# Jump-Start for the Vertebrates

## New clues to how our ancestors got a head

By RICHARD MONASTERSKY

*It's a long way from amphioxus, it's a long way to us.*
*It's a long way from amphioxus to the meanest human cuss.*
*It's good-bye to fins and gill slits, welcome lungs and hair.*
*It's a long, long way from amphioxus, but we all came from there.*
— Philip Pope

The small, fishlike oddity called amphioxus has long inhabited a zoological twilight zone. It's a familiar stranger—neither complete outcast nor accepted member of the household. Like humans, amphioxus falls in the phylum Chordata. But because it lacks a backbone, the paper-clip-sized creature lies on the other side of the vertebrate line.

That dubious position, however, makes amphioxus the darling of biologists who seek humanity's ancient origins. "Amphioxus is an animal that we think looks remarkably like what the ancestor of the vertebrates would have looked like [a half billion years ago]," says Peter W.H. Holland, a molecular zoologist at the University of Reading in England.

In Holland's laboratory and others around the world, new studies of amphioxus are starting to reveal critical clues about the biological leap that produced all vertebrates, from lampreys to lizards to lawyers. The emerging evidence suggests that a massive genetic expansion in one fateful group of invertebrates led to the evolution of a backbone, a bigger body, and most important, a much more complex head.

"There's a lot of data from my group and many labs around the world suggesting that many gene families expanded close to the origin of vertebrates. Whatever genes we look at, vertebrates have more of them than do invertebrates," says Holland, who discussed his recent work last fall at a meeting of the Society of Vertebrate Paleontology in Pittsburgh.

"This is the most exciting thing to happen in 80 years," comments biologist R. Glenn Northcutt of the Scripps Institution of Oceanography in La Jolla. "We can now come back to the question of the origin of vertebrates with a very powerful new set of data and ideas about genetic changes and how they relate to development changes to produce vertebrates."

Instead of tallying all genes in amphioxus and other animals, scientists have simplified the problem by comparing the numbers in select families of genes.

Nearly 2 years ago, Jordi Garcia-Fernàndez, Holland, and their coworkers discovered that amphioxus has just one cluster of master blueprint genes called *hox*. Found in all animals, *hox* genes play a critical role during the early stages of embryonic growth, helping to organize the body into a front, middle, and hind region. Whereas amphioxus and other invertebrates have only one group of *hox* genes, almost all vertebrates have four clusters, each on a separate chromosome (SN: 8/20/94, p. 116).

The same story emerges from studies of more than a dozen widely varying gene groups. These include some that, like *hox*, play roles in development and others that perform housekeeping functions in the cell. For example, Linda Z. Holland and Nicholas D. Holland of Scripps have studied genes that code for the myosin light chain, part of the body's muscle machinery. "We've found that amphioxus has only one myosin light chain gene. In vertebrates, there are dozens," says Nicholas Holland.

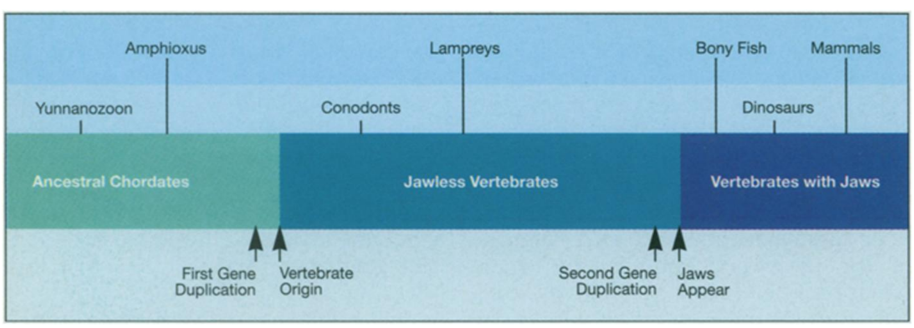
Peter Holland says he anticipated a very different picture before starting this research. "You might expect that as you look at a range of different animals, you would see widely varying numbers of genes. If you looked through the vertebrates, you could expect mammals to have more genes than reptiles and reptiles to have more genes than fish. But that turns out to be wrong.

"What our preliminary data suggest is that all the vertebrates have roughly the same number of genes, and all the invertebrates have roughly the same number of genes. But there was a jump between invertebrates and vertebrates."

From these numbers, a scenario has developed about the evolutionary innovation that led to vertebrates. Drawing on theories about gene duplication first proposed by Susumo Ohno in the 1970s, Peter Holland suggests that a random mutation gave an animal, which probably resembled amphioxus, a double set of chromosomes and hence a second copy of all genes.

Such a mix-up is not implausible, says Holland, because chromosome duplication occurs frequently in nature. Indeed, Down's syndrome and many other human birth defects result from inheriting an extra copy of a particular chromosome.

After the initial gene doubling that occurred more than 500 million years ago, the first set of genes went on performing its original role, while the duplicate set was co-opted to perform new functions, Holland proposes. Those extra genes—particularly the additional developmental genes—allowed the hypothetical vertebrate ancestor to evolve entirely




*From a spineless start: One scenario suggests that vertebrates appeared after an ancestral chordate acquired a duplicate set of genes. A second genetic doubling later gave rise to vertebrates with jaws.*

new body structures.

One of the most important novelties was a fancier head. In 1983, Northcutt and Carl Gans of the University of Michigan at Ann Arbor proposed that the origin of vertebrates is tied to the evolution of "a new head," packed with paired sensory organs, a complex, three-part brain, and other features lacking in invertebrates such as amphioxus.

In support of their theory, Northcutt and Gans noted a critical difference in the development of animals during the earliest stages of life. Vertebrates have three types of embryonic tissue not present in invertebrates: neural crest cells, ectodermic placodes, and a modified paraxial mesoderm. This triad of tissues gives rise to all the novel elements of the vertebrate head. The biologists therefore proposed that the appearance of such tissues far back in Earth's history marked the origin of the new head and thus the vertebrates.

The genetic expansion theory starts to explain how new body elements could have appeared. "We had no idea of the genetic basis for these changes; [now] we are beginning to understand that genetic basis," says Northcutt.

Buoyed by recent developments, biologists are finally making headway against a question that has vexed the field for 2 centuries. "Evolution of the vertebrate body plan is one of *the* great questions," says Nicholas Holland.

At the same time, new fossil evidence is helping to pinpoint the timing of these major steps in evolution. Paleontologists are pushing the vertebrates and amphioxuslike creatures much further back in Earth's history (see sidebar).

If genes doubled once just before vertebrates originated, the number of genes may have increased a second time, making possible a leap from the first simple vertebrates to the complex ones of today. The earliest known vertebrates, which shared characteristics of the modern lamprey, did not have jaws, paired fins on either side of the body, or true vertebrae.

Evidence of this second duplication is less firm, says Peter Holland. Biologists have only just started investigating the genetic makeup of lampreys and hagfish, the jawless animals that serve as proxies for the earliest vertebrates. Holland's preliminary studies of lampreys suggest that they have fewer clusters of *hox* genes than other vertebrates do. This observation supports the idea of a genetic expansion between vertebrates with and without jaws.

Genetic complexity apparently hit a wall after jaws appeared in early fish. Since those days, gene numbers have remained essentially static, though vertebrates have evolved to produce first amphibians, then reptiles, mammals, and birds. Peter Holland says, "I think that tells us there must be limits to the number of genes that an organism can cope with." □

## Vertebrate origins: The fossils speak up

As chroniclers of evolution, humans tend to place their own forebears on a pedestal. Generations of scientists have portrayed vertebrates and their kin as an advanced group that arose only after most of the other broad animal groups had appeared in the riotous days of the Cambrian period.

Now, evidence from the fossil record is knocking human ancestors from their vaunted heights and thrusting them back into the evolutionary melee with the other beasts. Vertebrates and their progenitors, according to the new studies, evolved in the Cambrian, earlier than paleontologists have traditionally assumed.

T. Bockelie, R. Fortey/NATURE

*Vertebrate or arthropod? Scales from* Anatolepis.

Last year, scientists at Leicester University in England demonstrated that enigmatic fossils known as conodonts in fact represent the earliest known vertebrates. Conodonts had puzzled scientists since the 1800s, when paleontologists started finding these isolated, toothlike objects in rocks from the late Cambrian through the Triassic period. The objects appeared to belong to an animal, but the shape of the missing creature remained unclear until 1983, when scientists discovered the toothlike pieces at the front end of an eel-shaped fossil from Scotland.

Paleontologists debated whether this conodont animal was a true vertebrate or an invertebrate chordate similar to amphioxus. After finding distinctive eye muscles not known in invertebrates (SN: 4/29/95, p. 261), however, the Leicester team identified it as a vertebrate. This work pushed the record of vertebrates back into the Cambrian.

Conodonts were not the only Cambrian vertebrates. Researchers from the University of Birmingham in England have identified a second group that reaches back to the time of conodonts, perhaps slightly earlier.

In a tale reminiscent of the conodont story, M. Paul Smith and Ivan J. Sansom are studying another enigma known only from tiny, isolated pieces. Scientists in 1976 identified the fossils, called *Anatolepis*, as the scales of a jawless fish. Subsequent workers have debated whether these plates belong to a fish or an arthropod—the phylum of segmented invertebrates that includes insects and crustaceans.

In histological studies of the microscopic structure of *Anatolepis*, Smith and Sansom determined that the scales contain dentine, a tissue found only in vertebrates. "We feel now that we've got conclusive evidence that *Anatolepis* is in fact a fish," says Sansom. The two published a brief report of their study last year.

Other researchers are less sure of the identification, because the shape of *Anatolepis'* body remains a mystery. The new analysis, says Leicester's Mark Purnell, "is evidence, but it is not conclusive proof that *Anatolepis* is a vertebrate."

Whereas putative vertebrates appear in the late Cambrian, around 520 million years ago, their chordate ancestors apparently reach back to the main burst of the evolutionary event known as the Cambrian explosion. This 10-million-year-long span, starting 530 million years ago, marks the appearance of almost all animal phyla known today.

Until last year, the oldest known chordate fossil was an amphioxuslike creature called *Pikaia*, which hails from Canada's Burgess Shale, a site postdating the Cambrian explosion. In the Oct. 26 NATURE, an international team of paleontologists reported the identification of an even older fossil chordate from an early Cambrian site in Chengjiang, China.

Jun-yuan Chen of the Nanjing Institute of Geology and Paleontology, Lars Ramsköld of the University of Uppsala in Sweden, and their colleagues determined that the animal, *Yunnanozoon*, was a chordate. Its key characteristics include a stiff, spinelike rod called a notochord, structures that supported gills in life, and a row of gonads on both the right and the left sides of the body.

Other Chinese researchers disagree, however. In preliminary studies, Shu Degan of Xian Northwest University places *Yunnanozoon* in another phylum, the hemichordates, which includes the modern acorn worms.

If Chen and his colleagues prevail, *Yunnanozoon* will indicate that the chordates began with all the other phyla during the Cambrian explosion. "If we see *Yunnanozoon* as something that could be our ancestor, because it is very close at least, it was just one simple little animal among all other animals in the Chengjiang fauna," says Ramsköld.

"Maybe we can see our place in nature a little more clearly and understand that we are not so special and so different. We have a humble origin; we had the same origin as all the other animals." —*R. Monastersky*