PUBLICATION REVIEW

In vivo imaging of influenza virus infection in immunized mice

Seasonal influenza is a serious and persistent threat to global health. Vaccination and immunotherapy are crucial for the control of seasonal influenza outbreaks, but must contend with antigenic drift and antiviral resistance. Since there is no universal influenza vaccine or immunotherapy, there remains a critical need for the development of novel vaccines, antiviral drugs, and monoclonal antibodies (mAbs). Current preclinical efficacy studies of candidate influenza vaccines and antiviral agents are routinely tested in animals, but are inherently limited in scope, time consuming, expensive, and require a large number of animals.

In vivo optical imaging with IVIS® technology has emerged as a powerful, non-invasive tool to track viral load and therapeutic efficacy of vaccines and immunotherapies in small animal models. In the present study, a bioluminescent reporter H1N1 influenza virus (H1N1pdm09-Nluc) was generated to evaluate virus replication in mice. Mice challenged with H1N1pdm09-NLuc exhibited robust chest bioluminescence and presented clinical signs and virus titers comparable to those of mice inoculated with a wild-type (wt) virus. Further, vaccination with a live attenuated influenza virus (LAIV) or administration of human mAbs protected mice following H1N1pmd09-NLuc virus challenge. Collectively, this study supports the potential of optical imaging to enhance traditional preclinical efficacy evaluation of candidate vaccines and immunotherapies for the prevention and treatment of influenza.

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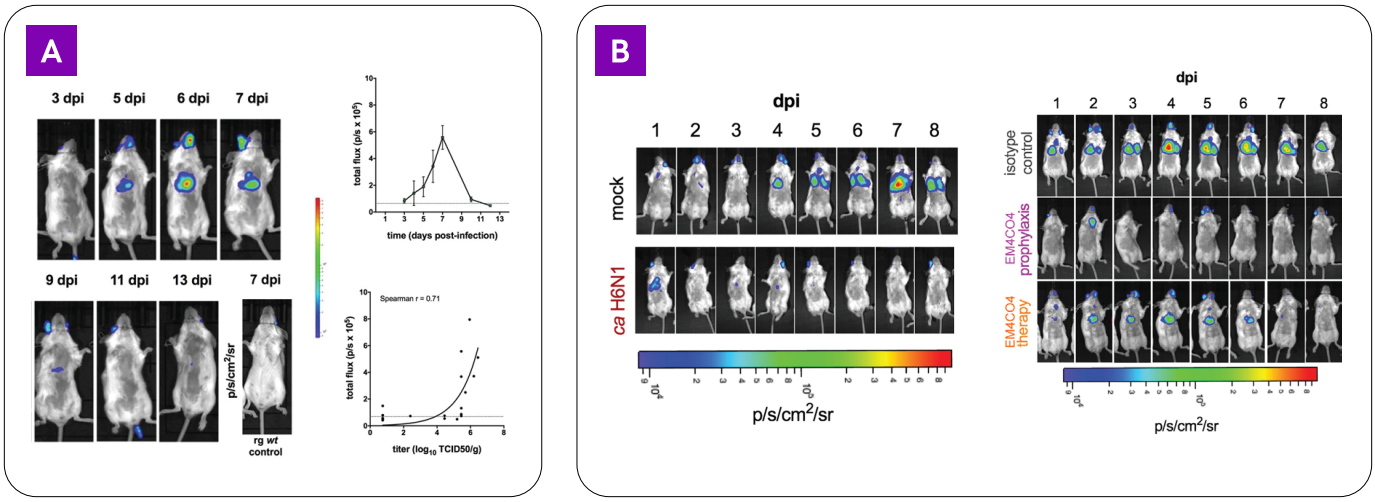
Publication highlights:

Non-invasive bioluminescent imaging using the Revvity IVIS platform successfully quantified H1N1pmd09-Nluc influenza viral load in mice and demonstrated that vaccination or human mAb administration has a protective or therapeutic effect in mice challenged with influenza virus. These results highlight the utility of IVIS imaging technology for preclinical viral research.



A) BALB/c mice were inoculated intranasally with H1N1pmd09-NLuc virus (103 TCID50) and imaged on an IVIS Imaging System at the indicated time points. A control mouse was inoculated with H1N1pmd09 wt virus. Sequential imaging revealed distinct spatiotemporal bioluminescence kinetics over the course of infection. Further, virus titers from lung homogenates collected from separate cohorts of mice support that bioluminescence signal correlates with the level of viral load present in the lung. **B)** Left image: Mice were inoculated with a single dose of caH6N1 LAIV or mock L-15 and challenged six weeks later with H1N1pmd09-NLuc virus (106 TCID50) and imaged at the indicated time point. Right image: Mice were immunized with a human mAb (EM4CO4) prophylactically (24 h pre-challenge) or therapeutically (72 h post-challenge). Results demonstrate that LAIV vaccination, prophylactic human mAb administration, or therapeutic human mAb treatment confers a protective or therapeutic effect to mice against influenza virus infection.

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