

When the British naturalist George Shaw received a weird specimen from Australia in 1799 -- one with a mole's fur, a duck's bill and spurs on its rear legs -- he did what any skeptical scientist would do: He looked for the stitching and glue that would reveal it to be a hoax.

"It was impossible not to entertain some distant doubts as to the genuine nature of the animal," Shaw wrote of the seemingly built-by-committee creature, which he eventually named "platypus."

Now, more than 200 years later, a team of scientists has determined the platypus's entire genetic code. And right down to its DNA, it turns out, the platypus continues to strain credulity, bearing genetic modules that are in turn mammalian, reptilian and avian.

There are genes for egg laying -- evidence of the animals' reptilian roots. Genes for making milk, which the platypus does in mammalian style despite not having nipples. Genes for making snake venom, which the animal stores in its legs. And there are five times more sex-determining chromosomes than scientists know what to do with.

"It's such a wacky organism," said Richard Wilson, director of the genome center at Washington University in St. Louis, who led the two-year international effort, described online Wednesday in the journal *Nature*.

Yet in its wackiness, Wilson said, the platypus genome offers an unprecedented glimpse of how evolution made its first stabs at producing mammals. It tells the tale of how early mammals learned to nurse their young; how they matched poisonous snakes at their own venomous game; and how they struggled to build a system of fertilization and gestation that would eventually, through relatives that took a different tack, give rise to the first humans.

"As we learn more about things like platypuses," Wilson said, "we also learn more about ourselves and where we came from and how we work."

Platypuses (preferred over "platypi" in U.S. dictionaries) live on a relative sliver of Earth along Australia's east coast, Tasmania and Papua New Guinea. But *Ornithorhynchus anatinus* has a global fan base, it seems, having been chosen as the mascot of countless companies, products and events.

The animal's complete genetic code, or genome, turns out to have 2.2 billion molecular "letters" of DNA, or about two-thirds as many as the human genome, and contains 18,500 genes, about the same as humans.

Finding the order of all those letters was grueling, scientists said, because no similar animal has ever been sequenced. The platypus inhabits an isolated branch on the evolutionary tree with just one other close cousin, the echidna, also of Australia.

That left researchers with no model to help them figure out how the platypus's DNA should fit together.

"It was quite a difficult thing," said Jennifer Marshall Graves of Australian National University in Canberra, who led part of the analysis after the St. Louis team derived the basic sequence. "The genome was completely unknown, and we knew it was going to be fairly weird," Graves said. "You'd look at some of these repetitive sequences and think, 'What on Earth is that?' "

One of the more surprising elements was the animal's system for sex determination. Most mammals have two sex chromosomes, either two X chromosomes (to make a female) or an X and a Y (to make a male). Not only do platypuses have 10 instead of two, but some of those resemble the Z and W chromosomes of birds more than standard-issue X's and Y's.

Moreover, the key gene on the Y chromosome that confers maleness in most mammals is not present on any of the platypus's sex chromosomes. It is on another chromosome, where it seems to have nothing to do with sex. In its place, another gene seems to be central to sex determination in platypuses -- evidence of a shakeout of various evolutionary efforts to settle on a system of sex determination in early mammals.

Other genes show how platypuses were transitional creatures on the road from egg laying to internal gestation. There is just one gene for one kind of yolk protein, for example, while chickens have three. That is consistent with the idea that the platypus represents a shift in strategy toward providing more nutrition after hatching, rather than during incubation, and lends credence to the poet Ogden Nash's famous appreciation of the platypus's approach to child-rearing: "I like the way it raises its family/Partly birdly, partly mammaly."

Platypus milk appears to be a modified version of a moisturizing fluid that ancestral platypuses once used to keep their leathery, lizard-like eggs from drying out during incubation. It is secreted from "milk patches" on the mother's abdomen.

As with kangaroos, platypus milk becomes more nutritionally complex over a period of months while the young suckle and grow, the result of at least five different genes turning on in sequence.

"The dairy industry is actually very interested in this and want to get their hands on the controlling gene elements that turn these milk genes on and off," Graves said. (End Optional Trim)!

Another surprise was that platypuses have a huge array of genes that help them detect chemical signals released underwater by other animals. That makes sense, scientists said, because platypuses close their eyes and nostrils while diving for the small aquatic crustaceans that make up the bulk of their diet.

These "vomeronasal organ" genes give the platypus perhaps the most sensitive

known system for detecting pheromones -- hormone-like signals -- allowing it to pick up the scents of potential mates or prey underwater.

One final surprise came from an examination of the genes involved in the production of venom, which the platypus can deliver from a sharp spur on each of its rear legs.

The platypus is the only mammal to make venom, and the chemicals in it are almost identical to those in some snake venoms. Yet the new analysis shows plainly that the two classes of animals came up with the innovation independently and by different evolutionary routes, though both built their poisons from the same starter molecule, an immune system chemical.

Disappointingly, scientists said, they have been unable to find any genes involved in the platypus's elaborate system for detecting electrical fields, which it does through its bill, perhaps to help navigate through narrow waterways. But that is just one of many avenues, they said, that promise to keep them busy with duck-billed DNA.

"We're going to be using the platypus genome for the next 50 years," said Ewan Birney of the European Bioinformatics Institute in Cambridge, England, which was involved in the analysis.

"The platypus gives us a perspective that is deep in time, that tells us what was going on 170 million years ago, when all these traits were being developed," Birney said. "Every time there's a difference in the DNA between human and dog, or human and some other mammal, and you want to know which one changed more recently, you need these outgroup species to be able to answer that."

