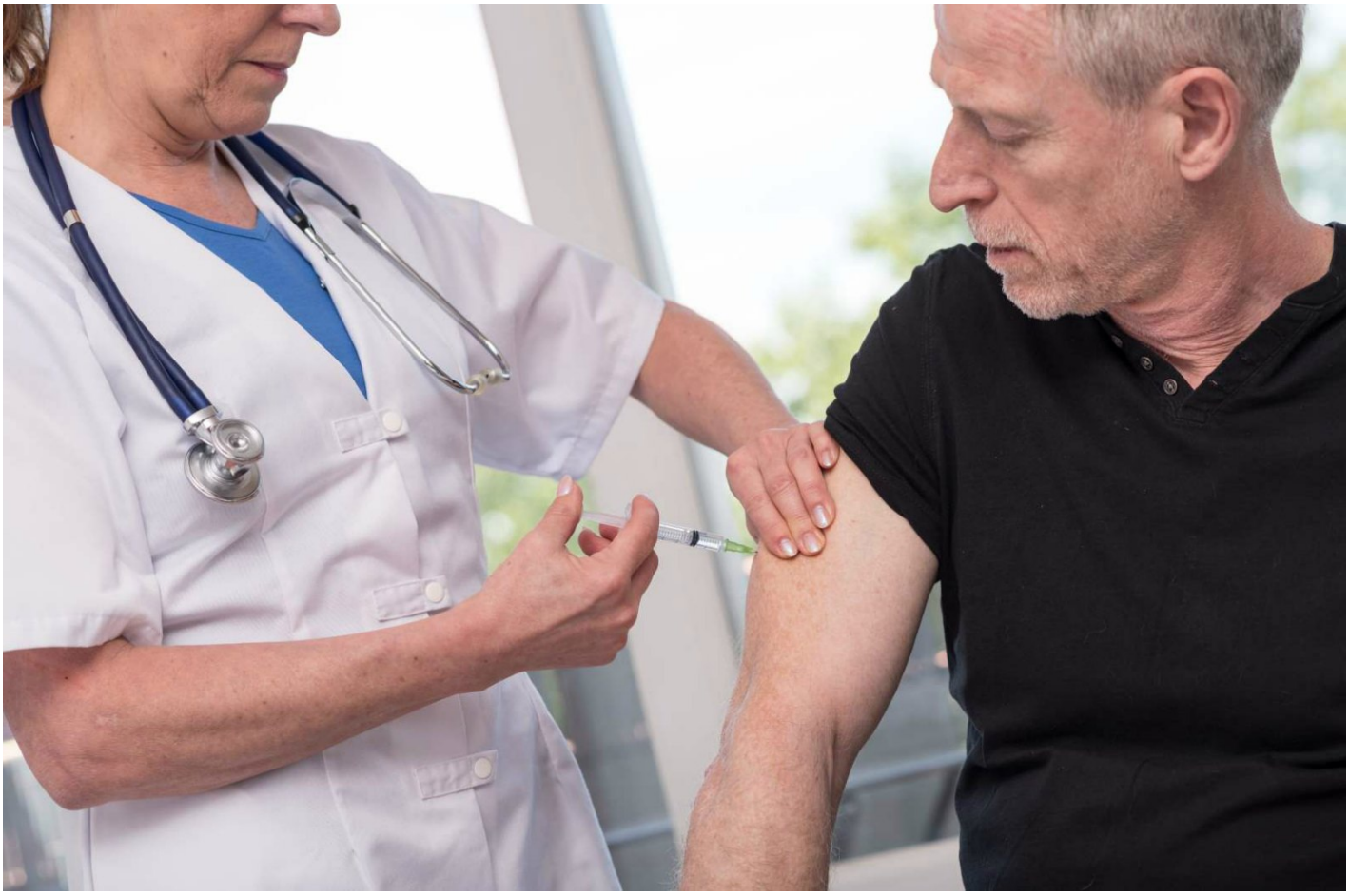
St. Jude Children's Research Hospital Tackles Universal Pneumonia Candidates

St Jude Children's Research Hospital



Pneumonia has been known for over 2,000 years, but in the United States its the most common hospital aquired infection and deadliest infectious disease, killing 40,000 to 70,000 each year.

The term "pneumonia" describes a severe inflammation of the lungs in which tissue around air spaces swells and fills with fluid. Though there are various causes, it results in fever and sharp chest pain made worse by breathing and coughing.

Pneumonia is a typical complication from seasonal influenza, and is often caused by a common bacterium, Streptococcus pneumoniae, which lives in the respiratory tract of 15 percent of the population without causing problems; howevr, it spread pneumonia only when inhaled deeply into the lungs. Germ travel to others through coughing, sneezing, and even talking in close proximity. Bacterial pneumonia is most common in winter and spring, when upper respiratory tract infections are frequent.

Bacterial pneumonia has been treated often with antibiotics, which lowered the pneumonia death rates in the United States 40 percent from 1936 to 1945. The more common viral pneumonia usually diminishes on its own, but all strains of pneumonia can be serious if neglected.

Current pneuminia vaccines only protect against a few of the over 100 serotypes, and many high-risk patients do not routinely receive them. Researchers at St. Jude Children's Research Hospital are working on Universal Pneumonia Candidates.

Live Vaccine Candidate (SJ-11-0001)

Jason Rosch, PhD, Department of Infectious Diseases, discusses St. Jude's Universal Live Attenuated Streptococcus Pneumonia Bacteria Vaccine and how it protects against pneumonia, acute sinusitis, and otitis media. It consists of a genetically modified bacterium that is unable to cause tissue damage or massive inflammation, does not translocate to the blood stream and is rapidly cleared from the body. Another advantage over currently approved vaccines is its ability to recognize bacteria independent of different serotypes, whereas approved vaccines only cover 13 of the over 100 serotypes. Our vaccine generates antibodies against both the bacteria's polysaccharide capsule and the bacteria's serotypes, or protein targets.

> *Acute otitis media caused by Streptococcus pneumoniae remains one of the most common infectious diseases worldwide despite widespread vaccination.*

A major limitation of the currently licensed pneumococcal vaccines is the lack of efficacy against mucosal disease manifestations such as acute otitis media, acute bacterial sinusitis, and pneumonia. We sought to generate a novel class of live vaccines that are fully attenuated and retain all major antigenic virulence proteins.

A live vaccine candidate based on deletion of the signal recognition pathway component ftsY induced potent, serotype-independent protection against otitis media, sinusitis, pneumonia, and invasive pneumococcal disease. Protection was maintained in animals coinfected with influenza virus, but was lost if mice were depleted of CD4+ T-cells at the time of vaccination. Compared to the commercial conjugate vaccine that promotes IgG1 production in mice, the live vaccine induced a strong serum IgG2a and IgG2b response that correlated with CD4+ T-cell mediated class switching. Deletion of genes required for microbial adaptation to the host environment is a novel strategy for development of live, attenuated vaccines that retain potentially antigenic virulence factors.

Attenuated Vaccine Candiate (SJ-05-0036, SJ-10-0028, SJ-13-0032)

Researchers at St. Jude are also working on a vaccine comprising synthetically linked domains of choline binding protein A (CbpA) from Streptococcus pneumonia and a new type of pneumococcus vaccine component in which a T-cell epitope (e.g. PneuImolysin toxoid) is fused to immunogenic fragments of choline binding protein A (CbpA). This new fused vaccine component provides an easier, less costly and more efficient way to elicit an immune response to both the T-cell epitope and CbpA as compared to a mixture of separate antigens. The CbpA fragment used preferably comprises synthetically linked domains of CbpA.

The CbpA peptide-pneumolysoid fusion construct is a viable broadly protective pneumococcal vaccine that potentially adds protection against other meningeal pathogens; and may be useful for treating or preventing infections such as sepsis, meningitis, and pneumonia. Also, SJ-13-0032, “YLN for Cardiac Indication,” involves using these vaccine components to avoid adverse cardiac events caused by pneumonia infections (This is co-owned with Univ. of Texas Health Science Center.) These cardiac events are common and deadly and can create a "ticking time bomb" scenario.

To see available technologies from research institutions, click here to visit the AUTM Innovation Marketplace.