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ePoster Viewing
Vaccine development

INTERLINEAGE CROSS-PROTECTION INDUCED BY A WEST NILE VIRUS LINEAGE 1 RECOMBINANT DOMAIN III VACCINE

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Objectives: West Nile virus (WNV) is a mosquito-borne flavivirus that is currently endemic in Africa, the Middle East, Europe and the United States. Of five lineages of WNV, lineage 1 and 2 are most widespread in the world, and both are currently circulating in Europe. To date, no vaccine is available for use in humans. This study aimed to explore the efficacy of recombinant domain III (rDIII) WNV vaccine, based on WNV lineage 1, in providing protection against both WNV lineage 1 and 2.

Methods: This study combined bioinformatics analysis and in-vivo experiment. Protein bioinformatics analysis was performed using BioEdit©, Pymol©, Swiss-model expasy©, Swiss pdb viewer ©, and DPX to assess sequence and structural differences between domain III of WNV lineage 1 and 2. Three-week old C57BL/6 mice were immunized twice (prime-boost strategy) with rDIII adjuvanted with Matrix-M™ and challenged with either WNV-NY99 (lineage 1) or WNV-578/10 (lineage 2). Half of each group (n=5) was sacrificed by day 8 post challenge to assess the ability of the vaccine to prevent dissemination of virus to the brain and the other half was assessed for survival.

Results: Domain III was found to be highly conserved across lineage 1 and 2 with only two non-conservative amino acid substitutions at position 312 and 369 of the envelope. Amino acids of WNV lineage 1 consisted of either lysine or phenylalanine at position 312 and alanine at position 369, while lineage 2 consisted of alanine and serine at position 312 and 369, respectively. So far, no known neutralizing epitope is known to be located at position 369, and only one study has documented a possible neutralizing epitope at position 312. Protein structural analysis also confirmed highly conserved nature between both lineages. No major differences in the location of neutralizing epitopes were found when comparing the two lineages. Vaccination-challenge experiments showed that immunized mice were fully protected against challenge with both homologous and heterologous virus . In addition, no virus was present in the brains of vaccinated mice on day 8 as compared to control mice. Interestingly, in vitro neutralization assays showed that serum from rDIII-vaccinated mice neutralized WNV-578/10 at much lower titers as compared to NY99.
Conclusions: These results demonstrate that a vaccine based on DIII of WNV is able to provide cross-protection against lethal challenge with both lineage 1 and 2 virus but induces lower neutralizing antibody titers against heterologous virus. This vaccine is therefore highly suitable for use in an area such as Europe, in which both lineages of WNV are circulating. Further study is needed to assess the role of amino acids at position 312 and 369 in altering the extent of the neutralizing antibody response against heterologous virus.