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Sendai virus: illuminating parainfluenza virus dynamics in living animals and a platform for vaccine development

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Abstract

Sendai virus is the murine counterpart of human parainfluenza virus 1 (HPIV1), the leading cause of pediatric croup. Sendai virus and HPIV1 are antigenically similar, and a team at St. Jude is currently conducting clinical trials to develop Sendai virus as a Jennerian vaccine for HPIV1. Sendai virus is a respiratory paramyxovirus with a single-stranded, negative sense RNA genome that is genetically stable upon inserting a foreign gene (reporter gene or foreign vaccine antigen). In collaboration with our colleagues, we have been using recombinant luciferase-expressing reporter Sendai viruses to visualize the dynamics of infection in living mice and viral glycoprotein-expressing Sendai virus vectors as vaccines for human paramyxoviruses such as RSV and HPIV3. Through the longitudinal measurement of reporter-virus infection as a function of inoculation method or transmission mode (contact or aerosol), our work has revealed that the mode of transmission determines the dynamics of primary respiratory infection and protection from reinfection while independent viral and host factors are responsible for pathogenesis. Basic virological studies on foreign gene positioning and antigen glycoprotein structural form are suggesting novel ways to enhance Sendai virus as a vaccine platform. Our studies with a host-matched virus (Sendai virus in mice) are providing a picture of the elements contributing to natural infection and transmission of a respiratory virus and hint at ways to exploit this understanding to prevent future infections.

Biography

Charles Russell completed his Ph.D. from the University of California at Berkeley where he studied the thermodynamics of membrane-peptide interactions. During his postdoctoral fellowship in the laboratory of Dr. Robert Lamb of the Howard Hughes Medical Institute at Northwestern University, he studied membrane fusion mediated by paramyxoviruses. He is currently a PI at St. Jude Children's Research Hospital in Memphis, TN, where his lab studies infectious diseases caused by influenza and paramyxoviruses. Research in the Russell lab runs the gamut from high-resolution structure to virus pathogenesis and transmission, making connections between the molecular and biological. Basic research in the lab addresses the impact of fusion glycoprotein activation on pathogenesis and host range while translational work focuses on viral envelope glycoproteins as vaccine candidates.