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Mucosal immunization with an unadjuvanted vaccine that targets *S. pneumoniae* PspA to human FcγRI protects against Pneumococcal infection via complement- and Lactoferrin-Mediated Bactericidal Activity

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Targeting antigen (Ag) to Fc receptors (FcR) can enhance the immune response to Ag in the absence of adjuvant. Furthermore, we recently demonstrated that intranasal (i.n.) immunization with FcR-targeted Ag enhances protection against a Category A intracellular mucosal pathogen, *Francisella tularensis*. To determine if a similar strategy could be applied to the important pathogen *Streptococcus pneumoniae*, we used an improved mucosal FcR-targeting strategy that specifically targets only human FcγR Type I (hFcγRI). A humanized single chain antibody (Ab) component in which the variable domain binds to hFcγRI [anti-hFcγRI (H22)] was linked in a fusion protein to pneumococcal surface protein A (PspA). PspA is known to elicit protection against pneumococcal sepsis, carriage, and pneumonia in mouse models when administered with adjuvants. Anti-hFcγRI-PspA or rPspA alone were used to immunize i.n. wildtype (WT) and hFcγRI transgenic (Tg) mice in the absence of adjuvant. The hFcγRI Tg mice receiving anti-hFcγRI-PspA exhibited elevated *S. pneumoniae*-specific IgA, IgG2c, and IgG1 Ab in sera and bronchoalveolar lavage. Neither immunogen was effective in protecting WT mice in the absence of adjuvant, but when PspA was targeted to hFcγRI as the anti-hFcγRI-PspA fusion, enhanced protection against lethal *S. pneumoniae* challenge was observed in the hFcγRI Tg mice, as compared to mice given non-targeted rPspA alone. Immune sera from the anti-hFcγRI-PspA-immunized Tg mice showed enhanced complement C3 deposition on bacterial surfaces and protection was dependent upon an active complement system. Immune sera also showed enhanced lactoferrin-bactericidal activity directed against *S. pneumoniae*. These studies were supported by NIH grants R01AI07640801 and R21AI06547601.

Biography

Edmund Gosselin received his Ph.D. in Medical Sciences at the University of Massachusetts, Worcester, MA, in 1988. He completed a postdoctoral fellowship at Dartmouth Medical School in 1993, where he focused on targeting Ag to FcR on APC to enhance T cell activation. Dr. Gosselin then moved to Albany Medical College, where his research has focused on the development of FcR-targeted immunogens as an adjuvant-independent approach for mucosal vaccination. In 2008, he published the first paper demonstrating that immunogens targeted to FcR intranasally can enhance protection against subsequent challenge with a mucosal Category A intracellular pathogen, *F. tularensis*.