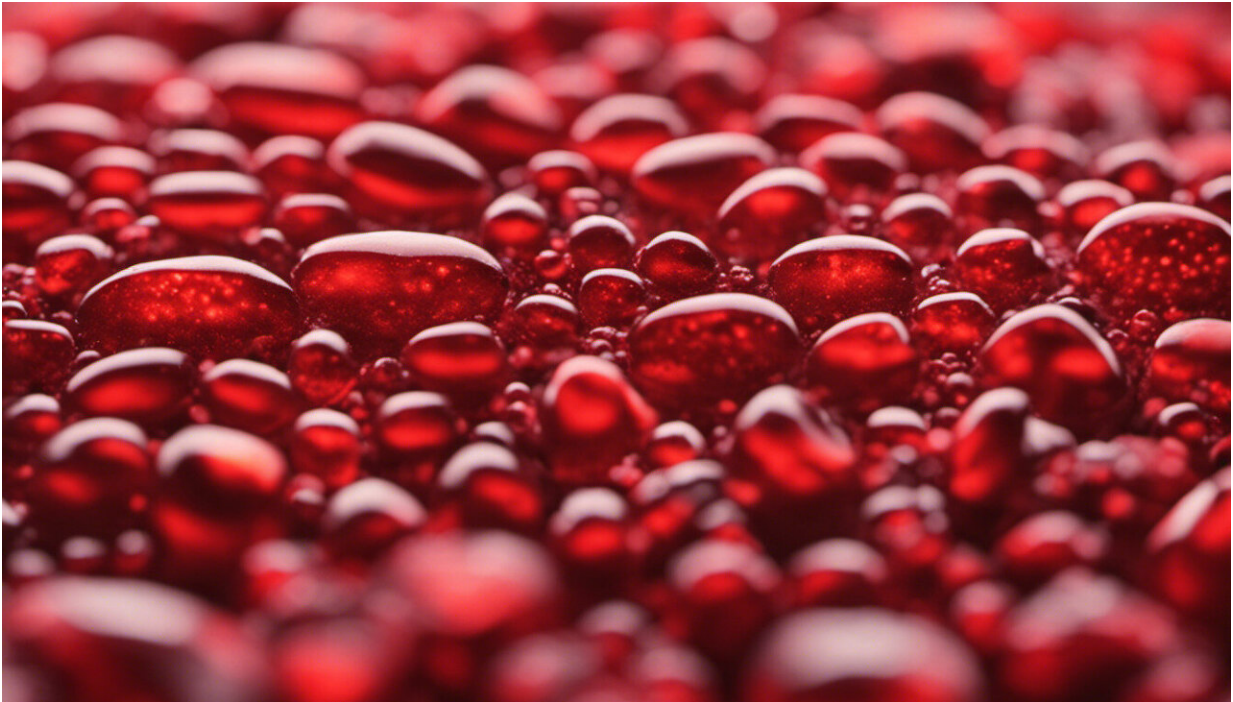


Microbial molecule stimulates both arms of the immune system to quell inflammation

April 10 2014, by Elizabeth Cooney



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(Medical Xpress)—Putting out the fires of inflammation takes more than the immune system itself, studies of the human microbiome have revealed. It also takes more than one arm of the immune system, according to new research from Harvard Medical School.

"Friendly" bacteria living in the gut amid the collective population called the microbiome are critical in helping the host's immune system extinguish inflammation by inducing immune cells to secrete an anti-inflammatory molecule, HMS scientists previously learned.

Now, researchers led by Dennis Kasper, the HMS William Ellery Channing Professor of Medicine and professor of microbiology and immunobiology, have shown that a molecule found on the surface of one specific bacterium regulates both arms of the immune system—innate and adaptive—to quell inflammation. This discovery reveals a central host-microbe strategy that limits the extent and severity of inflammatory diseases, Kasper and his colleagues report in *Cell Host & Microbe*.

Kasper and others had already shown how some microbes regulate components of the human immune system, modulating the way it responds to health threats. Certain of these microbiota are crucial for maintaining a balance between disease-causing organisms and their health-maintaining counterparts.

Bacteroides fragilis is one of those good guys. In mouse experiments Kasper had previously demonstrated the powerful effect that polysaccharide A (PSA), a molecule that sits on the bacterium's surface, has on harmful inflammation.

For the new study, Kasper's team focused on how PSA acts in mice induced to have inflammation modeled on two human diseases: colitis in the intestinal tract and multiple sclerosis in the brain. They have now found that PSA directs both innate—quick and general—and adaptive—later but more specific—immune responses to cooperate on instructing the immune cells to protect against inflammation.

In the innate immune response, PSA interacts with [immune cells](#) called plasmacytoid dendritic cells (PDCs) via the innate immune receptor Toll-

like receptor 2 (TLR2). This eventually induces PDCs to engage T cells in the [adaptive immune system](#) to stimulate secretion of anti-inflammatory molecules that turn off inflammatory processes within cells. This engagement of T cells by PDCs relies on adaptive molecules such as major histocompatibility complex II (MHCII) and co-stimulatory molecules on PDCs.

Both arms of immunity are needed to fight inflammation, as the scientists discovered when they tested dendritic cells combined or not combined with PSA in mice with the disease models of inflammation.

"It's that double signal," Kasper said. "It's that presentation of the PSA molecule through the adaptive arm, linked with all of the right signals from the innate [immune system](#), all contacting the T cell, that send the T cell in this direction. If you knock out the adaptive arm or the innate arm, you don't get this effect on inflammation. It requires both working together."

This work reveals a network of beneficial interactions between the host and microbial molecules through both the innate and adaptive immune mechanisms. The insights gained may be useful for pursuing therapeutic molecules beyond PSA, the researchers concluded.

"This opens the door for similar investigations with other molecules from the microbiota, to see if they follow a similar pattern," said Suryasarathi Dasgupta, HMS instructor in microbiology and immunobiology, and lead author of the paper.

More information: "Plasmacytoid Dendritic Cells Mediate Anti-inflammatory Responses to a Gut Commensal Molecule via Both Innate and Adaptive Mechanisms." Dasgupta, Suryasarathi et al. *Cell Host & Microbe*, Volume 15, Issue 4, 413 - 423. DOI: [dx.doi.org/10.1016/j.chom.2014.03.006](https://doi.org/10.1016/j.chom.2014.03.006)

Provided by Harvard Medical School

Citation: Microbial molecule stimulates both arms of the immune system to quell inflammation (2014, April 10) retrieved 29 June 2024 from <https://medicalxpress.com/news/2014-04-microbial-molecule-arms-immune-quell.html>

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