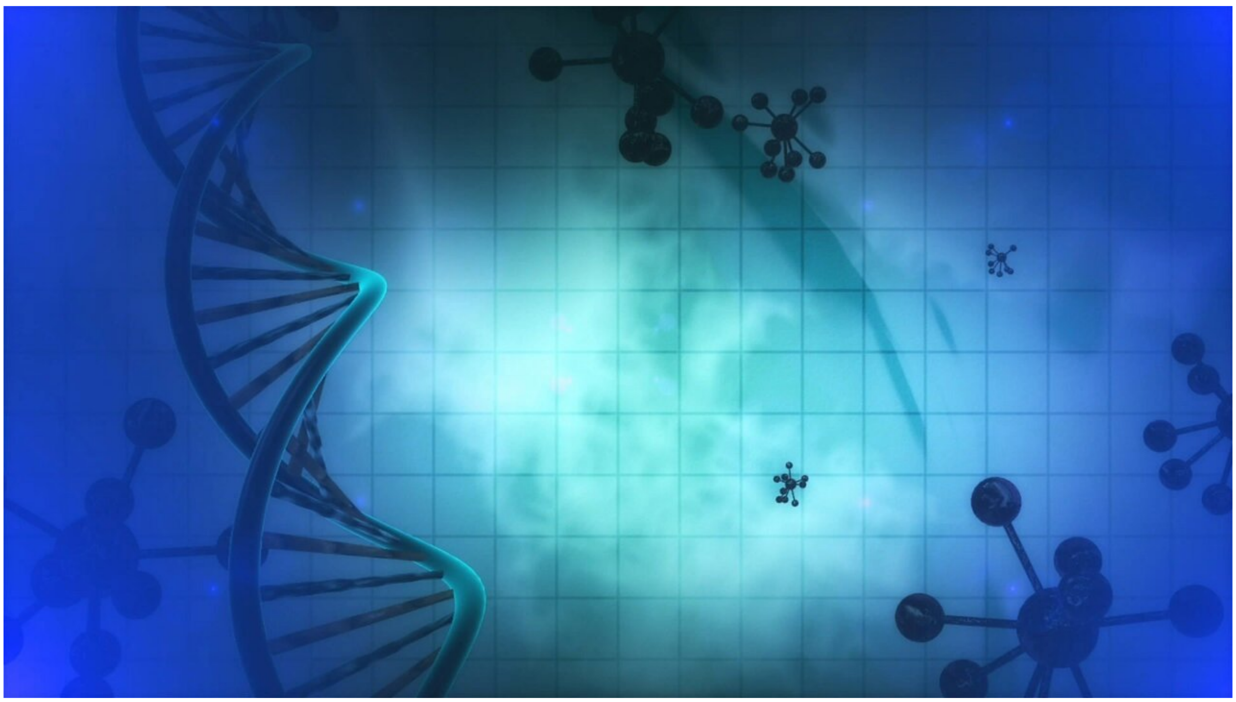
De novo genes far more common and important than scientists thought

February 17 2020, by Thomas Deane



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Scientists from Trinity and the University of Pittsburgh have discovered that de novo genes—genes that have evolved from scratch—are both more common and more important than previously believed.

Their findings appear in two studies, one forthcoming in *eLife* and one that was published earlier this month in *Nature Communications*.

DNA, genes, and de novo orphans

Over time, genes change via random mutations. Some of these changes result in serious defects and are rarely passed on to the next generations, others have little impact, and others confer significant advantages, which become favoured due to natural selection and end up being passed on to future generations.

This is the main source of genetic novelty and how organisms differ from each other. However, genetic novelty can also be generated by totally new genes evolving from scratch.

In the eLIFE study, the scientists devised a way of assessing just how frequently genes seem to evolve from scratch. Their results were surprising.

Explaining de novo genes, first author on the paper, Nikolaos Vakirlis, Trinity, said:

"Most of the genes in a genome have 'cousins' in the genomes of other species; genes made up of similar DNA sequences that, once translated into proteins, perform similar functions. However, some genes are unique and can only be found in a single, or small number of closely related species. We call these 'orphan genes' because they appear to have no relatives and are often responsible for unique characteristics and abilities of organisms. For example, a gene that is unique to cod fish living in the arctic allows them to survive in sub-zero temperatures."

Orphan genes pose a tough evolutionary problem though. They don't look like other genes, so where do they come from? One idea is that they can originate seemingly from nothing: over long, evolutionary timescales, a completely novel gene can emerge de novo out of a region in the genome that is made up of junk DNA. Alternatively, with enough time, two 'cousin' genes can diverge so much that we can no longer identify the relationship between them. Thus, a gene may at a glance appear to be an orphan without having really emerged de novo.

A new approach to assessing de novo gene frequency

For a long time, scientists thought the majority of orphan genes were simply cases of 'missing relatives', which could be explained by the divergence of the sequences through mutations during evolution. The new research suggests this is not the case.

Aoife McLysaght, professor in genetics at Trinity College Dublin, said:

"To our surprise, at most, around one third of orphan genes result from divergence. So, in turn, this suggests that most unique genes in the species we looked at are the result of other processes, including de novo emergence, which is therefore much more frequent than scientists initially thought."

Are de novo emerging genes important?

In the second piece of research, published recently in leading journal *Nature Communications*, the scientists sought an answer to the obvious question: Are de novo emerging genes important?

This may seem a paradoxical question because something that has not yet emerged fully in the world of evolution wouldn't be expected to be overly important. After all, how can a gene that was never used before suddenly appear and play a major role?

This paradox can be resolved if emerging genes have high potential to be beneficial for the organism. So, while they are expected to play no particular role in their current form, random changes that affect their sequences or increase the amount of protein they produce when translated should lead to beneficial effects.

The scientists tested whether this hypothesis may be true by doing a series of biological and computational experiments using baker's yeast as a model organism. And when they artificially allowed emerging sequences to be expressed at higher levels than they are naturally, the cells tended to grow faster.

Importantly, growth was not enhanced by overexpressing established genes. So, emerging sequences do indeed carry the potential to be important to the cells.

Anne-Ruxandra Carvunis, Ph.D., assistant professor of computational systems biology at the University of Pittsburgh, said:

"Order seems like something that's hard to achieve, but our results go completely opposite to that. We found that simple order is rampant everywhere in the genome. The propensity to make simple shapes that are stable is already there, waiting to be exposed. De novo gene birth is thus becoming less and less mysterious as we better understand molecular innovation."

More information: Nikolaos Vakirlis et al. De novo emergence of adaptive membrane proteins from thymine-rich genomic sequences, *Nature Communications* (2020). DOI: 10.1038/s41467-020-14500-z

Provided by Trinity College Dublin

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