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Vaccination with Streptococcus mitis could protect against virulent sibling, Streptococcus pneumonia

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Vaccinating laboratory mice with *Streptococcus mitis* bacteria prevents their virulent sibling, *Streptococcus pneumoniae* from infecting the mice. The research suggests that vaccination of humans with live *S. mitis* might offer protection from some of the many serotypes of *S. pneumoniae* that vaccines currently do not exist for. This pathogen is one of the most common causes of severe pneumonia, and can also cause meningitis, bloodstream and sinus infections, endocarditis, and middle ear infections in young children. The research is published in *Applied and Environmental Microbiology*.

S. pneumoniae afflicts about 14 million children, annually, killing 2-3 million, including around a million under age five. Resistance to antibiotics is an increasing problem, underscoring the need for vaccines, according to the report. And current vaccines target only 13 of more than 90 serotypes of *S. pneumoniae*.

S. mitis, which lacks many of the virulence genes present in *S. pneumoniae*, but is otherwise quite similar, commonly inhabits the oral cavity and the upper respiratory tract, living in peaceful coexistence with the host.

The investigators intranasally vaccinated mice with two different versions of *S. mitis*, to compare their efficacy: wild type *S. mitis*, and *S. mitis* which they had genetically engineered to express a sugar coat that is

found on the exterior of the cell wall of *S. pneumoniae*. Serotype 4, they posited, might strengthen the antibody response to S. penumoniae.

Vaccination with the *S. mitis* vaccine boosted production of IgG and IgA antibodies, as well as Th17 cells (the investigators did not examine production of such antibodies and cells following vaccination with the engineered vaccine), said principal investigator Fernanda C. Petersen, DDS, Ph.D., Professor of molecular microbiology, University of Oslo, Norway.

IgG is an important antibody in the blood and other bodily fluids, and IgA is critical in secretions, especially those of the mucus epithelium of the intestinal and respiratory tracts. Th17 cells are pro-inflammatory cells that play an important role in fighting invading pathogens.

The engineered vaccine worked as expected, boosting protection against *S. pneumoniae* serotype 4, but not against *S. pneumoniae* serotype 2, as compared to the wild type vaccine.

Co-corresponding author Sudhanshu Shekhar, Ph.D., a postdoctoral researcher in Dr. Petersen's group, noted that one must be cautious in extrapolating results from mouse models to humans, and emphasized that protection of humans would remain hypothetical until human studies have been performed.

The report also noted that commensal live vaccines circumvent the main limitation of vaccinations with attenuated live pathogens: reversion to virulence.

"Bacterial live vaccines can be highly efficient because they mimic the natural infection," said Dr. Petersen. "They have been known for decades to prevent respiratory and enteric infections in humans. The main challenge, however, is to engineer attenuated versions that are safe

as vaccines, but still offering protection. Our study reveals that *S. mitis* a natural human colonizer that resembles *S. pneumoniae* but seldom causes diseases, can be the answer offered by nature for a safe vaccine against *S. pneumoniae*."

More information: Sudhanshu Shekhar et al, Intranasal immunization with the commensal Streptococcus mitis confers protective immunity against pneumococcal lung infection, *Applied and Environmental Microbiology* (2019). DOI: 10.1128/AEM.02235-18

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