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Endurance Exercise, the Fountain of Youth, and the Mitochondrial Key

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Scientists have been searching for the proverbial fountain of youth for centuries, hoping that a newly discovered drug or exotic plant would hold the key to anti-aging riches. However, a recent study from Canada provides powerful evidence that the key was within each and every one of us the entire time.

Led by Dr. Mark Tarnopolsky, Professor of Pediatrics and Medicine, a team of researchers from McMaster University's Michael G. DeGroote School of Medicine recently published a study that found endurance exercise can prevent the signs of premature aging in virtually every tissue and organ system in the body. Published in the Journal of Proceedings of the National Academy of Sciences of United States of America, the study found that mice that were genetically engineered to age faster were protected against the phenotypic and biologic changes of aging by engaging in regular endurance exercise.[1] In an era that has seen the epidemic emergence of chronic diseases—likely a result of increasing sedentary behaviour, excess caloric intake, and obesity—this study should help promote the benefits of exercise for all those searching to stay forever young.[2]

Epidemiological evidence has established that endurance training greatly reduces the risk of chronic diseases and decreases mortality in humans; however, little is known about how endurance training affects aging.[3–14] The mitochondrial theory of aging postulates that lifelong accumulations of mitochondrial DNA mutations lead to a cellular energy crisis, resulting in progressive decline in tissue and organ function, and ultimately accelerating the aging process. Based on this theory and known evidence that exercise can induce mitochondrial biogenesis and metabolism, Dr. Tarnopolsky and his team of researchers set out to prove that endurance exercise could help prevent premature aging in mice.[15–19]

The study used mice with genetically modified dysfunctional mitochondria which caused them to age prematurely. Starting at three months of age, or about 20 human years, the mice were randomly assigned to moderate intensity endurance exercise three times per week for 45 minutes or to a sedentary group. The mice were studied over the next five months until the age of eight months, or approximately 60 human years, with startling findings.[1]

Although both groups of mice were genetically disadvantaged to prematurely age, the mice that engaged in endurance exercise looked as healthy as normal mice while the sedentary group showed many phenotypic features of aging, including hair loss, greying, physical inactivity, and social isolation. Furthermore, the exercised mice were protected against early mortality and multi-system organ degeneration, such as hearing loss, cataracts, sarcopenia, brain atrophy, cardiomyopathy, anemia, and infertility. Compelling evidence revealed that endurance exercised mice had decreased accumulations of mitochondria DNA mutations, increased mitochondrial biogenesis, and decreased mitochondrial apoptosis,[1] further highlighting the potential role of mitochondria in the aging process.

These findings strengthen the mitochondrial theory of aging, providing evidence that endurance exercise may prevent premature aging through the maintenance and recovery of mitochondrial function, which is crucial for organ health. "Every part of the body was protected by exercise," said Dr. Tarnopolsky, who believes "that exercise is the most potent anti-aging therapy available today and likely forever."[20] The poet John Gray wrote in 1716: "Rosy-complexion'd health thy steps attends, and exercise thy lasting youth defends."[21] It is interesting to think that maybe he was right all along.

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Unraveling the Role of Lipid Metabolism in Alzheimer's Disease

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Imagine the heartbreak of being unrecognizable to your spouse after 40 years of marriage or losing the capacity to remember one's only child—such are the features salient in the latter course of Alzheimer's dementia. Given that Alzheimer's Disease (AD) is estimated to affect up to 40 % of North Americans over the age of 85, it constitutes a substantial obstacle to healthy aging.[1,2]

Upon finishing her post-doctorate work with Dr. Michael Hayden at the University of British Columbia, Dr. Cheryl Wellington began investigating the link between neurodegenerative disease and lipid disorders. Given that the most important genetic risk factor for AD is apolipoprotein E (apoE), which is a major cholesterol carrier in the brain, Dr. Wellington set out to further investigate the relationship between cholesterol metabolism and AD.

One of the major neuropathological hallmarks of AD is the presence of amyloid plaques within the brain parenchyma and cerebral blood vessels. The plaques are deposits of Aβ peptide, a by-product of amyloid precursor protein that is continuously produced and then cleared from the brain. With aging, it is hypothesized that the clearance and degradation of Aβ become less effective. Dr. Wellington's lab has shown that the clearance rate of Aβ is strongly affected by how much lipid is carried on apoE.[3]

The natural function of apoE is to distribute lipids among various cell types in the brain, a function that is critical for repairing damaged neuronal membranes. The cholesterol transporter ABCA1 acts to move excess lipids from the cell surface to apoE. In humans, the polymorphic *apoE* gene is present in three different allelic isoforms (2,3, and 4), and *apoE4* has been shown to increase the risk of developing AD with each inherited copy. At least 50 % of patients with AD possess at least one *apoE4* allele.[3]

In accordance with ethical guidelines for preclinical research, Dr. Wellington has used murine models of AD to show that the whole degradation pathway of the Aβ peptide slows down in the absence of ABCA1. The mice deteriorate cognitively and develop more amyloid deposits in their brains. Dr. Wellington has also shown that lipid saturation of apoE can be increased by using genetic modifications or small molecule compounds that increase ABCA1 activity. This results in more rapid degradation of Aβ peptides and less amyloid formation. "This gives us the ability to possibly provide novel therapeutic strategies for Alzheimer's disease that can augment therapies being developed to slow the

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