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New Research Shows MicroRNAs Emerged Early in Evolution

Scientists have long wondered when the tiny gene-tweaking molecules known as microRNAs first arose during animal evolution. Their curiosity has been driven, in part, by lingering questions about whether these snippets of RNA helped shape the development of complex multi-cellular animals.

Now, Howard Hughes Medical Institute investigator David Bartel at the Whitehead Institute for Biomedical Research has found microRNAs in animal species whose last common ancestors were present on Earth about 1 billion years ago. Bartel's group teamed up with researchers at the University of California, Berkeley, and the University of Queensland to identify microRNAs—and similar gene-regulators known as piRNAs (piwi-interacting RNAs)—in a simple sponge and a sea anemone.

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— David P. Bartel

Their research paper, published in *Nature* on October 1, 2008, establishes that microRNAs existed in some of the earliest multi-cellular life forms. MicroRNAs have been available to regulate and shape gene expression as far back as we can go in animal evolution—they might even predate animals, says Bartel, a leader in the discovery and functional study of microRNAs. They might have helped to usher in the era of multi-cellular animal life.

First discovered in 1993, microRNAs are strands of RNA that are 21-24 nucleotides in length. They dampen gene expression by intercepting messenger RNA before it can turn the cellular crank that translates a gene into a protein. Earlier, Bartel's research team showed that each microRNA can regulate the expression of hundreds of genes.

The ability of microRNAs to silence gene expression likely evolved from a more ancient defense against viruses, bacteria, and other mobile genetic elements that can mutate host DNA. The question has been asked, `When in evolution did the microRNAs emerge in animals?' Bartel says. It just wasn't known.

Scientists had already found microRNAs in the Bilateria, a large group of animals that first appeared about 500 million years ago. Bilaterians—named because their body shape displays bilateral symmetry—include humans and most other animals but not sponges, jellyfish and sea anemones. Sponges and jellyfish have radial symmetry—meaning they have a top and bottom, but no defined front or back. They are also older than Bilaterians in evolutionary terms. But scientists had not found microRNAs in sponges or jellies, and had only hints of their existence in anemones.

Bartel and his colleagues used bioinformatics software to evaluate millions of small RNAs that they had isolated from radially symmetric creatures whose genomes had recently been sequenced and annotated. Those organisms included *Nematostella vectensis,* the starlet sea anemone; *Amphimedon queenslandica,* a sponge from Australia's Great Barrier Reef; and *Trichoplax adhaerens,* a primitive balloon-like marine animal.

The scientists determined that the starlet sea anemone has both microRNAs and piRNAs. In addition, the anemone makes proteins resembling those that interact with these small RNAs in humans. Both types of small RNA were also found in the sponge. The third target of their search, *Trichoplax,* did not contain any microRNAs, though Bartel suspects they may have existed in ancestral forms and later disappeared.

We now know that both we and the sponge have microRNAs, Bartel says. We can't prove that microRNAs were required for complex multi-cellular animal life on the basis of this study, but they certainly might have been useful. It could be that if you have a simple cell that acquires microRNAs, this additional mode of gene regulation increases the chances of evolving into something more complex.