Highlight—Making It Big: Salamanders Keep DNA Near and Dear

Danielle Venton

Corresponding author: E-mail: danielle.venton@gmail.com.
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In ancient lore, salamanders were magical creatures capable of leaping spontaneously from flame. Rather than being harmed by fire, they fed on it. In one of his less scientific moments, Da Vinci wrote the salamander "gets no food but from the fire, in which it constantly renews its scaly skin."

Although these powers are, unfortunately, not true, it is consoling to know salamanders are near-magical for other reasons. Among naturalists and school kids, these often spectacularly colored amphibians are famous for an ability to regenerate severed limbs. However, it was the incredible, out-sized genomes of these creatures that attracted molecular evolutionist Rachel Lockridge Mueller. Salamanders split from a common ancestor with frogs approximately 250 million years ago, yet their genomes are, on average, nine times larger. Compared with other animals such as birds, fish, and mammals, salamander genomes are 15–40 times larger.

"This is a strange phenomenon," says Mueller of Colorado State University. "We're interested because it's rare for genomes to get so big."

In a recently published study in *Genome Biology Evolution*, Mueller and coworkers examined the salamander's genomic peculiarities and found that they are uncommonly skilled at hanging on to DNA.

All genomes fluctuate in size—waxing with insertion mutations and waning with deletions. However, for salamanders, deletions are comparatively uncommon and, when they do happen, fewer than average base pairs are jettisoned, compared with other vertebrates. Salamanders are the genetic equivalent of hoarders by way of analogy, Mueller says. They might not "shop" (or accumulate DNA) more than other species, but they clean out their closets less often and, when they do, they take smaller bags to the thrift store.

In this study, the team from Colorado examined insertion, deletion, and substitution patterns in the transposable elements of four salamander species. For comparison, they estimated the loss rates in transposable elements from five other genomes: primates (humans), lizards, fish, birds, and another amphibian group (frogs). Sometimes called "selfish DNA" or "jumping genes," transposable elements are DNA sequences that seem to have lives of their own, set apart from the rest of the genome. They make copies of themselves, spread throughout the genome, but do not seem to do much for the organism. So far as we can tell, they do not code for proteins nor (for the segments used in this study) do proteins bind to them. They mutate and evolve neutrally, seemingly without selection pressure. Because transposable elements are used in many biotechnical and biomedical applications, Mueller is hopeful that a deeper understanding of these helps researchers tinker with them.

Current research into the causes of deletion mutations indicates that they are due to errors in DNA replication and recombination—when chromosomes swap sections during meiosis. "It's the core machinery that deals with keeping DNA intact from one generation to the next," Mueller says. "When there are problems with that core machinery, that's when you get deletion events."

Although the mechanism behind salamander's high-DNA fidelity is not known, Mueller suspects recombination in salamanders may work slightly differently than in other animals. "This little clue," she says, "points to differences in the core DNA machinery...it's fascinating to think about variation in something so central [to all life]."

These findings provide a harmonizing chord to recent work by Kiwoong Nam and Hans Ellegren (2012) demonstrating that recombination slims down genomes. Birds, for example, have relatively small genomes, and they tend to loose a lot of material through recombination events, further reinforcing their small genome size. Across the animal kingdom, in fact, there seems to be a link between DNA loss rates and genome size (similar patterns have been found in insects as well).

When first proposed by Harvard population geneticist Dan Hartl and his colleagues in the 1990s, this idea was controversial. "So there it sat. Now people are returning to it," Hartl says. Beyond seeing a validation of his and other's ideas, Hartl finds Mueller's work an interesting counterpoint to some of the current thinking in genomics, the ENCODE project in particular. ENCODE was launched in 2003 by the National...
Human Genome Research Institute to find all functional elements in the human genome. In September 2012, the project published results assigning “biochemical functions for 80% of the [human] genome”—an eye-popping figure.

The underlying assumption of ENCODE is that if a protein binds to a DNA section then it is important. “That’s not necessarily true,” Hartl says. “It could be functional, but this suggests much of the DNA is carried along passively. Is someone going to tell me that salamanders really need all of this material just to be salamanders?”

Likely not, and their mammoth-sized genomes cause traits that would be an expected inconvenience. Animals with enormous genomes need to have larger cells, for example, to house their abundant DNA. This increases the time needed for development and decreases how complex the brain can become for a given size. “You’d expect big genomes to be selected against for lots of reasons,” Jockush says. “Yet evolution hasn’t eliminated the big genome—it’s rather counter intuitive.”

The roles of noncoding DNA, and the degree to which genome size is hinderance or help, are still wide open questions and likely will be for sometime. For now, it is enough that the salamander’s remarkable behind-the-scenes genetics add to their mythical fascinating powers.

**Literature Cited**

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