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Development of a multiple epitope-based DNA vaccine against avian influenza and infectious bronchitis viruses

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Dedication

For my family

You are always first

Acknowledgment

*Praise is due to **Allah**; Dispenser of graces, merciful with no limits, and generous with no ends for his blessings and merits. For Allah all the gratitude returns, and for his satisfaction we seek and aspire. How limited what we call our knowing, and how tremendous and unlimited his wisdom and knowledge. Praise always is due to Allah the Provider of all sustenance; for what we have acquired, and for what we have learned. Praise always is due to Allah the Most Bountiful One for his graces during the dark moments and his help during the harsh times. Praise always is due to Allah, by the number of his creations, and as the vastness of his universe. Praise always is due to Allah, the sustainer of all the worlds.*

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Abstract

The high evolutionary dynamics of viruses renders it as moving targets that is arduous to cope with. This casts burdens on vaccine developers to innovate vaccines that can elicit broad cross-protective and enduring immune responses. In Egypt, both avian influenza virus (AIV) and infectious bronchitis virus (IBV) are considered to be among the most challenging viral infections. Multiple AIV subtypes and IBV variants are co-circulating in the Egyptian field and frequent outbreaks keep up-surging. Multi-epitope vaccines are proposed as innovative and flexible platforms that can accommodate multiple viral antigenic determinants within more flexible and immunogenic contexts. This flexible platform can easily adopt the use of immunogenic epitopes, removal of immunosuppressive epitopes, and utilizing multiple subsets of different types of epitopes. In this study, we have

utilized the biologically significant data as the main source for epitopes and/or immune-stimulatory sequences. Five prerequisites were set for the epitopes selection, in order to maximize the immunogenic potential of the incorporated epitopes. Three influenza B-cell epitopes, two IBV T-cell epitopes, and one TLR agonists were selected based on the aforementioned criteria. A novel linker was designed to provide enhanced stability, better presentation, and proper processing pattern. The designed novel molecule was evaluated using bioinformatics tools for the assessment of structural quality, immunological potential, and expected intracellular events post translation. This was followed by gene synthesis and cloning into the expression vector. In-vitro studies were carried out to evaluate the expression and stability. In-vivo studies were performed in mice and chicken to confirm the stimulation of the host immune system by the synthesized molecule. Chickens were challenged against either IBV or highly pathogenic avian influenza (HPAI) H5N1 virus. Our findings indicate very promising data concerning IBV with high protection level, and minimized shedding. Meanwhile, the vaccine couldn't protect the birds from morbidity or mortality following the HPAI H5N1 virus challenge. Overall, the novel designed platform represents a promising candidate for effective T-cell epitope vaccine while it requires further modifications to can adopt B-cell epitopes. This study is a step on a long and unpaved way that aims the development of vaccines more consistent with our contemporary viral challenges.

Keywords

Influenza virus; IBV virus; Vaccines; Virus evolution; Egypt; ME-DNA vaccines; Biologically significant data; Protective study.

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