Study sheds light on how patients with rare, severe immunodeficiency are still able to defend themselves

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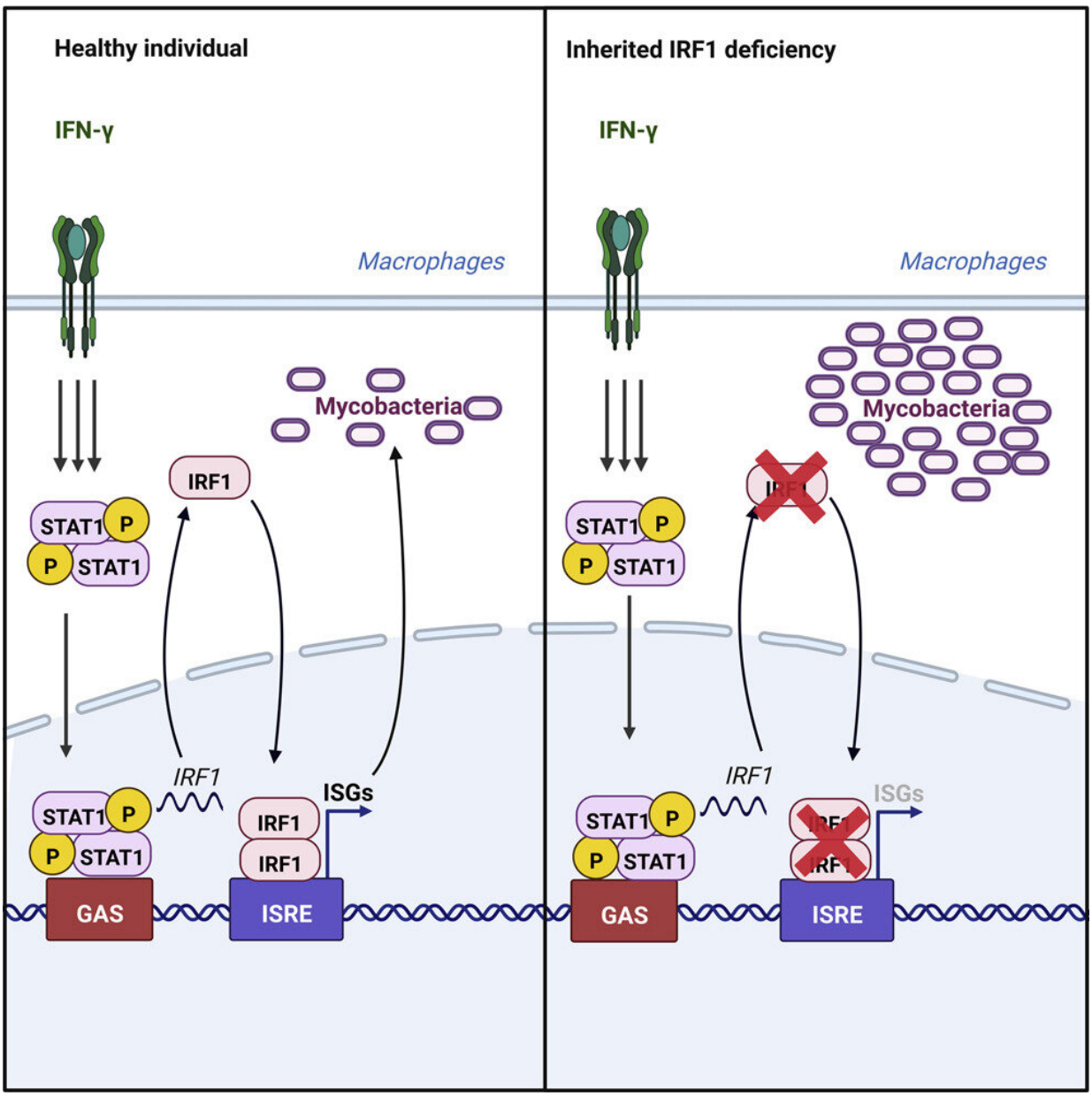

Graphical abstract. Credit: *Cell* (2023). DOI: 10.1016/j.cell.2022.12.038

The first study of humans with a rare immunodeficiency reveals how the immune system protects the body against pathogens known to cause serious diseases, such as tuberculosis and COVID-19. The research involving McGill University, paves the way for new therapies to treat autoimmune diseases, chronic inflammatory diseases, and new approaches to vaccine development.

The immune system responds differently to various types of pathogens, like bacteria, parasites, and viruses. However, scientists are still trying to uncover how this complex network functions together and the processes that can go wrong with immunodeficiencies.

"The immune system plays a vital role in protecting the body from harmful germs that make people ill. It's made up of a complex network of organs, cells, and proteins—like IRF1 or regulatory factor 1, which is key in the regulation of an early immune response to pathogens," says co-author of the study David Langlais, an Assistant Professor in the Departments of Human Genetics and Microbiology and Immunology at McGill University.

"A better understanding of these specific processes will help us pinpoint the cause of defective immune responses, and perhaps even allow to boost an appropriate immune response to better combat illness," adds Langlais who is also a Principal Investigator at the Victor Phillip Dahdaleh Institute of Genomic Medicine.

Understanding the role of IRF1 in immune responses

Previous studies on mice that were IRF1 deficient have shown that the animals were highly susceptible to many viruses. In studying the first human patients with IRF1 deficiency ever identified, the researchers found that while the patients were highly susceptible to some bacterial infections, surprisingly they can defend themselves normally against viruses, including COVID-19.

"This study provides new insight into the mechanisms underlying the human immune responses to mycobacteria, which includes pathogens known to cause tuberculosis, versus differences in the immune response to viruses. Unlike in mice, we show that in humans, the activity of IRF1 is not essential to anti-viral immunity," says co-author Jörg Fritz, who is also an Associate Professor in the Department of Microbiology and Immunology.

"Based on our findings, it could be possible to think of therapeutic avenues to block or activate the action of IRF1 and control the type and intensity of immune responses. Our findings shed light on our understanding of the specificity and selectivity of our immune responses towards different pathogens," says co-author Philippe Gros, a Professor in the Department of Biochemistry and Principal Investigator at the Victor Phillip Dahdaleh Institute of Genomic Medicine at McGill.

The findings are published in the journal *Cell*.

More information: Jérémie Rosain et al, Human IRF1 governs macrophagic IFN-γ immunity to mycobacteria, *Cell* (2023). DOI: 10.1016/j.cell.2022.12.038

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