Hospital del Mar Research Institute
Barcelona

Nota de prensa

The relationship between gut microbiota, immunoglobulin A, and vaccine efficacy

- ***A study led by the Hospital del Mar Research Institute has established the importance of immunoglobulin A, an antibody that is part of the immune system, in generating a response to pneumonia vaccines.***
- ***Researchers have found that the absence of this antibody leads to an overgrowth of gut microbiota, triggering an excessive and sustained immune system response, which ultimately becomes exhausted and fails to respond effectively to vaccines.***
- ***The study, published in Science Advances, opens the door to exploring the possibility of early immunoglobulin therapy administration to prevent this process and reduce the risk of potentially dangerous infections, even in at-risk individuals without a diagnosed immunodeficiency***

Barcelona, March 13, 2025 – Gut microbiota may be the key factor explaining why certain individuals **do not respond well to the pneumococcal vaccine**—a bacterium that can cause various diseases, such as pneumonia. This conclusion is drawn from a recent study led by the B Cell Biology Research Group at the Hospital del Mar Research Institute, published in *Science Advances*.

Researchers analyzed vaccine responses using **genetically modified mouse models to study two types of pneumococcal vaccines—one commonly used in children and another in adults**. Although these vaccines function through different mechanisms, both provide broad coverage. However, in individuals with a specific type of immunodeficiency, immunoglobulin A (IgA) deficiency, the immune system does not always mount an adequate response, leaving them vulnerable to respiratory infections that can lead to severe complications. The reason: **poor regulation of gut microbiota.**

Immunoglobulin A plays a crucial role in controlling gut microbiota. It regulates its function and ensures that its presence remains beneficial to the body. However, in the absence of IgA, the bacteria that make up the microbiota can overgrow and spread beyond the intestines. This overgrowth triggers an immune system response to keep the bacteria in check, but this response remains persistently active over time, leading to immune cell exhaustion.

According to Dr. Andrea Cerutti, a principal investigator at the Hospital del Mar Research Institute and ICREA Professor, "**The vaccine may be less effective in the absence of immunoglobulin A because the immune system produces an excessive amount of another antibody, immunoglobulin G (IgG), in response to bacteria originating from the gut. These bacteria overstimulate the immune system, leaving it depleted due to persistent stimulation**."

Under normal conditions, "**vaccines generate a response through pneumococcus-specific IgG antibodies. However, in patients with IgA deficiency, the lack of IgA reduces the vaccine's effectiveness,**" explains Mauricio Guzmán, a Ramón y Cajal Investigator at the Hospital del Mar Research Institute. This finding suggests that vaccination strategies should take this factor into account.

Early intervention

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The study's authors highlight that while IgA deficiency primarily affects adults**, its impact on the immune system can begin at a very early age**. The study's results indicate that the absence of immunoglobulin A and the immune response to gut microbiota overgrowth begin in childhood.

For this reason, "**we should explore the possibility of early supplementation with recombinant IgA antibodies, as a form of immunotherapy, to counteract the excessive immune response to gut bacteria and prevent immune system exhaustion,**" notes Dr. Cerutti. This approach could help prevent immune cells from failing to respond to vaccines after years of continuous immune activation caused by a lack of microbiota regulation provided by immunoglobulin A.

The research team believes these findings could be applied to at-risk groups for pneumococcal infections, such as individuals over 65, for whom vaccination is recommended. Additionally, the study's conclusions may extend to other vaccines as well. The researchers also point out that several clinical trials are already underway to develop treatments that address immunoglobulin A deficiency.

The study included researchers from the Vall d'Hebron Research Institute (VHIR) and the Sant Pau Biomedical Research Institute (IIB-Sant Pau), as well as the Icahn School of Medicine at Mount Sinai and Weill Cornell Medicine, both in New York, United States.

Reference article

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More information

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