



HUMAN EVOLUTION

Pathogen influence on human genetic variation

Human population genetic variation is known to be influenced by environmental pressures. By developing a novel statistical framework, Fumagalli and colleagues have been able to discern the relative contributions of environmental factors to evolution of genomes, and they found that local pathogen diversity had the strongest role in the selective process.

Recent genome-wide human population genetic analyses have revealed that genes involved in traits such as immune function, skin pigmentation and metabolism are non-neutrally evolving sequences and have therefore been under the influence of environmental pressures. However, although it has been possible to identify genes that have been influenced by selection, it has not been possible to pinpoint the pressures that have shaped these sections of the genome or their relative contributions. In this

study, the statistical framework that was developed by Fumagalli *et al.* enabled them to correlate allele frequencies for 500,000 SNPs in 55 distinct human populations with local environmental factors, such as diet, climate conditions and pathogen load.

Consistent with previous studies, the authors found a greater correlation of these environmental factors with the frequencies of genic SNPs and nonsynonymous SNPs than with non-genic SNPs. After correcting for demography, they showed that pathogen diversity has the strongest influence on local genetic variance, and they detected about 100 human genes for which the allele frequency significantly correlated with pathogen load. Interestingly, helminths seemed to have a stronger influence than viruses, protozoa or bacteria. Climate was shown to have a limited role. Furthermore, genes that were shaped

by pathogens were heavily enriched in genes that are associated with autoimmune diseases, such as coeliac disease and type 1 diabetes.

The finding that pathogens have left such a strong mark on human genomes is perhaps not surprising given the influence that pathogens have on the human lifespan. However, the trace left by these pathogens at autoimmune disease gene loci suggests an intriguing relationship between achieving protection against infection and maintaining disease-causing mutations

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ORIGINAL RESEARCH PAPER Fumagalli, M. *et al.* Signatures of environmental genetic adaptation pinpoint pathogens as the main selective pressure through human evolution. *PLoS Genet.* **7**, e1002355 (2011)

FURTHER READING Barreiro, L. B. & Quintana-Murci, L. From evolutionary genetics to human immunology: how selection shapes host defence genes. *Nature Rev. Genet.* **11**, 17–30 (2010)