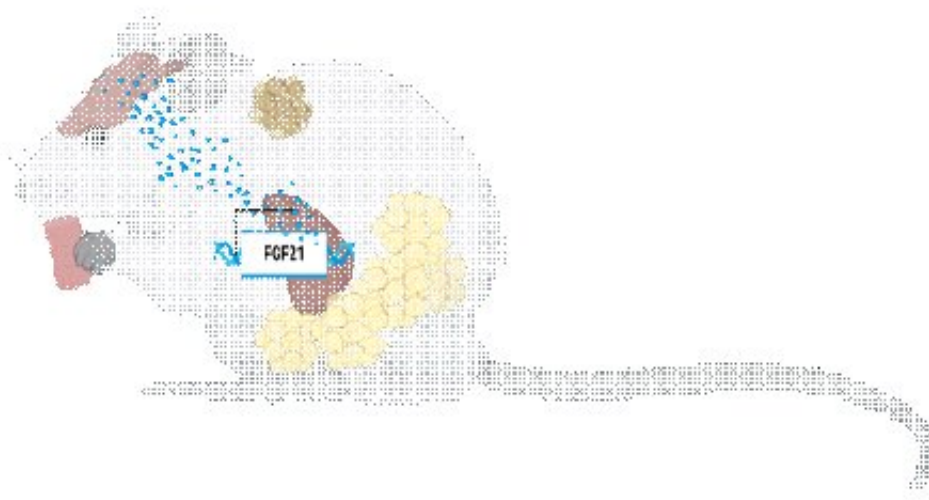


Mice live longer and lose weight while eating more when FGF21 is present

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When the liver detects low levels of protein, it activates cells that produce FGF21 and release the hormone into the bloodstream. FGF21 is then carried to target cells (neurons) in the brain. Those cells hit the alarm button when they see FGF21, signaling that protein intake is too low. The brain reacts by sending out a complex set of directions that, among other things, stop the mouse from growing, alter food intake, and increase the number of calories burned. Credit: Pennington Biomedical Research Center

A single hormone appears to coordinate the lifespan extension produced by a low-protein diet.

A new study from Pennington Biomedical Research Center, published in the journal *Nature Communications*, found that reducing the amount of protein in the [diet](#) produced an array of favorable [health](#) outcomes, including an extension of lifespan, and that these effects depend on a liver-derived metabolic hormone called Fibroblast Growth Factor 21 (FGF21).

It has long been known that reducing the amount you eat improves health and extends lifespan, and there has been increasing interest in the possibility that reducing protein or amino acid intake contributes to this beneficial effect. Several recent studies suggest that diets that are low in protein, but not so low that they produce malnutrition, can improve health. Conversely, overconsumption of high-protein diets has been linked to increased mortality in certain [age groups](#).

A few years ago, Pennington Biomedical's Neurosignaling Laboratory discovered that the metabolic hormone FGF21 was a key signal linking the body to the brain during protein restriction. Without this signal, [young mice](#) failed to change their feeding behavior or metabolism when placed on a low-protein diet.

"Our data suggest that FGF21 talks to the brain, and that without this signal the mouse doesn't 'know' that it is eating a low-protein diet. As a result, the mouse fails to adaptively change its metabolism or feeding behavior," said Christopher Morrison, Ph.D., Professor and Director of the Neurosignaling Lab.

The group's newest work, led by postdoctoral researcher Cristal M. Hill, Ph.D., demonstrates that low-protein diets produce beneficial metabolic effects in aged mice, improving metabolic health, reducing frailty, and extending lifespan. These beneficial effects were also apparent when protein intake was reduced in middle-aged mice, even protecting against the detriments of obesity. Importantly, these beneficial effects were lost

in mice that lacked FGF21, suggesting that its action in the brain is critical for the increase in health and lifespan.

"We previously showed that FGF21 acts in the brain to improve metabolic health in young mice fed a low-protein diet. These new data extend this work by demonstrating that FGF21 also improves metabolic health and extends lifespan. Collectively, these data provide clear evidence that FGF21 is the first known hormone that coordinates feeding behavior and metabolic health to improve lifespan during [protein](#) restriction," Dr. Hill said.

However, Dr. Hill said several questions remain. It's unclear exactly how these observations will translate to aging humans, but the hope is that this work will uncover novel molecular and neural pathways that can be leveraged to improve health in people.

"This groundbreaking research has important implications for extending the health and lifespan of people. If scientists can better understand how diets and nutritional hormones like FGF21 act to extend [lifespan](#), these discoveries could offset many of the [health issues](#) that occur in middle age and later," said Pennington Biomedical Executive Director John Kirwan, Ph.D.

More information: Cristal M. Hill et al, FGF21 is required for protein restriction to extend lifespan and improve metabolic health in male mice, *Nature Communications* (2022). [DOI: 10.1038/s41467-022-29499-8](#)

Provided by Pennington Biomedical Research Center

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