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Particle-based vaccines for transcutaneous vaccination

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Abstract

Immunization concepts evolve with increasing knowledge of how the immune system works and the development of new vaccination methods. Traditional vaccines are made of live, attenuated, killed or fragmented pathogens. New vaccine strategies can take advantage of particulate compounds—microspheres or nanoparticles—to target antigen-presenting cells better, which must subsequently reach the secondary lymphoid organs, which are the sites of the immune response. The use of the skin as a target organ for vaccine delivery stems from the fact that immature dendritic cells (DCs), which are professional antigen-presenting cells can be found at high density in the epidermis and dermis of human or animal skin. This has led to design various methods of dermal or transcutaneous vaccination. The quality and duration of the humoral and cellular responses to vaccination depend on the appropriate targeting of antigen-presenting cells, of the vaccine dose, route of administration and use of adjuvant. In this review, we will focus on the use of micro- and nano-particles to target the skin antigen-presenting cells and will discuss recent advances in the field of transcutaneous vaccination in animal models and humans.

Keywords: Nanoparticles; Skin; Immune responses; Vaccination

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Résumé

Les concepts d'immunisation évoluent avec nos connaissances approfondies du fonctionnement du système immunitaire et des nouveaux développements technologiques. Les vaccins conventionnels sont composés de pathogènes vivants atténués, tués ou fragmentés. Les nouvelles stratégies vaccinales peuvent tirer profit des composés particulaires des pathogènes-des microsphères ou des nanoparticules-pour améliorer le ciblage des cellules présentatrices d'antigène, qui doivent migrer vers les organes lymphoïdes secondaires où la réponse immunitaire est initiée. L'intérêt d'utiliser la peau comme organe cible pour la vaccination vient du fait que l'on retrouve de forte densité de cellules dendritiques immatures dans l'épiderme et le derme de la peau humaine. Ceci a mené à concevoir de diverses méthodes de vaccination par les voies intradermiques ou les voies transcutanées. L'intensité et la qualité des réponses immunitaires dépendent de l'optimisation de la vaccination par ces nouvelles voies, *i.e.* de l'immunogène, de la dose vaccinale et de l'adjuvant utilisé. Dans cette revue, nous discuterons l'utilisation des microparticules ou de nanoparticules permettant de cibler les cellules présentatrices d'antigène et des avancés récentes dans le domaine de la vaccination transcutanée dans les modèles animaux et chez l'homme.

Mots clés: Nanoparticules; Peau; Vaccination; Réponses immunitaires

1. Immunology of the skin

1.1. Why skin immunization?

Activating the immune system is the major challenge to be faced in vaccine development. The presentation of vaccine-derived antigen to the immune system is a rather inefficient process that is limited by the availability of functionally active antigen-presenting cells (APCs) at the site of inoculation. The muscle, a traditional site of vaccination, is not considered to be an efficient site for antigen presentation due to the lack of suitable quantities of APCs, whether dendritic cells (DCs) or macrophages [1]. In addition, myocytes lack expression of MHC-Class II and costimulatory molecules and thus cannot directly prime T cells. Adjuvants are therefore necessary to increase DC activation and infiltration into or around the intramuscular (IM) vaccination sites [2–6]. In contrast, the skin is one of the largest immune organs and is rich in potent APCs such as Langerhans cells (LCs) in the epidermis and DCs in the dermis [7–9]. These cells can efficiently initiate primary immune responses both *in vitro* and *in vivo* [8]. Thus, the skin appears to be a good target organ to generate cellular and humoral immune responses [7]. Many studies have found that intradermal (ID) immunization allows using quite smaller doses of antigen than IM immunization, probably because of the better availability of APCs at the site of inoculation [10–12].

In order to induce both a robust cellular and humoral immunity to combat cancer and infectious diseases, efforts need to be made in the administration and formulation of vaccines. Modern biotechnology has enabled the development of