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Lungfish fins reveal how hands and limbs evolved

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Since the nineteenth century, scientists have used fossil evidence to propose many different theories explaining the series of events that led up to this major transformation. However, it has remained a mystery how fish fins developed into hands with fingers and toes.

In a new study from the University of Konstanz, an international team of biologists has used embryos of the Australian lungfish to examine how limbs evolved from fins.

The Australian lungfish is the closest living fish relative of tetrapods. It is often referred to as a “living fossil” because it still resembles the fish that were present when the first four-limbed vertebrates began to walk on land.

The study revealed that a primitive hand is present in lungfish fins. However, the research also suggests that the unique anatomy of limbs with digits only evolved during the rise of tetrapods through changes in embryonic development.

“During embryogenesis, a suite of ‘architect’ genes shapes an amorphous group of precursor cells into fully grown limbs,” said study first author Dr. Joost Woltering.

The same architect genes also drive fin development, but due to evolutionary changes in the activity of these genes, the developmental process now produces fins in fish and limbs in tetrapods.

To compare this developmental stage in fins and limbs, the team studied architect genes in the embryos of the Australian lungfish.

“Amazingly, what we discovered is that the gene specifying the hand in limbs (hoxa13) is activated in a similar skeletal region in lungfish fins,” explained Woltering. This particular region has never been found in the fins of other fish that are more distantly related to tetrapods. “This finding clearly indicates that a primitive hand was already present in the ancestors of land animals.”

To understand the genetic basis for the lungfish hand, which lacks fingers and toes, the team analyzed genes that are known to be associated with the formation of digits. The study showed that a gene which is important for the formation of fingers and toes, hoxd13, was switched on in a dynamic manner during tetrapod limb development.

According to the study, the hoxd13 gene first becomes activated in the developing pinky finger and then expands all the way throughout the future hand towards the thumb. This process coordinates the correct formation of all five fingers.

While the experts observed a similar activation pattern of hoxd13 in lungfish fins, it only remained activated in exactly one half of the fin.

“All of this goes to show that while lungfish fins unexpectedly have a primitive hand in common with tetrapods, the fins of our ancestors also needed an evolutionary ‘finishing touch’ to produce limbs. In this sense it looks as if the hand was there first, only to be complemented with digits later during evolution,” explained Woltering.

Going forward, the researchers will conduct further analyses using techniques like CRISPR to gain more insight into the development of fins and limbs, focusing not just on lungfish but also on more modern fish species such as cichlids as their embryos.

“To complete the picture of what happened in our fish ancestors that crawled onto land hundreds of millions of years ago, we really rely on currently living species to see how their embryos grow fins and limbs so differently,” said Woltering.

The study is published in the journal *Science Advances*.

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