



## Learning to walk

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The coelacanth, an endangered fish found off the coast of South Africa, is helping UW professor Chris Amemiya and his team of scientists understand how fish made their evolutionary transition onto land more than 400 million years ago.

Known by some as a “living fossil,” the coelacanth is the second closest water-bound relative to tetrapods, a superclass that consists of the first four-limbed vertebrates and their evolutionary descendants, which include humans. Amemiya gathered more than 80 researchers from around the world to sequence, analyze, and annotate coelacanth’s genome.



The coelacanth provided an example of part of the transition that fish made to evolve into land animals. Over time, creatures repurposed the fish’s genes depending on their adaptive needs.

Technically, lungfish are closer relatives to tetrapods. But scientists have been unable to decipher their genetic code because it is 100 billion units long.

A coelacanth’s genome is just 2.8 billion units and therefore was easier for scientists to evaluate.

The researchers found that rather than sharing DNA directly responsible for the physical traits of tetrapods, coelacanths had special gene snippets known as enhancer sequences that drive the expression of genes for adaptive characteristics such as limb formation and placental development.

“The ancestor of the land vertebrates had to somehow develop the structures to not only crawl up on land and use their extremities for locomotion, but also had to develop other adaptations as well,” Amemiya said.

These physical developments include everything from the way terrestrial creatures breathe to the way they sense the world around them. Amemiya said his team’s research now makes it possible to theoretically postulate how these adaptations came to be through evolution.

As a test, researchers took the coelacanth enhancer sequences responsible for initiating limb formation and placed them into the appropriate DNA sections in developing mice.

The extremities of the mice grew normally, implying that although the enhancer sequence didn’t cause limbs to form in coelacanths, the enhancer sequences existed in the genes as a

framework that tetrapods used to evolve from the fish.

Leader of the Vertebrate Genome Biology group at the Broad Institute, Jessica Alföldi, helped to sequence the coelacanth genes for analysis. She said that discovering the enhancer sequence for limbs in a species with no apparent need for them was particularly interesting.

Furthermore, the enhancer sequences that humans and coelacanths share suggest the existence of a common ancestor, according to Axel Meyer, professor at the University of Konstanz in Germany who also contributed to the paper detailing the coelacanth findings.

“There was a common ancestor of coelacanths and humans,” he said. “[It] gave rise to coelacanths, lungfish, and tetrapods. So it’s a piece of the puzzle.”

His lab and prior research was instrumental in finding the transposable elements of the coelacanth genome. A transposable element is a piece of DNA that replicates and inserts itself into already existing DNA, and usually causes mutations that give rise to new enhancer sequences.

Tracking these mutations over time addresses how species adapt. More mutations in transposable elements suggest that it took longer to acquire them.

In the coelacanth, Meyer said the transposable elements have been evolving slowly so the tissue sample they are working with now is a reasonable reflection of its ancestor. And this means that data collected by researchers today can be used to draw conclusions about the evolution of creatures millions of years ago.

Although the research provided scientific insights, it was difficult to fund because it didn’t immediately address pressing biological matters such as disease or famine. However, Amemiya said that all the scientists working on the project were willing to do so without pay.

“We made a lot of phone calls to assemble experts who were willing to participate in this. They do it only because they’re interested in the science,” Amemiya said. “You just do it because you’re interested in the answer.”

The researchers are planning to make the information available on public access websites — a decision that Amemiya said came from a desire to spread the knowledge of our common ancestry.

“The genome itself is kind of a gift to the community, it’s a terrific resource,” he said.

According to Meyer, the research on enhancer sequences can open up new horizons for decoding the human genome through the lens of how it evolved over the last several million years.

He said that researchers have a strong conceptual grasp on the proteins responsible for expressing physical characteristics, but the genes that drive the formation of those characteristics remain difficult to ascertain in many cases.

“The genome will be around as a resource now, but many people will continue to work on their particular ... gene family,” Meyer said.

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