Altering Viral Diversity: How This Impacts Viral Infection

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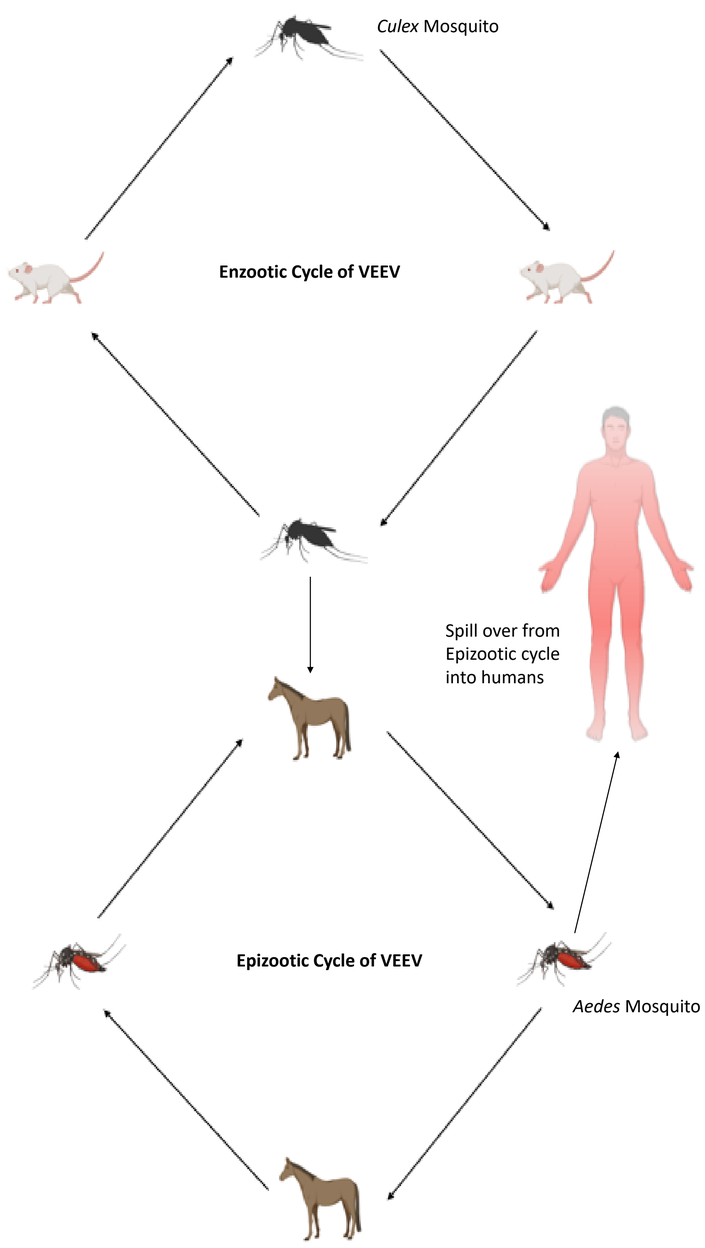
Introduction

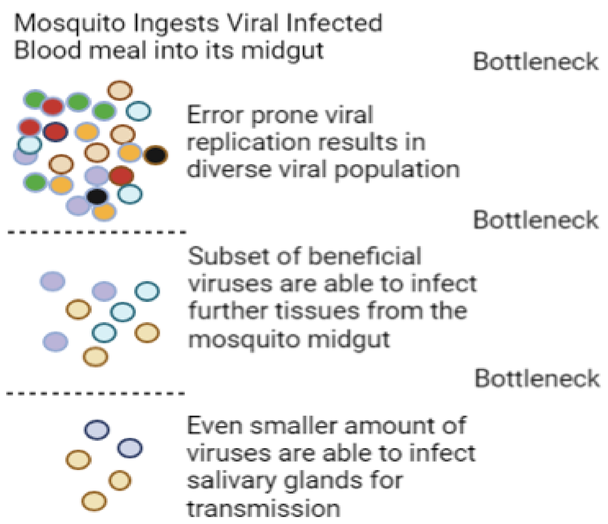
Diversity within a viral population is important for infection and transmission.
Diversity is generated during replication as the error prone polymerase creates mutations.
Venezuelan Equine Encephalitis Virus is an arbovirus; an arthropod borne virus that has an enzootic and epizootic cycle.
Since its discovery in 1838, it has caused several large outbreaks, with 75,000-100,000 people infected in a 1995 outbreak[1].
Understanding how viral diversity impacts infection is key to understanding transmission of this important virus.



The infection cycle of VEEV. Outbreaks occur when the virus moves into the epizootic cycle.

Arboviruses are mosquito-borne viruses that transmit between a mosquito and a host animal[2].

Arboviruses include viruses such as Zika Virus, Dengue Virus and West Nile Virus. We focused on an alphavirus called **Venezuelan Equine Encephalitis Virus (VEEV).**



Methods

Infect U4.4 cells with TC-83 and TC-83_3X

Illumina sequence viral RNA after 24 hours

Analysis using viRome (R programme)

Significance was determined in comparison to mock infections

We focused on the vaccine strain of VEEV: TC-83, and TC-83_3X which produces more diversity.

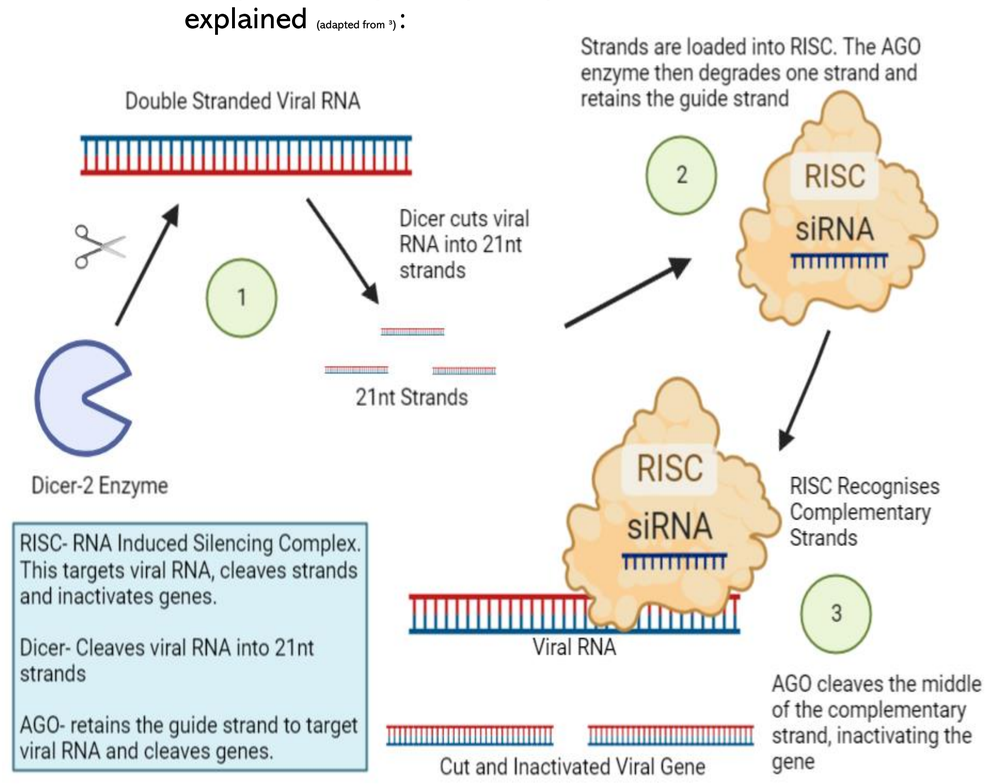
Both TC-83 and TC-83_3X show increased diversity to the wild-type VEEV.

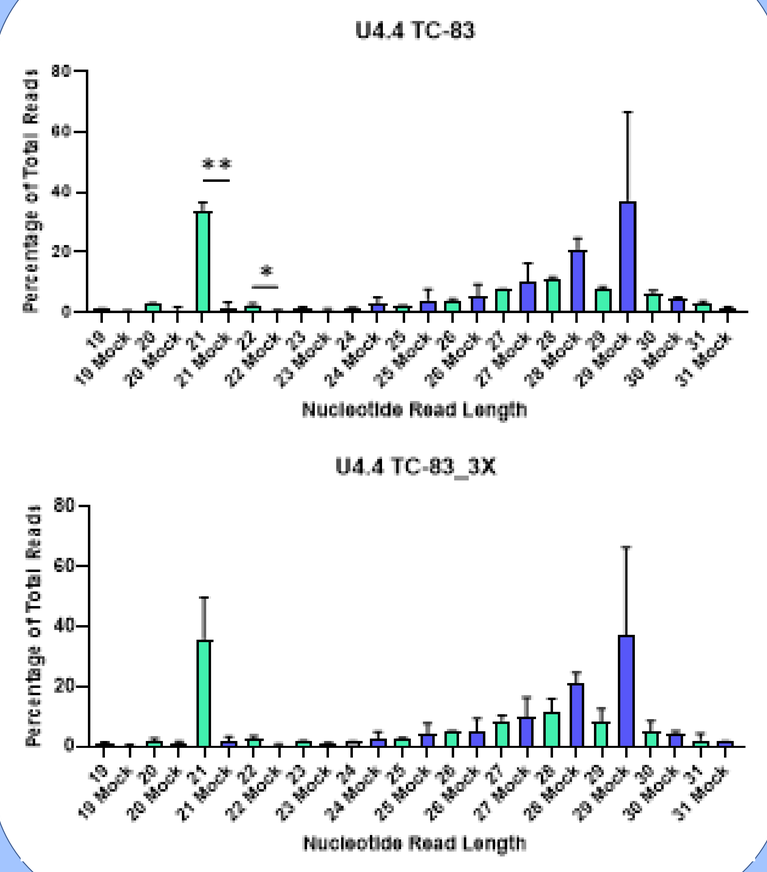
These viruses were unable to survive mosquito infection.

We wanted to see what stopped them from surviving and whether it was to do with the altered diversity.

We looked at a key antiviral mosquito immune response:

Small Interfering RNAi Response (siRNA) explained (adapted from [3]):





Future work

- Determine why TC-83_3X is unable to survive mosquito infection despite no siRNA immune response against it.
- Identify treatments that could target viral diversity.

Results

TC-83 produced reads characteristic of the siRNA response (21 and 22 nucleotide).
TC-83_3X produced no reads of significance.
These results show that altering the mutation rate, and subsequent diversity, of a virus directly impacts the host immune response against it.
This suggests that for TC-83, the siRNA immune response is preventing it from surviving infection in mosquitoes.

Conclusion

Changing the diversity of the viral population directly impacts the immune response of the host cell against the virus.

References
1. Weaver, S. C., Salas, R., Rico-Hesse, R., Ludwig, G. V., Oberste, M. S., Boshell, J., Tesh, R. B. 1996. Lancet, 348(9025): 436-40. doi: 10.1016/s0140-6736(96)02275-1.
2. Chamberlain, R. W. (1968). Arboviruses, the arthropod-borne animal viruses. Curr Top Microbiol Immunol, 42, 38-58. doi:10.1007/978-3-642-46115-6_3
3. Dana, H., Chalbatani, G. M., Mahmoodzadeh, H., et al., Molecular Mechanisms and Biological Functions of siRNA, 2017. International Journal of Biomedical Science, 13(2): 48-57.