Establishment of a Comprehensive Assay Platform for Supporting the Discovery of Agents against Acute and Latent Infections of Herpes Simplex Viruses

WuXi Biology

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Abstract

Herpes simplex virus 1 and 2 (HSV-1 and HSV-2) are globally prevalent human pathogens associated with a wide range of diseases, from mild conditions such as herpes labialis to serious infections such as encephalitis. Like other herpesviruses, HSV can establish lifelong latent infection in neurons of the peripheral nervous system, which can reactivate under certain circumstances. In addition, latent HSV infection is potentially associated with certain types of cancers. Despite ongoing research, the mechanisms underlying HSV latency remain incompletely understood.

Current HSV therapies are effective against active infections, but have no impact on the latent viral reservoir in neurons. Furthermore, no effective vaccines for HSV-1 or HSV-2 have been developed. Consequently, the HSV-related diseases remain incurable and challenging to prevent. Addressing the prevention and treatment of HSV infections, particularly latent infections, remains a critical unmet medical need.

To expedite the discovery of prophylactic and therapeutic agents targeting HSV reactivation, as well as to further deepen the understanding of HSV latency, we have developed a comprehensive platform encompassing both in vitro and in vivo HSV assays.

Cell-based Assays

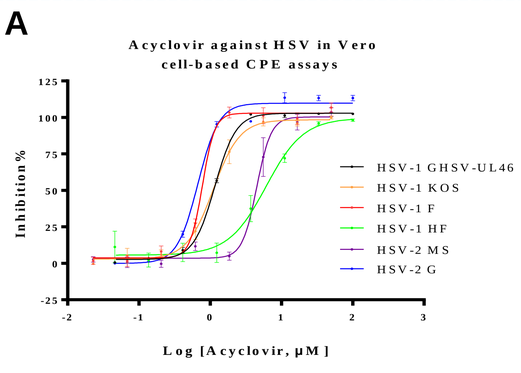

Fig. 1. Evaluation of the in vitro activity of drugs against HSV-1 and HSV-2 in Vero cell-based infection assays. **(A)** The activity of HSV polymerase inhibitor acyclovir in the Vero cell-based cytopathic effect assay. **(B)** The activity of acyclovir and HSV helicase-primase inhibitor pritelivir in the Vero cell-based qPCR assay.

HSV-2 Guinea Pig Infection Model

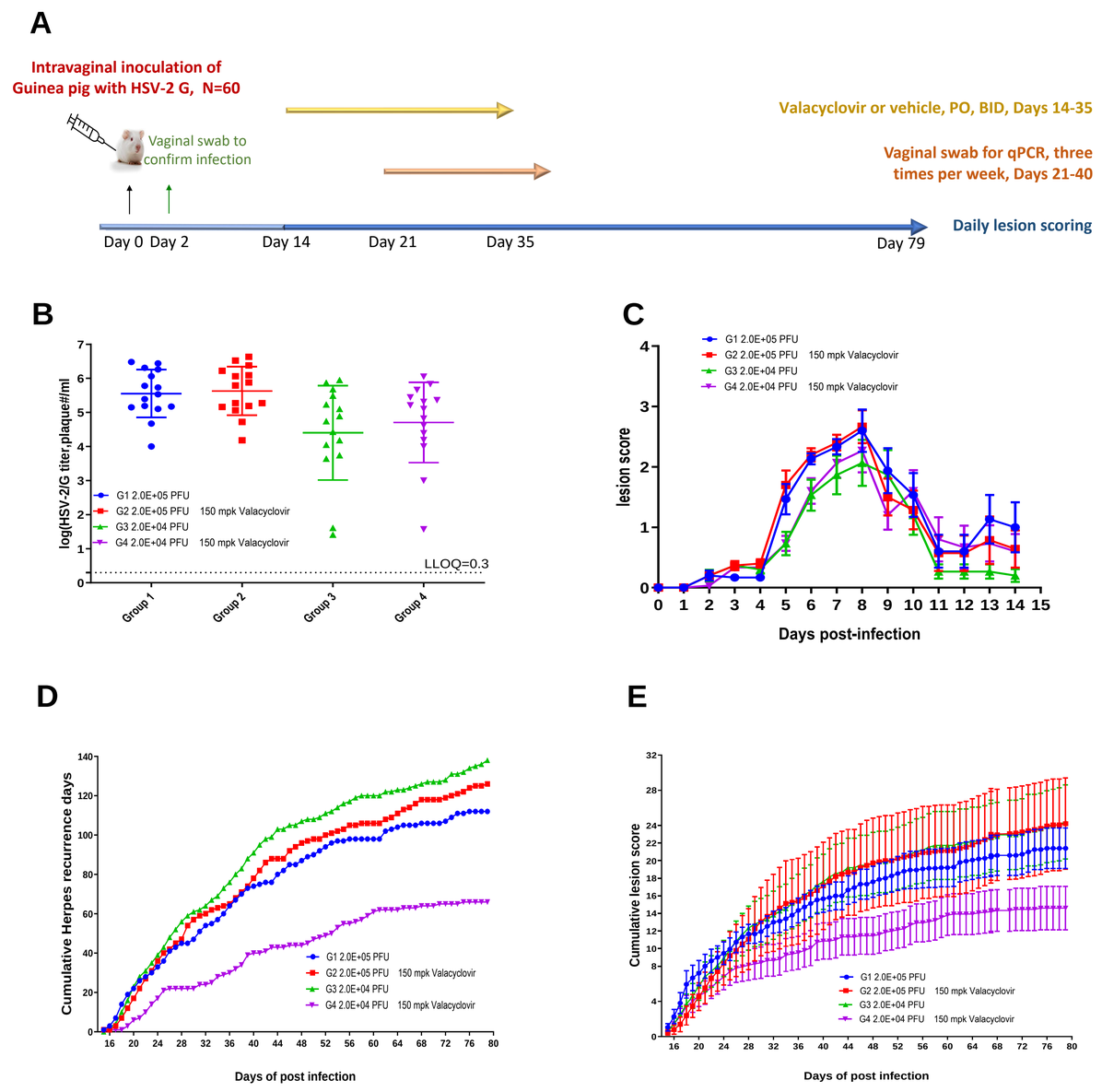

Fig. 4. The HSV-2 guinea pig infection model. **(A)** The scheme of HSV-2 intravaginal infection and the progress of the primary and recurrent infection. Hartley guinea pigs (female, 320 to 420 g) were intravaginally infected with $2x10^4$ or $2x10^5$ PFU of HSV-2 G strain. **(B)** The infection was confirmed by measuring the viral load from vaginal swabs collected 2 days post-infection using a plaque assay. **(C)** The symptoms of infected guinea pigs during the primary acute phase were scored based on the vaginal lesion. Cumulative herpes recurrence days **(D)** and lesion scores **(E)** from days 15 to 79 were used to assess infection recurrence.

HSV-1 Mouse Intranasal Acute Challenge Model

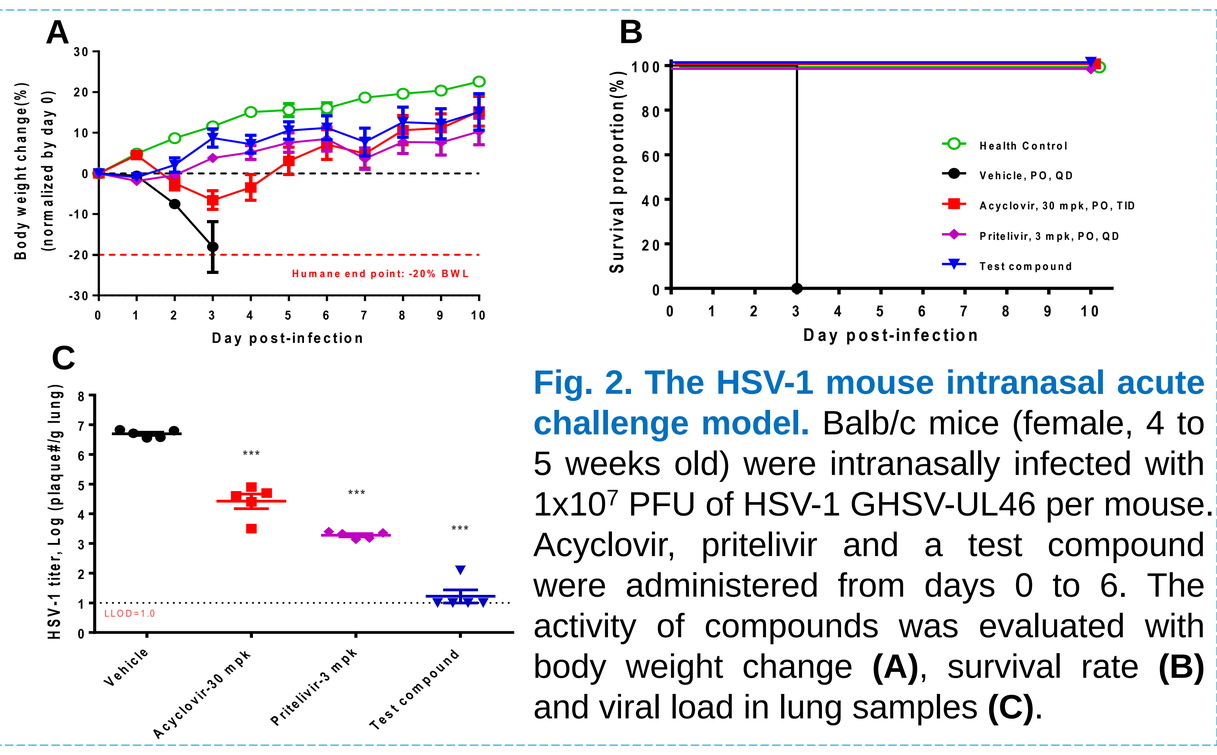

Fig. 2. The HSV-1 mouse intranasal acute challenge model. Balb/c mice (female, 4 to 5 weeks old) were intranasally infected with $1x10^7$ PFU of HSV-1 GHSV-UL46 per mouse. Acyclovir, pritelivir and a test compound were administered from days 0 to 6. The activity of compounds was evaluated with body weight change **(A)**, survival rate **(B)** and viral load in lung samples **(C)**.

HSV-1 Rabbit Keratitis (HSK) Model

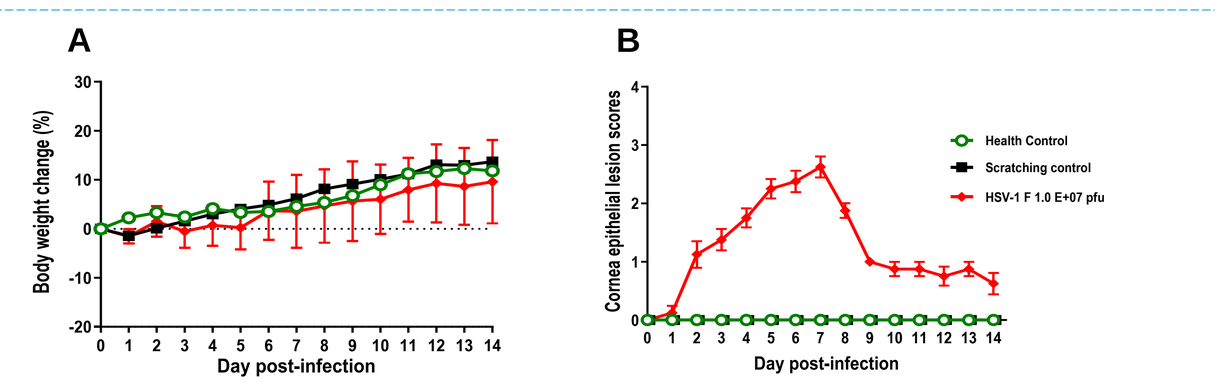

Fig 5. HSV-1 rabbit keratitis (HSK) model. New Zealand white rabbits (2.0 to 2.5 kg) were anesthetized, and their corneas were scratched and infected with $1x10^7$ PFU of HSV-1 F strain. **(A)** The infection did not significantly affect the body weight change. **(B)** The successful establishment of the animal model was demonstrated by the observed increase in corneal epithelial lesions.

HSV-2 Mouse Intravaginal Acute Challenge Model

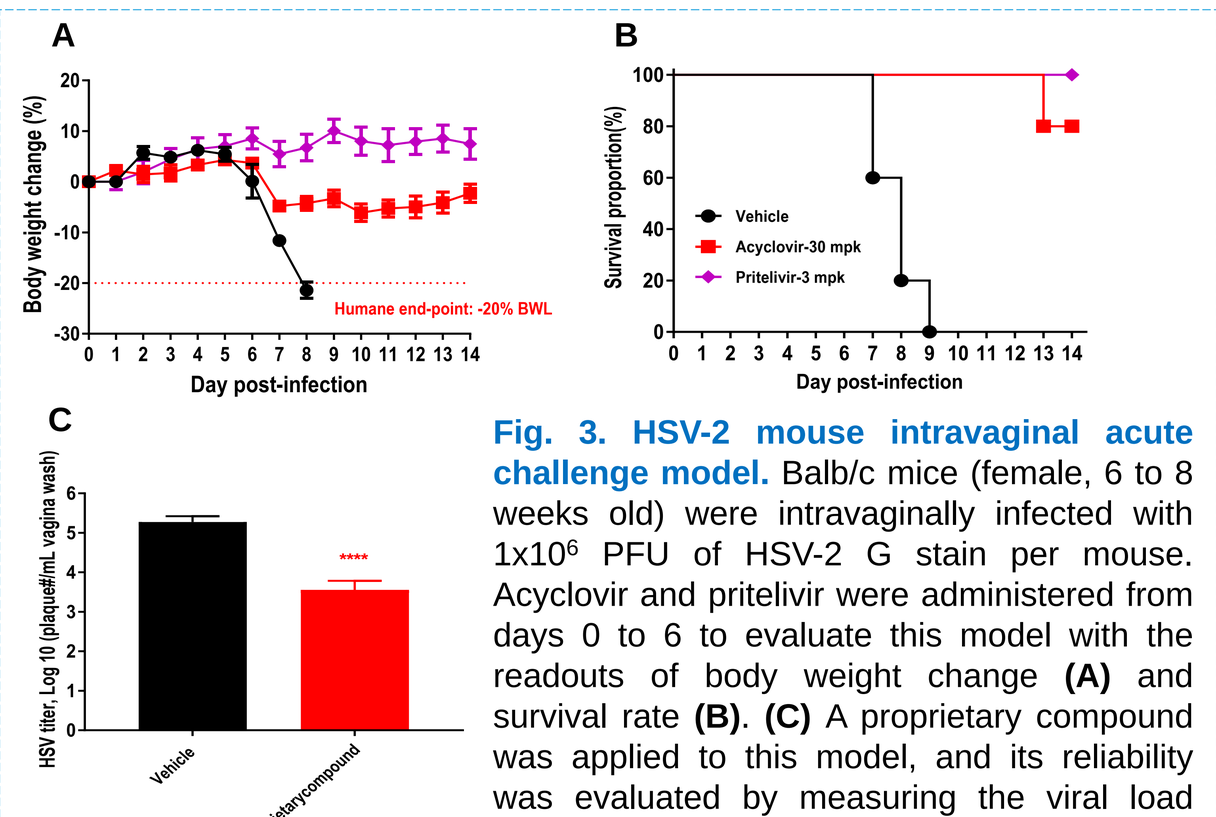

Fig. 3. HSV-2 mouse intravaginal acute challenge model. Balb/c mice (female, 6 to 8 weeks old) were intravaginally infected with $1x10^6$ PFU of HSV-2 G stain per mouse. Acyclovir and pritelivir were administered from days 0 to 6 to evaluate this model with the readouts of body weight change **(A)** and survival rate **(B)**. **(C)** A proprietary compound was applied to this model, and its reliability was evaluated by measuring the viral load from vaginal wash samples.

Summary

We have successfully established various HSV-1 and HSV-2 models to support the discovery of prophylactic and therapeutic agents against HSV infection. These cell-based and animal HSV models can also be applied to study various diseases caused by HSV-1 and HSV-2 infections to facilitate the understanding of antiviral treatment during HSV acute and latency infections.

Reference

1. Bernstein DI, Cardin RD, Smith GA, et al. The R2 non-neuroinvasive HSV-1 vaccine affords protection from genital HSV-2 infections in a guinea pig model. NPJ Vaccines. 2020. 5(1):104.
2. Zhu S, Viejo-Borbolla A. Pathogenesis and virulence of herpes simplex virus. Virulence. 2021. 12(1):2670.
3. Hussain MT, Stanfield BA, Bernstein DI. Small animal models to study herpes simplex virus infections. Viruses. 2024. 16(7):1037.

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Feel free to contact us for more info of Antiviral platform