

IRF7 HAPLOTYPE- HOST PROTECTION AND AUTOIMMUNITY. A TRADE-OFF

Why would a genetic variant that increases the risk of an autoimmune disease become the most common version of that gene across most of the world? That's the puzzle at the heart of a new paper in *The American Journal of Human Genetics* (1), and the answer is a beautiful illustration of an idea familiar to every biologist: evolution deals in trade-offs, not free lunches.

The gene is IRF7, the master regulator of our type I interferon response, the system that raises the alarm when a virus gets in. One coding variant of IRF7 is strongly linked to lupus risk, yet it's carried by 70% to 98% of people depending on ancestry, and ancient genomes show it has been common for over 10,000 years, surviving plague after plague.

Virolainen et al. (1) show why: this variant makes IRF7 bind DNA more strongly and produce more interferon. Mice engineered to carry it fought off a viral lung infection much more effectively than mice with the alternative version, but they also developed significantly more autoantibodies when their immune system was chronically stimulated, an early sign of lupus-like autoimmunity.

Better protection against viruses, at the price of a higher long-term risk of autoimmunity. For most of human history, shaped far more by infectious disease than by autoimmune conditions that often strike later in life, that trade seems to have been one worth making, and this haplotype is a striking example of it, hiding in the genome of most people alive today.

1. Virolainen et al., 2026, *Am J Hum Genet.*
<https://doi.org/10.1016/j.ajhg.2026.08.016>