# Genetic based human diseases are an ancient evolutionary legacy

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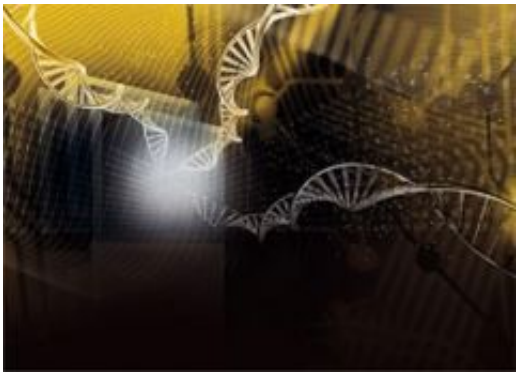

Artistic illustration of a phylostratigraphy. Image: Irena Andreic, Ruđer Bošković Institute, Zagreb

Tomislav Domazet-Lošo and Diethard Tautz from the Max Planck Institute for Evolutionary Biology in Plön, Germany, have systematically analysed the time of emergence for a large number of genes - genes which can also initiate diseases. Their studies show for the first time that the majority of these genes were already in existence at the origin of the first cells. The search for further genes, particularly those which are involved in diseases caused by several genetic causes, is thus facilitated. Furthermore, the research results confirm that the basic interconnections are to be found in the function of genes - causing the onset of diseases - can also be found in model organisms (*Molecular Biology and Evolution*).

The Human Genome Project that deciphered the human genetic code,

uncovered thousands of genes that, if mutated, are involved in human genetic diseases. The genomes of many other organisms were deciphered in parallel. This now allows the evolution of these disease associated genes to be systematically studied.

Tomislav Domazet-Lošo and Diethard Tautz from the Max Planck Institute for Evolutionary Biology in Plön (Germany) have used for this analysis a novel statistical method, "phylostratigraphy" that was developed by Tomislav Domazet-Lošo at the Ruđer Bošković Institute in Zagreb (Croatia). The method allows the point of origin for any existing gene to be determined by tracing the last common ancestor in which this gene existed. Based on this information, it is then possible to determine the minimum age for any given gene.

Applying this method to disease genes, the scientists from Plön came to surprising findings. The vast majority of these genes trace back to the origin of the first cell. Other large groups emerged more than one billion years ago around the first appearance of multi-cellular organisms, as well as at the time of origin of bony fishes about 400 million years ago. Surprisingly, they found almost no disease associated genes among those that emerged after the origin of mammals.

These findings suggest that genetic diseases affected primarily ancient cellular processes, which emerged already during the early stages of life on Earth. This leads to the conclusion that all living organisms today, i.e. not only humans, will be affected by similar genetic diseases. Furthermore, this implies that genetically caused diseases will never be beaten completely, because they are linked to ancient evolutionary processes.

Although it was already known that many disease associated genes occur also in other organisms distant to humans, such as the fruitfly Drosophila or the round worm Caenorhabditis, the analysis of Domazet-Lošo and

Tautz shows now for the first time that this is systematically true for the vast majority of these genes. At present it remains unknown why the more recently evolved genes, for example those involved in the emergence of the mammals, do not tend to cause diseases when mutated.

The research results of the scientists from Plön also have some practical consequences. It will now be easier to identify candidates for further disease genes, in particular for those involved in multi-factorial diseases. Furthermore, the results confirm that the functional knowledge gained about such genes from remote model organisms is also relevant for understanding the genes in humans.

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