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A 'spoonful of sugar' makes the worms' life span go down

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If worms are any indication, all the sugar in your diet could spell much more than obesity and type 2 diabetes. Researchers reporting in the November issue of *Cell Metabolism*, a Cell Press publication, say it might also be taking years off your life.

By adding just a small amount of glucose to *C. elegans* usual fare of straight bacteria, they found the worms lose about 20 percent of their usual life span. They trace the effect to insulin signals, which can block other life-extending molecular players.

Although the findings are in worms, Cynthia Kenyon of the University of California, San Francisco, says there are known to be many similarities between worms and people in the insulin signaling pathways. (As an aside, Kenyon says she read up on low-carb diets and changed her eating habits immediately - cutting out essentially all starches and desserts -- after making the initial discovery in worms. The discovery was made several years ago, but had not been reported in a peer-reviewed journal until now.)

"In the early 90s, we discovered mutations that could double the normal life span of worms," Kenyon said. Those mutations effected insulin signals. Specifically, a mutation in a gene known as daf-2 slowed aging and doubled life span. That longer life depended on another "FOXO transcription factor" called DAF-16 and the heat shock factor HSF-1.

Now, the researchers show that those same players are also involved in

numbering the days of worms who are fed on glucose. In fact, glucose makes no difference to the life span of worms that lack DAF-16 or HSF-1, they show. Glucose also completely prevents the life-extending benefits that would otherwise come with mutations in the daf-2 gene.

Ultimately, worms fed a steady diet containing glucose show a reduction in aquaporin channels that transport glycerol, one of the ingredients in the process by which the body produces its own glucose. "If there is not enough glucose, the body makes it with glycerol," Kenyon explained. That glycerol has to first get where it needs to go, which it does via the aquaporin channels.

Further studies are needed to see if these same effects of sugar can be seen in mice, or even people. But there is reason to think they may.

"Although we do not fully understand the mechanism by which glucose shortens the life span of *C. elegans*, the fact that the two mammalian aquaporin glycerol-transporting channels are downregulated by insulin raises the possibility that glucose may have a life-span-shortening effect in humans, and, conversely, that a diet with a low glycemic index may extend human life span," the researchers write. Kenyon also points to recent studies that have linked particular FOXO variants to longevity in several human populations, making the pathway the first with clear effects on human aging.

She says the findings may also have implications for drugs now in development for the treatment of diabetes, which are meant to block glucose production by inhibiting glycerol channels. The new findings "raise a flag" that glycerol channels might be doing something else, she says, and that drugs designed to block them might have a downside.

Source: Cell Press (news : web)