

Researchers find B cells drive responses of other immune cells, can be modified to prevent multiple sclerosis symptoms

May 6 2024

B cells can control responses of myeloid cells through the release of particular cytokines (small proteins that control the growth and activity of cells in the immune system), disproving the previous consensus that T cells are the only orchestrators of immune responses.

In individuals with [multiple sclerosis](#) (MS), abnormally active respiration in B cells drives pro-inflammatory responses of myeloid cells and T cells, leading them to attack the protective sheath (myelin) that covers nerve fibers, and leading to nerve damage that causes symptoms of MS.

An emerging class of drugs, called Bruton's tyrosine kinase (BTK) inhibitors may alter this abnormal B cell respiration and stop the signaling that leads to MS flare-ups. The research, led by the Perelman School of Medicine at the University of Pennsylvania, was [published](#) May 3 in *Science Immunology*.

"Experts previously thought that T cells were the main orchestrators of responses by other immune cell types, and that MS was principally caused by overly activated T cells," said Amit Bar-Or, MD, a professor of Neurology, and director of Penn's Center for Neuroinflammation and Neurotherapeutics.

"This research highlights that it is actually how multiple cell types interact that matters, and that B cells modulating myeloid cells play a

much more active role in the immune system than we thought."

A healthy immune system is always responding to stimuli by activating or suppressing immune responses, in part through release of different cytokines which tell other cell types how to respond. Normally, every [immune response](#) generates a counter response, and this constant "push-me-pull-you" helps maintain the proper balance between immune responses.

This way, an individual's immune system can, on one hand, respond to an infection but also ensure that the response does not become overactive and cause damage to the body, as might occur in an autoimmune disease like MS.

In this study, researchers used both human samples and mouse models of MS to show that not only does the cytokine signaling between B cells and T cells go awry in MS, but also that B cells of MS patients produce an abnormal cytokine profile that drives myeloid cells to generate an inflammatory response.

They found that these actions can all be traced back to metabolic dysregulation in a process within the B cells called [oxidative phosphorylation](#), a type of mitochondrial respiration. Researchers found that normal B cells can break down oxygen and release chemical energy signals that illicit a further response in the B cells themselves, and subsequently also in myeloid cells, telling them to produce a pro- or anti-inflammatory response.

However, when this B cell metabolism is over-active, as it is in MS, the signaling results in abnormal myeloid as well as T cell responses which have been implicated in MS symptom flare-ups.

"An exciting approach for new MS treatments, then, might be to

partially mute respiration in B cells, which could then stop the cascade of interactions between immune cells that drives inflammation and MS activity," said Bar-Or.

The authors [previously showed](#) that an emerging class of drugs, called BTK inhibitors, does just that. These agents slow overactive B cell respiration and "calm down" B cells of MS patients, so that they don't release the same abnormal cytokine profile that drives abnormal pro-inflammatory myeloid cell and T cell responses.

Existing MS therapies, like anti-CD20 treatments, deplete B cells. However, since B cells are eliminated, the individual's immune system may be compromised, struggling to mount certain immune responses—for example antibody responses to infections or vaccinations. In contrast, BTK inhibitors do not deplete B cells, but correct the metabolic abnormality, making the B cells less prone to drive pro-inflammatory responses of other cells.

More information: Rui Li et al, Oxidative phosphorylation regulates B cell effector cytokines and promotes inflammation in multiple sclerosis, *Science Immunology* (2024). [DOI: 10.1126/sciimmunol.adk0865](https://doi.org/10.1126/sciimmunol.adk0865)

Provided by Perelman School of Medicine at the University of Pennsylvania

Citation: Researchers find B cells drive responses of other immune cells, can be modified to prevent multiple sclerosis symptoms (2024, May 6) retrieved 8 August 2024 from <https://medicalxpress.com/news/2024-05-cells-responses-immune-multiple-sclerosis.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private

study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.