DESIGN OF VACCINES AGAINST MULTIPLE STRAINS OF THE ENCEPHALITIC ALPHAVIRUSES.

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Many alphaviruses are endemic in the US, and infections of horses and humans by the equine encephalitis viruses (EEV) have a high mortality, with long-term, severe sequelae in many survivors. Symptoms in humans include fever, chills, headache, back pain, nausea and vomiting, with eventual progression to encephalitis. Currently, no vaccines are commercially available for mass protection; the attenuated VEEV vaccine strain, TC-83 used for lab personnel is expensive and has significant side effects. While current alphavirus vaccines under development are based on single wild-type (wt) strains, using the envelope proteins E1 and E2 as antigens, this strategy explores vaccines with broad protection against diverse alphavirus strains. Design of vaccines that protect against multiple strains of alphaviruses is still a challenge due to the diversity of their envelope protein sequences. In this project, we obtained the genome sequences of many VEEV and EEEV strains through high throughput sequencing. The sequence analysis on the envelope protein E1 and E2 indicated residues with conserved and variable physico-chemical properties (PCP). In addition, we analyzed the surface exposed residues with the 3D structures of the envelope proteins, and predicted the potential antigen binding epitopes with our software InterProSurf. Combining the sequential and conformational analysis, we designed four hybrid E2 proteins representing the immunity features of both VEEV and EEEV. The VEEV TC83 was used as backbone and a few variable residues were replaced with two conserved epitopes from EEEV at corresponding positions. In collaboration with Dr. Forrester’s group, we have constructed viruses containing the hybrid proteins through multiple rounds of joint PCR. In vivo tests to verify the activities of the viruses and immune responses of animals are in progress.