

Intestinal bacteria needed for strong flu vaccine responses in mice

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Mice treated with antibiotics to remove most of their intestinal bacteria or raised under sterile conditions have impaired antibody responses to seasonal influenza vaccination, researchers have found.

The findings suggest that antibiotic treatment before or during vaccination may impair responses to certain vaccines in humans. The results may also help to explain why immunity induced by some vaccines varies in different parts of the world.

In a study to be published in *Immunity*, Bali Pulendran, PhD, and colleagues at Emory University demonstrate a dependency on gut bacteria for strong immune responses to the seasonal flu and inactivated polio vaccines.

Antibody responses to vaccines containing immune stimulating substances called adjuvants were not affected by a lack of gut bacteria. For example, bacteria were not critical for responses to the Tdap (Tetanus-Diphtheria-Pertussis) <u>vaccine</u>.

"Our results suggest that the gut microbiome may be exerting a powerful effect on immunity to vaccination in humans, even immunity induced by a vaccine that is given at a distant site," says Pulendran, Charles Howard Candler professor of pathology and laboratory medicine at Emory University School of Medicine and Yerkes National Primate Research Center.



The first author of the paper is postdoctoral fellow Jason Oh, PhD. Collaborators including Andrew Gewirtz, PhD, at Georgia State University and Balfour Sartor, MD, at the University of North Carolina contributed to the paper.

Pulendran says the impetus for this study was a previous study involving an analysis of the immune response to influenza vaccination in humans, using the "systems vaccinology" approach that his lab had pioneered. He and his colleagues had observed that in humans given the <u>flu vaccine</u>, the expression of the gene encoding TLR5, a few days after vaccination was correlated with strong <u>antibody responses</u> weeks later. TLR5 encodes a protein that enables <u>immune cells</u> to sense flagellin, the main structural protein for the whips (flagella) many bacteria use to propel themselves.

The ability of immune cells to sense flagellin appears to be the critical component affecting vaccine responses, the researchers found. Mice lacking TLR5 – but still colonized with bacteria—have diminished responses to flu vaccines, similar to antibiotic-treated or germ-free mice. Oral reconstitution of antibiotic treated mice with bacteria containing flagellin, but not with mutant bacteria lacking flagellin, could restore the diminished antibody response.

"These results demonstrate an important role for <u>gut bacteria</u> in shaping immunity to vaccination, and raise the possibility that the microbiome could be harnessed to modulate vaccine efficacy," says Pulendran. "The key question is the extent to which this impacts protective immunity in humans."

Pulendran says that his team is planning a study in humans to address this issue.

More information: *Immunity*, Oh et al.: "TLR5-mediated Sensing of *Gut* Microbiota Is Necessary for Rapid Induction and Persistence of



Antibody Responses to Seasonal Influenza Vaccination." www.cell.com/immunity/abstract ... 1074-7613(14)00303-3

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Provided by Emory University

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