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Primitive Microbe Offers Glimpse of Animal Evolution

A microorganism whose evolutionary roots can be traced to the era of the first multicellular animals may provide a glimpse of how single-celled organisms made a critical evolutionary leap.

In analyzing the single-celled choanoflagellates, scientists discovered that the organisms have a type of molecular sensor usually found in multicellular animals. This is the first time that such a sensor, called a receptor tyrosine kinase, has been found in a single-celled organism, said Sean B. Carroll , a Howard Hughes Medical Institute investigator at the University of Wisconsin, Madison. Carroll and Wisconsin colleague Nicole King reported their findings in the December 18, 2001, edition of the *Proceedings of the National Academy of Sciences* .

"In general, these discoveries have made us confident that we've picked the right organism to understand what happened on the eve of animal evolution. We believe we can discover in this organism more elements of the genetic toolkit that was first used to build animals."
— Sean B. Carroll

Choanoflagellates are a group of about 150 species of single-celled protists, which use a whip-like flagellum to swim and draw in food. Surrounding this flagellum is a circle of closely packed, finger-like microvilli that filter food from the water. Scientists have long suspected that choanoflagellates might represent modern examples of what the ancestors of multicellular animals, or metazoans, looked like. And the circumstantial evidence supporting that notion was compelling — choanoflagellates are nearly identical to cells called choanocytes in sponges that also carry out food-gathering and some species of choanoflagellates tend to form colonies.

"The existing scientific literature, however, has been conflicting or ambiguous about whether these protists are the closest living relatives of animals without actually being animals," said Carroll. "So, Nicole King proposed that we explore protein sequences that hadn't been examined before, and which might provide unambiguous support for the relationship between choanoflagellates and animals."

The researchers first compared genes in one species of choanoflagellate, *Monosiga brevicollis* , to four animal genes that express proteins that are highly conserved throughout the animal kingdom. These structural proteins — called elongation factor 2, alpha-tubulin, beta-tubulin and actin — are widely used as molecular markers to explore relationships among species.

"When we compared the sequences of the choanoflagellate and animal genes, we got a much clearer statistical signal than we expected that they were related," said Carroll. The comparisons constituted the strongest sequence-based support yet for the hypothesis of the kinship between choanoflagellates and metazoans, he said. Confident that they had established a kinship between the organisms, the researchers next surveyed the choanoflagellate genome for animal-related genes.

"It was something of a shotgun approach, but we tuned our search for genes for a few specific types of molecules that had not been found outside of the metazoans," said Carroll. The search concentrated on molecules involved in cell adhesion and cell signaling, which single-cell organisms would not be expected to have, said Carroll.

"Among several hundred common gene sequences we obtained, out popped this receptor tyrosine kinase, a molecule that has never before been found outside of metazoans," Carroll said.

Receptor tyrosine kinases are molecular sensors that nestle in the cell membrane. When an external chemical plugs into the receptor, like a key into a lock, a signaling pathway is activated inside the cell. The discovery of the receptor tyrosine kinase, called MBRTK1, is important because it implies that the choanoflagellates had evolved some of the machinery necessary to interact with one another like animal cells, said Carroll.

Further analysis of the MBRTK1 protein and comparison of its structure with kinases in other organisms could yield important evolutionary insights. "We'd like to know if this protein might be a founding member of this class of molecules — a common ancestor that may have appeared on the eve of animal evolution," said Carroll. Also, he said, the scientists hope to trace the signaling pathway activated by MBRTK1, to understand what effect the external signal produces in the choanoflagellate.

"In general, these discoveries have made us confident that we've picked the right organism to understand what happened on the eve of animal evolution," said Carroll. "Thus, we believe we can discover in this organism more elements of the genetic toolkit that was first used to build animals."

According to Carroll, the studies on choanoflagellates promise to be an important part of his laboratory's ongoing studies of animal evolution. The theme of this research is also reflected in Carroll's new book, *From DNA to*

Diversity: Molecular Genetics and the Evolution of Animal Design , which was written with Jennifer Grenier and Scott Weatherbee (Blackwell Science Publications, 2001).