

# Does dietary restriction protect against age-related leaky gut?

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Flies eating a Spartan diet are protected from leaky gut and the systemic inflammation associated with it as they age. Conversely, flies on a rich Atkins-like diet are more prone to developing intestinal permeability, a condition linked to a variety of human conditions including inflammatory bowel disease. Publishing in *PLOS Genetics*, researchers from the Kapahi lab at the Buck Institute show that gaps in the intestinal barrier are caused by an age-related increase in the death of intestinal epithelial cells, also known as enterocytes.

"The integrity of our gut declines with age and problems with [intestinal permeability](#) are now suspect in chronic inflammation, metabolic diseases and even neurological diseases like Alzheimer's," said Buck professor Pankaj Kapahi, senior scientist on the study. "The possibility that [dietary restriction](#), or the use of dietary restriction mimetics, could help prevent this decline in humans opens a new area of research that could influence healthspan and longevity."

Lead scientist Kazutaka Akagi, a former postdoc in the Kapahi lab who now runs his own lab at the National Center for Geriatrics and Gerontology in Aichi, Japan, zeroed in on dMyc, a gene involved in cell proliferation. He observed that levels of dMyc act as a barometer of cellular fitness in enterocytes, post-mitotic intestinal cells. He found that cells that have too little dMyc get eliminated by neighboring cells through a process termed "cell competition" in an attempt to maintain gut health. "But levels of dMyc naturally decline with age in enterocytes, leading to excessive cell loss and thus a [leaky gut](#)," he said. "In our study,

this decline in dMyc was enhanced by the rich diet, while dietary restriction maintained dMyc level in the flies, preventing leaky gut and extending the lifespan of the animals."

Researchers in the Kapahi lab also looked at the role of dysbiosis, an imbalance in the [intestinal bacteria](#) or microbiome of the flies, as a potential contributor to leaky gut. Even though dysbiosis has been proposed as a leading cause of leaky gut, researchers found that removing intestinal bacteria with antibiotics conferred only minimal protection to the animals and did not prevent age-related damage to enterocytes. "The intestinal epithelium is affected by everything that moves through the gut. It would make sense that diet would have major impact on the health of those cells, especially over a lifetime of eating," said Kapahi. "While we understand the interest in the role of the microbiome, we think that diet may ultimately be the primary driver in cellular changes leading to leaky gut."

**More information:** Kazutaka Akagi et al, Dietary restriction improves intestinal cellular fitness to enhance gut barrier function and lifespan in *D. melanogaster*, *PLOS Genetics* (2018). [DOI: 10.1371/journal.pgen.1007777](#)

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