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New pneumococcal vaccine approach successful in early tests
Vaccine inhibits bacteria by mimicking naturally-acquired immunity;
collaborators plan to further advance development of the vaccine candidate

[NOTE TO REPORTERS: In a 3.5-minute [video](http://vectorblog.org/affordable-pneumococcal-vaccines-that-work-globally/) <http://vectorblog.org/affordable-pneumococcal-vaccines-that-work-globally/> Malley gives some background on pneumococcal infection, its effects in the developing world, the challenges of developing useful vaccines, and other vaccine approaches his group is testing.]

Pneumococcus (*Streptococcus pneumoniae*) accounts for as much as 11 percent of mortality in young children worldwide. While successful vaccines like Prevnar® exist, they are expensive and only work against specific pneumococcal strains, with the risk of becoming less effective as new strains emerge. Through a novel discovery approach, researchers at Children's Hospital Boston and Genocea Biosciences, Inc., in collaboration with the international nonprofit organization PATH, developed a new vaccine candidate that is potentially cheaper and able to protect against any pneumococcal strain.

Tested in mice, the protein-based vaccine successfully inhibited *S. pneumoniae* from establishing a foothold in the body, the researchers report in the February 17 issue of *Cell Host & Microbe*.

The current multivalent conjugate pneumococcal vaccines work by inducing people to make antibodies against the sugars on the bacterium's outer capsule. The antibodies then help fight off development of disease after the bacteria have colonized the body. But these vaccines are complex to manufacture, requiring separate individual components for sugars produced by multiple pneumococcal strains. Since pneumococci can make more than 90 different types of sugars, the vaccines may become less effective over time.

The new protein-based vaccine takes a different approach. Based on close to a decade of research at Children's Hospital Boston and utilizing Genocea's novel vaccine discovery technology developed at Harvard Medical School, it stimulates a group of cells in the body known as T_H17 cells. These cells provide natural immunity to pneumococcal infection by clearing the bacteria from the surfaces of the upper respiratory tract where infection starts.

[Six years ago](#), Children's Richard Malley, MD, and colleagues showed in mice that while antibodies against surface proteins can protect against pneumococcal disease, there is another mechanism of protection that doesn't require antibodies: the body has natural defenses that act as security guards, preventing the bacteria from becoming squatters in the upper respiratory tract. More recently, they [showed](#) that this protection is centered in T_H17 cells and production of the chemical messenger IL-17A.

The current study, led by Malley and Kristin Moffit, MD of Children's and Todd Gierahn, PhD, and Jessica Flechtner, PhD, of Genocea Biosciences, began by evaluating a comprehensive library of *S. pneumoniae* proteins, seeking those that stimulated T_H17 cells in mice. They identified specific pneumococcal proteins that activated T_H17 cells and used them to make a new vaccine formulation.

When live mice were immunized with these antigens, they showed near-complete protection from *S. pneumoniae* upper respiratory tract colonization. These same antigenic proteins also potently stimulated human T_H17 cells from healthy adult volunteers, causing them to secrete IL-17A.

"The next steps, already in motion, are to optimize the formulation of this vaccine, confirm its efficacy and safety in animals, and then proceed to human trials," says Malley.

In further collaboration with PATH, the researchers will refine and test the most promising formulation in preclinical studies. If the vaccine proves to be effective and safe, the group will prepare an Investigational New Drug (IND) application to the FDA to begin clinical trials.

Unlike existing conjugate vaccine components, the new pneumococcal protein-based vaccine antigens are common to all strains of *S. pneumoniae*. The researchers hope that a combination of 3 to 5 antigens will protect against pneumococcal colonization and disease from all strains, thereby providing comprehensive immunity with a universal vaccine that would be significantly less complex and expensive to manufacture.

Malley believes that an approach focusing on stimulating T_H17 cells or IL-17A secretion may also be effective in providing protection against other pathogens such as *Staphylococcus aureus*, *Mycobacterium tuberculosis*, or *Listeria monocytogenes*.

"By combining advances in molecular biology, immunology and bioinformatics, the strategy we use at Genocea allows comprehensive, rapid, and unbiased screens of every protein produced by an infectious agent to identify the most effective T cell-stimulating antigens," says Flechtner. "We look forward to our continued collaboration and the development of an improved pneumococcal vaccine."

About Children's Hospital Boston

Children's Hospital Boston is home to the world's largest research enterprise based at a pediatric medical center, where its discoveries have benefited both children and adults since 1869. More than 1,100 scientists, including nine members of the National Academy of Sciences, 12 members of the Institute of Medicine and 13 members of the Howard Hughes Medical Institute comprise Children's research community. Founded as a 20-bed hospital for children, Children's Hospital Boston today is a 392-bed comprehensive center for pediatric and adolescent health care grounded in the values of excellence in patient care and sensitivity to the complex needs and diversity of children and families. Children's also is the primary pediatric teaching affiliate of Harvard Medical School. For more information about research and clinical innovation at Boston Children's visit: [Vector Blog](#).

About Genocea

Genocea Biosciences is a vaccine discovery and development company targeting major infectious diseases with high unmet medical needs, for which T cell responses help confer protection. The company's transformational discovery platform mines the natural immune response across diverse human populations in a way that radically reduces the risk, cost and time associated with antigen discovery. Genocea is currently developing vaccines for herpes simplex-2 (therapeutic and prophylactic), a sexually transmitted disease affecting roughly 15 percent of the U.S. population; Chlamydia trachomatis, a sexually transmitted disease agent causing an estimated 90 million cases worldwide; Streptococcus pneumoniae, the leading killer of children under the age of 5 worldwide; and Plasmodium falciparum (malaria), of which there are more than 100 million cases globally. Visit www.genocea.com for more information.

About PATH

PATH is an international nonprofit organization that creates sustainable, culturally relevant solutions, enabling communities worldwide to break longstanding cycles of poor health. By collaborating with diverse public- and private-sector partners, PATH helps provide appropriate health technologies and vital strategies that change the way people think and act. PATH's work improves global health and well-being. For more information, please visit www.path.org.