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How Urolithin A May Support Mitochondrial Renewal in Aging Immune Cells

Analysis by Dr. Joseph Mercola | November 06, 2026

STORY AT-A-GLANCE

- As you age, your thymus produces fewer newly formed cells responsible for responding to unfamiliar pathogens, reducing your immune system's adaptability. This shift, combined with persistent inflammation, defines the core features of immune aging
- Urolithin A, a postbiotic compound, has been studied for its effects on mitochondrial renewal in aging immune cells. In a small, four-week trial in 50 healthy middle-aged adults, those taking urolithin A showed a modest increase in naïve-like CD8 T cells and shifts in several other immune cell populations compared with placebo
- In that trial, urolithin A was associated with higher levels of PGC-1α, a protein linked to mitochondrial biogenesis, and a greater capacity of CD8 T cells to use fatty acids for energy
- Beyond immune health, laboratory and animal studies suggest urolithin A may influence pathways involved in fatty liver and obesity-related insulin resistance. Separately, two small, industry-funded human trials reported improvements in some measures of muscle endurance and strength
- Alongside the research on urolithin A, you can also support your mitochondria by lowering linoleic acid intake, eating the right carbohydrates, limiting environmental toxins, and supporting NAD^+ production with niacinamide

Most people tend to think of immune health mainly as a defense against seasonal colds or infections. In reality, its influence runs deeper. A well-balanced immune system helps regulate inflammation, maintain internal stability, and support energy and vitality. As the years pass, however, the immune system undergoes natural changes that are part of the aging process itself.[1]

Mitochondrial dysfunction is thought to be a major contributor to this decline, alongside the exhaustion of immune stem cells, yet clinical strategies to address immune aging are still lacking. To address this gap, a randomized, placebo-controlled trial published in Nature Aging investigated whether urolithin A, a postbiotic compound known to stimulate mitochondrial clean-up (mitophagy), could reshape the composition and function of aging immune cells.[2]

What Happens to Your Immune System as You Age?

As you grow older, your immune system undergoes what the Nature Aging study describes as "global remodeling of the immune system," which involves several well-documented shifts that change how effectively your immune system responds to everyday challenges.[3]

- **Thymic output declines, reducing newly formed T cells —** One of the core shifts involves the thymus, the organ that produces naïve T cells. With age, thymic activity declines, leading to fewer newly formed T cells entering circulation. Because naïve T cells are your front-line responders to unfamiliar pathogens, this reduction makes it harder for your immune system to mount strong first-time responses.

- **Memory T cells accumulate, limiting adaptability —** As naïve T cells drop, memory T cells become a larger share of your immune system. Memory cells help with threats you have already encountered but bring little support when something new appears. This shift helps explain why older adults respond less robustly to vaccines and face more risk from novel infections.

- **Inflammaging becomes a defining feature of later life —** As immune cell patterns shift with age, the body enters a state of persistent, low-grade inflammation. This phenomenon, known as inflammaging, reflects higher levels of inflammatory mediators circulating at rest and is considered one of the central characteristics of an aging immune system. Learn more about this in "**'Inflammaging' Is a Lifestyle Phenomenon, Not a Universal Aging Trait**."

Together, these changes outline the core features of immune aging. They show why an older immune system tends to be less flexible, slower to respond to new threats, and more prone to persistent inflammation.

Insights Into Urolithin A's Immune and Mitochondrial Actions

The featured study, which is a randomized, double-blind, placebo-controlled trial, involved 50 healthy adults between 45 and 70 who received either 1,000 milligrams (mg) of urolithin A per day or a placebo for four weeks. Researchers collected blood at the beginning and end of the study to observe how immune cells shift over that short window.[4]

This made it possible to see whether mitochondrial support translates into measurable changes in immune cell composition and behavior. Note that the trial was designed as a short proof-of-concept study and was funded by the manufacturer of the urolithin A product tested.

- **Urolithin A increased naïve-like CD8 T cells —** Participants who received urolithin A showed a small but statistically significant increase in naïve-like CD8 T cells, which resemble younger, freshly formed immune cells and carry fewer markers of exhaustion. Alongside this shift, their CD8 T cells became noticeably better at using fatty acids for energy than those in the placebo group, suggesting better metabolic flexibility.

- **Some innate immune cell populations increased —** Urolithin A supplementation increased CD56dimCD16bright natural killer (NK) cells, the most common NK cell subset in human blood. For context, NK cells help identify and eliminate infected cells, but the researchers note that the functional relevance of this particular shift remains unclear, and NK cell killing activity was not directly measured.*

- **Signs of increased mitochondrial biogenesis appeared within CD8 T cells —** Participants who took urolithin A showed higher levels of PGC-1α, the protein that guides mitochondrial growth and renewal.

  The researchers propose that urolithin A may prompt immune cells to clear out older, less efficient mitochondria and build new ones, strengthening their overall energy system. However, mitophagy itself was not directly measured in participants, and this proposed mechanism rests largely on the team's earlier mouse and laboratory work.

- **Laboratory tests showed changes in immune cell activity —** When researchers activated T cells in the lab, those from the urolithin A group produced more tumor necrosis factor (TNF), a cytokine that signals rapid immune engagement. Monocytes also demonstrated better uptake of E. coli particles, suggesting an improved ability to recognize and engulf microbial targets under laboratory conditions.*

- **Molecular programming shifts within immune cells —** Exploratory single-cell analysis suggested that urolithin A shifted inflammatory and metabolic pathways across multiple immune cell types. The researchers caution that these comparisons were exploratory and did not preserve randomization. As they explained:

  > *"Exploratory single-cell RNA sequencing demonstrated urolithin A (UA)-driven transcriptional shifts across immune populations, modulating pathways linked to inflammation and metabolism.*

> *These findings indicate that short-term UA supplementation modulates human immune cell composition and function, supporting its potential to counteract age-related immune decline and inflammaging."*[5]

Taken together, the featured trial suggests that urolithin A can shift several measures of immune cell composition and function within a relatively short period of time. Because this was a small, four-week proof-of-concept study in healthy adults, the researchers emphasize that further studies are needed to determine whether these changes translate into tangible benefits, such as fewer infections.

Even so, the findings add to the evidence that supporting mitochondrial health may play a meaningful role in maintaining immune resilience as you age.

**These findings are from research conducted in clinical settings. Results may not apply to all individuals.*

Urolithin A Research Beyond Immune Health

Beyond immune aging, urolithin A has been studied for a variety of other health effects as well. Research suggests that it interacts with several biological pathways relevant to long-term health, which has led scientists to examine it in the context of several conditions — mostly in laboratory and animal studies — including:[6]

- **Muscle strength and endurance —** In a randomized, placebo-controlled clinical trial of 66 older adults aged 65 to 90, published in JAMA Network Open, participants were given 1,000 mg of urolithin A or a placebo daily for four months. Urolithin A significantly improved muscle endurance, measured as the number of contractions until fatigue in both hand and leg muscles, compared with placebo.

  However, the trial's primary end points — six-minute walk distance and maximal adenosine triphosphate (ATP) production in the hand muscle — did not improve significantly versus placebo. Moreover, the study was funded by the urolithin A manufacturer.**[7]

A separate four-month trial in 88 overweight, untrained adults aged 40 to 64, published in Cell Reports Medicine, found that daily urolithin A supplementation (500 mg or 1,000 mg) improved hamstring muscle strength by about 10% to 12% compared with placebo and produced favorable shifts in several biomarkers associated with mitochondrial health.

Improvements in aerobic endurance and walking distance did not reach statistical significance against placebo, the trial's primary end point (peak power output) was not met, and the study was sponsored by the urolithin A manufacturer.**[8]

- **Fatty liver —** In a mouse model of fructose-induced fatty liver disease, urolithin A administration reduced hepatic steatosis (fat buildup in the liver) and improved the balance between fat creation and fat breakdown in the liver by impairing lipogenesis and enhancing β-oxidation.[9] In parallel, a Biomedicines review notes that urolithin A attenuated inflammation in liver tissue in animal models of metabolic disease.[10]

- **Metabolic disorders —** Urolithin A has been studied in laboratory and animal models of obesity, Type 2 diabetes, and metabolic syndrome. In laboratory studies using human fat and liver cells, urolithin A reduced triglyceride accumulation by lowering genes that drive fat creation and activating AMPK, an energy-sensing pathway that shifts cells toward burning stored fat instead of stockpiling it.[11]

  More detailed experiments in mouse preadipocytes (the precursor cells that eventually mature into fat cells) found that urolithin A lowered triglyceride content and suppressed the expression of several key genes that help regulate fat storage, glucose transport, and fatty acid binding, a change that may help limit fat accumulation while still allowing fat cells to form normally.*[12]

  Additional research also reported that urolithin A protected mice and rats from high-fat diet-induced obesity and insulin resistance by supporting thermogenesis, increasing browning responses (a shift toward a more metabolically active type of

fat cell), reducing oxidative stress, and lowering inflammatory activity within adipose tissue.[13]

**These findings are from laboratory or animal research and may not directly apply to human health.*

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How Urolithin A Is Formed and Delivered

To make sense of the research on urolithin A, it helps to understand how your body forms it, why many people produce very little, and why researchers are exploring different ways of delivering it.

- **Urolithin A is naturally produced in your body —** When you eat foods rich in ellagitannins, a class of polyphenols found in **pomegranates** and some berries, these plant compounds are first converted into ellagic acid and then transformed into different urolithins depending on which microbial species live in your gut.[14]

- **Not everyone forms urolithin A efficiently —** The ability to generate urolithin A depends on your gut microbiota composition. Factors such as age, diet, medication use, and overall microbial diversity may influence whether the conversion occurs.

  According to one review, this conversion is observed in only about 40% of the population, and output varies widely among those who do produce it.[15] This variability is one reason researchers have tested urolithin A directly in clinical trials, including those described above.

- **How it's delivered may matter —** Because urolithin A acts on mitochondria, some researchers are exploring ways to deliver it more directly to them. Mitochondria are under constant wear, so the body depends on recycling the damaged ones.[16]

They contain the furnace of energy production, and because most people consume excess linoleic acid (LA) from seed oils, their mitochondria may be damaged prematurely. These damaged mitochondria need to be recycled; if they accumulate instead, your cellular energy production can decline.

While research on delivery continues, you already have practical ways to strengthen mitochondrial function, many of which support the same pathways urolithin A influences.

Practical Strategies to Improve Your Mitochondrial Health

Recognizing how strongly your mitochondria influence immune aging gives you a clearer sense of where to focus your efforts. The choices you make each day shape how well your mitochondria function, which in turn affects your metabolic stability and long-term immune resilience. Several practical steps can help you support these organelles and create a healthier foundation for cellular energy and overall health:

1. **Remove processed foods and vegetable oils from your diet —** Processed products are typically made with seed oils that contain large amounts of LA, which can interfere with mitochondrial function and reduce your ability to generate energy efficiently.

   Nuts, seeds, and most restaurant meals contribute additional LA, since commercial kitchens rely heavily on these oils, so it's best to prepare most of your meals at home. When you do eat out, The Templeton List (templetonlist.com) can help you find healthier restaurants.

   Chicken and pork often contain higher levels of LA as well, due to the way they are commonly raised and fed. Center your diet around whole foods and choose low-LA fats such as grass fed butter, tallow, and ghee. Aim to keep your daily LA intake below 5 grams. Use the Seed-Oil Sleuth feature in the upcoming PAX, which can help track the LA in your food.

2. **Optimize your carbohydrate intake for cellular fuel —** A balanced diet rich in the right carbs and free of ultraprocessed foods feeds your mitochondria with the glucose they're designed to burn. Focus on whole fruits and white rice first, then gradually bring in root vegetables, legumes, and well-tolerated grains as your gut improves. Aim for 250 grams of targeted carbs daily — far more if you're active — to support healthy thyroid function and cellular energy production.

3. **Reduce exposure to environmental toxins —** Your cells are exposed to synthetic chemicals every day. Substances such as **endocrine-disrupting chemicals** (EDCs) from plastics, estrogen-mimicking compounds like **xenoestrogens**, and widespread **electromagnetic fields** (EMFs) can interfere with how efficiently your mitochondria produce energy. When these exposures accumulate, mitochondrial function can decline.

   Taking steps to limit this burden can make a meaningful difference. Choose household items made from natural materials whenever possible, and store food in glass instead of plastic. Creating a low-EMF sleeping environment is also helpful, as it allows your cells to recover overnight with less external stress. Collectively, these changes reduce the strain placed on your body.

4. **Get proper sun exposure —** Regular sun exposure supports cellular energy by stimulating your mitochondria to produce melatonin — most of your body's melatonin is made in the mitochondria in response to near-infrared light — which provides strong antioxidant protection inside your cells.

   However, it's best to avoid direct sun during peak hours (typically 10 a.m. to 4 p.m. in most parts of the U.S.) until you have minimized seed oils in your diet for four to six months, as the buildup of LA in your tissues makes your skin more prone to sunburn. After that, solar noon is the optimal time for sun exposure.

5. **Support healthy NAD^+ levels —** Taking **niacinamide** at a dose of 50 mg three times a day may help raise your NAD^+ levels, which supports mitochondrial energy production. NAD^+ also plays a role in normal cell-death signaling and in immune cell

function.

Frequently Asked Questions (FAQs) About Urolithin A

Q: What is urolithin A, and how does it work?

A: Urolithin A is a postbiotic compound that your body can produce when certain gut bacteria break down ellagitannins from foods like pomegranates and berries.

It is best known for stimulating mitophagy, the process that clears out damaged mitochondria from your cells, and research suggests it may also support the formation of new, healthy ones. This mitochondrial renewal may be particularly important for your immune cells, which need strong energy production to function effectively as you age.

Q: How does my immune system change as I get older?

A: As you age, your thymus produces fewer naïve T cells, which are your front-line responders to new threats. At the same time, memory T cells accumulate, making your immune system less adaptable to novel infections. You also experience persistent low-grade inflammation that becomes a defining feature of immune aging. Together, these changes make your immune system slower to respond and less flexible.

Q: Can my body produce urolithin A on its own?

A: Your body can produce urolithin A only if you eat foods that contain ellagitannins and you have the specific gut bacteria needed to convert them. Many adults lack the microbes required, which is why conversion is observed in only about 40% of people, even after consuming ellagitannin-rich foods.

Q: What does research suggest about urolithin A beyond immune health?

A: Small human trials have reported improvements in some measures of muscle endurance and strength and in mitochondrial biomarkers, although several of their primary outcomes were not met. Laboratory and animal studies have also examined its effects on metabolic function, fat storage, and cellular stress responses.

Q: What other steps can I take to improve my mitochondrial function?

A: You can support your mitochondrial health through several practical daily choices. Lowering your LA intake by cutting back on seed oils and processed foods helps protect your mitochondria from ongoing oxidative damage. Eating the right kinds of carbohydrates also gives your cells the steady glucose they rely on for energy.

Reducing your exposure to environmental toxins and creating a low-EMF sleeping environment further lightens the stress placed on your cells each day. Regular sun exposure adds another layer of support by stimulating your mitochondria to produce melatonin in response to near-infrared light, and taking niacinamide helps raise your NAD^+ levels, which your mitochondria rely on to function efficiently.

This article is for informational purposes only and does not constitute medical advice. Consult a qualified health care provider before making changes to your health regimen.

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