

Jumping genes shed light on how advanced life may have emerged

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A previously unappreciated interaction in the genome turns out to have possibly been one of the driving forces in the emergence of advanced life, billions of years ago.

This discovery began with a curiosity for [retrotransposons](#), known as "jumping genes," which are DNA sequences that copy and paste

themselves within the [genome](#), multiplying rapidly. Nearly half of the human genome is made up of retrotransposons, but bacteria hardly have them at all.

Nigel Goldenfeld, Swanlund Endowed Chair of Physics at the University of Illinois and Carl R. Woese Institute for Genomic Biology, and Thomas Kuhlman, a former physics professor at Illinois who is now at University of California, Riverside, wondered why this is.

"We thought a really simple thing to try was to just take one (retrotransposon) out of my genome and put it into the bacteria just to see what would happen," Kuhlman said. "And it turned out to be really quite interesting."

Their results, published in the *Proceedings of the National Academy of Sciences*, give more depth to the history of how advanced life may have emerged billions of years ago—and could also help determine the possibility and nature of life on other planets.

Along the way to explaining life, the researchers first encountered death—bacterial death, that is. When they put retrotransposons in bacteria, the outcome was fatal.

"As they jump around and make copies of themselves, they jump into genes that the bacteria need to survive," Kuhlman said. "It's incredibly lethal to them."

When retrotransposons copy themselves within the genome, they first find a spot in the DNA and cut it open. To survive, the organism then has to repair this cut. Some bacteria, like *E. coli*, only have one way to perform this repair, which usually ends up removing the new retrotransposon. But advanced [organisms](#) (eukaryotes) have an additional "trick" called nonhomologous end-joining, or NHEJ, that gives them

another way to repair cuts in their DNA.

Goldenfeld and Kuhlman decided to see what would happen if they gave bacteria the ability to do NHEJ, thinking that it would help them tolerate the damage to their DNA. But it just made the retrotransposons better at multiplying, causing even more damage than before.

"It just completely killed everything," Kuhlman said. "At the time, I thought I was just doing something wrong."

They realized that the interaction between NHEJ and retrotransposons may be more important than they previously thought.

Eukaryotes typically have many retrotransposons in their genome, along with a lot of other "junk" DNA, which doesn't have a well-understood function. Within the genome, there must be a constant interplay between NHEJ and retrotransposons, as NHEJ tries to control how rapidly the retrotransposons multiply. This gives the organism more power over their genome, and the presence of "junk" DNA is important.

"As you get more and more junk in your DNA, you can start taking these pieces and combining them together in different ways, more ways than you could without all the junk in there," Kuhlman said.

These conditions—the accumulation of "junk" DNA, the presence of retrotransposons and their interactions with NHEJ—make the genome more complex. This is one feature that may distinguish advanced organisms, like humans, from simpler ones, like bacteria.

Advanced organisms can also manage their genome by using their spliceosome, a molecular machine that sorts through the "junk" DNA and reconstructs the genes back to normal.

Some parts of the spliceosome are similar to group II introns, bacteria's primitive version of retrotransposons. Introns are also found in eukaryotes, and along with the spliceosome are evolutionarily derived from group II introns. Goldenfeld said this poses an evolutionary question.

"What came first, the spliceosome or the group II introns? Clearly the group II introns," he said. "So then you can ask: where did the eukaryotic cell first get those group II introns in order to build up the spliceosome early on?"

This study suggests that group II introns, the ancestors of introns in the spliceosome and retrotransposons in eukaryotes, somehow invaded early eukaryotic cells. Then, their interactions with NHEJ created a "selection pressure" that helped lead to the emergence of the spliceosome, which helped life become advanced billions of years ago.

The spliceosome helped life become advanced by enabling eukaryotes to do more with their DNA. For example, even though humans have roughly the same number of genes as *C. elegans*, a worm, humans can do more with those genes.

"There's not much difference between this very simple worm and humans, which is obviously insane," Goldenfeld said. "What's happening is that humans are able to take these genes and mix and match them in many combinations to do much more complicated functions than *C. elegans* does."

Not only did NHEJ and retrotransposons help with the creation of the spliceosome; this study suggests that they may also have assisted in making chromosomes—DNA molecules that contain genetic material—more advanced. Interactions between NHEJ and retrotransposons may have aided in the transition from circular

chromosomes (which [bacteria](#) generally have) to linear ones (which more advanced organisms have), another indicator of advanced life.

Goldenfeld said that before this research, many researchers studied the role of retrotransposons, but the importance of NHEJ was not fully appreciated. This research proves that it played a part, billions of years ago, in eukaryotes becoming the advanced organisms we know today.

"This certainly was not the only thing that was going on," Goldenfeld said. "But if it hadn't happened, it's hard to see how you could have complex life."

This study contributes to the larger questions that the Institute for Universal Biology, a NASA Astrobiology Institute that Goldenfeld directs, seeks to answer—questions like: what had to happen in order for life to become advanced?

Answering this question in greater detail could help scientists determine the possibility of life on other planets.

"If life exists on other planets, presumably one would expect it to be microbial. Could it ever have made this transition to complex life?" Goldenfeld said. "It's not that you're inevitably going to get advanced [life](#), because there are a bunch of things that have to happen."

The physics perspective of this study helps to quantify these theoretical questions. This quantification comes from simply taking measurements in a laboratory and using those measurements to make models of evolution, as was done in this study.

In doing so, basic measurements in a laboratory become a time machine to the past.

"We're doing laboratory evolution," Goldenfeld said. "We're looking at what evolutionary processes must have happened billions of years ago."

More information: Gloria Lee et al., "Testing the retroelement invasion hypothesis for the emergence of the ancestral eukaryotic cell," *PNAS* (2018). www.pnas.org/cgi/doi/10.1073/pnas.1807709115

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