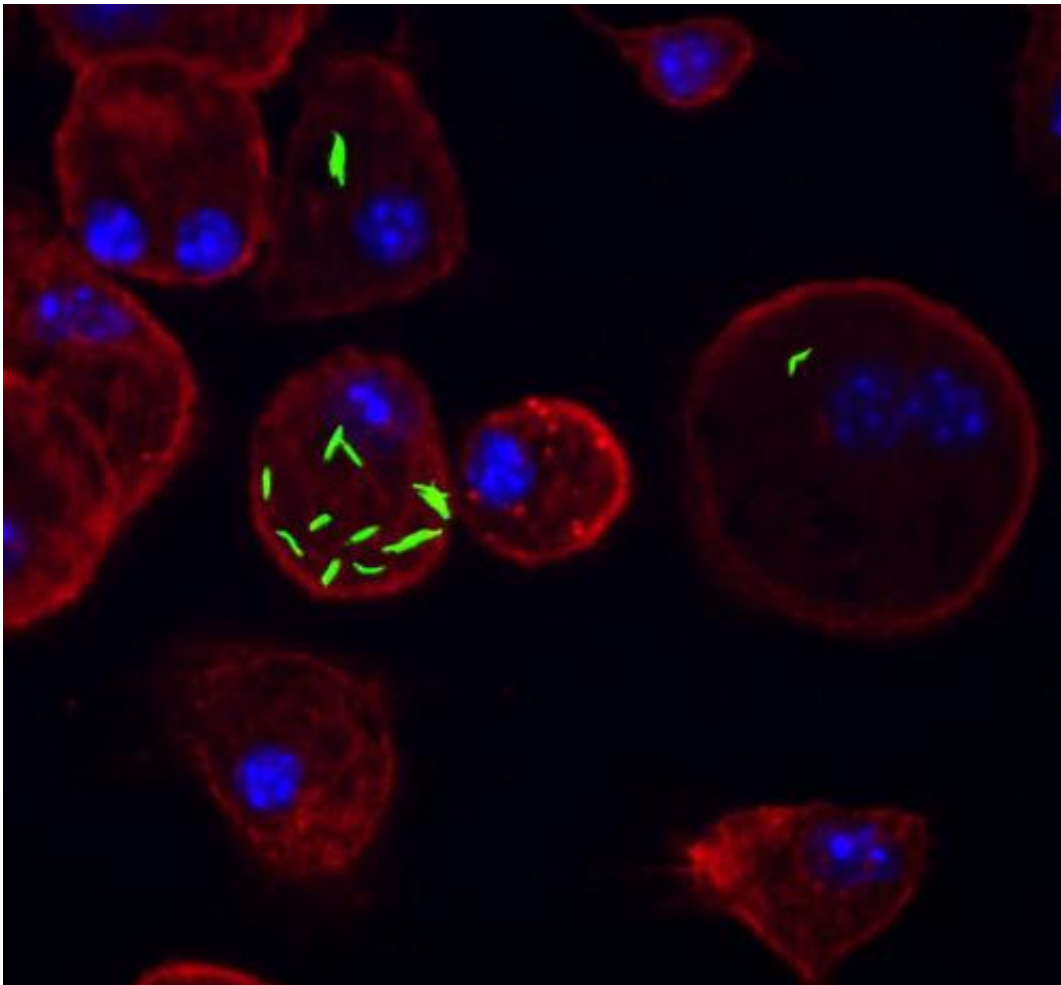


How invariant natural killers keep tuberculosis in check

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This shows macrophages infected with *Mycobacterium tuberculosis*. Credit: Alissa Rothchild

Mycobacterium tuberculosis is a major cause of death worldwide, and a formidable foe. Most healthy people can defend themselves against tuberculosis, but they need all parts of their immune system to work together. A study published on January 2nd in *PLOS Pathogens* reveals how a special class of immune cells called "invariant natural killer T cells" make their contribution to this concerted effort.

"We were interested in identifying the mechanisms that different types of T [cells](#) use to control *Mycobacterium tuberculosis* infection", says Samuel Behar, from the University of Massachusetts Medical School, US, the senior author of the new study.

He and his colleagues had previously shown that when invariant natural killer T (iNKT) cells encounter infected macrophages—the human target cells of *Mycobacterium tuberculosis*, or Mtb—the iNKT cells somehow prevented Mtb from growing and multiplying inside the macrophages.

In this study, the scientists focused on how the iNKT cells achieved this. Using a number of cell culture systems and experiments in mice to dissect the interaction, they found that when iNKT cells are confronted with Mtb-infected macrophages, they respond in two different ways. One is that they produce and release [interferon gamma](#), a broad-spectrum immune system activator. But when the scientists blocked interferon gamma action, they found that the iNKT cells could still inhibit Mtb growth in the macrophages.

After testing a few more known mediators of iNKT cell function and finding that they were dispensable as well, the scientists discovered that Mtb control depends on production and release by the iNKT cells of a soluble immune system factor called GM-CSF. When they blocked GM-CSF, they found that iNKT cells could no longer restrict mycobacterial growth. And when they exposed isolated Mtb-infected macrophages to GM-CSF, it turned out that this factor alone was sufficient to inhibit

Mtb growth.

These results are exciting in the context of previous findings that mice in which the GM-CSF gene had been deleted were more susceptible to Mtb infection, because they link iNKT cells and GM-CSF and identify a novel pathway of Mtb control by the [immune system](#).

Overall, the scientists say "Understanding how iNKT cells contribute to the control and elimination of Mtb in general and finding that GM-CSF has an essential function could lead to novel therapeutic approaches that strengthen their activity and boost the overall immune response during infection".

More information: *PLoS Pathog* 10(1):e1003805. [DOI: 10.1371/journal.ppat.1003805](#)

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