Employing XIAP to Enhance the Duration of Antigen Expression and Immunity Against an Avian Influenza H5 DNA Vaccine

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DNA vaccine represents a powerful approach for prevention of avian H5N1 influenza infection. Yet, DNA vaccine-induced immune responses might be limited by the short duration of antigen expression. As a strategy to enhance adaptive immune responses elicited by a hemagglutinin 5 (H5) DNA vaccine, we explored the effect of co-administration of a DNA encoding X-linked inhibitor of apoptosis protein (XIAP) as a modulator of apoptosis and a stimulator of inflammatory signaling. In cultured cells as early as 24 hours (h), we found that the DNA vaccine encoded H5 antigen was a potent stimulator of apoptosis, and the H5 pro-apoptotic activity was significantly suppressed by the co-expression of full-length XIAP or mutant XIAP (ΔRING). However, full-length XIAP showed a higher potency than mutant XIAP (ΔRING) in the inhibition of H5-induced apoptosis. We also compared the immunizing ability of transmembrane and secretory forms of H5. Mice vaccinated (twice with 3-week intervals) with the secretory form of H5 showed higher hemagglutination inhibition (HI) antibody titers than mice vaccinated with the transmembrane form of H5. Furthermore, co-administration of XIAP with the secretory form of H5 resulted into a stronger antibody response than the transmembrane form of H5. Our findings suggest that in the design of DNA vaccines for a given pro-apoptotic antigen, using an anti-apoptotic molecular adjuvant and the secretory form of antigen may be a greater stimulus to induce immune responses.

Keywords Apoptosis, avian H5N1 influenza, DNA vaccine, XIAP

INTRODUCTION

The H5N1 subtype of the avian influenza virus can cause a severe and fatal disease in humans and poultry. Susceptibility of the viral genome to mutation and reassortment might produce a virus with human to human transmission ability, and result into a pandemic and global crisis (Herfst et al., 2012; Imai et al., 2012). Among avian influenza viruses, highly pathogenic avian