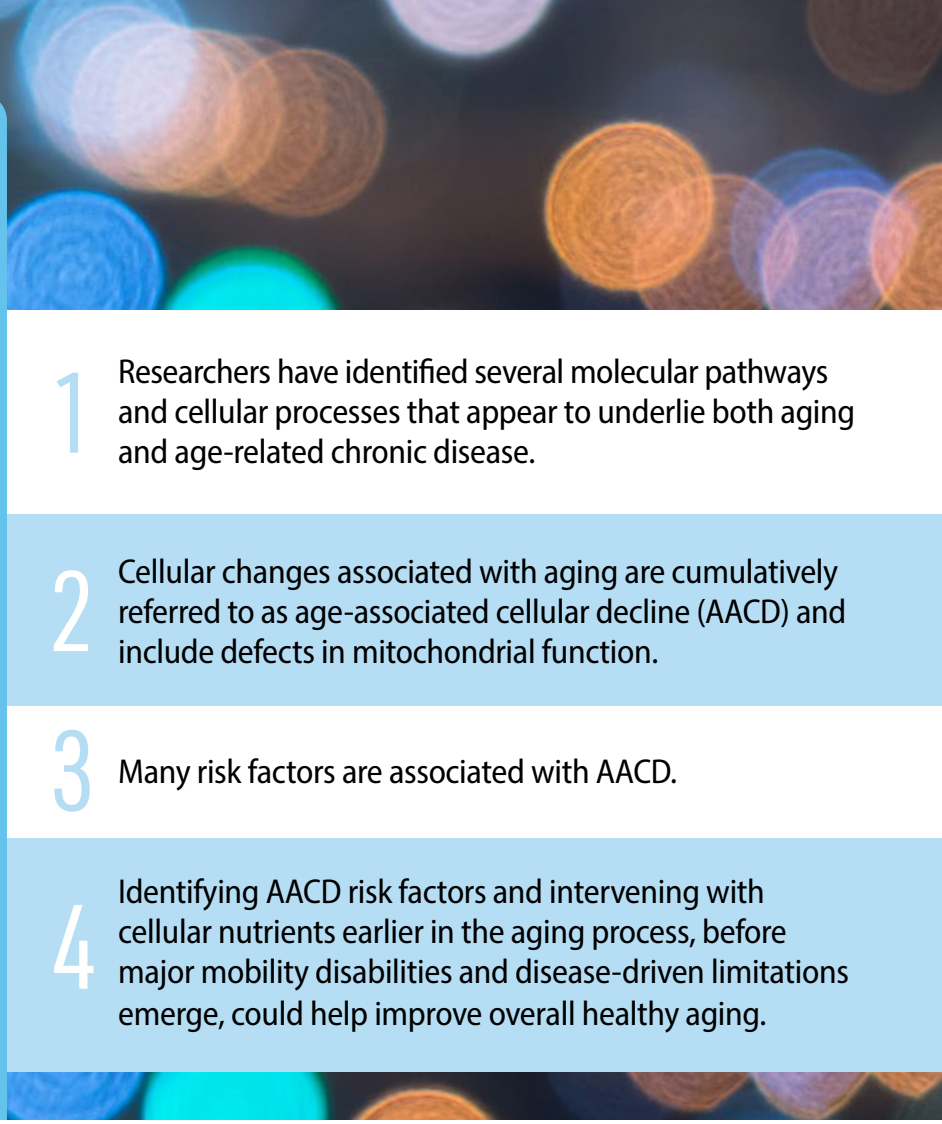
Cellular Nutrition and Its Influence on Age-Associated Cellular Decline (AACD)



1. Researchers have identified several molecular pathways and cellular processes that appear to underlie both aging and age-related chronic disease.
2. Cellular changes associated with aging are cumulatively referred to as age-associated cellular decline (AACD) and include defects in mitochondrial function.
3. Many risk factors are associated with AACD.
4. Identifying AACD risk factors and intervening with cellular nutrients earlier in the aging process, before major mobility disabilities and disease-driven limitations emerge, could help improve overall healthy aging.

Risk Factors Associated With AACD

Clinical Risk Factors

- Clinical conditions (e.g., cancer, cardiovascular, renal, or metabolic disease)
- Obesity
- Unfavorable genetic background
- Insulin resistance
- Low physical capacity (e.g., slow gait speed, muscle weakness)

Behavioral/Environmental Risk Factors

- Smoking
- Sedentary lifestyle
- Low physical activity
- Persistent physical or psychological stress
- Low socioeconomic status
- Alcohol abuse
- Inadequate nutrition
- Air pollution

Source: Reference 1.

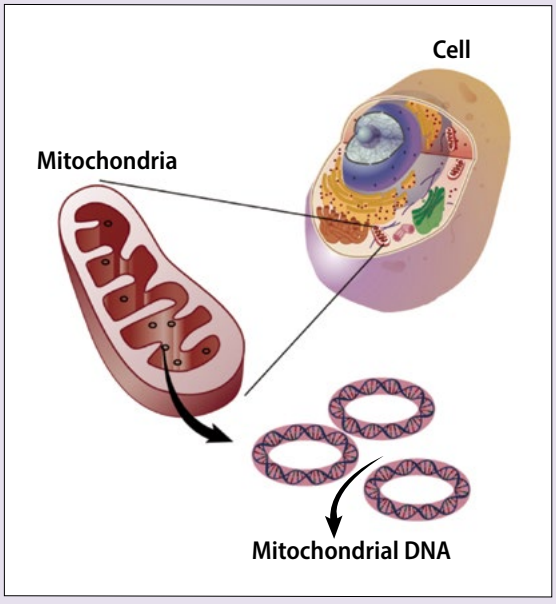
Mitochondria

- Mitochondria are organelles that produce cellular energy in the form of adenosine triphosphate (ATP).[2]
  - Other functions of mitochondria include regulating cellular metabolism, regulating apoptosis (programmed cell death), and signaling by producing reactive oxygen species.

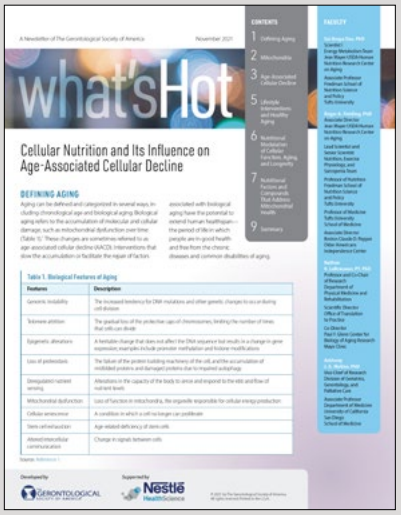
- Mitochondria are dynamic and can change size, shape, and position throughout their life cycle. They regularly undergo fission (division of a single mitochondrion into multiple mitochondria) or fusion (the combination of two or more mitochondria into a single mitochondrion).[3]

- Mitochondrial homeostasis is maintained through a balance of fusion, fission, mitochondrial biogenesis (creation of new mitochondria), and mitophagy (the selective degradation of mitochondria).

Mitochondria and Mitochondrial DNA



Source: Reference 2.



Learn more about Cellular Nutrition and Its Influence on AACD

Mitochondrial Function and AACD

- **Declining mitochondrial function results in AACD. These changes include:**
  - **Decreased** mitochondrial biogenesis.[4]
  - **Increased** mitochondria-mediated apoptosis.[4]
  - **Decline in** mitochondrial DNA (mtDNA).[4]
  - **Increased** mtDNA mutations.[4]
- **Abnormalities in mitochondrial function are associated with many diseases such as:**
  - Cancer, cardiovascular diseases, and neurodegenerative disease.

AACD Associations With Health and Physical Function

- AACD is often associated with fatigue, reduced strength and daily energy, and low physical activity.[5,6]

- Changes associated with AACD act as triggers for age-associated diseases and conditions. For example:
  - The age-related decline in nicotinamide adenine dinucleotide (NAD^+) has been associated with the development of diabetes, nonalcoholic fatty liver disease, atherosclerosis, Alzheimer's disease, retinal degeneration, chronic fatigue syndrome, and depression.[7,8] Conversely, research has shown that NAD^+ intermediates, such as nicotinamide mononucleotide and nicotinamide riboside, may potentially be effective for preventing and treating age-associated pathophysiology.[7]
  - Glutathione levels are lower and oxidative stress is higher in conditions associated with mitochondrial dysfunction, including aging, HIV infection, diabetes, neurodegenerative disorders, cardiovascular disorders, neurometabolic diseases, cancer, and obesity.

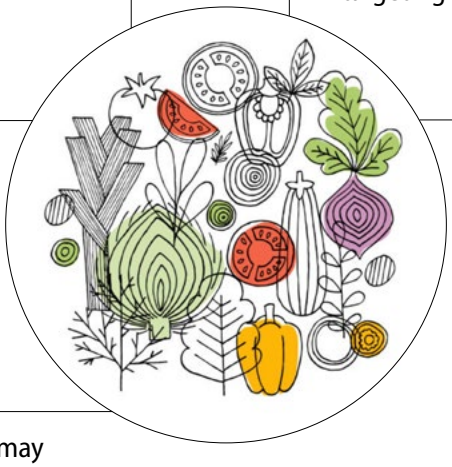
Nutritional Interventions to Address AACD

1

Adoption of healthful eating patterns and exercise has been shown to improve markers of age-associated diseases and attenuate biological aging.

2

Nutritional interventions may slow AACD and have the potential to extend human healthspan—the period of life in which people are in good health.



3

For example, calorie restriction (CR) may modulate cellular function and increase longevity.

- CR combined with exercise has some beneficial synergistic effects, such as improving insulin sensitivity, lowering systemic inflammation, and improving body composition. However, exercise may not provide an additive benefit for longevity when added to CR.[9,10]
- CR appears to improve markers of disease risk in humans, but its acceptability and feasibility particularly over the long term remains a challenge.

4

Emerging research indicates that nutritional components that target specific mechanisms associated with AACD hold promise for improving the health and well-being of adults.[6]

- Dietary supplementation with these components may be an alternative approach to lifestyle interventions targeting AACD.

5

Emerging research also indicates that some nutritional compounds can support healthy aging by influencing mitochondrial repair and preservation, quality control, and signaling.[6]

- Compounds that have been shown to address mitochondrial damage and clinical disease states include Szeto-Schiller (SS) peptides, coenzyme Q_{10} (CoQ_{10}), MitoQ, and glycine and *N*-acetylcysteine (GlyNAC).[11-14]
- Compounds that may address mitochondrial quality control include sirtuins, mitochondrial division inhibitor (mdivi), urolithin A, and epicatechin.[15-18]
- Compounds that have been shown to address mitochondrial signaling include nicotinamide riboside and nicotinamide mononucleotide.[19,20]

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