Neutral evolution has helped shape our genome

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Johns Hopkins researchers have added to the growing mound of evidence that many of the genetic bits and pieces that drive evolutionary changes do not confer any advantages or disadvantages to humans or other animals.

“For a long time, the basic belief of evolution was that all random genetic changes that manage to stick around have some selective advantage,” says Nicholas Katsanis, Ph.D., Associate Professor at Hopkins’ Institute of Genetic Medicine. “But our work adds to the case that frequently, we are what we are largely due to random changes that are completely neutral.”

“I am not at all discounting the role of natural selection, the persistence of genetic changes that confer some advantage,” Katsanis adds, “because it has been instrumental. What this study does is to reinforce and highlight the equal, and in some cases greater, importance of neutral genetic drift.”

Describing their contributions to genetic drift online in *PLoS Genetics*, Katsanis says the Hopkins experiments demonstrate that one of the major architectural markers of the human genome, DNA repeat elements that make up over 40 percent of our genome, rose to prominence without offering any benefits to the organism it inhabits. Repeat elements are fragments of DNA containing the same repetitive sequence of chemical base pairs several hundred times.

Katsanis and his team first stumbled onto one type of repeat element while looking at genes associated with Bardet Biedl syndrome, a rare disorder of substantial interest to the lab. While hunting for new genes, they found portions of DNA that had been copied from the mitochondria, the energy-making apparatus of human cells that has its own small genome. These mitochondrial sequences are known as numts.

When they expanded their study across the whole human genome, they found more than 1200 such pieces of mitochondrial DNA of various lengths embedded into chromosomes. While chimps have a comparable number, mice and rats only have around 600 numts. Since they increase in frequency as species advance, it suggested there was some evolutionary purpose to keeping them around.

Strikingly, however, none of these numts contained the blueprint (an actual gene) to make a protein that does anything, nor did they seem to control the function of any nearby genes. “At best, it seems numts are a neutral part of our genome,” says Katsanis. “If anything, they may be mildly negative since long repeat sequences can be unstable or get inserted inside genes and disrupt them.”

The researchers believe they have uncovered a possible reason why these potentially damaging but mostly neutral bits of DNA accumulate over time by comparing the sequences of human numts with those in different animals. How closely the different species’ sequences match can provide an estimate of when that particular sequence got inserted into the ancestor of the human genome.

Their calculations revealed that most numts became embedded in our genome over a 10-million-year period centered roughly 54 million years ago – right around the time when the first primates emerged. “When new species emerge, their numbers and therefore their genetic differences are very small,” Katsanis notes. “This creates a genetic bottleneck during

which any changes in the genome will either get eliminated quickly or spread to the whole population quickly."

Katsanis proposes that numts, being "neutral," were generally at low levels in ancient mammals, but during the primate emergence 54 million years ago, they accumulated and spread through the small early primate populations precisely because they were not detrimental enough to be eliminated. Then, as these populations expanded, numts reached stable but higher frequencies.

Source: Johns Hopkins Medical Institutions