Staphylococcus aureus Vaccine

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Staphylococcus aureus, an important bacterial pathogen in the hospital and in the community, causes a myriad of infection types, including bacteremia, endocarditis, pneumonia, osteomyelitis, and skin and soft tissue infections. *S. aureus* has become increasingly resistant to multiple antibiotics, and thus non-antimicrobial approaches to controlling this microbe are clearly needed. Because many individuals who are susceptible to staphylococcal infections are not competent to mount an effective immune response, passive as well as active immunization strategies have been explored. Numerous single-component *S. aureus* vaccines or immunotherapies have failed to meet their clinical endpoints in human phase III clinical trials: a capsular polysaccharide-based vaccine (StaphVAX), a human IgG preparation (Veronate) with elevated levels of antibodies to clumping factor A, a *S. aureus* protein (IsdB) vaccine, and a humanized monoclonal antibody to lipoteichoic acid. There is no evidence that natural infection by *S. aureus* leads to an adaptive immune response that protects against re-infection. Thus, inducing immunity to *S. aureus* by a vaccine approach presents a unique challenge. Given the multiple and often redundant nature of staphylococcal virulence factors that promote pathogenesis, if a vaccine is to prove effective, it will most likely be comprised of multiple components and target multiple immunologic mechanisms. Likely candidates include cell wall-associated proteins, secreted toxoids, and surface polysaccharides. A thorough understanding of the immune correlates of protection against *S. aureus* infection is sought, but this is accomplished in large part by preclinical vaccination studies in imperfect rodent models of staphylococcal disease. Whether the data obtained in these preclinical studies will predict protection against infection in humans is uncertain. Phase I and II clinical trials in progress test multicomponent vaccines designed to elicit opsonic and toxin-neutralizing antibodies, as well as memory T cells capable of enhancing phagocyte recruitment to sites of infection, thereby facilitating clearance of the

organism from tissues. Only by testing this second-generation vaccine approach against *S. aureus* in phase III clinical trials will its merit be demonstrated.