

THE ULTIMATE CATCH-22: WILL LIFE BE THE DEATH OF US?

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Whatever it is that you live, eat and breathe, the point is you eat and breathe.

Remarkably, these two simple (and occasionally pleasurable) activities are all that's needed to keep the biology of your body ticking over. By getting oxygen into your lungs and food into your stomach you are providing all the raw materials required for aerobic respiration: the chemical reaction that is constantly firing away in every cell of your body to give you energy. This fantastic life-giving reaction comes courtesy of a tiny organelle in your cells called the mitochondrion. But don't be fooled by their apparently selfless nature - they might just be the death of you.

While mitochondria have long been appreciated for their role in aerobic respiration, more recent scientific research has begun to uncover their darker side. From cancer to Alzheimer's, mitochondria have been shown to be involved in a number of life-threatening diseases and may even be responsible for human ageing itself. But in order to understand how mitochondria can be both friend and foe, we have to consider where mitochondria came from and how they work.

Mitochondria really are very tiny, each one no bigger than a single bacteria – and this is no coincidence. It is now widely accepted that mitochondria are in fact ancient bacteria that were once engulfed by our single-celled ancestors. Originally intended as a meal, the mitochondrion resisted digestion and instead made a home for itself inside the cell. This turned out to be much more beneficial than a quick dinner as they brought with them the ability to carry out aerobic respiration which, as discussed above, is the most important way that our body produces the energy essential for our continued survival. Indeed, without mitochondria the humans we are today would never have existed - we simply wouldn't have had the energy.

But there was a catch. Although mitochondria's way of making energy is about 19 times more efficient than what our cells would manage on their own, they can sometimes accidentally produce very destructive molecules called reactive oxygen species (ROS), a type of 'free-radical'. These ROS are to your cells what the Vikings were to quiet English villages and their chaste maidens: ROS will happily run riot through your cells, reacting with and degrading any cellular component they can find, including your DNA. There are a number of repair pathways in your cell, but they are not perfect and gradually 'oxidative damage' accumulates. This is thought to underpin the process of ageing: the gradual decline in cell and organ function that leads ultimately and inevitably to death.

We already know that damaged DNA can lead to cancer, but what other diseases could oxidative damage cause? A study in humans found that in the brains of people aged over forty, a number of genes required for normal brain function had already started to accumulate oxidative damage, implicating ROS in age-related dementias including Alzheimer's disease (Lin and Beal, 2006). Mitochondria also have their own genes to look after. If this DNA is damaged then over time the mitochondrion will stop working properly, resulting in a 'power failure' for the host cell and probably cell death. It's a two pronged attack of ROS-mediated destruction and energy system failure.

But does damage to mitochondrial DNA cause ageing, or is it just a consequence of the ageing process? A classic question of the 'chicken or the egg?' variety. To try and figure it out, scientists created a mouse whose mitochondria were incapable of copying their DNA without making mistakes, effectively forcing them to sabotage their own ability to function. What they found was that the mice got osteoporosis, lost weight and went bald - classic signs of premature ageing - suggesting that mitochondrial DNA damage can be what gets the ageing ball rolling (A. Trifunovic et al., 2004).

This 'free radical theory of ageing' involving ROS as the bringers of destruction and damaged mitochondria as the ultimate executioners is an attractive one, but not all scientists are happy with it (H. Fukui and C. T. Moraes, 2008, and D. Gems and R. Doonan, 2009). For example, although this theory forms the science behind antioxidant supplements that claim to improve on the job the body already does of mopping up excessive ROS and reducing their damaging effects, it doesn't appear that taking these pills will make you live longer. In fact, a review of recent trials showed that taking some antioxidant supplements may actually increase your chance of dying (G. Bjelakovic et al., 2007). This may be because while ROS can certainly damage DNA, they also play an important part in flagging up to the cell that it needs either to repair itself or undergo cell death (E. Sahin and R. A. DePinho, 2010). This makes sure that cells with damaged DNA don't hang around and turn into cancer.

So it's a tricky balance where everything is a trade off. In exchange for aerobic respiration and the ability to reach multi-cellular organism status, we get ROS, cellular damage and a dependency on mitochondria to produce our energy. Even antioxidants harbour a double-edged sword – too little and we can't keep ROS in check, too much and the body can't detect that it has some repairing to do. However, by better understanding mitochondrial biology and how ROS and mitochondrial function affect the cell, it is hoped that scientists may one day help to slow down the ravages of time and ward off some of the most feared diseases that are the natural bedfellows of ageing. It's no secret of eternal life, but it's a start.

But who would want to live forever anyway? And more importantly, what would happen if we did? There are a number of theories as to why humans and animals age. It seems bizarre that despite having undergone numerous rounds of natural selection and survival of the fittest that getting old and forgetful has not been wiped out. Some scientists believe that this is because animals actually need to age to make room for the next generation. As any woman may tell you, a more experienced man can be infinitely more attractive than his immature counterpart. Indeed, consider a world where seasoned lotharios ceased to be hampered by some of the less enticing aspects of ageing and were therefore able to continue their domination of the gene-pool: evolution and adaptation could come to a halt entirely.

In today's society where over 20% of under 25 year olds are unemployed and the number of people over 65 continues to increase, do we really want to find out how to make people live even longer? It is a challenging question. The science is interesting, no doubt, but when a tough economic climate requires us to make tough economic decisions, should we be funding research into ageing, or malaria? Cancer or tuberculosis? Alzheimer's or HIV?

It seems we're back to finding that balance, that necessary trade off. And nothing teaches us this lesson better than the mitochondrion that gives life in one breath and starts taking it away in another.

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