of human cells and the regenerative capacity of aging tissue.

Modified caloric intake depending on age

Studies on mice, wildlife birds and human blood donors revealed a correlation between telomere shortening and a shortened lifespan. The new study from the group of Lenhard Rudolph at FLI reveals experimental evidence that telomere shortening increases the energy demand of cells and tissue leading to an increased requirement of glucose substitution in old mice with short telomeres in order to maintain energy homeostasis and body functions. “Should these results hold true for humans, this would indicate that we need a different composition of our diet at old age in order to prolong the maintenance of both energy homeostasis and body functions”, indicates Lenhard Rudolph, director of the institute and lead author of the current study.

Aging mice with short telomeres that were switched to a glucose-rich diet exhibited a 20% increase in overall lifespan compared to mice on normal diet. “These results were very surprising and could provide an explanation for the change in correlation of body weight and lifespan in old compared to middle aged individuals”, explains Dr. Bernhard Böhm, co-initiator of the studies at Ulm University and director of Metabolic Medicine at NTU Singapore und Imperial College London. Indeed, increased body weight at mid age is associated with and increased risk of disease development and early death. In contrast, at advanced age it is the opposite, and more than 30% of geriatric patients exhibit signs of malnutrition associating with a shortened lifespan compared to old people with higher body weight.

„It now needs to be tested whether the results of our study hold true in humans. If so, we may need to change the composition of our diet at advanced age in order to maintain the functionality of our cells and tissues exhibiting an increased demand of glucose substitution for energy production“, explains Rudolph. First human trials have been initiated with Dr. Stephan C. Bischoff, M.D. and nutrition scientist from the University of Stuttgart Hohenheim. “It will be important to determine the influence of energy supplementation in controlled settings within clinical trials and to develop biomarkers that indicate the optimization of energy homeostasis”. In the end it could come down to the

question whether butter-cream cakes at old age may be equally important as calorie restriction at middle age in order to achieve a maximization of our health span?

Publication:

Pavlos Missios, Yuan Zhou, Luis Miguel Guachalla, Guido von Figura, Andre Wegner, Sundaram Reddy Chakkarappan, Tina Binz, Anne Gompf, Götz Hartleben, Martin D. Burkhalter, Veronika Wulff, Cagatay Günes, Rui Wang Sattler, Zhangfa Song, Thomas Illig, Susanne Klaus, Bernhard O. Böhm, Tina Wenz, Karsten Hiller & K. Lenhard Rudolph. Glucose substitution prolongs maintenance of energy homeostasis and lifespan of telomere dysfunctional mice. *Nature Communications* 2014, doi: 10.1038/ncomms5924. www.nature.com/naturecommunications

About the FLI:

The Leibniz Institute for Age Research – Fritz Lipmann Institute (FLI) is the first German research organization dedicated to biomedical aging research since 2004. More than 330 members from over 30 nations explore the molecular mechanisms underlying aging processes and age-associated diseases. For more information, please visit *www.fli-leibniz.de.*

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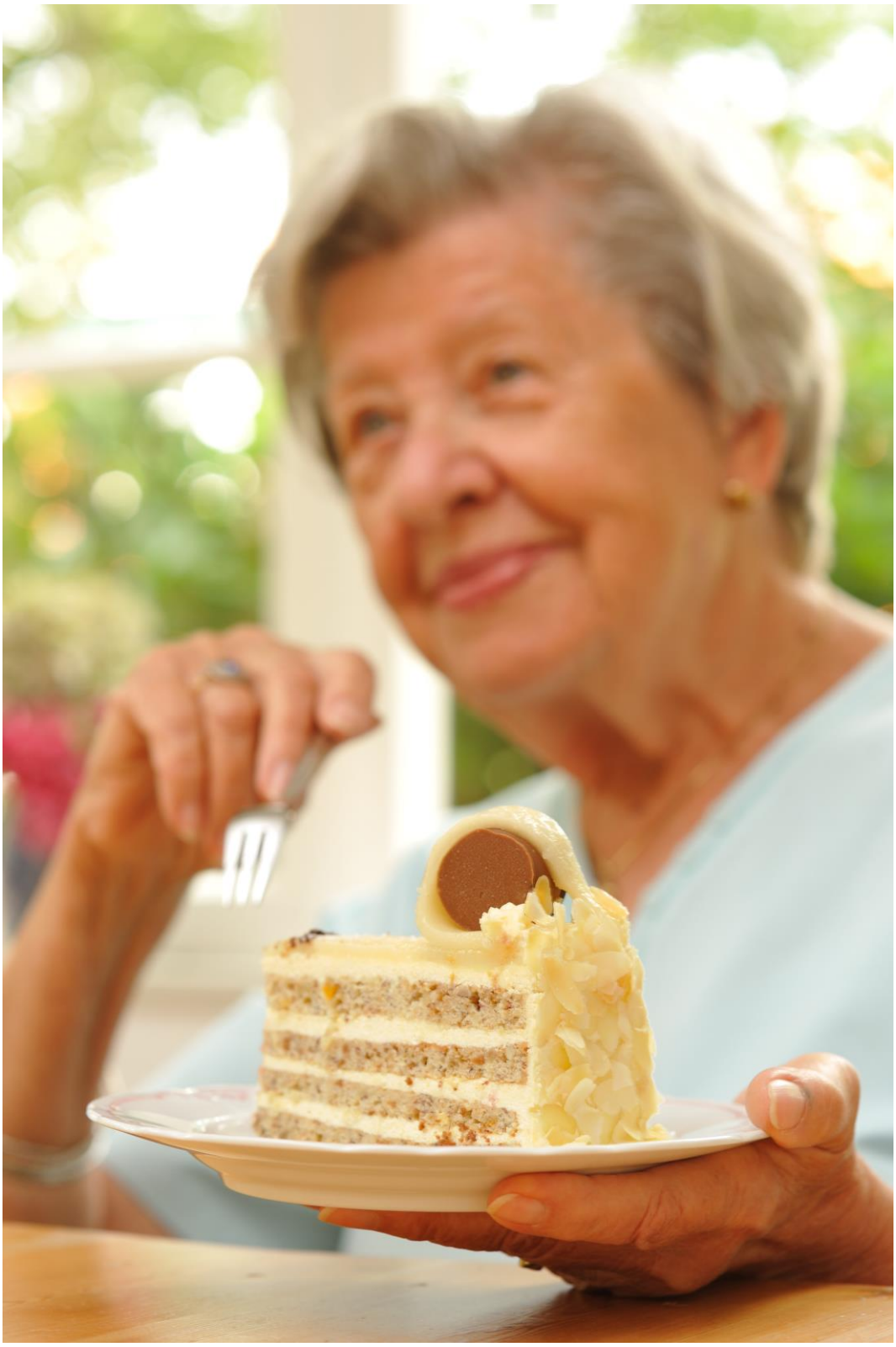

Should the results of the current study hold true in humans, a glucose-rich diet could help to improve the maintenance of aging cells and tissues as well as to prolong the health span at advanced age.

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