Losing genes and surviving—when less is more in the evolution of life

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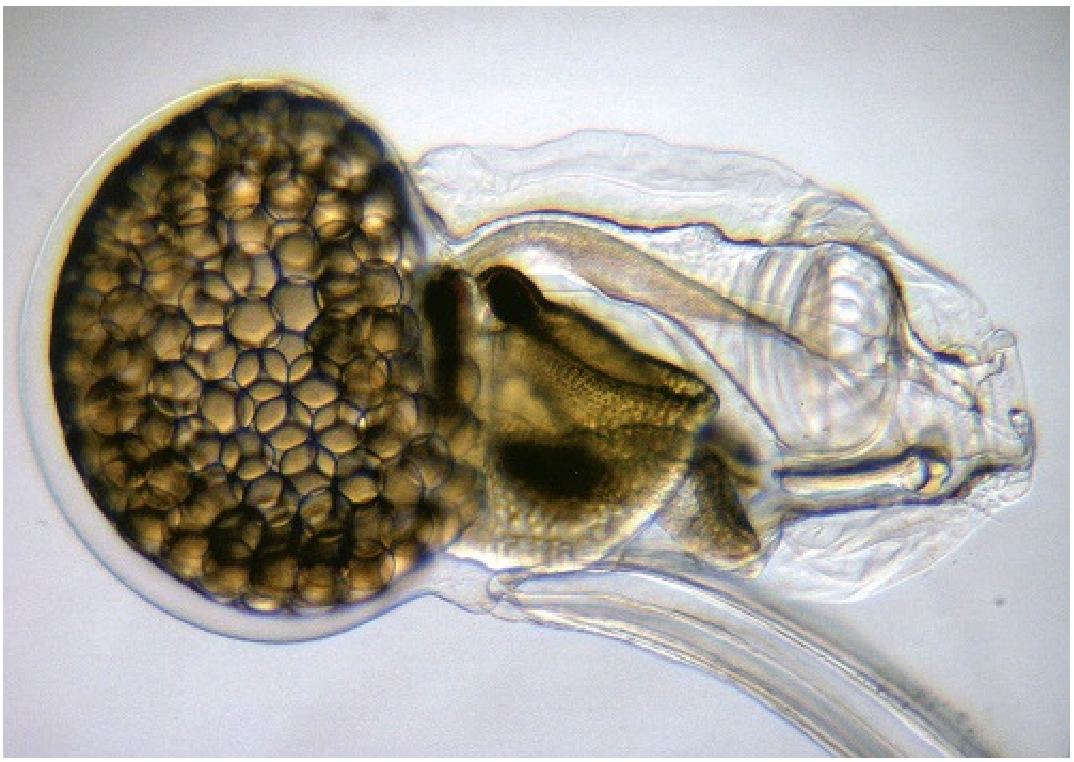

The chordate O. dioica, despite losing lots of genes, maintains a typical body plan with organs and structures (heart, brain, thyroids, etc.) which can be considered to be homologues to the vertebrates. Credit: University of Barcelona

"Loss is nothing else but change and change is nature's delight" says the quote by the philosopher and emperor Marcus Aurelius, which opens a scientific article that analyses the gene loss phenomenon and its impact on the evolution of living beings.

The study was published in *Nature Reviews Genetics* and signed by professors Ricard Albalat and Cristian Cañestro, from the Department of Genetics, Microbiology and Statistics and the Biodiversity Research Institute (IRBio) of the University of Barcelona.

Thinking of gene loss as an evolutionary force is a counterintuitive idea, for it is easier to think that only when we gain something—genes in this case—can we evolve. However, the new work by these authors, who are members of the Research Group on Evolution and Development (EVO-DEVO) of the UB, characterizes gene loss as a great potential process of genetic change and evolutionary adaption.

Losing genes is also an evolution engine

A gene is lost when the genome is physically removed (by illegitimate recombination, transposition, etc.) or when it is still in the genome but with unused due to a mutation (particular changes, insertions, deficiencies, etc.). "The genome sequencing of very different organisms has shown that gene loss has been a usual phenomenon during evolution in all life cycles. In some cases, it has been proven that this loss might mean an adaptive response towards stressful situations when facing sudden environmental changes," says Professor Cristian Cañestro.

"In other cases, there are genetic losses," says Cañestro, "which, even though they are neutral per se, have contributed to the genetic and reproductive isolation among lineages, and thus, to speciation, or have rather participated in the sexual differentiation in contributing to the creation of a new Y chromosome. The fact that genetic loss patterns are not stochastic but rather biased in the lost genes (depending on the kind of function of the gen or its situation in the genome in different organism groups) stresses the importance of the genetic loss in the evolution of the species."

Losing to win: an evolutionary paradox

Traditionally, it was believed that insects tended to lose genes. However, the genome sequencing of a beetle (Tribolium castaneum), which has few gene losses, challenges that view. In the chordate phylum, which includes vertebrates, there are also some differences among the species, with particular cases such as the planktonic organism Oikopleura dioica, that are very prone to gene loss.

According to Professor Ricard Albalat, "it has been shown that the possibility of losing genes is linked to the lifestyle of the species. Parasites, for instance, show a greater tendency of gene loss. Because they reuse their host's resources, lots of their genes become dispensable and end up disappearing. Species with lots of redundant genes such as the vertebrates and lots of plant species and yeasts that have doubled their genomes, have also suffered from gene loss over the course of evolution.

"Interestingly, the massive gene losses are not always linked to radical morphological changes in the affected organism's body plan. The chordate Oikopleura dioica, for example, despite losing lots of genes. Some are essential to the embryo development and design of the phylum body plan, maintaining a typical body plan with organs and structures that can be considered to be homologues to the vertebrates'. However, this contradiction, which we have defined as 'inverse paradox' of EvoDevo, is still very difficult to explain".

Lost genes in the human evolutionary history

Gene loss can be positive. This has been proven through laboratory experiments (in yeast or bacteria) and population studies on humans. Some of the best studied cases on humans are coding gene losses with cell receptors (CCR5 and DUFFY), which make individuals more resistant to HIV infection and to plasmodium caused by malaria. In nature, there are gene losses from which some organisms benefited: losses that caused colour changes in flowers which attract new pollinators, losses which made warmness-resistant insects to be able to colonize new habitats, etc.

Some studies also suggest that gene loss has been decisive in the origins of the human species. Chimpanzees and humans share more than the 98% of their genomes, and in this context it is tempting to speculate that perhaps it would be necessary to look for the differences not in the shared genes but in the missing ones, which have been lost across human and primate evolution. "For example, it is believed that gene loss reduced the jaw muscular structure, which allowed the human brain to grow its size, or that gene losses were important in the improvement of our defence system against illnesses," says Cristian Cañestro.

How many gens can a living being lose?

A gene can be lost only if it is dispensable and, therefore, its loss doesn't involve a disadvantage for the individuals. What makes a gene to be dispensable? A gene becomes dispensable when the organism can do its function in an alternative way (functional redundancy) or when the gene is no longer needed because the organism lost its structure or the physiologic requirement in which the gene participated (regressive evolution). For this reason, some changes in the species' lifestyle can make some genes dispensable, as seen in the gene loss related to pigmentation and vision of the species who adapted to cave living.

Discovering how many genes an organism can lose and how is essential to understanding how many human genes are dispensable and why certain mutations are irrelevant while others are vital for our health. Actually, the recent genome sequencing in individuals from several communities around the world has shown that any healthy person has an average amount of 20 non-functioning genes and it does not seem to provoke any unfavourable consequence.

When genes are dispensable: less is more

According to Ricard Albalat, "Probably, the presences of redundant genes or environmental conditions in which we live make us to have fewer unnecessary genes. Research on the differences of gene losses among different human communities has allowed, for instance, discovering that lipoprotein A gene loss grants resistance to coronary illnesses among the Finnish population who have fat-rich diets. This experimental approach relating genes to diseases is called 'genotype first,' and opens the door to the discovery of genes absences that give an advantage towards some environmental tensions (diets, climate, toxics, pathogens, etc.) and therefore it could help identifying new genes with therapeutic interests".

Oikopleura dioica: a new model organism in UB's research

Nowaday,s the Evo-Devo-Genomics team of the UB is one of the few research groups around the world that studies the Oikopleura dioica from an evolutionary developmental biology perspective (Evo-Devo).

The Oikopleura dioica is a small animal with a short life cycle, very prolific and easy to keep in the laboratory. These conditions make it an excellent model animal. Its genome, sequenced, is extraordinarily compact—three times smaller than the Drosophila fly—and has lost a lot of genes. Currently, the UB experts use O. dioica as evolutionary mutant that has lots important genes for embryo development. The research group works in two research lines. On the one hand, they use O. dioica to research on the toxic compound effect in marine animal development and reproduction, as well as its impact on the ocean trophic chains. On the other hand, they use O. dioica to study how genetic losses have affected cardio development mechanisms.

"We hope these studies enable us to identify the essential 'minimum gene set' to produce a heart, and would help us to better understand the genetic basics of certain cardiomyopathies and discover new genes to improve the diagnosis," say Ricard Albalat and Cristian Cañestro.

More information: Linda Koch. Complex disease: A global view of regulatory networks, *Nature Reviews Genetics* (2016). DOI: 10.1038/nrg.2016.36

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