

Mucosal vaccines: Strategies and Challenges

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Abstract

Adjuvant, Nasal vaccination, Mucosal immune response, and Drug delivery method avenues for administration, Immunological reactions at the mucosa specific tactics By evoking immune response in both mucosal and systemic tissue to guard against pathogen invasion at mucosal surfaces, mucosal vaccination has the potential to be more advantageous than standard parenteral immunisation. Mucosal vaccines, which have been designed to offer a first line of defence at these entrance ports, show great potential for lowering the burden of infectious illnesses. However, there have only lately become a few mucosal vaccinations accessible. This study provides an overview of current developments in a few key areas related to mucosal vaccination, such as suitable delivery routes, acceptable formulations, antigen-sampling and immunological responses of mucosal immunity, as well as methods for enhancing the efficiency of mucosal vaccines. Lastly, the difficulties in creating effective mucosal vaccinations and possible solutions are discussed.

Since mucosal surfaces are constantly in contact with the outside world, they constitute the body's greatest lymphoid organ. Gut-associated lymphoid tissues (GALTs), such as Peyer's patches and isolated lymphoid follicles, are crucial for the generation of antigen-specific immune responses in the gut in the mucosal immune system. GALTs interact with the network of T cells and dendritic cells to simultaneously induce and regulate IgA responses and oral tolerance due to their distinct organogenesis properties. Antigens are picked up by M cells in the epithelial layer of these lymphoid organs, and GALT cells then start antigen-specific immune responses. The respiratory tract's main organised lymphoid structures, the nasopharynx and tear duct-associated lymphoid tissues (NALTs and TALTs), respectively, have been shown to interact with each other. The development of mucosa-associated lymphoid tissues, as well as the induction and control of innate and acquired mucosal immune responses, are all influenced by host-microbe interactions on mucosal surfaces.

Keywords: Adjuvant; Nasal vaccination; Mucosal immune response; Administration methods; Mucosal immune responses specific tactics

Introduction

Beyond the vaccinated persons, vaccinations have a significant influence on the prevention and treatment of infectious illnesses. The achievement of a level of coverage adequate to halt disease transmission is necessary for the vaccination programme to be successful overall. The mucosa, which serves as the barrier between the inside of the body and its external environment, does in fact allow the majority of infectious agents or antigens to enter the body. Numerous pathogens, including rotaviruses (RVs) and influenza viruses, which infect the GI and respiratory tracts, respectively, are to blame for a significant portion of the world's illness burden and the high morbidity and death rates they cause in both people and animals [1]. The currently approved vaccinations, however, are injected subcutaneously or intramuscularly and delivered via systemic pathways. Traditional vaccination methods are efficient in triggering protective systemic immune responses, but it is challenging to trigger antigen-specific immune reactions at mucosal surfaces. In order to combat viruses that enter the body through mucosal locations, mucosal vaccines are given a lot of attention [2].

The demand for vaccinations against many of the diseases that infect or emerge from mucosal tissues is still quite considerable. The infections may only cause disease after spreading to non-mucosal tissues, as is the case with the poliovirus and Salmonella typhi, but more frequently, they exert their pathogenic effects locally on the mucosal tissue. By generating more than 3 billion illness episodes and 3 million fatalities annually, these diseases collectively have a major detrimental effect on world health. They also pose a major obstacle to the creation of vaccines [3]. Although parenteral immunisation can occasionally provide protection against mucosal infections, mucosal vaccination is often required. Mucosal vaccinations would generally be simpler to manufacture, less likely to spread illnesses, and easier to give compared

to injectable immunizations. However, compared to the more than 30 injectable vaccinations, there are still very few mucosal vaccines for human use [4].

Differential mucosal permeability

The permeability of mucosal tissues to serum-derived antibodies varies. The small intestine is basically impermeable to blood proteins unless it is afflicted by inflammation, in contrast to the lower respiratory tract and the female genital system, which are both rather permeable. In line with this, injectable pneumococcal vaccinations can offer some protection against lung pneumonia in addition to providing protection against blood-borne infection through the transudation of serum anti-capsular antibodies. Contrarily, non-inflammatory small intestine illnesses like cholera and enterotoxin genic Escherichia coli (ETEC) infection are instances of which vaccine protection is mediated by locally generated secretory IgA (SIgA) antibodies and often needs oral-mucosal delivery [5].

Invasion and inflammation

Parenteral vaccination may also be effective against enteric

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infections, such as Shigella bacteria, that enterocytes from the basolateral side, where serum-derived antibodies are in touch with them, through Peyer's patch 'M' cells. The majority of Salmonellae spp. and Campylobacter jejuni are two examples of pathogens that may be efficiently attacked by serum antibodies after causing inflammation in the sub mucosal lymphoid tissues, other examples include S. typhi and the polio virus [6].

Mucosal immunological priming

Another factor is prior exposure to the pathogen, which results in mucosal priming. Even while the traditional injectable whole-cell cholera vaccines never produced a strong or long-lasting immunity, they were able to provide a small level of protection for a few months in the elderly population in cholera-endemic areas. In the same way, parenteral polio immunisation may lessen faecal transmission in areas where polio is endemic in addition to protecting against paralysis. These outcomes are explained by the vaccines' capacity to elicit protective SIgA antibody responses in people who have already been primed by natural mucosal exposure in the gut [7].

Choice of mucosal vaccination route for site-directed immune responses

Initially, it was believed that immune responses triggered at one mucosal location would spread extensively to adjacent mucosal tissues. Later research, however, has demonstrated the mucosal immune system's high anatomic compartmentalization, which is connected to the migratory characteristics of lymphocytes activated at various mucosal locations. This places clear limitations on the selection of the mucosal vaccination delivery method [8].

Discussion

Chemokines, cytokines, and their receptors have a large therapeutic promise since they are crucial for lymphocyte formation, migration, function, and homeostasis. The co-delivery of chemokines and cytokines as vaccination adjuvants may have a major impact on immune responses and challenge results, according to promising preclinical findings from our group and others. After parenteral immunisation, the reported prime-and-pull approach of administering chemokines to mucosal surfaces to attract activated lymphocytes to pertinent mucosal surfaces has shown notable preclinical success. However, there haven't been many clinical investigations looking at the impact of co-administering chemokine or cytokines with vaccines. We have found that co-delivery of plasmids expressing human interleukin-12 (IL-12) improves cellular and humoral responses to synDNA antigens in susceptible individuals in the field of infectious diseases [9].

Large numbers of chemokines and cytokines may be required to mediate in vivo effects, but their large-scale manufacturing is technically difficult. Here, we took advantage of the synDNA platform's special capacity to parentally co-deliver chemokine and antigen in vivo. Our findings show that immune cell exposure to antigen and mucosal chemokines changes their trafficking patterns and promotes improved mucosal immunity in vivo [10,11].

Conclusion

Mucosal immunity and mucosal vaccines haven't received their fair share of research and development for a long time. Mucosal vaccine development has seen a sharp rise in interest as a result of recent breakthroughs in our understanding of the mucosal immune system and methodological advancements in the measurement of

local immune responses, including antibodies and cell-mediated immunity. Several novel mucosal vaccines, including potential better replacements for current vaccinations and vaccines against additional mucosal illnesses, such as, for example, ETEC diarrhoea, shigellosis, and calicivirus infections, are in various phases of clinical development.

However, the development of a broader range of mucosal vaccines, especially subunit vaccines based on purified antigens, will require access to improved antigen delivery systems as well as effective adjuvants. Significant advances have recently been made in both of these fields leading to products that are now in clinical testing. Still, their usefulness in genetically diverse human subjects who also may differ significantly in their intestinal flora, nutritional status and previous immunological experience, all of which are factors that have been found to affect mucosal vaccine efficacy, remains to be defined.

However, access to better antigen delivery mechanisms and efficient adjuvants will be necessary for the development of a wider variety of mucosal vaccines, particularly subunit vaccines based on purified antigens. Both of these domains have lately seen significant progress, resulting in technologies that are currently undergoing clinical trials. Although these variables have been proven to impact the efficiency of mucosal vaccines, their utility in genetically varied human patients who may also differ greatly in their gut flora, nutritional condition, and prior immunological experience is yet unknown.

It is noteworthy that two recently developed mucosal vaccines for human use, a first-generation live attenuated oral rotavirus vaccine (RotaShield) and a nasal influenza subunit vaccine given together with (unmodified) E. coli LT as adjuvant were withdrawn after a short period on the market due to adverse reactions. Despite the fact mucosal vaccine administration in general is safer than parenteral vaccination. This emphasises how tricky it is for all vaccinations to balance adjuvant and vaccine effectiveness with safety and widespread acceptance.

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None

Conflict of Interest

The authors have no conflict of interest to declare.

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