Making a better mouse model to understand the pathogenesis of respiratory syncytial virus infection

Respiratory syncytial virus (RSV) is the number one cause of infant hospitalizations in the United States. RSV infection is very common, with all children infected with this virus at least once by two years of age. Severe RSV infection has been correlated with increased morbidity and asthma development. Despite extraordinary research efforts, an effective vaccine to prevent RSV still does not exist. Our lack of knowledge of infant immunity has significantly impeded development of such a vaccine.

It has been shown that immune responses during infancy are vastly different from that of adults. Our ability to study immunity in human infants is limited; thus mouse models have been employed to define the reasons for the difference in immune responses. One limitation using mouse models to study human RSV infection is that common strains of RSV (e.g. A2 and Long strain) used in mouse experiments do not readily infect mouse cells. To overcome this limitation, an RSV mutant (rA2-19f) was created by Dr. Martin Moore. The rA2-19f virus is modified from the A2 RSV strain, with the A2 fusion protein (f) portion of the virus replaced with the f protein from the RSV line 19 strain. Infection of adult mice with rA2-19f resulted in greater amounts of virus in the lungs. Importantly, our studies demonstrated that infecting infant mice with rA2-19f closely mimics RSV disease symptoms in human infants. Infant mice infected with rA2-19f had higher amount of virus in their lungs compared to infant mice infected with RSV-A2 strain. The mutant virus also induced significant inflammation, mucus production, and lung dysfunction in infant mice, which are clinical hallmarks of severe RSV infection in human infants. Hence, the use of rA2-19f mutant RSV in mouse models of RSV disease represents a significant experimental advancement over use of the RSV-A2 strain, and will facilitate vaccine development.

Publication

Building a better neonatal mouse model to understand infant respiratory syncytial virus disease.
You D, Siefker DT, Shrestha B, Saravia J, Cormier SA
Respir Res. 2015 Aug 1