**ABSTRACT**

Alphavirus diseases are rapidly emerging global public health concerns. Understanding the molecular interactions essential for viral infection is vital to developing antiviral strategies and therapeutics to mitigate the burden of disease. Interactions between viral capsid protein and genomic RNA are essential for the formation of infectious particles and represent an excellent target for the development of antiviral therapeutics. SINV C:R interaction site mutations exhibit attenuated replication and pathogenicity in a murine model of infection as mice infected with C:R mutant SINV particles did not display overt signs of disease and exhibited steady weight gain over the experimental period. Taken together, the attenuation observed for SINV C:R mutant viruses indicates strong promises as a rational approach towards antiviral interventions.

**METHODS**

Using a CLIP-seq approach we have identified sites of interaction between genomic RNA and the viral capsid protein for Chikungunya (CHIKV) and Sindbis (SINV) during infections of tissue culture cells. Deep sequencing and bioinformatic analysis of cDNA libraries led to the identification of viral C:R interaction sites. Interestingly, as shown below, several discrete Capsid:RNA (C:R) interactions were identified for SINV and CHIKV, however, further bioinformatic analyses have not yet led to the identification of any consensus binding sites or motifs amongst the C:R interaction sites.

**SUMMARY and CONCLUSIONS**

Mutations to individual C:R sites resulted in decreased viral growth kinetics relative to wild type parental virus. The importance of the C:R interaction sites was observed in SINV, and its medically relevant relative CHIKV. Importantly, RNA synthesis and structural protein expression were unaffected by mutation of SINV C:R interaction sites. Furthermore, mutation of SINV, and CHIKV, C:R interaction sites significantly reduced the number of infectious particles, but not the total particles produced during infection. Taken together these data suggest that C:R mutations negatively affecting particle quality or function rather than particle assembly.

**FUTURE DIRECTIONS**

- Further characterize the mechanism for the decrease in viral kinetics
- Observe the effects these mutations have on viral growth in mosquito cell lines, the natural vector for Alphaviruses
- Characterize the difference in RNA synthesis and protein expression with CHIKV C:R mutants
- Infect CHIKV C:R mutants in mouse model