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HUMAN GENETICS

Pleiotropic mutations

A large-scale analysis of SNPs and genes that are reported to be associated with common complex diseases and traits has found abundant pleiotropy: that is, each individual gene mutation may have a role in multiple diseases.

The authors analysed data from the publicly available US National Human Genome Research Institute's catalogue of published genome-wide association studies (GWASs), in which all statistically significant SNP–trait associations are deposited. They developed a novel statistical framework in which to search for pleiotropic effects among variants and genes that are associated with complex non-Mendelian phenotypes.

Pleiotropic effects were found for 16.9% of the 1,380 genes and for 4.6% of the 1,687 SNPs analysed, indicating a wide role for pleiotropy in common disease. Sivakumaran *et al.* also showed that pleiotropic genes are significantly longer than non-pleiotropic genes and that pleiotropic mutations are mainly located in exons, as well as being predicted to influence protein structure. Immune-mediated disease and metabolic syndromes are the diseases that have the highest proportions of pleiotropic genes.

Notably, the authors believe that their estimate of pleiotropy in common disease is probably an underestimate and hence that this is probably a widespread phenomenon. Furthermore, this demonstration of pleiotropy in common disease has implications for genetic testing; it may be found that a mutation that predisposes an individual to one common disease also predisposes them to, or protects them from, other diseases.

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ORIGINAL RESEARCH PAPER
Sivakumaran, S. *et al.* Abundant pleiotropy in human complex diseases and traits. *Am. J. Hum. Genet.* **89**, 607–618 (2011)
FURTHER READING Wagner, G. P. & Zhang, J. The pleiotropic structure of the genotype–phenotype map: the evolvability of complex organisms. *Nature Rev. Genet.* **12**, 204–213 (2011)