STANDARD DEVIATIONS: Getting Old is a Weighty Matter

Greetings,

“If mitochondria are working so hard why do I still gain weight?”

The simple answer is aging.

I think of aging as getting old. I’m being ignorant.

Turns out, that the scientific community looks a little deeper and “aging” has a huge body of research that sees it more exactly as “progressive functional decline of organisms with time and likely caused by the simultaneous deterioration of various interconnected cellular functions.”

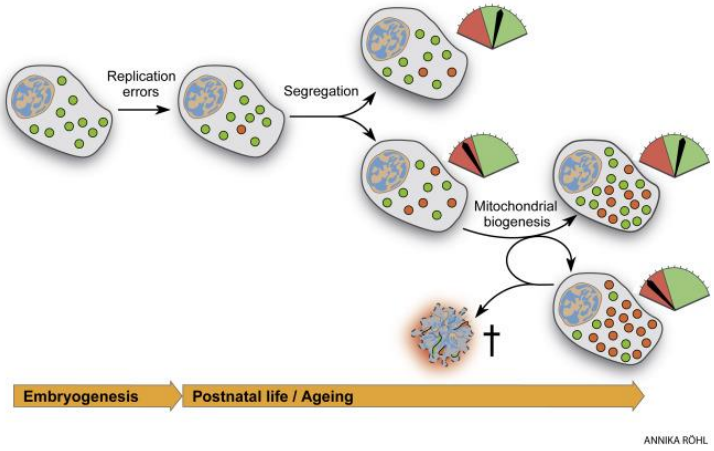
Mitochondria are to blame.

The dysfunctions we call aging, and observe in wrinkles, gray hair, memory loss, and more serious pathologies like obesity, diabetes, cancers, and dementia are merely reflections of **mitochondrial dysfunction**.

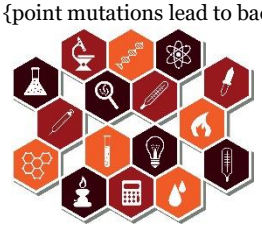
The process of aging involves a bunch of complex biological phenomena. A decline in mitochondrial turnover and function, caused by reduced mitochondrial biogenesis, inefficient mitochondrial degradation, and mutation seems to be particularly crucial.

Mitochondrial DNA has an estimated *10-fold greater mutation rate than nuclear DNA* and less repair capacity, and this plays an important role in aging and cancer. Human mtDNA codes for 13 polypeptides that are members of the OXPHOS system, along with 22 transfer RNAs (tRNAs) and 2 ribosomal RNAs (rRNAs), all of which are required for their synthesis.

Aging results in an accumulation of point mutations that impair our ability to regenerate healthy mitochondria. As a result, we lose their functionality.



{point mutations lead to bad copies}



As evidence, if we knock out effective mitochondrial replication in mice, we see signs of premature aging with symptoms such as reduced lifespan, reduced fertility, anemia, osteoporosis, hair graying, and hair loss.

One side effect in retro-viral HIV therapy is premature aging. These antiviral drugs target polymerases and work by hampering replication, but they're not awfully specific, so they affect mitochondria as well as virus. So, along with lower viral load, we also see poor metabolism, graying hair and other evidence of aging in these patients.

A decline in mitochondrial function plays a key role in the aging process and increases the incidence of age-related disorders.

Yeah, but …. Why do we gain weight?

As you get older, you require fewer calories to meet your daily needs—partly because we get less active and our muscle mass decreases, so there's less muscle tissue burning ATP.

Because ATP is fragile, you can't store energy in the form of ATP. You store energy in other ways.

One way is to store energy as starch (basically sugar that can be used when the body needs an extra source of fuel).

The other way you store energy is as fat.

A 20-year-old might require about 2,000 calories a day, whereas for women after menopause or men in their 60s, daily calorie needs drop below 1,500 and sometimes below 1,200 calories.

As you get older your body will store more of that fuel as fat.

Your entire neuroendocrine system (hormones and neurotransmitters) exerts its effects largely through mitochondria. Your body uses neurotransmitters and hormones as signals to tell mitochondria what to do. Mitochondria burn fat by up-regulating metabolic pathways, directly triggering fat-cell death, and also by increasing thyroid hormone.

What does thyroid hormone do? It basically turns on your mitochondria, which is why weight gain is a hallmark of low thyroid hormone (hypothyroidism).

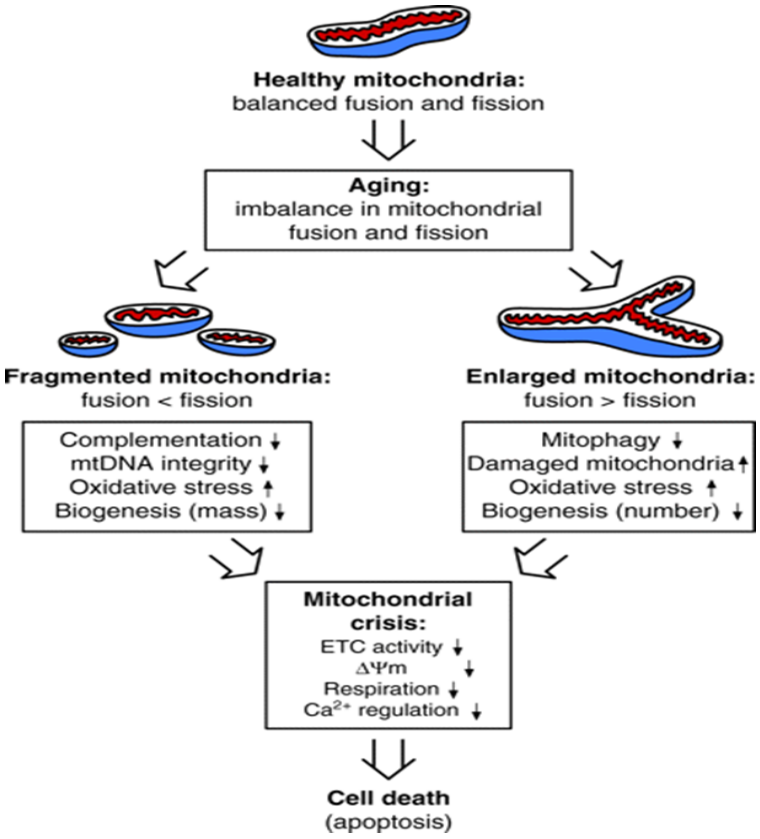
The feedback loops that regulate endocrine messaging are disrupted by mitochondria dysfunction. The aging process reinforces a downward spiral in metabolic efficiency.

As we age, we store more and more energy in fat and our mitochondria become less and less able to metabolize it. That's why we gain weight.

The billions of tiny motors that run much of our cellular machinery eventually just wear out. Specifically, the problem seems to be the point mutations that accrue in their little mitochondrial genomes.

But that ain't all.

Mitochondria are essential to a plethora of bodily functions, from muscle motion to mental acuity. Protective mechanisms are impaired in aging and faulty mitochondrial dynamics are involved in the aging process. Aging leads to dysfunction.



{we lose function as we age}

Mitochondria are essential in powering and regulating our immunity. Problems with viral immunity are big these days. The underlying issues are evident in the sequalae of disease in the aging. Next week we'll look at the mitochondrial role in COVID-19 and the disproportional severity in older populations (almost done with Mitochondria Month!!).

Have a great week and be safe,

Bryan

p.s. Mitochondria are the primary organelle affected during chronological and UV-induced skin aging, the wrinkles we develop are the direct consequence of mitochondrial dysfunction. Gray hair is also predominately due to mitochondria losing potency. Their plasticity is crucial to neuron function and maintenance and play an increasingly more understood role in age-onset dementia.