

Although our genetics differ significantly, we all look alike

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The genetic variation within a species can be significant, but very little of that variation results in clear differences in morphology or other phenotypes. Much of the diversity remains hidden 'under the surface' in buffered form. This has been revealed by research conducted by the University of Groningen, Wageningen University and Research Centre (both Netherlands) and the British research centre Rothamsted Research. The research was published on 25 January 2009 in *Nature Genetics*.

The researchers crossed two ecotypes of *Arabidopsis* and investigated the offspring for molecular and phenotypic differences, for example the number of proteins and metabolites that are formed and susceptibility to disease. It turned out that of the hundreds of thousands of differences in the DNA, only six 'hotspots' had major molecular and phenotypic effects.

The DNA of the two crossed ecotypes of *Arabidopsis thaliana*, a small plant that serves as a model organism in genetic research, differs on no fewer than 500,000 points, i.e. there is significant genetic variation. Of the offspring of the crossbreeding, 162 plants were investigated on 139 external characteristics (classic phenotypic traits such as the height of the plant, flowering time or resistance to disease) and 40,000 molecular traits. The latter category covers the products of the genes, i.e. the transcripts and proteins formed in the plant cell and the healthy or toxic compounds (metabolites) that these proteins generate in their turn. Many of these traits show substantial phenotypic variation.

Research leader Prof. Ritsert Jansen: ‘You’d expect the mutations - the genetic causes of these phenotypic differences - to be evenly divided over the DNA, that they would be spread out over the whole genome, in a manner of speaking. This was clearly not the case in this experiment. We could point out exactly six areas in the genome where the genetic causes of thousands of differences were located. In other words, the genetic causes turned out to be clustered into six hotspots. The other 500,000 mutations in the genome only had a relatively very minor influence.’

As described in the publication, this is a type of buffering - the 500,000 genetic differences do influence the activity of thousands of genes, but that diversity gradually diminishes the further you move away from the genetic source, the DNA; it is buffered. Eventually, only a small number of hotspots remain and these cause phenotypic differences at the highest levels, in metabolites and classic phenotypic traits. ‘The genetic variation is significantly present deep in the cell but is muffled more and more the further you move towards the outside’, Jansen explains.

Although buffering has a muffling effect on the evolution of a species, it certainly does not hinder it. Jansen: ‘I’d say that it’s lucky there’s buffering. Just imagine if each of the 500,000 differences was immediately expressed in the next generation. From the point of view of the “robustness” of a species, it’s necessary that the offspring do not vary too dramatically. But if there’s a change in the environment that requires an evolutionary adaptation, then the necessary genetic variation is ready and waiting.’

The discovery means that life scientists should in particular examine the hotspots in the genome when searching for the causes of genetic disorders. In that regard the results of the current research agree with the results of Prof. Cisca Wijmenga of the University Medical Center Groningen, which was published in Nature Reviews Genetics in

December. Her research revealed that only a limited number of hotspot genes are involved in the development of numerous immune-related diseases, such as type 1 diabetes, coeliac disease, Crohn's disease and rheumatoid arthritis. Just like Arabidopsis, people differ from each other in millions of positions in their genome, but it's the genotype in the hotspots that is the most relevant. 'When it comes down to it, we are more similar to each other than the major differences in genome sequences suggest.'

Source: University of Groningen

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