mitophagy and aging

Mitophagy is the selective autophagic removal of damaged or superfluous mitochondria, and declining mitophagy is now viewed as a key driver of aging and age-related disease.[1] [2]

What mitophagy does

- Mitophagy continuously culls dysfunctional mitochondria, limiting mitochondrial DNA (mtDNA) mutations, excess reactive oxygen species (ROS), and impaired ATP production.[3] [1]
- By doing so, it helps maintain mitochondrial network quality, supports normal metabolism, and prevents activation of cell death and inflammatory pathways.[2] [1]

How mitophagy changes with age

- Aging tissues typically show mitochondrial structural abnormalities, reduced oxidative phosphorylation capacity, increased ROS, and accumulation of mtDNA mutations.[1]
- At the same time, mitophagy and broader autophagy pathways become less efficient, allowing damaged mitochondria to accumulate and reinforcing a vicious cycle of mitochondrial dysfunction and cellular damage.[4] [1]

Impact on healthspan and disease

- Impaired mitophagy is implicated in neurodegenerative disorders, cardiovascular disease, cancer, and other chronic age-related conditions.[2] [3] [1]
- Genetic and experimental models indicate that enhancing mitophagy can delay onset of aging phenotypes and is considered a pro-longevity mechanism that supports organismal healthspan.[5] [6]

Longevity and experimental evidence

- In model organisms such as *C. elegans*, mitophagy genes (for example dct-1/NIX, pink-1, parkin orthologs) are required for lifespan extension induced by mild mitochondrial stress and certain small molecules (such as tomatidine).[5] [1]
- Mouse models with enhanced mitophagy show protection against age-related neuromuscular and neurological decline, while those with defective mitophagy exhibit premature aging-like traits.[7] [6] [1]

Interventions that modulate mitophagy

- Strategies being investigated include: pharmacological activators of PINK1/Parkin or receptor-mediated mitophagy, agents that stimulate mitochondrial biogenesis in parallel with mitophagy, and lifestyle approaches such as exercise that activate AMPK–ULK1 signaling to promote mitochondrial turnover.[4] [1] [2]
- Early clinical and translational work suggests that safely boosting mitophagy may help counteract age-related mitochondrial dysfunction and reduce chronic inflammation, thereby potentially slowing aspects of biological aging.[6] [7] [2]

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rate of mitophagy, how long to mitochondria function before their functionality ends and they are replaced

There is no single fixed “rate of mitophagy,” but in mammals most mitochondria function for days to weeks before being turned over, and this varies strongly by tissue and context.[9] [10] [11]

Typical mitochondrial lifetimes

- In mouse liver, mitochondrial half-life is about 1.8 days under normal conditions, and can accelerate to roughly 1.2 days with dietary restriction.[10]
- In mouse heart, reported mitochondrial half-life is around 14 days, while earlier work in non-proliferating tissues suggested ranges of roughly 5–25 days depending on organ and method.[11] [9]

Tissue differences and proteins vs organelles

- Newer isotope-labeling studies show median half-lives of mitochondrial proteins of about 3–4 days in mouse liver and around 25–26 days in brain synaptic mitochondria, underscoring slower turnover in long-lived neuronal compartments.[12]
- In neurons and myotubes, organelle-level mitochondrial protein half-lives of about 5–7 days have been reported, somewhat slower than many other organelles in the same cells.[13] [14]

What this means for mitophagy rate

- Mitophagy is one arm of “mitochondrial quality control,” so effective mitophagy plus biogenesis together produce the observed organelle half-lives in each tissue.[15] [16]
- A mitochondrial half-life of, for example, 7 days means that in a week roughly half of the mitochondrial mass in that tissue has been functionally replaced, but individual mitochondria and mtDNA molecules can persist longer or shorter depending on local damage and stress.[17] [9]

Key caveats

- Turnover is highly context-dependent: stress, ROS, nutrient status, and disease can all accelerate mitophagy and shorten mitochondrial lifespan locally.[18] [19]
- Methods differ (radio-labeling, fluorescent reporters, proteomics), so absolute numbers vary between studies, but they consistently place mitochondrial functional lifetimes on the order of several days to a few weeks in most mammalian tissues.[20] [9] [10]

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mitophagy rate in brain mitochondria

Mitophagy in brain is relatively slow and heterogeneous: most neuronal mitochondria turn over on the order of weeks, but individual mitophagy events can take more than a day to complete and are strongly activity-dependent.[24] [25] [26]

Bulk turnover (weeks scale)

- In mice, metabolic ^15N labeling shows the median half-life of striatal synaptic mitochondrial proteins is about 25.7 days, much longer than hepatic mitochondria (~3.8 days), indicating slower basal turnover in brain synapses.[24]
- This implies that, under resting conditions, roughly half of the mitochondrial proteome in synaptic regions is renewed about once per month, although some mitochondrial proteins are much shorter- or longer-lived.[27] [24]

Single-organelle mitophagy events (day scale)

- Live-cell work in neurons indicates that, once a mitochondrion is tagged for PINK1/Parkin-dependent mitophagy and engulfed, its degradation through lysosomal acidification can exceed 24 hours, making lysosomal breakdown the rate-limiting step.[25]
- Neuronal mitophagy proceeds more gradually than in many non-neuronal cell types, with autophagosome–lysosome fusion and acidification occurring hours after the initial mitophagy trigger.[26] [25]

Spatial and activity dependence

- Axons and synapses tend to initiate mitophagy locally and then transport mitophagosomes retrogradely toward the soma for degradation, which further slows effective clearance compared with compact cells.[28] [29]
- High oxidative phosphorylation activity (for example, during intense firing) can markedly enhance mitophagy and mitochondrial turnover in neurons, whereas mitophagy is lower at rest, so the “rate” is tightly coupled to neuronal workload and stress.[30] [28]

Aging and disease context

- In aging and neurodegenerative disease models, mitophagy in brain often becomes inefficient: initiation may increase, but trafficking or lysosomal degradation is impaired, causing retention of mitophagosomes and functionally “old” mitochondria in synapses.[29] [31] [28]
- Such slowing of effective mitophagic clearance is thought to contribute to accumulation of damaged brain mitochondria and rising vulnerability to neurodegeneration over time.[32] [33] [30]

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mitophagy rate changes with age

In most tissues mitophagy becomes less efficient with age, but some organs show compensatory increases in mitophagy signaling in response to accumulating mitochondrial damage and inflammation.[40] [41] [42]

General age-related trend

- Many studies in muscle, liver, heart, and hematopoietic stem cells report a decline in autophagy/mitophagy activity with age, leading to accumulation of structurally abnormal, ROS-producing mitochondria.[42] [43] [40]
- Reduced expression or function of core autophagy proteins (for example LC3, LAMP2, Atg proteins) and mitophagy regulators (such as PINK1, Parkin, BNIP3, NIX) is commonly observed in aged tissues and correlates with impaired mitochondrial quality control.[44] [43] [42]

Brain and nervous system

- In the aging nervous system, mitophagic activity generally declines, aggravating mitochondrial dysfunction and increasing vulnerability to neurodegenerative diseases like Alzheimer’s and Parkinson’s disease.[45] [46] [47]
- Aging brains often show downregulation of several autophagy–lysosome genes alongside dysregulated PINK1/Parkin signaling, which together indicate inefficient initiation and completion of mitophagy rather than a simple uniform increase or decrease.[46] [43]

Compensatory upregulation and inflammation

- Newer whole-animal mitophagy-reporter studies in mice found that, in physiological old age, basal mitophagy levels can be upregulated in multiple organs, apparently as a response to chronic mitochondrial stress and cytosolic mtDNA-driven cGAS–STING inflammation.[41]
- Despite this increased mitophagy signal, old tissues still accumulate swollen, damaged mitochondria, suggesting that upregulation is only partially compensatory and that degradation or biogenesis steps remain limiting.[41] [42]

Functional consequence for “rate”

- Functionally, aged tissues often show slower effective clearance of dysfunctional mitochondria (slower flux), even when some mitophagy markers are elevated, because of bottlenecks in autophagosome–lysosome fusion, lysosomal function, or NAD^+-dependent signaling.[43] [42]
- Genetic or pharmacological enhancement of mitophagy (for example NAD^+ boosters, urolithin A, tomatidine, or direct PINK1/Parkin pathway activators) can restore more youthful mitochondrial turnover rates and improve healthspan in animal models.[48] [49] [44]

Key takeaways

- With aging, basal mitophagy signaling can either decline or become chronically activated depending on tissue and context, but mitochondrial quality control almost always becomes less effective overall.[40] [42] [41]
- The net result is a reduced capacity to remove defective mitochondria at the needed **rate**, contributing to hallmarks of aging such as increased ROS, chronic inflammation, and organ-specific degeneration.[50] [44] [43]

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ways to boost mitophagy for anti-aging

Several lifestyle strategies and a few emerging compounds can enhance mitophagy, but evidence in humans is still limited and mostly indirect.

Foundational lifestyle approaches

- **Exercise**: Endurance and high-intensity training increase mitophagy and mitochondrial biogenesis in muscle, improving mitochondrial biomarkers and performance with age.[55]
- **Caloric restriction / intermittent fasting**: Energy stress activates AMPK and inhibits mTOR, which promotes autophagy and mitophagy in multiple tissues in animal models.[56] [57]

Urolithin A (UA)

- UA is a gut-microbiome–derived metabolite from ellagitannins (in pomegranates, some berries, nuts) that directly induces mitophagy in animals and human cells.[58] [56]
- Randomized trials in older or middle-aged adults (500–1,000 mg/day for 4–12 weeks) show improved muscle strength and endurance plus changes in mitochondrial gene expression and acylcarnitines consistent with enhanced mitochondrial health, interpreted as mitophagy activation.[59] [56] [55]
- Early work also suggests UA may remodel immune cells and improve markers of immune aging, again via mitophagy and mitochondrial biogenesis.[60] [61] [62]

NAD⁺ boosters and sirtuin activators

- Restoring NAD⁺ levels (for example with precursors like NR or NMN in models) enhances SIRT1–PGC-1α signaling, improves mitochondrial quality, and restores DCT-1/ULK1-dependent mitophagy in premature-aging models.[63] [64] [65]
- In worms and flies, NAD⁺ repletion improves mitophagy and extends lifespan, suggesting a potential geroprotective mechanism, though large, long-term human anti-aging data are not yet available.[65]

Other candidate nutraceuticals (preclinical/early)

- Compounds such as spermidine, resveratrol, and some polyphenols are reported to induce autophagy/mitophagy and improve mitochondrial function in preclinical studies, and are proposed as synergistic with UA, NAD⁺ boosters, exercise, and fasting.[66] [57]
- These remain less well validated in rigorous human anti-aging trials compared with UA, and optimal doses or combinations are not established.[67] [66]

Practical and safety considerations

- Focusing on regular aerobic/interval exercise, maintaining a healthy weight, and avoiding chronic overnutrition likely provides the strongest, safest mitophagy support at present.[68] [56] [55]
- UA supplements (typically 500–1,000 mg/day) have shown good short-term safety and mitochondrial benefits in trials, but should still be considered experimental for systemic "anti-aging," and used in consultation with a clinician, especially with chronic disease or medications.[56] [59] [58]

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SS 31 effect on mitophagy

SS-31 (elamipretide) is not a classic mitophagy drug, but in multiple models it improves mitochondrial quality control and can enhance mitophagy-related processes, especially the engulfment and clearance of damaged mitochondria.[70] [71] [72]

Direct effects on mitophagy/autophagy

- In INS1 β-cells exposed to nutrient excess, elamipretide increases the engulfment of mitochondria into LC3-positive autophagosomes and prevents the nutrient-induced reduction in mitophagosome formation, indicating a stimulation of the mitophagy step where mitochondria are sequestered for degradation.[73] [70]
- In ischemic skeletal muscle and C2C12 myotubes, SS-31 restores impaired autophagic flux (more effective autophagosome clearance, fewer damaged mitochondria) by inhibiting AKT–mTOR signaling, which normally suppresses autophagy.[71]

Mechanistic links

- SS-31 binds cardiolipin on the inner mitochondrial membrane and stabilizes mitochondrial structure, which is thought to help normalize mitochondrial dynamics and signaling events that flag damaged mitochondria for autophagy.[74] [75]
- Because externalized cardiolipin can act as a mitophagy signal by binding LC3 on autophagosomes, one proposed mechanism is that SS-31 modulates cardiolipin–LC3 interactions and thereby supports efficient mitophagosome formation under stress.[75] [70]

Disease and aging models

- In models of nutrient excess, diabetes, or tissue ischemia, SS-31 reduces mitochondrial ROS, limits fragmentation, and preserves mitochondrial number and morphology, consistent with better mitochondrial turnover and quality control that includes mitophagy.[76] [77] [78]
- A 2024 cardiomyopathy model (Barth syndrome) shows SS-31 improves abnormal mitochondrial morphology and defective mitophagy in the heart, further supporting a role in rescuing impaired mitophagy in disease states.[79]

How to interpret this for anti-aging

- Current evidence suggests SS-31 mainly acts as a mitochondria-targeted antioxidant/structure-stabilizing peptide that secondarily normalizes or enhances mitophagy and autophagy under stress, rather than a dedicated mitophagy inducer like urolithin A.[72] [76] [70]
- Human trials with elamipretide focus on mitochondrial diseases, heart failure, and kidney disease; they evaluate safety and functional outcomes, but they have not yet established SS-31 as a general anti-aging mitophagy drug in otherwise healthy older adults.[80] [74] [72]

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MOTS-c effect on mitophagy

MOTS-c appears to upregulate mitophagy-related pathways and overall mitochondrial quality control, but the evidence is still mostly preclinical and indirect.

Evidence for mitophagy effects

- In cell and animal studies, MOTS-c increases expression of mitophagy-associated genes such as PINK1, PARK2 (Parkin), and ATG7, alongside genes for mitochondrial biogenesis and fusion, suggesting coordinated activation of mitochondrial turnover.[85]
- In these models, MOTS-c treatment reduces the number of mitochondria per cell while improving cristae structure and respiratory capacity, consistent with more aggressive fusion plus autophagic removal of damaged mitochondria.[86] [85]

Mechanistic context

- MOTS-c activates AMPK and modulates mTOR, key regulators of autophagy and mitophagy, and also boosts PGC-1α-driven mitochondrial biogenesis.[87] [88] [85]
- Reviews summarize that MOTS-c "promotes mitochondrial biogenesis, mitochondrial fusion and mitophagy processes," improving mitochondrial homeostasis and lowering ROS and inflammatory signaling in aged or stressed cells.[89] [90] [85]

Anti-aging implications

- In older mice, MOTS-c improves exercise capacity, metabolic flexibility, and skeletal-muscle homeostasis, which has been attributed in part to better mitochondrial quality control (biogenesis + fusion + mitophagy).[91] [87]
- Human data are still early; MOTS-c is viewed as a promising mitochondrial-derived peptide with potential geroprotective effects, but specific, direct measurements of mitophagy flux in humans are not yet well established.[90] [85] [89]

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mitochondria, how are new ones produced and what affects the quality of new mitochondria

New mitochondria are made by a process called **mitochondrial biogenesis**, where existing mitochondria grow and divide, coordinated with gene programs in the nucleus and in mitochondrial DNA.[100] [101]

How new mitochondria are produced

- Mitochondria do not arise from scratch; they enlarge and then divide (fission), so all new mitochondria come from pre-existing ones.[102] [101]
- Most mitochondrial proteins are encoded in the nucleus, made in the cytosol, and then imported into mitochondria, while mtDNA encodes a small number of key respiratory chain subunits plus rRNA and tRNA.[101] [100]
- Biogenesis is driven by transcriptional coactivators such as PGC-1α, which activate nuclear respiratory factors (NRF-1, NRF-2) and TFAM to replicate mtDNA and increase expression of oxidative-phosphorylation components.[103] [104] [105]
- Fusion and fission proteins (Mitofusins Mfn1/2, Opa1, and Drp1) remodel the network, mix contents, and help distribute new and old components across the mitochondrial population.[100] [101]

What affects the quality of new mitochondria

- **Energy and stress signaling:** AMPK and SIRT1 sense low energy and NAD^+ levels and activate PGC-1α, generally promoting higher-quality, stress-resistant mitochondria; chronic nutrient excess and mTOR overactivation impair this program.[106] [104] [103]

- **mtDNA integrity:** Mutations or deletions in mtDNA, or poor TFAM-mediated replication, reduce the quality of new mitochondria by limiting proper assembly of respiratory complexes.[105] [101]
- **Protein import and folding:** Defects in import machinery or chaperones cause misfolded or missing proteins inside nascent mitochondria, compromising their function.[101] [100]
- **Mitophagy balance:** Effective mitophagy removes damaged templates and low-quality mitochondria; if clearance is weak, biogenesis may simply expand a pool of already defective mitochondria.[104] [102] [101]
- **Cellular environment:** Oxidative stress, calcium dysregulation, and inflammation all damage lipids, proteins, and mtDNA during or after biogenesis, lowering the functional quality of the new organelles.[105] [101]

In practice, signals that activate AMPK–SIRT1–PGC-1α (for example exercise, transient nutrient stress) tend to yield better-functioning new mitochondria, while chronic overnutrition, oxidative stress, and defective mitophagy degrade their overall quality over time.[107] [103] [104]

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Factors impairing mitochondrial biogenesis quality

Mitochondrial biogenesis quality drops when the signaling that coordinates it is disrupted and when new organelles are assembled in a damaged, pro-oxidant environment.[110] [111]

Signaling and transcriptional issues

- Reduced PGC-1α, NRF-1/2, and TFAM activity (central controllers of mitochondrial biogenesis) leads to poorly coordinated expression of respiratory chain subunits and mtDNA replication, producing less efficient mitochondria.[112] [111] [113]
- Aging, chronic high-glucose/high-fat conditions, and some drugs (for example cyclosporine A, XCT790, 2-methoxyestradiol) are reported to suppress PGC-1α/AMPK signaling and directly inhibit mitochondrial biogenesis programs.[114] [111]

Oxidative stress and inflammation

- Excess mitochondrial and cytosolic ROS damages mtDNA, lipids, and newly synthesized proteins during or soon after assembly, locking in defects in “new” mitochondria.[115] [116] [110]
- Chronic low-grade inflammation and cGAS–STING activation by leaked mtDNA further impair mitochondrial function and biogenesis signaling, creating a vicious cycle of poor-quality replacements.[117] [118] [114]

mtDNA damage and genomic instability

- Accumulated mtDNA mutations and deletions in progenitor mitochondria are copied into daughter organelles, so even active biogenesis can expand a defective mitochondrial genome pool.[116] [115] [110]
- Telomere damage and nuclear DNA stress repress PGC-1α and PGC-1β, indirectly reducing the fidelity and capacity of mitochondrial biogenesis.[114]

Dynamics, mitophagy, and quality control

- Oxidative stress shifts dynamics toward excessive fission and suppresses fusion proteins (Mfn1/2, Opa1), fragmenting networks and impeding the content-mixing that normally helps dilute local defects.[110]
- When mitophagy and proteostasis are impaired with age, damaged mitochondria and misfolded proteins are not efficiently removed, so biogenesis mainly increases the amount of dysfunctional mitochondria rather than improving average quality.[119] [113] [120]

Environmental and lifestyle factors

- Sedentary behavior, chronic overnutrition, and exposure to toxins that target mitochondria (some pollutants, drugs) all promote oxidative stress and inflammation, thereby degrading the quality of newly formed mitochondria.[121] [122] [115]
- In contrast, transient, moderate mitochondrial stress from exercise or caloric restriction tends to upregulate AMPK–SIRT1–PGC-1α and improve the coordination and quality of biogenesis, illustrating how context determines whether stress is harmful or hormetic.[123] [111] [119]

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1. https://pmc.ncbi.nlm.nih.gov/articles/PMC7113588/
2. https://www.nature.com/articles/s42255-023-00930-8
3. https://www.sciencedirect.com/science/article/pii/S1050173817301809
4. https://www.fightaging.org/archives/2026/01/targeting-mitophagy-to-slow-aging/
5. https://www.frontiersin.org/journals/cell-and-developmental-biology/articles/10.3389/fcell.2020.00239/full
6. https://pubmed.ncbi.nlm.nih.gov/34889504/
7. https://www.nature.com/articles/s41467-024-47840-1
8. https://iubmb.onlinelibrary.wiley.com/doi/10.1002/iub.2585
9. https://pmc.ncbi.nlm.nih.gov/articles/PMC4333239/
10. https://pmc.ncbi.nlm.nih.gov/articles/PMC2659384/
11. https://pmc.ncbi.nlm.nih.gov/articles/PMC2928637/
12. https://www.nature.com/articles/s41598-023-38484-0
13. https://pmc.ncbi.nlm.nih.gov/articles/PMC8664086/
14. https://www.sciencedirect.com/science/article/pii/S1534580721008091

15. https://www.sciencedirect.com/science/article/pii/S1016847823004673
16. https://pmc.ncbi.nlm.nih.gov/articles/PMC3335292/
17. https://www.biorxiv.org/content/10.1101/2020.02.15.950410v1.full?dm_t=0%2C0%2C0%2C0%2C0
18. https://pmc.ncbi.nlm.nih.gov/articles/PMC3359476/
19. https://rupress.org/jcb/article/219/11/e202004029/152083/Mitophagy-pathways-in-health-and-disease Mitophagy
20. https://pmc.ncbi.nlm.nih.gov/articles/PMC2861545/
21. https://pmc.ncbi.nlm.nih.gov/articles/PMC12159423/
22. https://en.wikipedia.org/wiki/Mitophagy
23. https://febs.onlinelibrary.wiley.com/doi/10.1016/j.febslet.2007.01.010
24. https://www.nature.com/articles/s41598-023-38484-0
25. https://elifesciences.org/articles/50260
26. https://pmc.ncbi.nlm.nih.gov/articles/PMC8724472/
27. https://pmc.ncbi.nlm.nih.gov/articles/PMC8664086/
28. https://pmc.ncbi.nlm.nih.gov/articles/PMC8726713/
29. https://pmc.ncbi.nlm.nih.gov/articles/PMC7507095/
30. https://journals.biologists.com/jcs/article/136/11/jcs260638/316553/Mitophagy-and-long-term-neuronal-homeostasis
31. https://pmc.ncbi.nlm.nih.gov/articles/PMC8392649/
32. https://pmc.ncbi.nlm.nih.gov/articles/PMC11612451/
33. https://pmc.ncbi.nlm.nih.gov/articles/PMC2861545/
34. https://www.sciencedirect.com/science/article/pii/S002228362500227X
35. https://www.frontiersin.org/research-topics/76223/mitophagy-and-mitochondrial-quality-control-in-brain-aging-and-neurodegeneration
36. https://www.nature.com/articles/s41392-023-01503-7
37. https://rupress.org/jcb/article/197/4/535/36795/Mitochondrial-division-ensures-the-survival-of
38. https://www.science.org/doi/10.1126/science.aba9760
39. https://www.embopress.org/doi/full/10.1038/s44318-024-00275-2
40. https://www.frontiersin.org/journals/cell-and-developmental-biology/articles/10.3389/fcell.2020.00239/full
41. https://www.nature.com/articles/s41467-024-45044-1
42. https://pmc.ncbi.nlm.nih.gov/articles/PMC9898045/
43. https://pmc.ncbi.nlm.nih.gov/articles/PMC5565781/
44. https://pmc.ncbi.nlm.nih.gov/articles/PMC7113588/
45. https://pmc.ncbi.nlm.nih.gov/articles/PMC9593040/
46. https://pmc.ncbi.nlm.nih.gov/articles/PMC12755872/
47. https://www.frontiersin.org/journals/cell-and-developmental-biology/articles/10.3389/fcell.2022.978142/full
48. https://pubmed.ncbi.nlm.nih.gov/34889504/
49. https://www.nature.com/articles/s41420-025-02913-y

50. https://pmc.ncbi.nlm.nih.gov/articles/PMC12159423/
51. https://www.sciencedirect.com/science/article/abs/pii/S0047637420300014
52. https://pubmed.ncbi.nlm.nih.gov/37124925/
53. https://pmc.ncbi.nlm.nih.gov/articles/PMC7179682/
54. https://www.fightaging.org/archives/2026/01/targeting-mitophagy-to-slow-aging/
55. https://pmc.ncbi.nlm.nih.gov/articles/PMC9133463/
56. https://pmc.ncbi.nlm.nih.gov/articles/PMC10791945/
57. https://pmc.ncbi.nlm.nih.gov/articles/PMC8617978/
58. https://pubmed.ncbi.nlm.nih.gov/32694802/
59. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2788244
60. https://www.nature.com/articles/s43587-025-00996-x
61. https://ascopubs.org/doi/10.1200/JCO.2024.42.16_suppl.e14562
62. https://pubmed.ncbi.nlm.nih.gov/41174221/
63. https://pubmed.ncbi.nlm.nih.gov/31754102/
64. https://pmc.ncbi.nlm.nih.gov/articles/PMC6872719/
65. https://www.nature.com/articles/s41467-019-13172-8
66. https://www.genesispub.org/urolithin-a-a-novel-geroprotectant-capable-of-stimulating-mitophagy
67. https://www.sciencedirect.com/science/article/pii/S1568163724002241
68. https://www.fightaging.org/archives/2024/08/reviewing-the-development-of-urolithin-a-as-an-age-slowing-intervention/
69. https://www.sciencedirect.com/science/article/pii/S2666379122001586
70. https://pmc.ncbi.nlm.nih.gov/articles/PMC6290358/
71. https://pmc.ncbi.nlm.nih.gov/articles/PMC9046554/
72. https://pmc.ncbi.nlm.nih.gov/articles/PMC11816484/
73. https://pubmed.ncbi.nlm.nih.gov/30389435/
74. https://www.pnas.org/doi/10.1073/pnas.2002250117
75. https://pmc.ncbi.nlm.nih.gov/articles/PMC7334473/
76. https://pmc.ncbi.nlm.nih.gov/articles/PMC6588449/
77. https://pmc.ncbi.nlm.nih.gov/articles/PMC9192202/
78. https://pubmed.ncbi.nlm.nih.gov/31466264/
79. https://www.nature.com/articles/s41598-024-64368-y
80. https://www.sciencedirect.com/science/article/pii/S0753332225002501
81. https://www.sciencedirect.com/science/article/pii/S0009279724003120
82. https://pubmed.ncbi.nlm.nih.gov/29405550/
83. https://onlinelibrary.wiley.com/doi/10.1155/2022/1295509
84. https://www.sciencedirect.com/science/article/abs/pii/S1567724924000047
85. https://pmc.ncbi.nlm.nih.gov/articles/PMC9854231/
86. https://www.nature.com/articles/s41598-021-93735-2
87. https://www.nature.com/articles/s41467-020-20790-0

88. https://pmc.ncbi.nlm.nih.gov/articles/PMC9866798/
89. https://pmc.ncbi.nlm.nih.gov/articles/PMC9905433/
90. https://pubmed.ncbi.nlm.nih.gov/36761202/
91. https://www.aging-us.com/article/102944/text
92. https://pmc.ncbi.nlm.nih.gov/articles/PMC4350682/
93. https://www.usada.org/spirit-of-sport/what-is-mots-c-peptide/
94. https://www.nature.com/articles/s12276-025-01521-1
95. https://swolverine.com/en-ca/blogs/blog/mots-c-for-beginners-benefits-dosage-stacking-and-side-effects
96. https://www.sciencedirect.com/science/article/pii/S2589004224024374
97. https://pmc.ncbi.nlm.nih.gov/articles/PMC5116416/
98. https://www.alzdiscovery.org/uploads/cognitive_vitality_media/MOTS-c.pdf
99. https://www.frontiersin.org/journals/physiology/articles/10.3389/fphys.2025.1602271/full
100. https://en.wikipedia.org/wiki/Mitochondrial_biogenesis
101. https://pmc.ncbi.nlm.nih.gov/articles/PMC3175594/
102. https://www.sciencedirect.com/topics/medicine-and-dentistry/mitochondrial-biogenesis
103. https://pmc.ncbi.nlm.nih.gov/articles/PMC7205802/
104. https://pmc.ncbi.nlm.nih.gov/articles/PMC3685894/
105. https://www.nature.com/articles/s41392-024-01839-8
106. https://taylorandfrancis.com/knowledge/Medicine_and_healthcare/Physiology/Mitochondrial_biogenesis/
107. https://pubmed.ncbi.nlm.nih.gov/32279443/
108. https://pubmed.ncbi.nlm.nih.gov/24606795/
109. https://www.sciencedirect.com/topics/neuroscience/mitochondrial-biogenesis
110. https://pmc.ncbi.nlm.nih.gov/articles/PMC12159213/
111. https://pmc.ncbi.nlm.nih.gov/articles/PMC7205802/
112. https://pubmed.ncbi.nlm.nih.gov/19371772/
113. https://pmc.ncbi.nlm.nih.gov/articles/PMC3404634/
114. https://pmc.ncbi.nlm.nih.gov/articles/PMC12241157/
115. https://www.nature.com/articles/s41392-025-02253-4
116. https://pmc.ncbi.nlm.nih.gov/articles/PMC3184498/
117. https://pubmed.ncbi.nlm.nih.gov/40500258/
118. https://www.nature.com/articles/s41392-024-01839-8
119. https://www.sciencedirect.com/science/article/pii/S2666337625001106
120. https://pmc.ncbi.nlm.nih.gov/articles/PMC3175594/
121. https://www.explorationpub.com/Journals/em/Article/1001129
122. https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/mitochondrial-biogenesis
123. https://pmc.ncbi.nlm.nih.gov/articles/PMC2562606/
124. https://pmc.ncbi.nlm.nih.gov/articles/PMC11114788/

125. https://www.pnas.org/doi/10.1073/pnas.0911570106