Immune genes adapt to parasites

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Thank parasites for making some of our immune proteins into the inflammatory defenders they are today, according to a population genetics study that will appear in the June 8 issue of the *Journal of Experimental Medicine* (online May 25). The study, conducted by a team of researchers in Italy, also suggests that you might blame parasites for sculpting some of those genes into risk factors for intestinal disorders.

Parasite-driven selection leaves a footprint on our DNA in the form of mutations known as "single nucleotide polymorphisms" (SNPs). Making sure that genetic variation (in the form of multiple SNPs) is maintained within certain immune genes over time helps ensure that the host can fend off different infections in different environments.

In the new study, Matteo Fumagalli and colleagues sift through 1,052 SNPs in genes that code for immune proteins called interleukins from roughly 1000 people worldwide. Of 91 genes assessed, 44 bore signatures of evolutionary selection, meaning that the genetic variation was neither due to chance nor to the migration of populations over time. And some of that variation correlated with the diversity of parasites that live alongside humans. The data suggests that having lots of different parasites around has shaped the evolution of our interleukin genes.

In general, parasitic worms appear to have had a more powerful influence on certain interleukin genes than smaller microbes such as viruses, bacteria, and fungi. That isn't surprising, says senior author Manuela Sironi, because worms typically evolve slower than bacteria or viruses, giving their human hosts time to adapt in response. Some of the

genes that were shaped by worm diversity made perfect sense, as the proteins they encode help generate the precise type of immune response required to rid the body of worms.

Other genes, however, seemed to be influenced more by the diversity of viruses, bacteria, and fungi than by that of worms. SNPs in some of these genes are known risk alleles for inflammatory bowel diseases, such as Crohn's and celiac disease. These "risky" alleles were probably maintained during evolution because they promote the kind of immune response needed to fend off viruses and bacteria. But this type of response also contributes to inflammatory bowel diseases.

More information: Fumagalli, M., et al. 2009. J. Exp. Med. doi: 10.1084/jem.20082779

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