Nanoparticulate Vaccine Delivery Systems

edited by
Martin J. D’Souza
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In recent years, there has been an unprecedented explosion of research and applications in the field of nanotechnology. Nanotechnology has the potential to significantly improve the prevention, detection, and treatment of diseases. There is a tremendous amount of excitement, that this field of nanotechnology will build momentum and produce new avenues for the treatment of diseases. Inherent to this optimism, are the related challenges in the areas of medical applications. For example, it is difficult to adequately assess the biological effects of nanoparticles due to the fact that because of their small size, their properties may be rather unpredictable in the body. Further, changes in the overall nature and properties, route of administration, and dose administered can significantly affect the response and toxicity. Despite the fact that better-engineered and much more sophisticated nanomaterials will continue to be evaluated and utilized to a greater extent in the future for a wide range of biomedical applications, there is also a growing concern that unexpected toxicity may arise from desired properties, such as higher hypersensitivity, and accessibility to cells, which newer materials possess in the nano range.

This book addresses novel nano and micro-vaccines that can be administered orally or via the transdermal route. The proposed oral vaccines can be administered in the form of suspensions or capsules. Also, research focused on improving stability, biocompatibility and limiting toxicity with novel nanoparticles are discussed. This book discusses at length, vaccines for two major classes of diseases: (1) infectious diseases and (2) cancer vaccines.

Advances in nanotechnology have paved the way to the discovery of innumerable methods for prevention or treatment of various diseases. Its impact on immunotherapy potentiates vaccine delivery and efficacy. Immunotherapy is a specialized method of eliminating diseases, where it primes the immune system to combat foreign antigens (in case of infectious diseases) or self-antigens (in case of cancer). It has withstood the test of time and
has been a cost-effective mechanism to prevent or treat diseases. With the evolution of different challenging diseases, and the identification of cancer antigens, there is an urgent need for vaccine development to save lives of millions throughout the world. Moreover, in case of existing vaccines, there is still a need to address issues with respect to safety, effectiveness, ease of administration, time of preparation, and, most importantly, the cost. Recent developments in immunology and molecular biology explore new vaccine materials and aim at triggering memory response to vaccines. The threat of cancer and its metastatic incidences has been a concern for over a century, and attempts to combat this “smart disease” have not yet paved the way for successful cancer therapy. Surgery and chemotherapy have not succeeded in eliminating tumor cells, which results in relapse of tumors within a few years of post-treatment in various cancers. Several clinical studies in cancer vaccines are under way and most of them have not progressed beyond phase III studies. It has been observed that even though antigen-specific response is obtained with different approaches of antigen specific immunization, there is no consistency in clinical benefit. Recently, a therapeutic prostate cancer vaccine (Provenge®) was introduced into the market in April 2010 by Dendreon Corporation (Seattle, WA), which involves isolating white blood cells from prostate cancer patients and stimulating them ex vivo. The cells are activated with a prostate-specific fusion protein and are then re-introduced into the patient. This procedure when carried out three times was found to result in marginal increase in median survival rate of prostate cancer patients by 4 months in clinical trials. These approaches are encouraging. However, the cost for the vaccine is over $90,000. Therefore, there is an urgent need to find new and, more importantly, affordable approaches. Unlike infectious disease vaccines, cancer vaccines need to be custom-designed for individual patients because of the diverse gene mutations in cancer cells. Therefore, cancer vaccine development requires a design that is rapid and potent and can be used to develop custom-designed vaccines for individual patients. Among various approaches being evaluated to combat cancer, microparticulate vaccine using whole cell lysate provides a unique and the simplest strategy, as microparticles represent a promising approach to deliver antigens to immune cells. Although specific antigen cancer vaccines or dendritic cells pulsed with antigens are now used due
to the advancement in recombinant technology and gene expression, the whole cell lysate vaccine still remains a very promising approach, as it can overcome the demerits associated with a single antigen/epitope vaccine. Whole cell lysate provides a pool of tumor-associated antigens (TAAs), which can induce both CD8+ and CD4+ T cells.

This book addresses many of the problems associated with the current vaccine therapies such as time involved in vaccine preparation, specific antigen isolation/purification, and the high vaccine costs. Therefore, cancer immunotherapy is being evaluated in conjunction with chemotherapy. The microparticulate system has several advantages over the use of the antigens by themselves without incorporation into a delivery vehicle. It has been demonstrated that particulate antigens are more immunogenic when compared to soluble antigens. Improved uptake of the particles compared to the solution results in higher cytotoxic T-lymphocyte response against the cancer cells. Another potential advantage of the microparticulate delivery system is that various immunopotentiators can be included in the delivery systems to enhance the immune response. The microparticulate delivery systems are of similar dimension as compared to a pathogen. The antigen-presenting cells in the body easily phagocytose these microparticles and generate a robust immune response. Although various cancer antigens are being identified and evaluated for cancer immunotherapy, there is still a concern with the lack of progress in formulation and routes of administration currently used. In this book, we present nano- and microparticulate carrier systems, which can deliver the antigens effectively to generate an immune response via non-invasive routes such as oral and transdermal administration.

Transdermal microneedle-based particulate vaccine delivery is an attractive mode of immunization because of its ease of administration and requires no specially trained personnel and thus may eliminate many problems associated with needle injections. Briefly, the microneedle device creates microchannels to allow passage of the vaccine particles into the dermis and thus initiating vaccine response due to particle uptake by immune cells. Transdermal delivery is considered a promising route for vaccine administration because of the skin-associated lymphoid tissue, which comprises the Langerhans cells, dermal dendritic cells,
lymph nodes, and subsets of T-lymphocytes. The microparticles are taken up by these immune cells in the skin, which trigger mucosal as well as systemic immune response. Langerhans cells are dendritic cells that activate T cells and induce a strong immune response and occupy around 20% of the skin’s area. They can induce immunity by either endogenous antigen or exogenous antigen uptake. The endogenous antigen is processed and presented by MHC Class I to CD8+ T cells and MHC Class II presents the exogenous antigen to CD4+ T cells. Also, the vaccine microparticles can generate better immune response when compared to the solution form. The microparticles are prepared using a single-step process with the use of a spray dryer. Avoidance of organic solvents and minimal exposure of antigens to high temperatures during spray drying techniques ensured retention of their bioactivity. This book discusses oral vaccines for infectious diseases such as tuberculosis, typhoid, influenza, pneumonia, meningitis, and hepatitis B, as well as vaccines for cancers such as melanoma and prostate, breast, and ovarian cancer. The vaccine particles for oral administration can be formulated using enteric biodegradable material. The oral microparticles are targeted to M cells of Peyer’s patches of small intestine using M cell targeting ligands, which generates immune response via immune cells in gut. Thus, the oral as well as transdermal microparticulate vaccines described in this book provide a promising approach in terms of cost-effectiveness, ease of production, and patient compliance.

In summary, this book presents the most recent advances in the field of vaccines and will serve as a useful tool for both researchers and students to further their knowledge in the field of vaccines for both cancer and infectious diseases.