



## [How to Increase Autophagy for Lifespan Extension](#)

### **The four pathologies of aging**

Aging can be defined as a breakdown of homeostasis; that is, the organism as it gets older finds it increasingly difficult to regulate itself and to maintain all systems in a state of balance and of health.

A more practical way of defining aging is as increasing susceptibility to disease. Aging is the prime factor in disease risk.

There are four main cellular derangements of aging:

- increased inflammation
- increased oxidative stress
- increased mitochondrial dysfunction
- lower levels of autophagy.

They are all related and linked through cellular sensors and pathways, most notably through [the cellular energy sensor AMPK, which regulates aging](#).

Improving the parameters of any one of these factors also improves the others. Lowering oxidative stress, for example, also entails lower levels of inflammation and better mitochondrial function.

### **Autophagy**

Autophagy, from the Greek for “self-eating”, is the regulated process through which the cell breaks down parts of itself and by sequestering them into vacuoles and digesting them. The parts that are broken down are mainly organelles and proteins that have passed their expiration dates.

In this way, autophagy provides for a continuous process of self-renewal by

breaking down older structures, allowing for new ones to be built in their place.

One characteristic of aging is the accumulation of damage, and this is largely due to the failure of autophagy to attain normal functional levels. It can be seen that bringing levels of autophagy to youthful levels can ameliorate aging by clearing out damaged parts of the cell.

In rats, stimulating autophagy by either fasting every other day, or by fasting once a week together with the anti-lipolytic drug Acipimox, fully restored levels of autophagy in older rats to those of 3-month-old rats. Acipimox is a derivative of niacin (vitamin B3) and works the same way. ([Experimental Gerontology](#)). Markers of accumulated damage also decreased to those of young animals.

In old rats (27 months), the rate of autophagy was only 1/6 that of young animals. ([Journal of Gerontology.](#))

That's a huge difference. Think of the functional decline of an older person: depending on the exact comparison made, it wouldn't be an exaggeration to say that many older people have only 1/6 the physical function of a young man in his prime. That difference may largely be due to autophagy.

In aging, the importance of maintaining clean cells is paramount. ([Autophagy.](#))

## **Autophagy is central to life extension**

A number of different treatments and protocols, for example resveratrol, calorie restriction, and genetic manipulation of IGF-1 signaling, have been found to extend the lifespans of experimental animals.

These treatments and protocols have something in common: they all cause an increase in autophagy.

Autophagy is central to extending lifespan and to avoiding the diseases of aging.

**There is no such thing as healthy aging.** Aging means increasing susceptibility to disease and the breakdown of the organism. Being healthy when older requires *retarding* the aging process.

How central is autophagy to life extension? It is not only necessary, but sufficient: "Essential role for autophagy in life span extension" ([Journal of Clinical Investigation](#)). This article by the world-class scientific team led by Guido Kroemer states:

Life and health span can be prolonged by calorie limitation or by pharmacologic agents that mimic the effects of caloric restriction. Both starvation and the genetic inactivation of nutrient signaling converge on the induction of autophagy, a cytoplasmic recycling

process that counteracts the age-associated accumulation of damaged organelles and proteins as it improves the metabolic fitness of cells. **Here we review experimental findings indicating that inhibition of the major nutrient and growth-related signaling pathways as well as the upregulation of anti-aging pathways mediate life span extension via the induction of autophagy. Furthermore, we discuss mounting evidence suggesting that autophagy is not only necessary but, at least in some cases, also sufficient for increasing longevity.** [my emphasis]

## **Autophagy can be increased easily**

The beauty of autophagy as a life-extending process is that, in the right physiological milieu, that is, under conditions over which we have a great deal of control, it can be strongly increased. Kroemer himself explicitly states that autophagy is “a druggable process that is deregulated in aging and human disease” ([JCI](#)).

**Autophagy (“self-eating”) constitutes one of the most spectacular yet subtly regulated phenomena in cell biology.** Similarly to cell division, differentiation, and death, autophagy is perturbed in multiple diseases, in that excessive or deficient autophagy may contribute to pathogenesis. Numerous attempts have been launched to identify specific inducers or inhibitors of autophagy and to use them for the therapeutic correction of its deregulation. At present, several major disease categories (including but not limited to age-related, cardiovascular, infectious, neoplastic, neurodegenerative, and metabolic pathologies) are being investigated for pathogenic aberrations in autophagy and their pharmacologic rectification. Driven by promising preclinical results, several clinical trials are exploring autophagy as a therapeutic target.

Increasing autophagy to youthful levels is, in my view, essential to any anti-aging protocol.

Much of the decrease in autophagy seen in aging is also less related to aging *per se* than it is to types of behavior associated with aging.

Even in older animals, autophagy can be robustly increased through, for example, fasting and exercise, two interventions that have nothing to do with aging in itself.

Before we get to ways to increase autophagy, how can you completely screw up the process and ensure that your autophagy levels decline and that you get old and unhealthy in a hurry?

- First of all, eat all the time: graze, eat snacks, never let your body out of the fed state.

- Second, be sedentary and gain weight. Doing this increases levels of inflammation and oxidative stress and causes a decline in autophagy.
- Third, make sure all your food is processed and that you never eat a vegetable.

## How to increase autophagy

Several reliable interventions increase autophagy, and you can do them on your own.

1. **Exercise:** Exercise induces autophagy in the body and in the brain ([Autophagy](#)). Since it's been shown that autophagy is required for the beneficial effects of exercise, including performance adaptation, exercise would have to be intense enough to cause these adaptations for autophagy to take place.

The benefits of weightlifting are in part caused an increase in autophagy: "Chronic resistance training activates autophagy and reduces apoptosis of muscle cells" ([Experimental Gerontology](#)).

Autophagy Is Required to Maintain Muscle Mass. ([Cell Metabolism](#).) Absence of autophagy causes profound muscle atrophy.

2. **Fasting:** Autophagy is "potently triggered by fasting" (Kroemer again, [Cell](#)). How much fasting? In young animals and humans, overnight fasting is enough to get it started. When older, longer periods of fasting may be necessary, which is why I regularly fast for 16 hours or more.

Even better news is that fasting can strongly protect against cognitive decline, dementia, Alzheimer's, and Parkinson's: Short-term fasting induces profound neuronal autophagy ([Autophagy](#)). **"Our data lead us to speculate that sporadic fasting might represent a simple, safe and inexpensive means to promote this potentially-therapeutic neuronal response."**

If you want to keep your mind as well as your body in youthful condition, fasting should be added to the arsenal.

3. **Chemical autophagy boosters:** See my article "[Intermittent Fasting Boosters / Autophagy Enhancers](#)". These chemical autophagy boosters include resveratrol, hydroxycitrate, nicotinamide, curcumin, lithium, and EGCG (from green tea). These are all readily available over-the-counter, and are cheap and safe.

Insulin signaling from food could override the autophagy-boosting effects of these supplements, so take them during the fasted state.

4. **Ketosis.** [Ketosis](#) results from relatively prolonged abstention from dietary carbohydrates. It stimulates autophagy ([JBC](#)) and promotes autophagy in the brain ([Medical Hypotheses](#)), which is likely important to the neuroprotective effects of the ketogenic diet.

## Conclusion

Virtually every known method of life extension, as well as methods that protect the organism from disease, are mediated by autophagy. Fortunately for us, we have many methods at our disposal for increasing autophagy to youthful levels.

**PS:** For more on this, see my book [Stop the Clock: The Optimal Anti-Aging Strategy](#).

**PPS:** [Check out my Supplements Buying Guide for Men.](#)