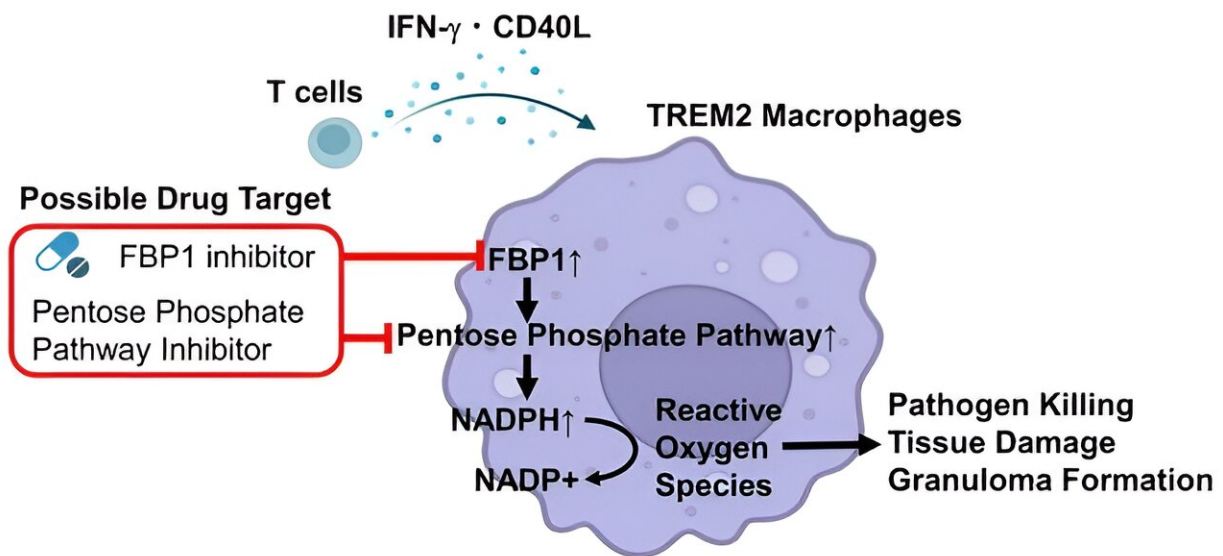


Researchers discover metabolic pathway specific to granuloma formation in patients

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Credit: *Journal of Clinical Investigation* (2023). DOI: 10.1172/JCI171088

On good days, the immune system can effectively handle pathogens that invade the body. However, when foreign matter takes the upper hand, the body builds a wall of immune cells called granuloma around the pathogens to isolate them.

Occasionally, abnormal clusters of granuloma become granulomatous diseases, such as sarcoidosis and Crohn's disease—with typical symptoms of blindness, [irregular heartbeat](#), pulmonary fibrosis, and

diarrhea—but their causes are unknown. And no approved non-steroidal treatments exist.

Now, a team of researchers at Kyoto University has found that macrophages—[white blood cells](#) that consume pathogens—produced the granulomas by a hyperactive metabolic pathway called the pentose phosphate pathway (PPP). The findings are [published](#) in the *Journal of Clinical Investigation*.

"Inhibition of this pathway also inhibited granuloma formation both in vitro and in a mouse tissue model, showing possible therapeutic efficacy," says Satoshi Nakamizo of the Graduate School of Medicine.

Using single-cell RNA sequencing, Nakamizo's team found evidence of the macrophages not only in the skin of sarcoidosis patients but also in lesions throughout the body. Using PPP inhibitors in vitro human and in vivo mouse granuloma models consistently reduced granuloma formation.

"Our results also indicate that the metabolic enzymes may have diagnostic and therapeutic applications, encouraging us to collaborate with the [pharmaceutical industry](#) for [drug development](#)," says team leader Kenji Kabashima.

"We used patient samples—not just animal studies—which underscores our finding's clinical relevance and importance," adds Nakimizo.

"All cases we analyzed showed elevated expression of PPP enzymes, such as fructose biphosphatase, suggesting the unexpected regularity of sarcoidosis."

More information: Satoshi Nakamizo et al, Activation of the pentose phosphate pathway in macrophages is crucial for granuloma formation in

sarcoidosis, *Journal of Clinical Investigation* (2023). [DOI: 10.1172/JCI171088](https://doi.org/10.1172/JCI171088)

Provided by Kyoto University

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