Mitochondrial process may predict lifespan of organisms

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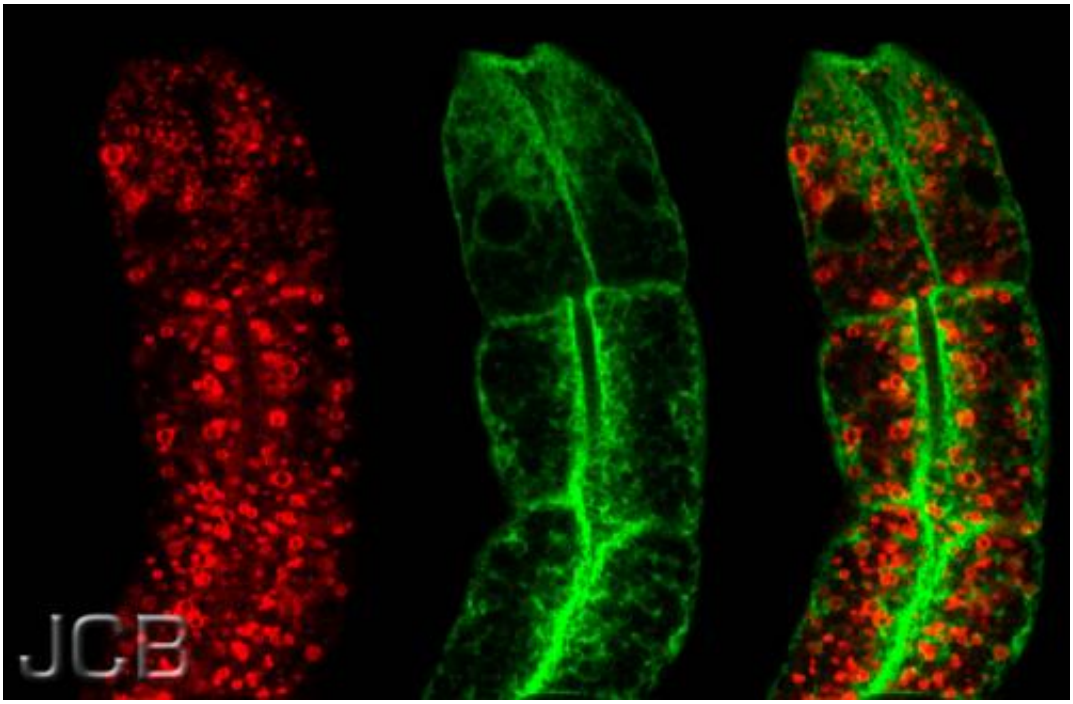

Glow-in-the-dark worm. Credit: thejcb

The complexity in biology is astounding. That is why biologists are thankful that model organisms, like the roundworm *Caenorhabditis elegans*, can be used to breakdown biological processes into simpler units.

C. elegans is a particular favourite. It grows in the exact same way from a single fertilised egg cell to 959 cells as an adult. Its body is transparent

which has allowed scientists to map its growth and study internal changes to great detail.

In a paper published in Nature recently, En-Zhi Shen at the National Institute of Biological Sciences in Beijing and colleagues have used *C. elegans* to make an intriguing discovery. Based on a process that occurs in each cell's power house, mitochondria, they claim to be able to predict the lifespan of that organism.

In nature, electrons are found in pairs in orbit around the atom's nucleus. A free radical is created when an atom has an unpaired electron whizzing around the nucleus. Inside mitochondria, there is formation of such free radicals called reactive oxygen species.

The mitochondria produces many types of reactive oxygen species (ROS) as by-products of the normal metabolic process, including superoxide, hydrogen peroxide, and nitric oxide. These free radicals propelled by their unpaired electrons seek to find other molecules in the cells from whom they can steal an electron and thereby damage them. Thus, free radicals can damage DNA and stop proteins and lipids from performing their functions in the cell. This process of stealing electrons from functional molecules by reactive oxygen species and its resulting damage is known as oxidative stress.

Shen thought that if they were able to measure the amount of oxidative stress in the worms they may be able to predict how long they would live. Shen had previously discovered that the mitochondria in cells produce sudden short bursts of free radicals which could be counted.

When Shen studied *C. elegans* with added proteins that glow in the dark because of oxidative stress, she could detect levels of oxidative stress by measuring the flashes of light, termed mitoflash, emitted by proteins which detect free-radicals produced by the mitochondria. The more

mitoflashes that happen within a certain window of time, the higher the amount of free radicals produced by the mitochondria.

Using the mitoflash method, an individual worm can be observed during the entirety of its 21-day lifespan. These worms are at the peak of their reproductive ability during the second and third day of their lives. Soon after this, the worms start their steady decline towards old age and by about the fifteenth day most of them are considered old.

Shen discovered that there were two periods in the lifespan of the worm when oxidative stress increased. The first was around the third day, when the worms are laying their eggs and the other was around the fifteenth day when the worms were old.

They then compared these finding using other worms who were engineered to have longer or shorter lifespans. Consistently, they found that worms with low amounts of mitoflashes during the third day of their lives lived longer compared to worms with higher mitoflashes. Interestingly, the number of mitoflashes on ninth day was not predictive of lifespan. Shen, therefore, thinks that oxidative stress levels of a worm during early life can determine how long they can live.

Telling age in a flash

Shen's work improves on previous worm studies by hinting that free radicals produced by mitochondria especially in early life may be a central mechanism driving the decline during ageing.

Also, the results of this study agree with the free radical theory of ageing, which assumes that the diseases of ageing result due to the increasing inability of cells to repair damage caused by oxidative stress. This theory predicts that organisms that have long lives must lower their oxidative stress by producing more antioxidants.

Unfortunately, this doesn't happen in real life. Human beings live much longer lives in spite of producing much fewer antioxidants compared to rats, hamsters, mice and rabbits. And studies involving dietary supplementation of antioxidants show an inverse relationship between antioxidant levels and life span. The claim that oxidative stress in early life may be a predictor of lifespan may work in some worms but it will certainly be of no use in humans.

More information: *Nature* DOI: 10.1038/nature13012"