Abstractions

LAST AUTHOR

Despite numerous medical advances, heart disease remains a dominant cause of death worldwide. Many fish and amphibians can regenerate and repair damaged heart tissue; humans, unfortunately, cannot. However, work by Benoit Bruneau at the Gladstone Institute of Cardiovascular Disease in San Francisco, California, and his colleagues has thrown light on the little-understood topic of mammalian and reptilian heart evolution. Two findings, which centre on how the protein Tbx5 regulates the growth of a subset of heart cells, may lead to new treatments for human heart disease. The first revelation was that this protein, along with two others, could be manipulated to induce embryonic mouse cells to develop into cardiac cells (J. K. Takeuchi and B. G. Bruneau *Nature* **459,** 708–711; 2009). Now, Bruneau and his team show that, in two reptiles, Tbx5 is a key determinant in the heart's division into two chambers — and that, in mice, the protein's absence has a drastic effect on heart structure (see page 95).

You began by studying mouse heart-cell growth, then moved on to reptilian hearts. Why the interest in different organisms?

By comparing different organisms, we can often gain insight into similar processes. To try to understand the function of Tbx5 in heart disease, we deleted the *Tbx5* gene from specific chambers of the heart, essentially turning the mouse heart into what looked like a frog heart. We then studied reptilian hearts to look into the patterned expression of *Tbx5* and gain a broader perspective on the gene's role. We didn't know how important *Tbx5* might be in cardiac chamber formation, or in its evolution.

What was the hardest part of the work?

Locating literature on reptilian heart development. The newest paper I could find that described the embryology was a German monograph from 1903. Some of its predictions were right on the money, but there were dissenting responses from others also studying the reptile heart. Reptiles have a broad spectrum of morphology, and no one could make head nor tail of their hearts. People offered differing interpretations of the same morphology in their own papers.

Is your work important to human health?

Now that we understand how important *Tbx5* is to ventricular separation, we can focus on how it helps the heart develop a septum. Human *Tbx5* mutations cause septation defects, which are very common in children with congenital heart disease. Understanding the role of *Tbx5* in building and separating the heart into ventricles will probably be broadly applicable to understanding and treating heart diseases caused by genetic defects. ■

MAKING THE PAPER

Bess Ward

Nitrogen loss in the oceans is a genuine puzzle still to be solved.

Why are some areas of the world's oceans rich in plant growth, whereas others are biological deserts? The answer is that more than half the ocean has too little nitrogen to support the growth of microscopic plants, or phytoplankton. But where does the missing nitrogen go?

For decades most oceanographers, including Bess Ward at Princeton University in New Jersey, thought 'denitrification' was responsible for virtually all nitrogen loss in the ocean. In oxygen-poor areas of the ocean, anaerobic bacteria, which do not rely on oxygen for their growth, use biologically available forms of nitrogen, such as nitrates and nitrites, for energy generation, producing, through several intermediate steps, dinitrogen (N_2) — a form of nitrogen that plants cannot use.

But starting in 1995, investigators in the Netherlands, Germany and Denmark uncovered an additional biochemical reaction, called anaerobic ammonia oxidation, or anammox, that produces N_2 in ocean waters. Here, the bacteria responsible use up nitrite (NO_2^-) and ammonia (NH_4^+) to directly generate N_2.

The Europeans showed that anammox, in the absence of denitrification, accounted for most, if not all, N_2 generation. "But given the chemistry of the two processes it was impossible for us to understand how that could be," says Ward.

The problem, she thought, was that nitrite and ammonium are intermediate products in the denitrification process. And in oxygen-poor waters, denitrification is the only substantial source of these chemicals. "We couldn't understand how anammox could be occurring in the absence of denitrification," says Ward, "so that's what we set out to resolve."

This involved sending postdoc Jeremy Rich, now a researcher at Brown University in Providence, Rhode Island, on a trip to Europe. The European investigators had devised new methods for measuring anammox and denitrification in small (10 millilitre) samples of ocean water. "The methods were so new and so different that a lot of people were suspicious there might be some artefact involved," says Ward. "So Jeremy visited some of our European colleagues and learned the methods, so we could go out and try to reproduce their results." Ward and her colleagues also developed their own methods for measuring denitrification and anammox in larger (10 litre) samples.

The next step was to apply the techniques to different parts of the ocean. First stop was Chesapeake Bay, on the east coast of the United States, where Ward's team found "exactly what we expected in our own backyard, which was both anammox and denitrification" occurring together, she says. In the Eastern Tropical South Pacific, however, off the coast of Peru, "we got exactly what the Europeans had, which was all anammox and no denitrification", she says. Convinced that their methods were working, Ward and her colleagues made an additional stop in the Arabian Sea, "where it turned out that it was all denitrification and very little anammox" (page 78).

So in different parts of the ocean, and at different times, a variety of mechanisms may be responsible for marine nitrogen loss. "We used to think we understood denitrification and now we know we don't," says Ward. The current study "does not increase clarity", she says. "But it makes it more compelling that we find the answer." ■

FROM THE BLOGOSPHERE

If you weren't one of the 200 or so people invited to Science Foo Camp this year, you can experience a snippet of the "gathering of geeks" that took place earlier this summer at Google's headquarters in Mountain View, California. A video produced by *Nature* podcast producer Charlotte Stoddart has been posted on The Great Beyond blog (http://tinyurl.com/mfe4g4).

The film shows just how an 'unconference' runs — with attendees rushing to scribble down their own agenda on the first day. Talks such as "Can biology help us understand the financial crisis?" and "Is 'evil' in our brains and can we control it?" peppered the whiteboard. The gathering included people such as the mathematician who designed a non-reversing mirror and the co-founder of DIYbio.org, an online community for amateur scientists.

Tim O'Reilly, chief executive of O'Reilly Media and after whom Foo is named (friends of O'Reilly), points out, "If you had a bunch of really smart people over to your house, would you think you had to have a programme? Of course they're going to find things to talk about!" ■

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