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Short Communication

Evaluating the Longitudinal Antibody Response Following a Novel Prime-Boost Vaccine Regimen for Respiratory Syncytial Virus

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Description

The Respiratory Syncytial Virus (RSV) is a major respiratory pathogen responsible for significant morbidity and mortality worldwide, especially in young infants, immunocompromised individuals, and older adults [1]. In infants, RSV is the leading cause of bronchiolitis and pneumonia, resulting in substantial hospitalization rates [2]. In older adults, RSV infection can exacerbate underlying chronic conditions and lead to severe outcomes, including death [3]. Despite the significant global health burden of RSV, there is currently no licensed vaccine available for widespread use in these vulnerable populations. The RSV fusion (F) protein, which mediates viral entry into host cells, is a primary target for neutralizing antibodies and a key immunogen for vaccine development [4]. The F protein exists in two major conformational states: prefusion (pre-F) and postfusion (post-F). Antibodies targeting the pre-F conformation have been shown to exhibit significantly higher neutralizing activity compared to those targeting the post-F conformation [5]. Therefore, stabilizing the F protein in its prefusion conformation has become a central strategy in the development of next-generation RSV vaccines.

A prime-boost vaccination strategy, involving an initial immunization with one type of vaccine (prime) followed by a subsequent immunization with a different but related vaccine (boost), has shown promise for eliciting strong and durable immune responses against various pathogens [6]. This approach can leverage the advantages of different vaccine platforms to induce both robust initial responses and long-lived immunological memory. Recombinant adenovirus vectors are effective at eliciting strong cellular and humoral immune responses due to their ability to efficiently deliver antigens to antigen-presenting cells and induce potent immunostimulatory signals [7]. Subunit protein vaccines, particularly those incorporating stabilized antigens, can elicit highly specific and potent antibody responses, especially upon boosting of a primed immune system [8]. This study aimed to evaluate the longitudinal antibody response following a novel prime-boost vaccine regimen for RSV in preclinical models. The regimen consisted of a recombinant adenovirus vector prime expressing a stabilized prefusion F protein of RSV, followed by a boost immunization with the purified stabilized prefusion F protein. We assessed the kinetics and durability of both neutralizing antibodies and binding antibodies specific to the RSV F protein over an extended period to determine the potential of this prime-boost strategy for inducing sustained protective immunity against RSV [9,10].

The prime-boost vaccination regimen induced a rapid and robust increase in F-specific binding antibody titers following both the prime and boost immunizations (Figure 1A). The prime-only group also developed significant binding antibody titers after the initial immunization, but these titers plateaued and gradually declined over the longitudinal follow-up period. The boost immunization in the prime-boost group resulted in a substantial and sustained increase in binding antibody titers that remained significantly higher than those in the prime-only and boost-only groups throughout the study ($p<0.001$ at all time points post-boost). The boost-only group showed a delayed onset of binding antibody responses, with lower titers compared to the prime-boost group at later time points. The control group showed no detectable F-specific binding antibodies.

This study demonstrates the potential of a novel prime-boost vaccine regimen, utilizing a recombinant adenovirus vector expressing stabilized prefusion RSV F protein followed by a protein subunit boost, to elicit robust and sustained antibody responses in preclinical models. The prime-boost strategy induced significantly higher and more durable neutralizing antibody titers compared to single-dose vaccination with either the adenovirus vector or the protein subunit. The booster immunization elicited a strong anamnestic response, indicating the effective induction of immunological memory by the priming immunization.

The superior antibody responses observed in the prime-boost group are likely due to the complementary mechanisms of the two vaccine platforms. The adenovirus vector prime efficiently

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delivers the antigen and induces strong cellular and initial humoral responses, establishing memory B and T cells [7]. The subsequent protein subunit boost, formulated with an adjuvant, effectively reactivates these memory cells, leading to a rapid and substantial increase in high-affinity, neutralizing antibodies [8]. The use of a stabilized prefusion F protein as the immunogen in both the prime and boost likely contributed to the elicitation of potent neutralizing antibodies, as this conformation exposes critical epitopes that are highly conserved and targeted by protective antibodies [5].

The longitudinal assessment of antibody responses is crucial for evaluating the potential durability of vaccine-induced immunity. The sustained high levels of neutralizing antibodies observed in the prime-boost group over the 112-day study period suggest the potential for long-lasting protection against RSV infection. While this preclinical study provides promising data, further investigations are needed to assess the long-term immunogenicity and protective efficacy of this prime-boost regimen in relevant animal models and ultimately in human clinical trials.

The findings of this study are consistent with previous research demonstrating the benefits of prime-boost strategies for viral vaccines [6]. The use of an adenovirus vector prime followed by a protein subunit boost has shown promise for other respiratory pathogens as well [10]. The stabilized prefusion F protein has emerged as a leading candidate antigen for RSV vaccine development, and its incorporation into a potent delivery strategy like a prime-boost regimen holds significant potential for overcoming the challenges that have hindered the development of an effective RSV vaccine for decades.

In conclusion, our preclinical evaluation of a novel adenovirus prime–stabilized prefusion F protein boost vaccine regimen for RSV demonstrates the induction of robust and sustained antibody responses, including high levels of neutralizing antibodies. These findings support the further development of this prime-boost strategy as a promising approach for achieving long-lasting protection against RSV infection in vulnerable populations.

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