

Research in aging fruit flies may explain roots of metabolic dysfunction in aging humans

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Have you ever wondered why young children can eat bags of Halloween candy and feel fine the next day – compared to adults who experience all sorts of agony following the same junk food binge? Evolution and a gene called Foxo may be to blame. Working in fruit flies, scientists at the Buck Institute have identified a mechanism that helps the flies adapt to changes in diet when they're young; they've discovered that same mechanism gets misregulated as the flies age, disrupting metabolic homeostasis, or balance.

In a study appearing in *Cell Reports*, researchers focus on the function of the Foxo gene in the intestines of fruit [flies](#). Foxo is widely expressed throughout the body (both in flies and in humans), particularly in muscle, the liver and pancreas – and can regulate many aspects of metabolism in response to [insulin signaling](#). Lead author Jason Karpac, PhD, Assistant Research Professor at the Buck, says when young animals experience a change in diet, insulin signaling gets repressed, which turns on Foxo. "In normal young animals, Foxo turns on and off quite easily, allowing for a seamless adjustment to changes in diet," said Karpac. "The process is evolutionarily conserved, it protects young animals and helps guarantee their survival," he said.

But Karpac says as the animals age, Foxo stops responding to insulin signaling (not a good thing for non-youngsters who crave that Halloween candy). "In the flies Foxo gets chronically turned on, which disrupts [lipid](#)

[metabolism](#). The process reflects the development of a general inflammatory condition in the aging gut."

"It has been proposed that our modern high-sugar/high fat diets can lead to misregulation of evolutionarily conserved dietary responses," said Buck Institute faculty Heinrich Jasper, PhD, lead scientist on the study. "That may be the case. Metabolism is a very complex process – lots of things can go wrong which increases stress in the animals." Jasper says age-related loss of metabolic balance is a risk factor for many human pathologies. The goal is to identify age-related changes in metabolic pathways with the hope of being able to intervene. "Our aim is to develop treatments that would preserve well-functioning [metabolism](#) as part of healthy aging – something that would likely not ever include indulging in candy binges."

More information: "Misregulation of an Adaptive Metabolic Response Contributes to the Age-Related Disruption of Lipid Homeostasis in *Drosophila*," *Cell Reports*, epub, September 12, 2013. [www.cell.com/cell-reports/abstract ... 2211-1247\(13\)00428-2](http://www.cell.com/cell-reports/abstract/S2211-1247(13)00428-2)

Provided by Buck Institute for Age Research

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