

Mitochondria behind life span extension

Study in flies suggests low-protein diet works through power-producing organelles

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Web edition : Thursday, October 1st, 2009

The life-extending power of a low-protein diet may come from mitochondria, at least in fruit flies, researchers report in the Oct. 2 *Cell*. The finding may help researchers explain how dietary restriction lengthens the lives of organisms including yeast, worms, mice and monkeys.

The new work “is really exciting, especially because it starts to get to the mechanisms,” says molecular biologist John Tower of the University of Southern California in Los Angeles.

Although researchers have known that restricting calories can extend lives, the way the process works hasn’t been completely clear. Past studies have shown that when calories are cut, cells respond by changing the degree to which they convert the DNA of some life-extending genes into messenger RNA (a process called transcription). These RNA sequences can then be turned into proteins (translation). Many scientists have focused on the first step in the process by figuring out which messenger RNAs get turned up or down when calories are reduced. But researcher Pankaj Kapahi of the Buck Institute for Age Research in Novato, Calif., and his colleagues took a different approach.

“A lot of our focus has been on the DNA to RNA conversion,” Kapahi says, “but we thought we should also look into the next step.”

Kapahi and his team fed fruit flies a low-protein diet and then assessed how the translation of messenger RNAs changed in response to the diet. Translation of several hundred messenger RNA sequences increased as a result of the dietary restriction, the scientists found. Some of the genes that encode the resulting proteins had not previously been identified as important for life span extension. “This says that translation is very important,” Kapahi says.

What’s more, many of these messenger RNAs encode proteins known to work in the mitochondria, the energy factories of the cell that have been implicated in aging. Flies on a low-protein diet had higher mitochondrial activity, meaning they might operate more efficiently, the team found. “Mitochondria are very intimately linked to the aging process,” Tower says.

To see whether the mitochondria were really responsible, the researchers mutated several of the mitochondrial genes that they had identified as linked to dietary restriction. The benefits of the diet on life span diminished, indicating that the proteins encoded by the mitochondria-related genes were required for life span extension, Kapahi says.

The researchers also found that a protein called 4E-BP is important for mitochondrial function.

Typically, 4E-BP halts the translation of protein in cells. Kapahi says that 4E-BP's job "is to tell the cell that it doesn't need to go around making protein it doesn't need." But the researchers found that, in flies on a low-protein diet, 4E-BP actually increases the translation of certain mitochondrial proteins.

By increasing the levels of 4E-BP in flies on a normal diet, the researchers were able to extend the life span of those flies too, suggesting 4E-BP is crucial for the mitochondrial activity that boosts life span. "You can reverse this age-related decline in mitochondria" by bumping up the levels of 4E-BP, Kapahi says.

The new study's results fit with recent work that found low-protein diets for humans may have anticancer and antiaging effects (*SN:10/25/08, p. 17*). "Proteins matter," Kapahi says.