Safe pseudovirus infecting mouse models in BSL-2 for filovirus entry study

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Background: Ebola virus and Marburg virus belong to filovirus family, which cause severe viral hemorrhagic fever in humans. Due to their high pathogenicity and mortality, live viruses require Biosafety Level 4 (BSL-4) facilities, which restrict the development of anti-filovirus vaccines and drugs. Methods: For enveloped viruses, HIV-based pseudovirus is a powerful technique for viral entry study. In our study, the pseudo-filoviruses were prepared by co-transfection of the HIV-core plasmid (pNL4-3.Luc.R-E-) containing a luciferase gene as reporter gene, with the filovirus envelope glycoprotein (filovirus-GP) expressing plasmid into 293T cells. The pseudo-filoviruses can be used to infect cells in vitro and mice in vivo. The infectivity was represented by the luciferase activity in the infected cells and bioluminescence imaging in mice. Two known filovirus entry inhibitors, clomiphene and toremiphene, were used to validate the models. Results: Ten pseudo-filovirus models covering all filovirus genera in vitro were established, and three representative viruses, Zaire ebolavirus, Marburg virus, and Lloviu cuevavirus, infected mice in a viral dose dependent manner. The bioluminescence peak in mice was reached on day 5 post-infection. All models were proved by tool compounds, clomiphene and toremiphene. Conclusions: Pseudo-filoviruses are infectious both in vitro and in vivo, and the mouse models can be used for compounds pharmacodynamics evaluation in vivo. Our sequential in vitro and in vivo filovirus entry inhibitors evaluation system provides a safe and efficient platform for screening and assessing anti-filovirus agents in BSL-2 facilities.

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