Genetic mutation identified as culprit in rare infectious disease

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At some point in life, most of us will contract Tropheryma whipplei without even knowing it. For one in a million infected people, however, this bacterium will make itself blatantly known by causing Whipple's disease, an intestinal inflammatory disorder that causes diarrhea, pain, and weight loss.

In an article published in *eLife*, Jean-Laurent Casanova has uncovered the human genetics factors that make these outliers susceptible to infection. His team suspected that Whipple's is the latest in a growing number of genetic defects that increases people's vulnerability to specific microbes. The researchers studied four related patients with Whipple's and identified an extremely rare mutation in a gene called IRF4, which plays a role in the immune system.

For decades after the first case of Whipple's was reported, in 1907, scientists thought it was an inflammatory disorder, before finding that it is in fact an infectious disease. "Our recent discovery of Whipple's genetic component is a second paradigm shift in the history of the disease," Casanova says. "Understanding why the disorder progresses in some people but not in others due to genetics could lead to new ways to diagnose and treat it."

More information: Antoine Guérin et al. IRF4 haploinsufficiency in a family with Whipple's disease, *eLife* (2018). DOI: 10.7554/eLife.32340

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