Both calorie restriction and resveratrol—a compound found in grapes, red wine, and nuts—ward off several age-related diseases in animal models. Researchers have been exploring the molecular mechanisms involved. Recent studies have implicated an enzyme called AMP-activated protein kinase (AMPK). AMPK senses and maintains energy levels in the cell. Among its many effects, it helps to regulate autophagy, a recycling process that continually breaks down and recycles waste within our cells. Autophagy has also been linked to aging and lifespan.

The Research
A team led by Dr. David Walker at the University of California, Los Angeles, used transgenic technology to manipulate AMPK levels in specific organs of fruit flies (Drosophila) and explored the impact on autophagy, cellular signs of aging, and lifespan.

The Results
The researchers found that boosting AMPK levels in the nervous system (neurons) induced autophagy within the brain and prolonged the flies’ lifespan. Surprisingly, boosting neuronal AMPK also induced autophagy in the flies’ intestines and improved a measure of intestinal aging. It induced autophagy and reduced signs of aging in muscle as well.

Autophagy can be directly induced in Drosophila by increasing expression of the gene Atg1. When the researchers raised expression of Atg1 in adult fly neurons, it also improved intestinal function during aging and prolonged lifespan. Further experiments showed that the anti-aging effects of neuronal AMPK disappeared when Atg1 was blocked.
The team next raised levels of AMPK in the intestine. This similarly boosted autophagy, both in the intestine and the brain. It also reduced signs of aging in muscle tissue and prolonged life.

To investigate how AMPK and Atg1 might exert these system-wide effects, the researchers explored the insulin/insulin-growth-factor-1-signaling pathway, which had previously been linked to lifespan in flies and mammals. Their results suggest that AMPK and Atg1 affect other tissues by altering insulin-like peptide signaling.

“We have shown that when we activate the [AMPK] gene in the intestine or the nervous system, we see the aging process is slowed beyond the organ system in which the gene is activated,” Walker says.

**What’s Next?**

Autophagy may slow the aging process by increasing the turnover of damaged cell components. Which of these components might be relevant to aging remains to be discovered. Researchers will also need to test whether activation of autophagy in a single tissue in mammals can slow aging in other tissues as well.

“We have shown that when we activate the [AMPK] gene in the intestine or the nervous system, we see the aging process is slowed beyond the organ system in which the gene is activated.”