Preface

Most pathogens exploit mucosal surfaces for entry into the host, and vaccines which most effectively concentrate immune effectors in tissues at these sites are those which are most likely to provide optimal immune protection: complete blocking of pathogen entry or local elimination of the pathogen in the tissue before it spreads. The superior potential to accomplish this by applying vaccines directly to a mucosal surface is the overarching advantage of mucosal vaccination over conventional intramuscular vaccination. But mucosal vaccine development is challenging because vaccine must be able to penetrate epithelial barriers and to survive luminal innate defenses. The present book collects a group of articles that review advances in mucosal vaccine delivery strategies and formulations. Regulatory issues, safety concerns, and advances in manufacturing are integral components of these reviews.

Success in the development of a mucosal vaccine requires that mucosal tissues be recognized and approached as separate entities. Each is unique overall with regard to its physiological function, luminal defenses, environmental stimuli (including commensals), the types of epithelia present, lymphoid organization, and endocrine influences. Local vaccination typically elicits the greatest immune responses within each compartment, but cross-talk can be negligible. This must be considered when local immunization is impractical and alternative delivery routes are being contemplated. In the first chapter of this volume, Czerkinsky and Holmgren review the mechanisms responsible for regionalization within the mucosal immune system and address other critical factors that should be taken into account when designing and evaluating mucosal vaccines. The mucosal tissues most effectively seeded by antigen-specific lymphocytes after immunization by different routes are reviewed, with an emphasis on the ability to populate numerous distal tissues using the sublingual route, which may have considerable advantages over the nasal route in terms of safety.

Needle-free topical application of antigen with appropriate adjuvant on the skin can also induce mucosal immune responses and may be an ideal delivery strategy for vaccines that are especially susceptible to denaturation in the mucosal lumen. In the following chapter, Lawson, Clements and Freytag review the transcutaneous

immunization route and the adjuvants, including toll-like receptor agonists, which have proved effective for inducing mucosal responses using this route. Notably, enterotoxin adjuvants can be safely administered to humans by the transcutaneous route and may be optimal for generating cellular and humoral immunity in the gastrointestinal, respiratory or female genital tract.

Vaccine platforms and formulations for the delivery of mucosal vaccines are the focus of the next five chapters. Yamamoto, Pascual and Kiyono review recently identified molecules that facilitate the delivery of oral or nasal vaccines specifically to intestinal or tonsillar M cells, which may be the most efficient antigen-sampling cells in the body. Schneider-Ohrum and Ross describe the production and use of recombinant noninfectious virus-like particles (VLP) to generate protective immunity against specific viruses or co-expressed foreign antigens, while McNeela and Lavelle review new formulation strategies that improve mucosal uptake of polymer-based microsphere and nanoparticle delivery vehicles. Mason and Herbst-Kralovetz discuss advances in the manufacture of plant-based vaccines and the challenges associated with the development of edible vaccines. In turn, Hickey and Staats discuss the advantages of dry vaccines over liquid formulations for pulmonary or nasal immunization. Invaluable information on the manufacture of powder vaccines, absorption enhancers, mucoadhesives, delivery devices and methods for evaluating safety in the respiratory tract is also included.

The final chapters review two of the greatest challenges in vaccine development: human immunodeficiency virus type 1 (HIV-1) and biodefense weapons. There is no longer any doubt that HIV is a mucosal disease and optimal vaccine-mediated protection will likely require that immune effectors be established not only at mucosal portals of entry but also throughout the gastrointestinal tract, which is home to the largest reservoir of HIV target cells. Belyakov and Ahlers review vaccination strategies that have augmented HIV-specific immunity in the intestinal mucosa and increased the protective efficacy of immunodeficiency virus vaccines. Mantis, Morici and Roy discuss the unique and daunting hurdles facing the development of biodefense vaccines for the numerous microbes and toxins that have been deemed potential biothreats in the respiratory or gastrointestinal tract. It is clear from the reviews in this volume that significant progress has been made in mucosal vaccination strategies over the last decade. However, further basic research on mucosal host defense mechanisms, adjuvants, and delivery vehicles is still needed for the optimal design of mucosal vaccines and prevention of infectious diseases.

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