Enzymes linked with immune cell activity could hold key to better understanding inflammation

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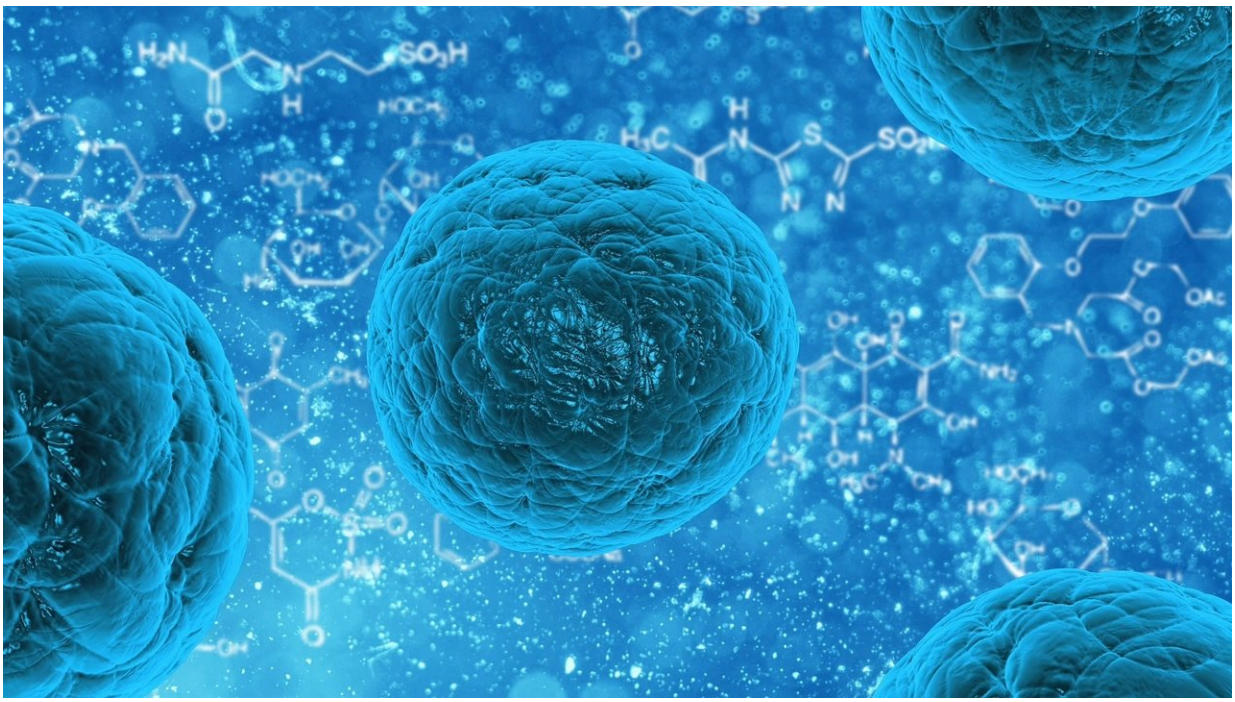

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New research shows a group of enzymes may have a critical role in the process of how immune cells are activated and then migrate to certain sites in the body—findings that could improve our understanding of inflammation and potentially lead to new treatments.

In a recent study published in *The FASEB Journal*, researchers explored a particular family of enzymes called neuraminidases. "We wanted to know whether these enzymes were involved in inflammation, whether they do anything important in the immune system," says Chris Cairo.

Cairo and his team found that certain neuraminidase enzymes act as either pro-inflammatory or anti-inflammatory. They help to regulate the way the immune cells move and interact within the body.

The findings show promise for developing potential inflammatory therapeutics, and could be useful in treating diseases, explains Cairo, a professor in the Department of Chemistry. For example, in an autoimmune disorder where too many immune cells are being recruited to a particular area, an enzyme with a subtly anti-inflammatory effect may help turn down the intensity of that immune response while not completely eradicating the person's immune system.

Neuraminidases cleave a specific carbohydrate residue from proteins and lipids in cells. Many important protein molecules in the immune system are glycosylated—meaning they have a carbohydrate attached to them—and these enzymes could influence specific interactions.

When immune cells move through the body, they search for something they recognize in the form of receptors or carbohydrates on the exterior of cells. If these receptors or the carbohydrate on them are modified in any way, the immune cell's ability to find and bind to those sites is compromised. When these enzymes cleave off the neuraminic acid on immune cells, the immune cells are activated in a different way, although researchers are still trying to refine their understanding of the process.

"Biology doesn't do things for no reason. You don't have a whole family of enzymes that are just there by accident—they serve a role," says

Cairo.

In the study, researchers looked at animal models missing specific neuraminidase enzymes. They found that this family of enzymes was unique in that some acted in an anti-inflammatory way, whereas others acted in a pro-inflammatory way.

"As an enzyme family they're both positive and negative regulators, which I think was not at all expected," says Cairo.

Cairo and his team took a broader approach, looking at the enzyme in a more general sense rather than examining a niche question or specific disease-related issue.

"We have a better idea of what this is doing to the whole immune system rather than just what it's doing to one cell type or one protein," he says.

These neuraminidase enzymes aren't as well studied because they're challenging to work with, explains Cairo, but they hold a lot of promise.

"We're probably coming across a whole enzyme system that could be very valuable in the future. But we've got to understand the mechanisms much better."

More information: Md. Amran Howlader et al, The Janus-like role of neuraminidase isoenzymes in inflammation, *The FASEB Journal* (2022). DOI: 10.1096/fj.202101218R

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