Medical Xpress

# Rare diseases point to connections between metabolism and immunity

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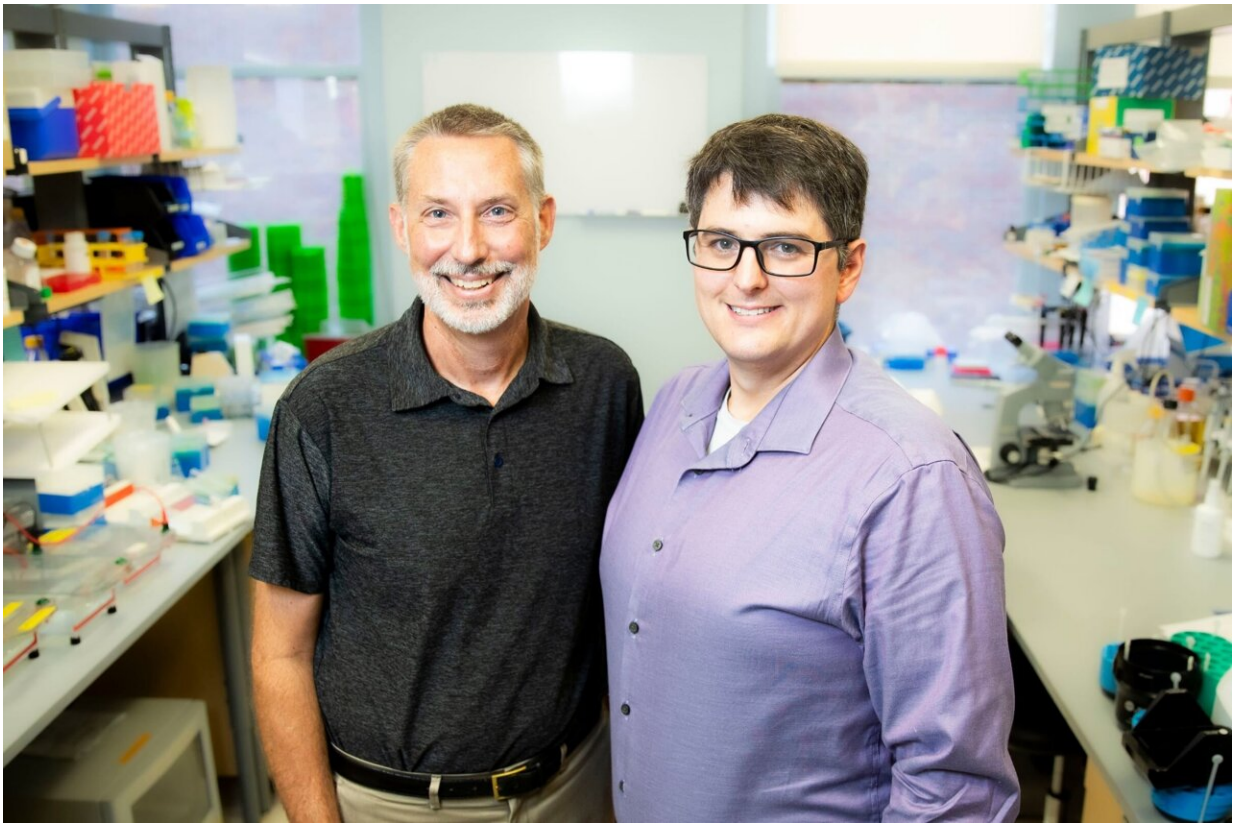

Jeffrey Rathmell, Ph.D., left, and Andrew Patterson, Ph.D., have discovered a new set of metabolic genes that are important for immune cell function. Credit: Vanderbilt University Medical Center

## Inherited diseases of metabolism and immunity have more in common

than previously recognized, according to a new study published in the journal Science Immunology. The findings point to a new set of metabolic genes that are important for the function of immune system T cells, and they offer insights that could improve care for patients with these disorders.

The study examined genes that cause inborn errors of metabolism (disorders of the processes that cells use to convert food to energy) and inborn errors of immunity (disorders that affect immune system function). These rare and complex diseases are not fully understood.

"There had previously been only a small number of genes that were on both lists of diseases, but we found that many more have overlap," said Andrew Patterson, Ph.D., who led the study as a postdoctoral fellow working with Jeffrey Rathmell, Ph.D., at Vanderbilt University Medical Center. "Our study showed that a large number of genes associated with inborn errors of metabolism can also potentially affect T cell function when they are mutated."

The findings suggest that patients with an inborn error of metabolism may also have immune defects that could impact their care, and conversely that metabolic defects may contribute to symptoms in patients with inborn errors of immunity.

"There's a lot more that will have to be learned, but these connections might point to different therapies," said Rathmell, Cornelius Vanderbilt Professor of Immunobiology and director of the Vanderbilt Center for Immunobiology. "Rather than different categories, these diseases are part of a continuum; there's a gray zone between them and a potential new class of inborn errors of immunometabolism that intersects the two."

Patterson and the research team used a gene-editing CRISPR approach

to screen the inborn errors of metabolism genes for immune defects and the inborn errors of immunity genes for metabolic defects. They further analyzed one example from each set—one metabolic gene that had an immune defect; one immunity gene that had a metabolic defect—to more carefully examine the mechanistic impact.

Overall, Rathmell's team is interested in discovering how metabolic pathways regulate T cell function, with the goal of developing targeted therapies for immune-mediated disorders.

"What we've done is lay the foundation for further investigation," Patterson said. "The two examples we studied in detail point to new biology and new mechanisms, and there are hundreds of other genes we identified to analyze for their roles in T cell function."

The findings are available on a website for other researchers to use.

"If you're trying to understand the connections between metabolism and immunity, this is a great place to start," Rathmell said.

Patterson recently joined the faculty of the University of Louisville as an assistant professor of Biochemistry and Molecular Genetics. Vanderbilt collaborators Vivian Gama, Ph.D., associate professor of Cell and Developmental Biology, and Janet Markle, Ph.D., assistant professor of Pathology, Microbiology and Immunology, were important contributors to the study.

**More information:** Andrew R. Patterson et al, Functional overlap of inborn errors of immunity and metabolism genes defines T cell metabolic vulnerabilities, *Science Immunology* (2024). DOI: 10.1126/sciimmunol.adh0368