A Virus-Like Particle (VLP) Vaccine Displaying Zika Envelope (E) Protein CD Loop Antigen Elicits Protective and Specific Immune Response in a Murine Model

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Abstract
Zika virus (ZIKV) is a mosquito-borne flavivirus associated with Congenital Zika Syndrome (CZS), which comprises a wide range of congenital abnormalities in fetuses and infants infected with ZIKV before birth (1 and 2). In a small number of patients, Zika infection is strongly associated with the neurological autoimmune disorder Guillain Barré Syndrome (GBS) (3). To date, no vaccines or antiviral strategies are licensed for Zika virus. Our aim is the development of a novel Zika vaccine candidate safe from antibody-dependent enhancement (ADE).

Methods
We developed novel ZIKV vaccine candidates by using a Woodchuck Hepatitis core antigen (WHcAg) virus-like particle (VLP) scaffolding system (4) for displaying specific antigens from the ZIKV Envelope (E) protein, which is conserved across ZIKV strains, as the vaccine immunogen (Fig. 1).

Results
Vaccine candidates were developed and tested using WHcAg chimera VLPs displaying selected ZIKV antigens from the E protein: (i) full length EDIII (WHcAg EDIII), (ii) the EDIII sub-structural domain CD Loop (WHcAg CD Loop), and (iii) the EDII sub-structural domain Fusion Loop (WHcAg Fusion Loop). While EDIII domain antigens are highly conserved or identical among flaviviruses, VLPs were recombinantly expressed in the serum dilution. The limit of detection (dotted line) is 100. A. The WHcAg CD Loop VLP induced a high level of IgG response against ZIKV E protein, DENV-2 E-protein and 6-Histidine tag (6-His) demonstrate ELISA analysis of serum from mice immunized with Zika-VLP vaccine candidates demonstrated that the WHcAg CD Loop induced a strong immune response and elicited a strong antibody response against ZIKV after prime immunization alone (Fig. 3A). Analysis of serum immunoglobulins demonstrated induction of both Th1- and Th2-mediated immune response (Fig. 3B).

Conclusions
The WHcAg CD Loop VLP vaccine candidate demonstrated immunoprotection in a C57BL/6N hisd murine model of ZIKV infection that employs anti-IFNAR1 antibody preconditioning prior to viral challenge (Fig. 5A). The WHcAg CD Loop immunization stimulated protective, but not neutralizing (Fig. 5B), antibodies associated with antibody-dependent cell-mediated cytotoxicity (ADCC) (Fig. 5C), and complement-dependent cytotoxicity (CDC) (Fig. 5D) activities.

References

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