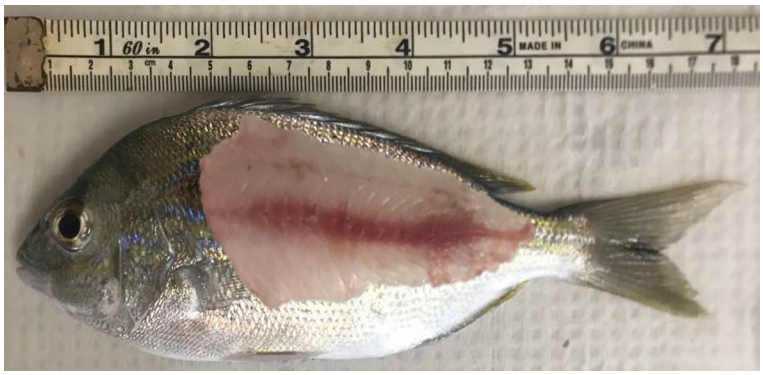
INSIDE JEB

Mitochondria are responsible for reactive oxygen species damage in fish muscle



A pinfish (*Lagodon rhomboides*), showing the distinct regions of red and white muscle. Photo credit: Erik Paulson.

Ever since the Great Oxygenation Event approximately 2.4 billion years ago, when cyanobacteria flooded the atmosphere with oxygen, life has been in a Faustian pact with the colourless gas. Oxygen reacts with glucose in cells to produce the energy that powers life through a chain of events that culminates within the mitochondria. However, these reactions with the life-giving gas also produce a plethora of toxic by-products, known as reactive oxygen species, which can in turn damage DNA, proteins and lipids in cells. The question was whether the mitochondrial powerhouses are the main source of harmful oxygen toxins, or whether they are generated by other sources in the cell. 'People have assumed that mitochondria are the main culprits in reactive oxygen species production, but Yufeng Zhang and Hoi Shan Wong challenged this notion in a Commentary in *Journal of Experimental Biology* in 2021', says Stephen Kinsey from the University of North Carolina Wilmington, USA.

Fortunately, Kinsey and graduate student Julie Neurohr (University of North Carolina Wilmington) knew of a unique tissue that could help to answer the question: fish muscle. 'Fish red and white muscle is easily delineated and metabolically distinct', says Kinsey, explaining that red muscle is packed with mitochondria and consumes large quantities of oxygen, while the larger white muscles are largely devoid of mitochondria and depend instead on anaerobic metabolism. By comparing the amount of damage caused by reactive oxygen species in the two tissues – and how both forms of muscle deal with the collateral damage – Kinsey and Neurohr might be able to begin unravelling whether mitochondria are the key culprits in the oxidative damage sustained by fish muscle.

After fishing for pinfish (*Lagodon rhomboides*) in the Intracoastal Waterway at Wrightsville Beach, USA, Kinsey, Neurohr and Erik Paulson (University of North Carolina Wilmington) used an electron microscope to scrutinise both forms of muscle, revealing that the red muscle was packed with 7 times more mitochondria (comprising 6.9% of the muscle volume) than the white muscle (0.89% muscle volume). And when Neurohr checked the amount of damage caused by reactive oxygen species to DNA, proteins and lipids in both forms of muscle, the red muscle came out on top, suffering the most damage in all three categories, despite having higher levels of the reactive oxygen species neutralising proteins – superoxide dismutase and catalase – for protection. The red muscle with larger quantities of mitochondria seemed to be at most risk from the damage caused by reactive oxygen species produced by the cell's powerhouses.

So, how do vulnerable red muscle cells deal with the increased risk of tissue damage caused by oxygen? Knowing that cells resort to two different forms of disposal – an engulfing system to clear up larger clusters of damaged proteins and a more targeted strategy, the ubiquitin–proteasome system, to dispose of individual unravelling proteins – the team checked for evidence of both and found that the red muscle was best prepared for mopping up individual damaged proteins. In contrast, the white muscle allows damaged proteins to form larger clumps before engulfing them.

And, when Neurohr checked how quickly both forms of muscle produced new proteins, the red muscle was working at almost double the rate of the white muscle to replace the damaged proteins. 'Together, these results suggest that higher mitochondrial content, which imparts the capacity for endurance in muscle, is associated with greater oxidative damage and cellular maintenance', says Kinsey.

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Neurohr, J. M., Paulson, E. T. and Kinsey, S. T. (2021). A higher mitochondrial content is associated with greater oxidative damage, oxidative defenses, protein synthesis and ATP turnover in resting skeletal muscle. *J. Exp. Biol.* **224**, jeb242462.

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