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Immunization with Mixtures of Pneumococcal Virulence Molecules Can Prevent Pneumococcal Disease

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Streptococcus pneumoniae is still a major cause of morbidity and mortality in both the developed and developing world. Problems with this disease have been aggravated by the increasing rate of antibiotic resistance among pneumococci. Vaccines have been developed for both adults and children. The vaccine for adults is of low efficacy in high risk populations and is not effective in young children, a group that has over 1 million deaths a year in some of the poorest countries in the world. The vaccine for children contains only 7 of the 91 known capsular types. This vaccine is quite expensive >$200 per child and pneumococcal disease in children is beginning to evolve around the vaccine by shifting to some of the types not in the vaccine.

One way around this problem is to develop a vaccine based on highly cross-reactive protection-eliciting pneumococcal proteins. Since the vaccine would be made of recombinant proteins it should be inexpensive to produce. However, since the proteins are not quite as protective as a strong response to the capsular polysaccharide, it appears that more than one protein will be required. Our data indicates that mixtures of more than one protein can increase protection by 10-100 fold.

One protein that has been long considered for use in such as vaccine is pneumococcal surface protein A. This protein inhibits complement fixation and antibodies to the protein reverse this effect. The protein also protects against killing of pneumococci by lactoferrin, which is present in secretions. Antibody to PspA also blocks this inhibition and therefore enhances killing of pneumococci in saliva by lactoferrin.