

Neutrophils are key to mounting an effective immune response when receiving a pneumonia vaccine

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Essi Tchalla, doctoral student, Department of Microbiology and Immunology Jacobs School of Medicine and Biomedical Sciences. Credit: University at Buffalo

University at Buffalo scientists exploring the nature of immunity after vaccination against *Streptococcus pneumoniae*, which causes pneumonia in people, have discovered that a specific type of white blood cell called neutrophils plays a more critical role than was previously known.

The research is especially relevant for the elderly because immunity declines with age.

Researchers at the Jacobs School of Medicine and Biomedical Sciences at UB have found that in order to generate a [protective response](#) when vaccinated against *Streptococcus pneumoniae*, an individual must have a sufficient level of neutrophils.

The [preclinical study](#) is important because it is the first to use Prevnar-13, one of two pneumonia vaccines on the market, instead of a model antigen to study the nature of the [immune response](#) triggered by the [vaccine](#).

Better vaccines

"The idea behind our research is ultimately to make a better pneumonia vaccine," said Elsa Bou Ghanem, Ph.D., assistant professor of microbiology and immunology in the Jacobs School and senior corresponding author on the paper, published in the *Journal of Infectious Diseases* in May.

While B cells are a key factor in the immune response because they produce antibodies that fight viruses and pathogens, Bou Ghanem said the new findings about neutrophils could be relevant to potential improvements in developing vaccines against *S. pneumoniae*.

"Now we have to think about the other [immune cells](#) in the mix as well," she said. "Now we understand that it's a little more complicated."

Bou Ghanem described neutrophils as "the first defenders," noting that "whenever any foreign object appears in the lungs, neutrophils are the first infection-fighting cells to appear."

That fact has long been known about neutrophils, also known as polymorphonuclear leukocytes (PMNs). They play key roles in the body's rapid response to bacterial infection, known as the innate response.

But the UB researchers found that they also play a role in generating the adaptive response, the immune system's slower, more customized response to a specific infection.

Orchestrating the whole immune response

"We have learned now that neutrophils orchestrate the whole immune response, both innate and adaptive," said Essi Tchalla, first author on the paper and a doctoral student in the Department of Microbiology and Immunology in the Jacobs School.

They made the discovery while studying how two groups of mice responded after being vaccinated with the polysaccharide conjugate vaccine: One group was normal and one group had had its neutrophils significantly depleted.

When exposed to *S. pneumoniae* a month after vaccination, all of the mice with normal neutrophil levels were able to mount a strong immune response and all of them survived, with only 12.5% of them showing any symptoms.

But in the group that had been depleted of neutrophils at the time of vaccination, nearly 80% became severely ill and more than half of the mice did not survive. These mice exhibited between 10 and 100 times

more bacteria in their lungs than was seen in the normal controls.

The researchers report it was the lack of neutrophils at the time when mice were vaccinated, not at the time of exposure to the bacteria, that caused them to suffer the worst outcomes. The neutrophils were required for the production of protective antibodies against *S. pneumoniae* following vaccination.

"Now we want to figure out what is the contribution of neutrophils in regulating this vaccine response," said Tchalla.

She said the team is looking at interferon gamma, which is involved in the innate immune response, and the possibility that neutrophils can produce interferon gamma, which in turn helps B cells to produce better antibodies against pathogens.

The long-range goal for Bou Ghanem and Tchalla is to investigate how the reduction in the efficacy of neutrophils in the elderly affects their ability to mount an immune response to *S. pneumoniae* when vaccinated.

One of their projects, currently on hold because of the pandemic, involves studying [neutrophils](#) provided by donors recruited through UB's Clinical and Translational Research Institute, a collaboration with Sanjay Sethi, MD, professor and chief of the Division of Pulmonary, Critical Care and Sleep Medicine in the Jacobs School.

The findings may also be relevant to understanding the ability of elderly patients to generate an adequate immune response when vaccinated against other pathogens, including COVID-19, the UB researchers said.

More information: Essi Y I Tchalla et al. Neutrophils Are Required During Immunization With the Pneumococcal Conjugate Vaccine for Protective Antibody Responses and Host Defense Against Infection, *The*

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