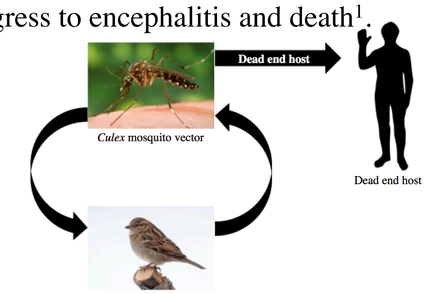
Re-emerging St. Louis Encephalitis virus in California

Kelly Symmes, Cody Steiner, Lark L. Coffey

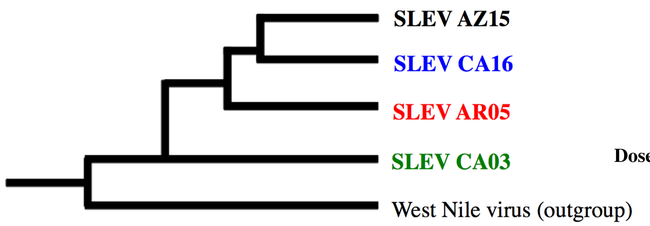
Department of Pathology, Microbiology and Immunology, School of Veterinary Medicine
University of California, Davis, California

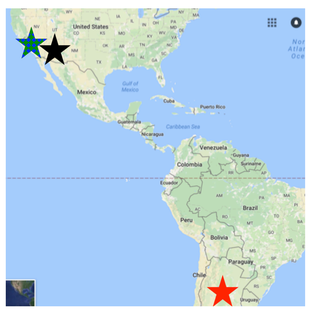
St. Louis encephalitis virus (SLEV)

- SLEV is a flavivirus that cycles between mosquitoes and birds.
- Humans are dead end hosts and usually asymptomatic. Symptomatic patients develop fever, lethargy and headache. Rare cases can progress to encephalitis and death[1].



- Between 2003-2014, no SLEV was detected in mosquitoes, birds or humans in California.
- SLEV activity was detected in California in 2015. This was concurrent with an outbreak Arizona that caused 23 cases and 1 fatality[2].
- Phylogenetic analyses revealed the closest relative to SLEV in CA 2015 and Arizona (AZ) 2015 is SLEV from an outbreak in Cordoba, Argentina in 2005[3].
- Understanding the factor(s) behind the re-emergence of SLEV will help us to better predict and prevent future outbreaks.



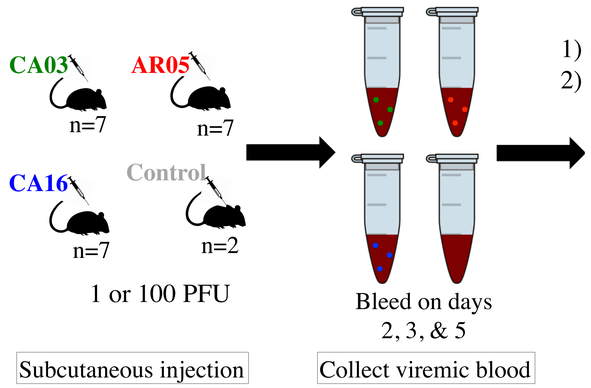


Hypothesis

Re-emergence of St. Louis encephalitis virus in California in 2015 after an 11-year absence of activity was promoted by augmented pathogenicity, resulting in enhanced magnitude of replication, morbidity, and mortality compared to ancestral strains from Argentina and historical strains from California.

Methods

Swiss albino mice were used as a model of human disease as established by Marques et. al. 2017, and Rivarola et. al. 2014.

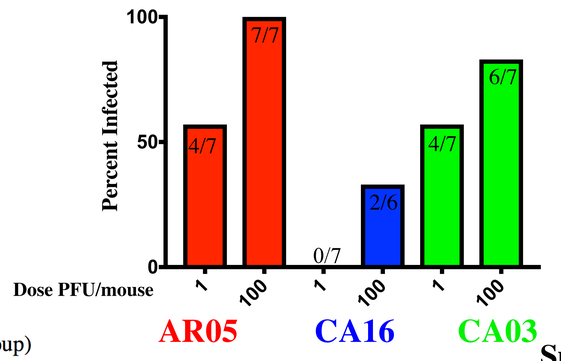


1) qRT-PCR for viral RNA quantification
2) Monitor for signs of lethal infection, including:
   - >20% total weight loss
   - >10% weight loss in 48hrs
   - Inability to feed or drink
   - Inability to groom self
   - Obtunded mentation

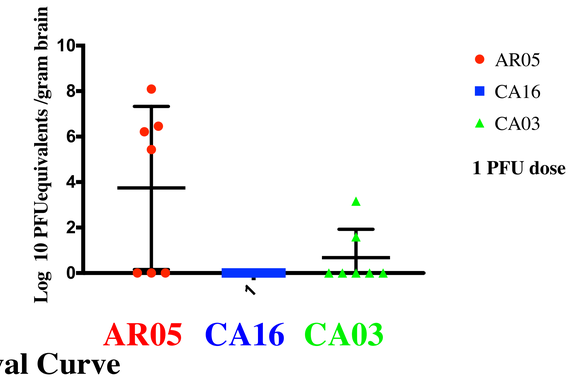
Quantify Disease

Results

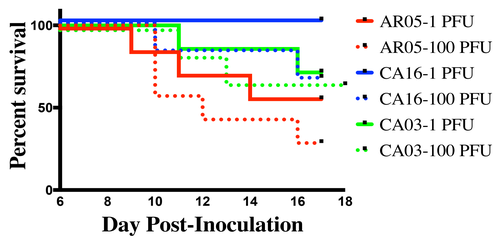
Infection Rate



SLEV RNA levels in mouse brains

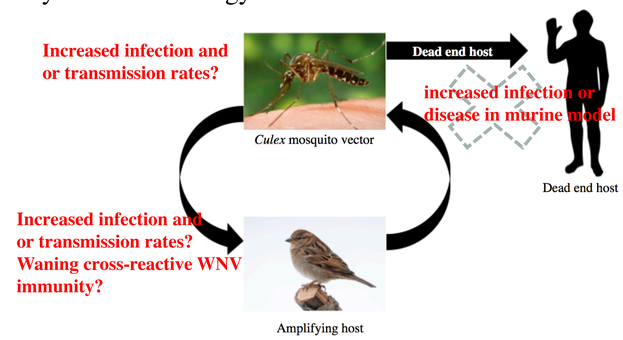


Survival Curve



Discussion

- Inoculated mice showed varying morbidity and mortality depending on the strain and dose of SLEV.
- Infection rates in mice inoculated with both doses of SLEV AR05 and CA03 were similar and contrasted with lower rates in mice inoculated with CA16.
- The lethal dose that killed half of mice infected with SLEV AR05 was ~1 PFU. By contrast, mortality in mice infected with 1 PFU of CA03 was 25%. Lethality was not correlated with SLEV titers in brains; mice with both high AR05 and low CA03 titers both succumbed to fatal disease. No mice inoculated with CA16 became infected or died. Mice infected with 100 PFU also showed a similar mortality pattern where AR05 produced higher fatality than CA03. CA16 was the least fatal.
- These infection and mortality data contrast with our hypothesis, and indicate that re-emerging CA16 SLEV is less infectious and virulent than both the ancestral AR05 and historical CA03 strains.
- Other factors may be promoting the re-emergence of SLEV in California, including changes in transmission dynamics or ecology.



References

[1]Centers for Disease Control and Prevention (https://www.cdc.gov/sle/technical/symptoms.html
[2]Centers for Disease Control, *Notes from the Field:* Concurrent Outbreaks of St. Louis Encephalitis Virus and West Nile Virus Disease — Arizona, 2015 https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6448a5.htm
[3]White, G. S., Symmes, K., Sun, P., Fang, Y., Garcia, S., Steiner, C., ... & Coffey, L. L. (2016). Reemergence of St. Louis Encephalitis Virus, California, 2015. *Emerging infectious diseases*, *22*(12), 2185.
[4]Marques, R. E., Del Sarto, J. L., Rocha, R. P., Gomes, G. F., Cramer, A., Rachid, M. A., ... & Teixeira, M. M. (2017). Development of a model of Saint Louis encephalitis infection and disease in mice. *Journal of neuroinflammation*, *14*(1), 61.
[5]Rivarola, M. E., Tauro, L. B., Llinás, G. A., & Contigiani, M. S. (2014). Virulence variation among epidemic and non-epidemic strains of Saint Louis encephalitis virus circulating in Argentina. *Memorias do Instituto Oswaldo Cruz*, *109*(2), 197-201.

Acknowledgements

- Students Training in Advanced Research (STAR) at UC Davis School of Veterinary Medicine
- NIH T35 Training Grant
- Department of Pathology, Microbiology and Immunology