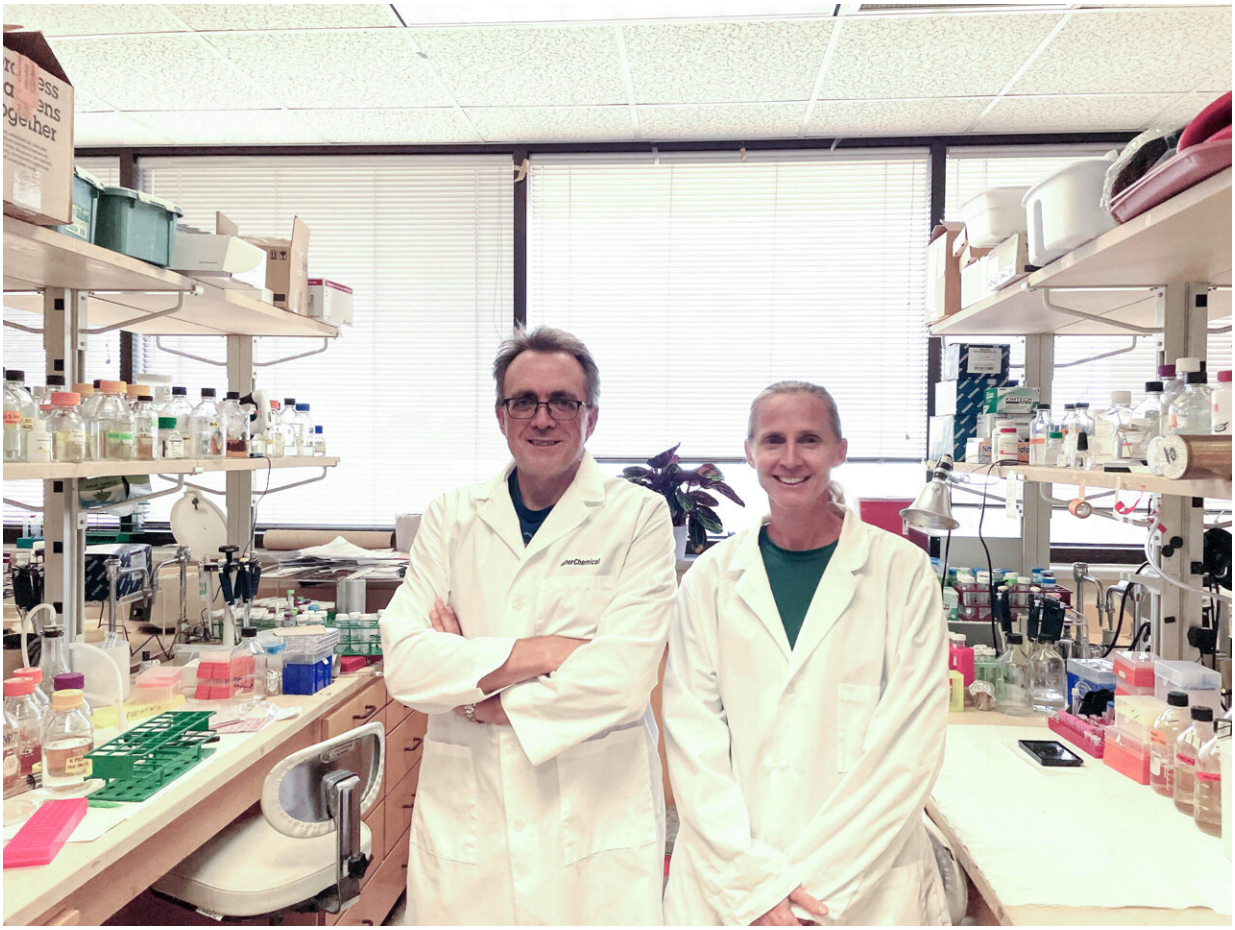
Reduction in folate intake linked to healthier aging in animal models

August 2 2024, by Ashley Vargo



Michael Polymenis, Ph.D., principal investigator, and Heidi Blank, Ph.D., first author of the study published in *Life Science Alliance*. This is the latest study by the researchers in their continuous investigation of the effects of folate in biological models. Credit: Eun-Gyu No, Ph.D./Texas A&M AgriLife

In a study published in *Life Science Alliance*, Texas A&M AgriLife Research scientists found that decreasing folate intake can support healthier metabolisms in aging animal models, challenging the conventional belief that high folate consumption universally benefits health.

The study was led by Michael Polymenis, Ph.D., professor and associate head of graduate programs in the Texas A&M College of Agriculture and Life Sciences Department of Biochemistry and Biophysics.

Folate, a B vitamin essential for cell growth and development, is widely recognized for its role in preventing birth defects. It's found naturally in foods like leafy greens, and it is typically added to refined grains. Despite its prevalence, the long-term health implications of consuming high amounts of folate throughout life are unclear.

By limiting folate in animal models, the researchers saw a decrease in processes related to growth and building new cells, but enhanced metabolic flexibility, which Polymenis said could lead to healthier aging.

"Optimal folate intake may vary depending on an individual's age," he said. "While higher folate is crucial during early life for growth and development, a lower intake later in life may benefit metabolic health and longevity."

The study supports the concept of precision nutrition, advocating for personalized dietary recommendations. This is a research pillar of the Texas A&M AgriLife Institute for Advancing Health through Agriculture, IHA, where Polymenis is an affiliate member.

Polymenis said further research is needed to explore the mechanisms behind this phenomenon and to develop safe and effective therapeutic interventions to promote healthy aging.

Shifting needs over a lifetime

Folate, or vitamin B9, is an essential dietary component used in the body to form red blood cells, as well as DNA, RNA and proteins. Polymenis said it's especially vital for children, young adults and pregnant women because of its role in growth processes.

He and the other Texas A&M AgriLife researchers wanted to explore its impact in lesser studied age groups. To simulate the effects in older adults, the researchers cut folate from the diets of animal models at an age corresponding roughly to human middle-age. A comparison group was raised the same but continued a typical diet inclusive of folate.

The researchers found the female folate-limited models were able to transition quicker between carbohydrate metabolism and fat metabolism across night and day compared to females on a typical diet.

"When you sleep, your metabolism burns fat," Polymenis said. "And when you're awake and active, you're typically burning carbohydrates for quicker energy. As you get older, it takes longer to switch between these fat-burning and carbohydrate-burning states, but this metabolic plasticity seems to be better maintained in animal models on a folate-limited diet."

The males on folate-limited diets had an overall increase in their metabolic rate during active periods, potentially helping them to maintain energy levels and physical activity.

Blank said the folate-limited group maintained their weight and body fat into old age as opposed to the control group. And despite folate's importance for red blood cell production, the folate-limited models showed no signs of anemia or other negative health consequences.

A series of studies

Polymenis said he and his team weren't surprised to see the folate-limited group age healthier.

The research team began this work a few years ago by using methotrexate to reduce folate intake in yeast cells, then in the worm C. elegans. In both cases, cutting folate led the models to live longer.

Looking forward, the team's next step will be to repeat the experiment in more genetically diverse models, simulating the genetic diversity of humans.

The researchers will also expand their study of novel compounds to limit folate intake, which could later transition to clinical trials.

Therapeutics to limit folate

Packing nutrients into commonly consumed food products—vitamin D in milk, calcium in fruit juices—has proven to help address public health problems. For instance, thyroid issues challenging the U.S. during the early 20th century were a result of widespread iodine deficiencies, which were corrected by adding iodine to consumer salt.

In 1998, the U.S. mandated that staple foods, particularly grains, be "enriched" or "fortified" with folic acid and other B vitamins following the refinement process. While helpful for some age groups, it might do more harm than good for older adults.

As a result, Polymenis said this research opens a new avenue for developing drugs to limit dietary folate uptake for individuals who don't need as much, rather than cutting foods that contain folate or folic acid,

the synthetic version often added to foods and supplements.

In the meantime, Polymenis said he doesn't recommend avoiding folate entirely.

"Based on our findings, we believe older adults may need less folate than they're likely getting now," he said. "We still have more to investigate in this area, and we would not advocate for absolute dietary eradication for anyone."

More information: Heidi M Blank et al, Late-life dietary folate restriction reduces biosynthesis without compromising healthspan in mice, *Life Science Alliance* (2024). DOI: 10.26508/lsa.202402868

Provided by Texas A&M University