

Autophagy Finally Considered for Viral, Bacterial Treatment

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STORY AT-A-GLANCE

- › Autophagy refers to your body's process of eliminating damaged cells by digesting them. It's an essential cleaning out process that encourages proliferation of new, healthy cells, and is a foundational aspect of cellular rejuvenation and longevity
- › Autophagy also destroys foreign invaders such as viruses, bacteria and other pathogens, and detoxifies the cell of harmful materials
- › Autophagy slows down with age, and autophagy defects are known to contribute to a wide variety of diseases, including Alzheimer's and Parkinson's
- › By activating autophagy, or repairing the mechanism in cases where dysfunction has set in, researchers believe neurodegenerative diseases such as Alzheimer's and Parkinson's can be successfully treated
- › There are a number of ways to activate and increase autophagy, including fasting, exercising, eating autophagy-boosting foods and taking AMPK-activating supplements such as berberine and PQQ

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Autophagy literally means "self-eating" and refers to your body's process of eliminating damaged cells by digesting them. It's an essential cleaning out process that encourages

the proliferation of new, healthy cells, and is a foundational aspect of cellular rejuvenation and longevity.

Autophagy also destroys foreign invaders such as viruses, bacteria and other pathogens, and detoxifies the cell of harmful materials. Autophagy slows down with age, and autophagy defects are known to contribute to a wide variety of diseases, including Alzheimer's and Parkinson's. The good news is there are a number of different ways to activate and increase this natural process, thereby preventing many health problems before they begin.

Autophagy Activation Is a Powerful Way to Treat Many Diseases

Researchers are now also latching on to autophagy as a viable way to treat disease.¹ As explained in the 2012 paper, "Autophagy Modulation as a Potential Therapeutic Target for Diverse Diseases:"²

"Autophagy occurs at a basal rate in most cells, eliminating protein aggregates and damaged organelles in order to maintain cytoplasmic homeostasis. This includes the degradation of dysfunctional mitochondria via mitophagy, a cytoprotective process that limits both the production of reactive oxygen species (ROS) and the release of toxic intramitochondrial proteins ...

In addition to its vital homeostatic role, this degradation pathway is involved in various human disorders, including metabolic conditions, neurodegenerative diseases, cancers and infectious diseases ... Autophagy may be dysregulated in several disorders, including metabolic diseases, neurodegenerative disorders, infectious diseases and cancer.

In some conditions, autophagy is inhibited and this can occur at different stages of the process to enhance disease, whereas in other cases autophagic activity may be permissive toward pathogenesis. In addition, the induction of autophagy has been shown to increase longevity in a large panel of species,

thus raising the possibility that ageing and longevity may be therapeutic targets for autophagy induction.

Given these observations, pharmacological approaches to upregulate or inhibit this pathway are currently receiving considerable attention. For example, autophagy upregulation may be of therapeutic benefit in certain neurodegenerative diseases ... whereas autophagy inhibition is being investigated as a strategy for treating some cancers."

Autophagy May Be Used to Treat Parkinson's Disease

In 2016, the Nobel Prize in medicine was given to the Japanese biologist Yoshinori Ohsumi³ for his discovery of the actual mechanisms of autophagy, i.e., how cells recycle their contents. As reported by The Conversation:⁴

"Ohsumi identified key genes and molecules behind autophagy. In so doing, he shifted scientific paradigms about cellular quality control. He opened the gate for researchers ... to understand how defects in autophagy are associated with neurological diseases ...

In neurodegenerative diseases, toxic proteins accumulate within brain cells called neurons. Neurons are irreplaceable. They must continue to recycle proteins and break them down into small amino acids to avoid a toxic buildup of abnormally large proteins. That is what autophagy lets them do.

The process works by sequestering unwanted proteins into pipelines called 'autophagosomes.' Then they dump those proteins into a part of the cell called a 'lysosome,' where they are recycled. When this process doesn't work properly, harmful proteins can accumulate."

Activating Autophagy Helps Prevent Neurological Degeneration

By activating autophagy, or repairing the mechanism in cases where dysfunction has set in, researchers believe neurodegenerative diseases such as Alzheimer's and Parkinson's can be successfully treated, as the autophagy process will naturally clear out harmful proteins.

Interestingly, researchers have demonstrated that certain cancer drugs can trigger autophagy by activating a protein called parkin. Parkin is involved in the autophagy process, and some cancer drugs specifically activate this protein. As reported by Charbel Moussa, assistant professor of neurology at Georgetown University:⁵

"Keep in mind that cancer drugs work by killing cancer cells and can also be toxic to other cells. So our first step was to find out how these drugs worked in cancer cells and neurons. Our initial observation in cell culture models was stunning: Cultured cancer cells died while cultured neurons survived after treatment with several autophagy-stimulating cancer drugs.

Next we introduced toxic proteins into cultured neuronal cells and treated them with several cancer drugs that activate autophagy and destroy tumors. The cells treated with these drugs survived and cleared their toxic proteins, while untreated cells died.

Activating autophagy is a double-edged sword. On the one hand, the process clears toxic or infectious materials from cells. On the other hand, if the autophagy process goes beyond 'recycling' and clearing out proteins, it can start to destroy the cell, leading to cell death. This means that autophagy must be carefully manipulated to avoid the death of nonrenewable and irreplaceable neurons."

Cyclical Autophagy, the Natural Way to Improve Health

Likely the safest way to achieve these benefits is simply to boost autophagy naturally, and there are many healthy lifestyle strategies that will do just that. Perhaps one of the

most important and most effective is fasting. As explained in "Autophagy Modulation as a Potential Therapeutic Target for Diverse Diseases:"⁶

"Autophagy is stimulated during various pathological and physiological states, such as starvation ... Starvation induced autophagy, an evolutionarily conserved response in eukaryotes, enables the degradation of proteins, carbohydrates and lipids, which allows the cell to adapt its metabolism and meet its energy needs.

Indeed, the induction of autophagy in newborn mice has a major role in maintaining energy levels in various tissues after the maternal nutrient supply via the placenta ceases. Moreover, starvation-induced autophagy has a cytoprotective effect by blocking the induction of apoptosis by mitochondria."

Longer water-only fasts are a form of "starvation" that will induce autophagy. As little as 200 calories can thwart the process, and the starvation period needs to be at least 16 hours or 72 hours or even longer, so it's important to be strict if autophagy induction is your chief aim.

On the flip side, autophagy cannot remain continuously activated all the time. You also need to allow the cells to rebuild and rejuvenate, which occurs during the refeeding phase, which is why cyclical fasting and feeding is so important.

Fasting Is a Powerful Way to Activate Autophagy

Based on the research that has emerged in recent years, I'm now convinced that multiple-day water fasting is one of the most profound metabolic interventions you can do to radically improve your health, as it allows your body to upregulate autophagy and mitophagy to remove damaged senescent cells, including premalignant cells. It's also an extremely effective way to shed excess weight and extend your life span.

For a refresher on how to do water fasting safely, check out the website⁷ of Dr. Jason Fung, whom I interviewed a few years ago after he wrote his book, "The Complete Guide to Fasting." Many have irrational fears about water fasting, even for a few days, and Fung expertly shreds many outdated myths about fasting.

There are a few caveats, however. If you're on medication, you need to work with your doctor to ensure safety, as some medications need to be taken with food and/or can become toxic when your body chemistry normalizes. Those taking hypoglycemic or antihypertensive medication are particularly at risk, as they may end up overdosing.

It's also recommended to continue taking nutritional supplements during your fast. You also need to take a high-quality salt. Certain health conditions may also need more stringent medical supervision to ensure safety when fasting.

A gentler way that can still improve autophagy is intermittent fasting, provided you're not eating for at least 16 hours at a stretch. This is the time needed to activate autophagy. That then means you need to eat all of your meals for the day within an eight-hour window, and not snack on anything during fasting hours.

If you want to try a water-only fast, I recommend starting out by intermittently fasting about 16 hours a day, and slowly working your way up to 20 hours a day. Once you've done that for a month, it will be a lot easier to do a water fast for five days.

Fasting Regenerates Your Pancreas

A powerful example of the regenerative power of fasting was demonstrated in a study⁸ that showed a fasting-mimicking diet — characterized by periods of feast and famine — can reverse diabetes and actually regenerate your pancreas. The experiment, conducted on mice, was led by Valter Longo, Ph.D., professor of gerontology and biological sciences and director of the USC Longevity Institute.

What they discovered was that by starving and refeeding the animals in cycles, insulin-producing beta cells were generated, resembling that observed during pancreatic development. Beta cells detect sugar in your blood and release insulin if blood sugar levels get too high. As a side effect of restoring pancreatic function, diabetic symptoms were also reversed. Insulin secretion and glucose homeostasis were restored in both Type 1 and Type 2 diabetes models. According to Longo:

"Our conclusion is by pushing the mice into an extreme state and then bringing them back – by starving them and then feeding them again –the cells in the pancreas are triggered to use some kind of developmental reprogramming that rebuilds the part of the organ that's no longer functioning ...

Medically, these findings have the potential to be very important because we've shown – at least in mouse models – that you can use diet to reverse the symptoms of diabetes. Scientifically, the findings are perhaps even more important because we've shown you can use diet to reprogram cells without having to make any genetic alterations."

The fasting-mimicking diet developed by Longo involves restricting your calories to 75 percent less than your normal calories per day for five days each month. This approach greatly improves compliance, as many find a five-day, water-only fast to be too difficult. During these five days of calorie restriction, it's important to select foods low in carbohydrates, low in protein and high in healthy fats.

The rest of the month, you are free to eat whatever you want. The goal is to mimic periods of feast and famine. However, while it may sound simple enough, Longo is quick to suggest this particular diet is best undertaken with medical guidance, as it's far more sophisticated than most people realize.

Other Strategies That Will Activate Autophagy

- **Cyclical exercise** – Every other day, do 30 minutes of high-intensity interval training or resistance training. The acute stress of exercise triggers autophagy much in the same way as fasting.
- **Eating autophagy-activating foods** – In her New York Times best seller book, "Glow 15: A Science-Based Plan to Lose Weight, Revitalize Your Skin, and Invigorate Your Life," Naomi Whittel includes 140 different types of foods that help activate autophagy – such as citrus bergamot tea, green tea and turmeric.

- **Activating adenosine monophosphate-activated protein kinase (AMPK) through proper diet and nutritional supplements** — AMPK is an enzyme that stimulates mitochondrial autophagy (mitophagy) and mitochondrial biogenesis, as well as five other critically important pathways: insulin, leptin, mammalian target of rapamycin (mTOR), insulin-like growth factor 1 and proliferator-activated receptor gamma co-activator 1-alpha.

It also increases nerve growth factor and helps protect against the type of oxidative stress that leads to Parkinson's disease. With age, your AMPK levels naturally decline. Certain dietary habits, such as eating too much unhealthy fat and not enough of healthy fats and getting insufficient amounts of flavonoids (antioxidants) also inhibit AMPK activity. Insulin resistance is also a powerful inhibitor of AMPK.

So, keeping this enzyme activated through proper diet is another important factor for maintaining healthy autophagy. Two dietary supplements known to activate AMPK — thereby triggering mitophagy and mitochondrial biogenesis — are pyrroloquinoline quinone (PQQ) and berberine. Both of these supplements also benefit your mitochondrial function and health.

A Simple Way to Boost Health and Prevent Disease

Considering your health is dependent on well-functioning cells, addressing autophagy is of significant importance and can go a long way toward preventing disease, including neurodegenerative disorders and cancer. Without autophagy, your cells will eventually become gunked up with toxins and debris, and once they start to malfunction and/or die, your body will be unable to efficiently clear those cells out, which will further exacerbate the problem.

The good news is, it's not very difficult to optimize autophagy. Fasting appears to be the most efficient way, but exercise and adding certain foods and supplements are also helpful strategies. If you're truly dedicated, you'd do your best to incorporate all of these strategies.

Sources and References

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