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Growth hormone's link to starvation may be clue to increasing life span

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Researchers at UT Southwestern Medical Center have determined that starvation blocks the effects of growth hormone via a mechanism that may have implications in treating diabetes and extending life span.

"It's been well-established that growth is blunted during starvation. But our work shows that this is not just from running out of energy. It's much more sophisticated than that," said Dr. Steven Kliewer, professor of molecular biology and senior author of a study available online and appearing in today's issue of the journal *Cell Metabolism*.

Using genetically altered mice, the researchers found that during fasting, the actions of growth hormone are blocked by a fat-burning hormone called FGF21.

"It's something that we hadn't anticipated," said Dr. Kliewer.

Growth hormone has many functions in the growth and reproduction of cells, such as controlling the length of developing arm and leg bones in children.

Growth hormone has several other functions, however, even in adults. It promotes the breakdown of fats, stimulates creation of protein and increases levels of IGF-1 (insulin-like growth factor-1), a hormone that promotes growth. Too much growth hormone can cause insulin resistance, resulting in diabetes, and lead to other disorders.

In the current study, mice that were genetically altered to produce excess FGF21 grew to be much smaller than ordinary mice, even though they ate more and had more fat in proportion to their size.

Paradoxically, and to the researchers' surprise, the altered, smaller mice produced much greater amounts of growth hormone than normal.

Why didn't the altered mice grow larger than normal in response? The researchers found that FGF21 does not block the production of growth hormone; rather, it works to prevent growth hormone from activating the genes it normally controls.

Interfering with the actions of growth hormone has been shown to increase life span in mice, Dr. Kliewer said.

"In addition, intermittent fasting – which increases FGF21 concentrations – also extends life span in mice. This raises the intriguing possibility that FGF21 might be a longevity factor," Dr. Kliewer said.

"This is something that we're beginning to test in the lab," he said. "But our genetically engineered mice have all the classic hallmarks of extended life span: growth hormone resistance, low concentrations of IGF-1, increased insulin sensitivity and small size."

FGF21 is already being tested in human clinical trials for treatment of obesity and diabetes in adults, but the new findings linking FGF21 to interference with growth hormone might indicate that caution is needed before using it in children or teens, Dr. Kliewer said.

Source: UT Southwestern Medical Center