INSIDE JEB

Thin-blooded icefish relocate carbonic anhydrase to gill

A *Champsocephalus gunnari* icefish. Photo credit: Michael Axelsson.

Few animals can justifiably be called 'thin blooded', but Antarctic icefish genuinely are. They lack the brightly pigmented red blood cells that usually carry oxygen around the body, although the blood is still capable of transporting oxygen to their tissues thanks to the high solubility of the gas in the frigid Antarctic waters. But the fish face another problem. In most bony fish, waste carbon dioxide is carried in the blood to the gills in the form of bicarbonate, where it is converted back into carbon dioxide in red blood cells by an enzyme known as carbonic anhydrase, before it is exhaled. 'However this strategy is impossible in icefishes, which have lost red blood cells', says Till Harter from the University of British Columbia, Canada. While there is some evidence that the essential bicarbonate converting protein is harboured somewhere in the gills, the precise location was not clear.

Reasoning that it might be might be situated on the inner surface of gill blood vessels, Harter, Colin Brauner and their international team of collaborators began searching for the elusive enzyme in the gills of *Champsocephalus gunnari* icefish.

Although Harter was unable to visit Antarctica himself, he was fortunate that Kristin O'Brien from University of Alaska Fairbanks, USA, and Lisa Crockett from Ohio University, USA, sent *C. gunnari* that they had caught during the 2015 Antarctic field season. After the fish arrived, he cautiously isolated the outer membrane from the cells lining the inside of the gill blood vessels before bathing it in water saturated with CO_2 and measuring how the pH changed – in the hope that any carbonic anhydrase present on the membrane surface may convert the gas into bicarbonate. The pH decreased rapidly, confirming that the enzyme is located on blood vessel cell membranes. And when Jonathan Wilson stained the cell membranes with a series of specialised dyes that could only bind to molecules of carbonic anhydrase, he found one form of the enzyme (carbonic anhydrase 4) attached to the membranes lining the inner surface of the gill blood vessels. To confirm the presence of the enzyme, Harter and David Metzger then collected RNA from the fish's gills, eventually identifying an mRNA molecule that could be translated to produce the carbonic anhydrase 4 enzyme. However, when the team searched for carbonic anhydrase proteins in the gills of a close relative, *Notothenia rossii*, which has retained its red blood cells despite sharing *C. gunnari*'s icy waters, they found none.

So, it seems that icefish have relocated carbonic anhydrase to their gills to overcome the difficulties of carbon dioxide disposal after trading in their red blood cells. But they suspect that red-blooded fish are unlikely to follow their apparently 'bloodless' cousin's convenient example, as the enzyme could drastically disturb the delicate balance that allows their red blood cells to keep hold of their oxygen cargo when exercising hard.

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Harter, T. S., Sackville, M., Wilson, J. M., Metzger, D. C. H., Egginton, S., Esbaugh, A. J., Farrell, A. P. and Brauner, C. J. (2018). A solution to Nature's haemoglobin knockout: a plasma-accessible carbonic anhydrase catalyses CO_2 excretion in Antarctic icefish gills. *J. Exp. Biol.* **221**, jeb190918.

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