




Australia

Researchers identify a gene that plays vital role in the innate human immune system

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Cedars-Sinai researchers identify gene which plays an important role in the innate human immune system. gene, *NLRP11* helps activate the inflammatory response that causes the body's white blood cells to attack the foreign presence.

Findings published in *Nature Immunology* bring medical science closer to understanding the biological process, which can both help and harm the body.



Chronic inflammation is the root cause of countless human diseases. If you study the molecular mechanisms involved in how inflammation occurs and how it is regulated, you will find something that can be applied very widely."

*Christian Stehlik, PhD, study co-author
and director of pathology research at
Cedars-Sinai*

When the immune system detects the presence of bacteria, viruses, toxins, or other foreign substances in the body, it sends white blood cells to surround the unwanted substance and release

chemicals to attack it. This reaction leads to inflammation, which causes redness, pain, fever, and swelling in the affected area as the body heals itself. Sometimes this defensive reaction lasts longer than it should, leading to chronic inflammation. Or the immune system may mistakenly attack healthy cells, resulting in an autoimmune disease.

"Acute inflammation is necessary and beneficial to eradicate infection and initiate wound healing," said Andrea Dorfleitner, Ph.D., co-author of the study and assistant professor of academic pathology and biomedical sciences at Cedars-Sinai. "However, chronic, long-term, uncontrolled inflammation is harmful and can damage organs and tissues in the body."

The key to controlling the inflammatory response and preventing chronic inflammation may lie in the ability to influence the expression *NLRP11* gene.

The researchers used a gene-editing system called CRISPR/Cas9 to remove genes or introduce gene mutations into human white blood cells called macrophages. They noticed that when they removed *NLRP11* it prevented an immune system sensor called the NLRP3 inflammasome from activating and triggering an inflammatory response.

When the investigators recovered *NLRP11* The inflammasome gene NLRP3 sent attack signals that triggered a typical inflammatory process. The researchers chose to focus on this gene because it is not expressed in mice, leading them to hypothesize that it is an integral part of the complex immune system found in humans.

"Now that we have a clearer understanding of the mechanisms of inflammation, we can come up with completely new strategies to

combat it that were not possible before," Dorfleitner said.

The study's first authors are Anu Gangopadhyay, Savita Devi, PhD, and Shivendra Tenguriya, PhD, all researchers from Stelik and Dorfleitner's lab.

Source:

Link to the journal:

Gangopadhyay, A., and others. (2022) NLRP3 licenses NLRP11 to activate inflammation in human macrophages. *natural immunology*. doi.org/10.1038/s41590-022-01220-3.

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