Researchers uncover how Gram-negative bacteria can trigger immune system reaction

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Researchers at the University of Toronto have uncovered how Gram-negative bacteria -- a broad class of bugs that cause diseases ranging from gonorrhea to diarrhea and pneumonia -- can trigger a reaction from our immune system. This discovery could lead to new therapies and treatments that use the immune system to fight infections instead of antibiotics.

Graduate student Ryan Gaudet, who works in the lab of Professor Scott Gray-Owen, made the breakthrough while investigating gonorrhea.

"This is a great example of how basic science research can lead to an unexpected discovery," says Gray-Owen, who is a professor of molecular genetics. He investigates how bacteria are able to invade healthy tissue and evade our otherwise effective immune responses. *Neisseria gonorrhoeae*, the bacteria that causes gonorrhea, is especially crafty.

Gonorrhea is a re-emerging problem because antibiotic-resistant superbugs have begun to appear, including in the USA and Canada. The World Health Organization estimates that there are nearly half a million new cases of gonorrhea occurring each day. Many people infected show no signs or symptoms as these stealthy bacteria avoid detection by the immune system. However, if it becomes exposed, the immune system kicks into high gear, sometimes with devastating results. In these cases, it can cause an overwhelming immune response that attacks not only the bacteria, but also surrounding tissue. In fact, gonorrhea remains a leading cause of uterine scarring and sterility in women, and it can blind infants who are born to infected mothers.

Gonorrhea also has a complex relationship with HIV. People with gonorrhea are more susceptible to HIV, and people with HIV become more infectious when they encounter gonorrhea. Previous research has shown that this was tied to the immune response gonorrhea can trigger, but no one was sure why.

Gaudet's research found that a type of sugar produced by Gram-negative bacteria -- called heptose -- could trigger an immune response. Heptose is not made by humans, so it represents a clear signal that bacteria have invaded the tissues. Such triggers are called pathogen-associated molecular patterns -- or PAMPs -- that act like flares to alert the immune system of a harmful presence.

So what does this mean for HIV? HIV infects T-cells, which are part of the immune system. It stays dormant until an immune response is initiated. Once it is, T-cells are activated and HIV can rapidly infect other cells. So gonorrhea's "flares" help HIV spread quickly.

Knowing how to trigger an immune response, without the threat of spreading harmful bacteria, can lead to new therapies Gaudet explains.

"There are a range of applications where we can use PAMPs to direct a productive immune response instead of using traditional drugs, ranging from treatments for infectious disease to autoimmune disease and cancer," he says. Gaudet plans to investigate those options as he completes his PhD.

"The curious thing is that other bacteria try to hide their heptose, while gonorrhea seems to release it intentionally. What we don't understand is why gonorrhea is sending out its' flares. Why does it want to cause an immune response?" says Gray-Owen. Further research will be done to answer that question.

Source:
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