Adjuvantaing of Fluzone® with JVRS-100 in Mice, Rabbits and Non-Human Primates
Demonstrates Increased Immunogenicity and Dose-Sparing

Bernadette Callejo1, Maria Lay1, Timothy D Carroll2, Shannon Matzinger3, Linda Fritts2, Christopher J Miller2, Stella Chang1, John F. Warner1, Jeffery Fairman1
1Juvairy BioTherapeutics, Pleasanton, CA, 2California National Primate Research Center, University of California-Davis, Davis, CA

INTRODUCTION

JVRS-100 (lipid-DNA complexes) is a unique and promising adjuvant for vaccine applications that require high levels of antibody and T-cell immunity. The JVRS-100 adjuvant was mixed with a split influenza vaccine (Fluzone®, Sanofi Pasteur) and administered either subcutaneous to mice, or intramuscular to rabbits and non-human primates. Vaccination with JVRS-100-Fluzone® resulted in a significant increase in total IgG, IgG1 and IgG2a influenza antibodies. Furthermore, hemagglutination inhibiting (HAI) antibodies were higher compared with Fluzone® alone. Administration of decreasing amounts of Fluzone® mixed with JVRS-100 resulted in a -50-fold dose-sparing effect based on HAI titer. In vitro stimulation of splenocytes from JVRS-100-Fluzone® vaccinated mice with Fluzone® demonstrated increased antigen-specific T cell responses (IFN-γ production) compared with Fluzone® alone. Splenocytes from JVRS-100-Fluzone® vaccinated mice responded to unmatched H1N1, H3N2, and influenza B viruses, suggesting induction of cross-reactive T cell responses to conserved viral antigens. Analysis of T-cell responses from vaccinated non-human primates demonstrated significant enhancement of both interferon-gamma positive and IL-2 positive cells (intracellular cytokine staining) indicating the enhancement of both primary and memory responses to influenza antigens.

This work was supported by NIAID grants R41AI068260-01 and U01AI075412

RESULTS

Vaccine was administered at day 0, 14, and 29 and HAI response quantitated at day 14, 28, and 56. The administration of JVRS-100 with Fluzone® increased the antibody response in rabbits both in magnitude and duration.

A dose-ranging study was conducted in non-human primates (Macaca mulatta). Groups of macaques (n=4) were vaccinated on day 0 and 14 (IM) with graded doses of JVRS-100 adjuvant mixed with a fixed dose (22.5µg) of Fluzone® vaccine.

PBMC samples from non-human primates were restimulated with pediatric Fluzone®, blocked with brefeldin A and analyzed for intracellular accumulation of interferon-gamma or IL-2 as an indicator of primary or memory immune response.

CONCLUSIONS

These results suggest that use of the JVRS-100 adjuvant enhances immune responsiveness and reduced antigen doses needed for strong immune responses to a licensed flu vaccine. The JVRS-100 adjuvant has also been shown to potentiate immune responses to multiple viral and bacterial antigens, and could be a broadly applicable adjuvant for human and veterinary vaccines.