Evaluating herpes simplex virus type 2 acute and recurrent disease in a mouse skin infection model

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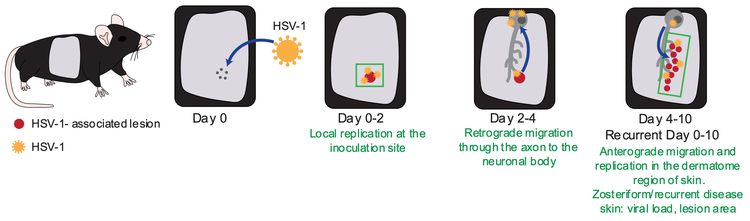
Abstract

Herpes simplex virus type 2 (HSV-2) is a sexually transmitted virus that infects more than 15% of US adults, causing genital herpes. Following epithelial infection, HSV-2 spreads to innervating sensory neurons in which it establishes a lifelong persistent (latent) infection. HSV-2 can reactivate from latency and cause recurrent epithelial lesions. Although the greatest burden of genital herpes disease is due to recurrent infections, the mechanisms by which HSV-2 establishes and reactivates from latency are not well understood. Our lab recently developed a new mouse model to study reactivation of the closely related virus HSV-1. In this model, we infect mice with HSV on depilated flank skin and the virus establishes latency in dorsal root ganglia; manual fur plucking is sufficient to stimulate viral reactivation, producing skin lesions. The goal of my project was to adapt this HSV-1 reactivation model to study HSV-2. While we typically infect mice with 106 focus-forming units (FFU) of HSV-1, we found that similar doses of HSV-2 produced 100% lethality, precluding reactivation studies. However, when we infected mice with 1x103 FFU of HSV-2 we found that skin lesion areas peaked 6 days post-infection (dpi) and resolved by 10 dpi. We waited 35 dpi to allow the virus to establish latency, then we re-plucked the mice and evaluated recurrent disease, which presented as dermatome lesions in the same site as the acute infection. We plan to use this model to study the stimuli that induce HSV-2 reactivation and the immune mechanisms that control skin lesion severity.

Approach



References

- Heather Bradley, Lauri E. Markowitz, Theda Gibson, Geraldine M. McQuillan, Seroprevalence of Herpes Simplex Virus Types 1 and 2—United States, 1999–2010, *The Journal of Infectious Diseases*, Volume 209, Issue 3, 1 February 2014, Pages 325–333

Results

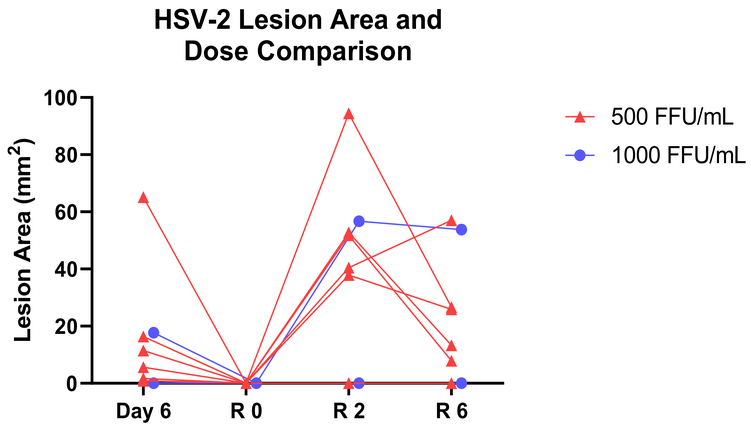


Figure 1. Using an HSV-2-adapted skin infection and reactivation model results in recurrent disease. C57/BL6 mice were infected with 500FFU/mL or 1000FFU/mL of HSV-2. Lesions were analyzed at 6 dpi, R0 (immediately after re-plucking), R2 (two days after re-plucking), and R6 (6 days after re-plucking).

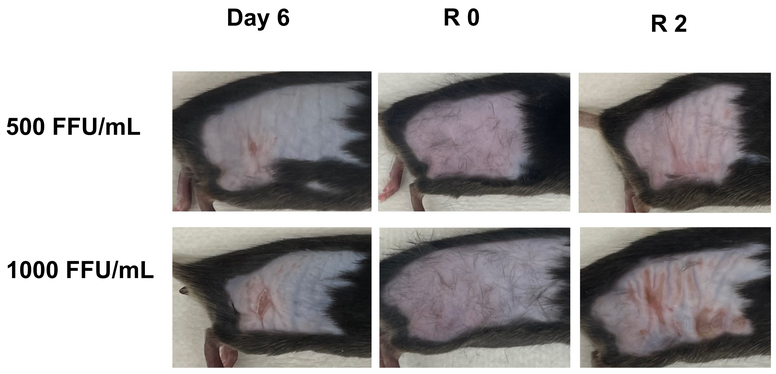


Figure 2. HSV-2 recurrent disease severity is dependent on inoculation dose during primary infection. Lesions were analyzed at 6 dpi, R 0, and R 2.

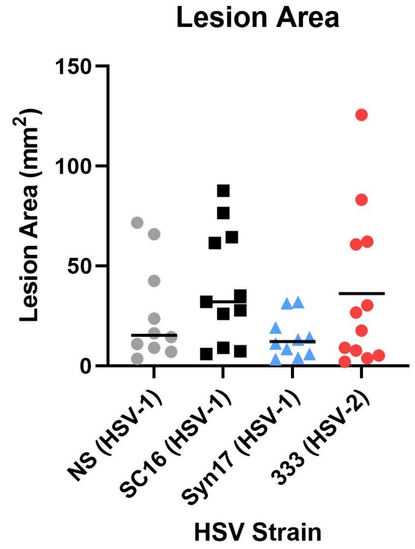


Figure 3. HSV-2 strain 333 exhibits increased pathogenicity compared to various HSV-1 strains. Mice were infected with HSV-1 (either strain NS, Syn17, and SC16) or HSV-2 (strain 333) and lesions were analyzed at 6 dpi.

Conclusions

- **A model used for studying HSV-1 skin pathogenesis is adaptable for HSV-2**
- **HSV-2 is more pathogenic than HSV-1**

Acknowledgements

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