Vaccines in the 21st Century: Gene-Based Vaccines

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Gene-based vaccines are being developed for prophylaxis and therapy of diseases that have not been successfully addressed by traditional vaccine approaches. The targets for these vaccines include not just infectious diseases but also autoimmune diseases, allergy, and cancer. Gene-based vaccines include plasmid DNA and other polynucleotides (both RNA and DNA), heterologous viral vectors, and bacterial expression vectors. The rationale for these vaccines includes the desire to generate different types of immunity (e.g., MHC Class I-restricted cytolytic T lymphocytes) than can be generated by, for example, recombinant proteins. These vectors can result in the production of both humoral and cellular immune responses, and thus target both accessible (i.e., generally external) antigens, as well as internal or structural proteins that tend to be more highly conserved between different strains of the pathogen. In addition, gene-based vaccines can stimulate novel immune responses based on the nature of the vector itself; for example PAMPs (Pathogen Associated Molecular Patterns) of the vectors stimulate innate immune responses, which in turn augment the antigen-specific immunity directed against the antigen encoded by the vector. Licensed gene-based vaccines to date have been limited to those for veterinary use. Human clinical trials of gene-based vaccines have demonstrated immunogenicity, but have largely been disappointing in terms of potency. Recent improvements in potency have been seen with prime-boost regimens, wherein different modalities are used for the priming and boosting immunizations, such as a DNA plasmid prime followed by a viral vector or recombinant protein boost. Additional changes have been made to the vectors and delivery systems resulting in increased potency. Improvements of gene-delivery vaccines will be discussed and examples and rationale provided.

Staphylococcus aureus vaccines: where are we now?

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Staphylococcus aureus is a commensal Gram-positive bacterium which persistently or intermittently colonizes most healthy adults, and yet globally is one of the most important causes of nosocomial infection. S. aureus is estimated to be responsible for 20-25% of all healthcare-associated infections,1 the manifestations of which range from skin and soft-tissue infections to life-threatening sepsis, in addition to toxin-mediated diseases. Healthcare-associated S. aureus infections result in 3 times the length of hospital stay, and 5 times the risk of in-hospital death as patients without S aureus infection.2 In comparison to other organisms, S. aureus infections result in longer average duration of treatment and hospitalization, and mortality rates as high as 25%.3 Over the past 15 years, rates of healthcare- as well as community-associated S. aureus infections have increased, largely due to the emergence and spread of epidemic MRSA strains. Infection control practices directed at the spread of MRSA have resulted in widespread and varied approaches to the screening and treatment of patients admitted to healthcare facilities. Despite such measures, the estimate from US Nationwide Inpatient Sample (NIS) data is that approximately 1% of all US hospitalizations involve S. aureus infections, at a cost of $14.5 billion, with $12.3 billion attributable to postsurgical S aureus infection alone.4 The SENTRY surveillance system reports S. aureus as the most prevalent cause of bloodstream infection (22%), lower respiratory infection (23%), and skin and soft tissue infection (39%), as well as overall infection throughout North America, Latin America, Europe, and Western Pacific nations.5 In many parts of the world, including the US as well as Asian nations of Japan, Korea, Taiwan, Hong Kong, Singapore, and Sri Lanka, healthcare-associated MRSA infections are now responsible for the majority of S. aureus infections. True vancomycin-resistant S. aureus (VRSA) has emerged during the last decade, and will likely increase over time and with more extensive antibiotic usage. The need for an effective vaccine to prevent S. aureus infection is clear.