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Visualizing influenza and parainfluenza virus infection non-invasively in living mice with non-attenuated reporter viruses

Content

Infection has classically been measured by titering infectious virus recovered from euthanized animals or respiratory washes. In contrast, bioluminescence imaging measures in living animals the expression of luciferase, a marker for the extent of infected cells. It is a powerful tool for studying virus-host interactions yet luciferase insertions attenuate replication and virulence. Propagating lung samples having the highest ratios of bioluminescence-to-titer, we used directed evolution of a luciferase-expressing pandemic H1N1 (pH1N1) 2009 influenza A virus in mice to restore fitness and increase bioluminescence signal. Mouse-adapted virus had 10-fold higher bioluminescence signal compared to wild-type and had wild-type-like replication and virulence in mice. Fitness was restored by PA-D479N and PB2-E158G amino-acid mutations and PB2 non-coding mutations C1161T and C1977T, which collectively increased mRNA transcription. The adapted reporter virus will be a useful tool for noninvasive imaging of pH1N1 influenza virus infection and its clearance while analyzing virus-host interactions and developing new therapeutics and vaccines. We are currently using the virus to study in pharmacologically immunosuppressed mice prolonged infection, immune reconstitution, and clearance. Future studies will explore treatment options in the immunocompromised host, building on our previous studies using a non-attenuated Sendai reporter virus (murine parainfluenza virus 1). Collectively, our studies demonstrate the unique power of visualizing viral infection non-invasively in living animals.

Choose primary session

Visualising Flu

Choose secondary Session

Pathogenesis

Contribution Type : Oral presentation