



Since the turn of the twentieth century, zoologists have set out from coastal marine stations at dawn to sieve peppercorn-sized worms from sea-bottom muck. These creatures, called acoels, often look like unremarkable splashes of paint when seen through a microscope. But they represent a crucial stage in animal evolution — the transition some 560 million years ago from simple anemone-like organisms to the zoo of complex creatures that populate the world today.

There are about 370 species of acoel, which gets its name because it lacks a coelom — the fluid-filled body cavity that holds the internal organs in more-complex animals. Acoels also have just one hole for both eating and excreting, similar to cnidarians — a group of evolutionarily older animals containing jellyfish and sea anemones. But unlike the simpler cnidarians, which have only an inner and outer tissue layer, acoels have a third, middle tissue layer. That is the arrangement found in everything from scorpions to squids to seals, suggesting that acoels represent an intermediate form.

That hypothesis has gained considerable support in recent years, but a report published in *Nature* this week<sup>1</sup> is causing scientists to rethink the storyline. The study by an international team of researchers, who used new analytical techniques and data, removes acoel worms from their position near the trunk of animal evolution and instead places them closer to vertebrates (see ‘Competing views of animal evolution’).

The rearrangement has triggered protests from evolutionary biologists, who are alarmed that they may lose their key example of that

*An obscure group of tiny creatures takes centre stage in a battle to work out the tree of life.*

BY AMY MAXMEN

crucial intermediate stage of animal evolution. Some researchers complain that the evidence is not strong enough to warrant such a dramatic rearrangement of the evolutionary tree, and claim that the report leaves out key data. In any case, the vehemence of the debate shows just how important these worms have become in evolutionary biology.

“I will say, diplomatically, this is the most politically fraught paper I’ve ever written,” says Max Telford, a zoologist at University College London and last author on the paper.

The debate focuses on where acoels fit in the family tree of bilaterians, three-layered animals with bilateral symmetry. Biologists divide these animals into two branches. The larger group,

called protostomes, contains invertebrates such as earthworms, squids, snails and insects. The smaller group, known as deuterostomes, includes both vertebrates and invertebrates, such as sea urchins, humans and fish.

Zoologists have generally placed acoels on the earliest branch of the bilaterians — before the split between protostomes and deuterostomes — because the worms lack so many key features such as a

separate mouth and anus, a central nervous system and organs to filter waste. Although the position of acoels has moved around a bit over the decades, a DNA analysis in 1999 (ref. 2) and several since then have placed them back in their earlier spot. In particular, a genetic study of 94 organisms in 2009 solidified the conclusion that acoels belonged at the very base of the bilaterians<sup>3</sup>. That study, led by Andreas Hejnol, a developmental biologist at the Sars International Centre for Marine Molecular Biology in Bergen, Norway, confirmed that acoels and their kin occupied an intermediate spot between cnidarians and the more-complex bilaterians.

“I suddenly had the feeling that everything had finally fallen into place,” says Claus Nielsen, an evolutionary biologist at the Natural History Museum of Denmark, who has followed acoels for 40 years as they wandered across the tree of life.

### SHAKING THE TREE

But the study by Telford and his colleagues<sup>1</sup> has shaken the tree again and placed acoels within the deuterostome branches, next to the echinoderms (which include sea urchins) and acorn worms. Their genetic analyses suggest that the acoels — and a marine worm named *Xenoturbella* — descended from a more complex ancestor and lost many of the features seen in other deuterostomes.

The researchers used several approaches and examined three independent data sets to come to their conclusions. First, they reanalysed data from Hejnol’s 2009 study<sup>3</sup>, using 66 species instead of 94. Hervé Philippe, a bioinformatician at the University of Montreal in Quebec, Canada, and first author of the *Nature* paper<sup>1</sup>, says that the team removed species that had

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incomplete genetic data or were ‘fast-evolving’ — meaning that some of their genes had accumulated many changes, when compared with genes from animal groups that emerged around the same time. Phylogenetic computer programs have a well-known problem with these kinds of species and tend to group them together even though they are not related.

Philippe and his co-workers used a more sophisticated mathematical model to analyse sequence evolution, which helped to minimize this problem. Without this model and careful species selection, Philippe says, acoels can fall at the base of the animal tree.

After analysing sequences from nuclear DNA, the group made a separate evolutionary tree based on genes in mitochondria. They also studied microRNAs, which regulate gene expression but do not code for proteins. According to co-author Kevin Peterson, a palaeontologist at Dartmouth College in Hanover, New Hampshire, microRNAs are particularly useful for studying deep evolutionary relationships. The team found that acoels have a type of microRNA known to be specific to deuterostomes, suggesting that they are related.

The authors acknowledge that no single data set clinches the case for placing acoels within

the deuterostomes. But taken together, says Telford, “the fact that our evidence points in the same direction makes me think it’s right”.

If acoels do fit within the deuterostomes, the worms must have evolved from an ancestor with a central nervous system, a body cavity and a through-going gut that connected an anus and mouth — features seen in existing deuterostomes. So researchers would need to explain how acoels and *Xenoturbella* lost those and other characteristics. They would also be left to search for another primitive-looking lineage that represents the evolutionary step between jellyfish-like animals and bilaterians. (If one even exists. Peterson says that many complex features may have emerged all at once.)

Some researchers are not ready to give up on the old ideas of where acoels fit. “I’m sad about their paper, but I’m not upset,” says Hejnl. “I’d be upset if their analysis was excellent and it meant we lost a representative animal to bridge an important transition in the tree of life.”

Hejnl and his colleagues have doubts about the reliability of the tree that Telford and his team built from nuclear genes, which

is their main evidence. Critics say that the key branches of the tree are not as statistically strong as they should be.

Because of this, Brian O’Meara, a phylogeneticist at the University of Tennessee in Knoxville, calls the new tree “suggestive, but not definitive”.

The study has also come under fire for leaving out data that some scientists say would

have weakened the researchers’ conclusions. An author on the paper had previously analysed a species of worm closely related to acoels known as *Meara stichopi*, and did not find deuterostome microRNA. But the authors

defend their decision to keep *M. stichopi* out of their microRNA analysis owing to concerns about the quality of those data.

Moreover, not everyone is convinced by the power of microRNA analysis, which has only recently been adopted for evolutionary studies. This report marks the method’s most high-profile appearance yet as a tool to resolve relationships. Because microRNAs can be lost during evolution, it is possible that the deuterostome microRNA in acoels originated in the ancestor of all bilateral animals but was later lost in the protostome line.

With so much at stake, researchers are keen to resolve the issue. The US National Science Foundation has been specifically soliciting proposals that target deep divergences in evolutionary history, as part of an initiative called Assembling the Tree of Life, says Tim Collins, a programme director at the foundation. “We’ve done a good job within groups, but we’ve had a hard time reconstructing the deepest branches of the tree of life,” he says. “These are the events that happened in a relatively short time compared with the amount of time that has passed since then, which makes things hard.”

Last summer in Kristineberg, Sweden, Hejnl and Telford shared a room while teaching a class together. They debated their differences and discussed an ongoing joint project that might settle them: sequencing the full genomes of an acael, a species of *Xenoturbella* and the controversial *M. stichopi*. With that influx of new genomic information, the researchers are confident that they can reach an agreement about where acoels fit in evolutionary history.

“We’re talking about a very close result with a humongous impact,” says Hejnl, of the newly proposed tree. “The good thing is, we know how to resolve this issue.” ■

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1. Philippe, H. *et al.* *Nature* **470**, 255–258 (2011).
2. Ruiz-Trillo, I., Riutort, M., Littlewood, D. T., Herniou, E. A. & Bagaña, J. *Science* **283**, 1919–1923 (1999).
3. Hejnl, A. *et al.* *Proc. R. Soc. B* **276**, 4261–4270 (2009).

## COMPETING VIEWS OF ANIMAL EVOLUTION

The traditional view of acoels places them at the base of the bilaterians, before the evolution of animals with a separate mouth and anus. After acoels and *Xenoturbella* split off, bilaterians diverged into protostomes and deuterostomes.

Development of bilaterians — animals with three tissue layers and bodies with symmetrical left and right sides.

Like other bilaterians, acoels and *Xenoturbella* have three body layers but they have only one hole for eating and excreting.

The new analysis by Telford and his team<sup>1</sup> puts acoels and *Xenoturbella* up within the deuterostomes, suggesting that these groups lost many features present in the ancestral deuterostome.

