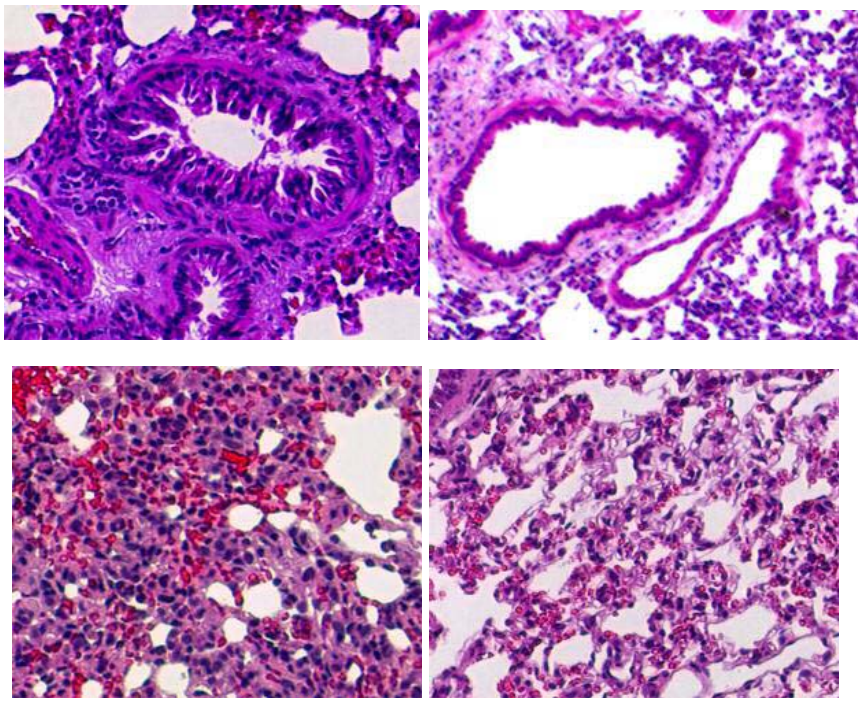
Attenuation of Respiratory Syncytial Virus Infection with Short Interfering RNA

Respiratory syncytial virus (RSV) causes severe bronchiolitis, and the infection is a risk factor for later development of asthma. Since there is no commercially available vaccine, alternative therapies to decrease the infection and associated inflammation would be valuable. Kong and colleagues have evaluated the use of short interfering RNA (siRNA), small RNA molecules that activate the body's innate defense mechanisms to destroy the target RNA. They used an siRNA vector targeted to the NS1 gene, which encodes a protein essential for viral replication. The siRNA was complexed to chitosan nanoparticles as a delivery agent, and delivered intranasally.



Treatment of rats with siRNA against NS1 (right) versus control siRNA-treated (left) decreases goblet cell hyperplasia (top) and infiltration of inflammatory cells (bottom).

Prophylactic treatment with siRNA against NS1 24 hours prior to RSV infection significantly reduced the amount of RSV in the lung and decreased airway hyperreactivity, the increase in airway resistance in response to a test challenge. Goblet cell hyperplasia and lung inflammation, both characteristics of asthma, were reduced (figure). Chitosan has mucoadhesive properties that help to target the siRNA to the lung mucosa for uptake and expression in endothelial cells and macrophages. Protein expression from nanoparticle complexes has been found to persist *in vivo* for 2 to 3 weeks, and mice treated with a chitosan-interferon gamma plasmid complex were resistant to repeated RSV infections. The use of siRNA prophylaxis against the RSV NS1 gene provides a potential strategy to stop the worldwide morbidity and mortality associated with RSV infection in infants and immunodeficient adults.

Kong X, Zhang W, Lockey RF, Auais A, Piedimonte G, Mohapatra SS. Respiratory syncytial virus infection in Fischer 344 rats is attenuated by short interfering RNA against the RSV-NS1 gene. *Genetic Vaccines and Therapy* 5:4 doi:10.1186/1479-0556-5-4. February 1 2007.

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