The next revolution in biology isn't reading life's code - it's writing it. (...) Writing DNA holds even greater promise - the potential to cure any disease. Andrew Hesel. October 23, 2025. Source.

This month's theme: Mitochondria

The Powerhouse and the Clock: How Mitochondria Shape Aging

About 2,3 billion years ago, an organism absorbed a bacterium that would become mitochondria. This was, for animals, the most successful symbiosis in the history of life. Nowadays, mitochondria, often called the "powerhouses" of the cell, do far more than just produce energy. These small but mighty organelles generate ATP—the essential molecule that fuels nearly every cellular process—while also regulating calcium balance, apoptosis (programmed cell death), and key metabolic pathways. What makes them especially intriguing is that they contain their own DNA, separate from the cell's nucleus, which makes them uniquely vulnerable to damage over time.

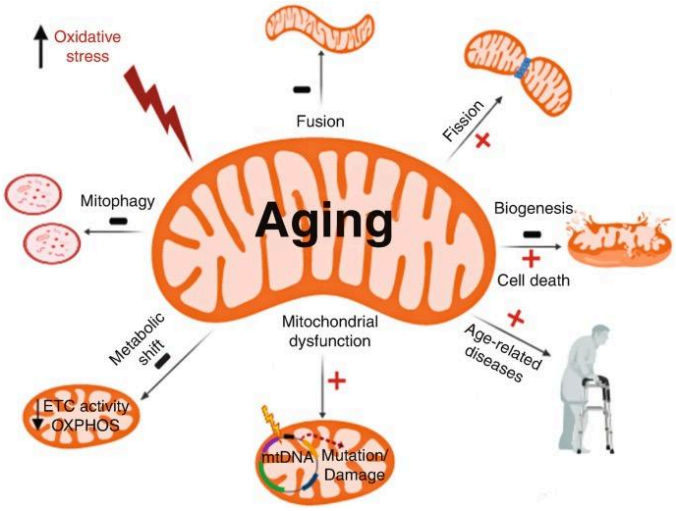

Image from S. L. Morales-Rosales et al, 2020

Mitochondria undergo wear and tear that affects their ability to function properly.

1. Damaged DNA, Damaged Cells

Mitochondria possess their own DNA (mtDNA), separate from the cell's nuclear DNA. Unlike nuclear DNA, mtDNA lacks the robust protective histones and repair systems that guard against damage. This makes it particularly vulnerable to oxidative stress — the constant bombardment of reactive molecules produced during energy generation. Over time, oxidative stress introduces mutations into mtDNA, disrupting the genes responsible for key components of the electron transport chain.

2. The ROS Paradox

Reactive oxygen species (ROS) are a double-edged sword in biology. On one hand, they are natural byproducts of mitochondrial respiration and play important signaling roles in cell adaptation, repair, and immune defense. In youthful, healthy cells, low levels of ROS act as beneficial messengers that fine-tune metabolism and trigger protective antioxidant responses — a process known as *mitohormesis*. However, as mitochondria age and become less efficient, they produce excessive ROS that overwhelm the cell's antioxidant defenses. This oxidative overload damages DNA, lipids, and proteins, impairing cellular structures and signaling pathways. Over time,

these molecular injuries accumulate, accelerating tissue degeneration and contributing to diseases such as Alzheimer's, Parkinson's, and cardiovascular decline.

3. Out with the Old — or Not

Cells have a sophisticated quality-control system to maintain mitochondrial health, and a central part of this system is mitophagy — the targeted degradation and recycling of damaged mitochondria. Under normal conditions, faulty mitochondria are tagged and removed to make way for new, fully functional ones. However, with age, this self-renewal process slows down. The mechanisms that detect and dispose of defective mitochondria become less responsive, leading to the accumulation of dysfunctional organelles within the cell. These impaired mitochondria not only produce less energy but also leak harmful molecules that exacerbate oxidative stress. The gradual buildup of damaged mitochondria is a critical contributor to the decline in cellular vitality and resilience seen in aging tissues.

4. Inflammation from Within

When mitochondria become damaged beyond repair, they can release fragments of their own DNA and proteins into the cytoplasm or bloodstream. Interestingly, because mitochondrial DNA evolved from ancient bacteria, the immune system often mistakes it for a foreign invader. Over time, this persistent low-level inflammation — termed *inflammaging* — becomes a major driver of age-related tissue damage and chronic diseases, including atherosclerosis, diabetes, and neurodegeneration. In this way, failing mitochondria act not only as victims of cellular aging but also as active participants that amplify the inflammatory processes underlying it.

Focus on Mitochondria for anti-aging interventions

Recent advances in nanoengineered mitochondria (biohybrid systems that integrate isolated mitochondria with functional nanomaterials) may soon allow us to repair and enhance them, opening new paths toward better health and longevity. Unlike conventional mitochondrial transplantation, which simply transfers healthy mitochondria to damaged tissues, these nano-biohybrids enhance organelle stability, boost ATP production, and enable targeted delivery. Preclinical studies show promising results in cardiovascular, neurodegenerative, and age-related disorders, including breakthroughs where engineered mitochondria prevented intervertebral disc degeneration in rats by restoring mitochondrial function and modulating key signaling pathways such as mtDNA/SPARC-STING. By bridging materials science and mitochondrial biology, nanoengineered mitochondria could emerge as a powerful new tool in longevity therapeutics, revitalizing energy metabolism at its source.

Several strategies are being developed to counteract mitochondrial decline. One major approach involves antioxidants targeted specifically to mitochondria, such as **MitoQ** and **MitoVitE**, which aim to neutralize excess ROS and reduce oxidative damage. Another focuses on stimulating mitochondrial biogenesis, often through pathways like PGC-1α activation; exercise remains the best-validated method for this, but pharmacological enhancers are under investigation. Therapies that enhance mitophagy — the selective clearance of damaged mitochondria — are also of

growing interest, as impaired mitophagy is a hallmark of aging cells. Other approaches include **modulating mitochondrial metabolism**, for instance by increasing NAD^+ levels, which support mitochondrial redox reactions and energy metabolism.

Among the most promising experimental therapies is **Elamipretide (SS-31)**, a mitochondria-targeted peptide that binds to cardiolipin in the inner mitochondrial membrane, stabilizing its structure and improving the efficiency of the electron transport chain. In preclinical studies, Elamipretide improved muscle endurance, cardiac function, and mitochondrial energetics, and early human trials have shown enhanced ATP production in older adults.

Collectively, these mitochondrial-targeted interventions represent one of the most active areas in aging research. While most remain at early stages of development, they illustrate a broader therapeutic shift—from treating single age-related diseases to addressing the underlying cellular dysfunctions that drive aging itself. Lifestyle interventions such as exercise and caloric moderation remain the most reliable means to preserve mitochondrial health, but ongoing trials of peptides like Elamipretide, NAD^+ precursors, and mitophagy activators could soon expand the toolkit for promoting healthier aging. The field's success will depend on overcoming key challenges such as long-term safety, delivery specificity, and demonstrating true improvements in human healthspan rather than just cellular biomarkers.

The good news of the month- Human cells reduce senescence markers in aged macaques.

In a study published in Cell (September 4, 2025), scientists demonstrated that infusing senescence-resistant human mesenchymal progenitor cells (SRCs) into aged macaques significantly reduced markers of aging and improved cognitive, bone, and reproductive function.

This is very promising. It is hoped that those monkeys will live long enough to demonstrate that the progenitor cells prolong the healthy lifespan.

For more information

- Heales, Longevity Escape Velocity Foundation, International Longevity Alliance, Longecity, and Lifespan.io
- Heales Monthly Science News
- Heales YouTube channel
- Contact us
- S. L. Morales-Rosales et al, 2020