Nanomedicine & Biotherapeutic Discovery

Extended Abstract

Anti-fusion targeted nanomicellar theranostics: Novel antiviral strategies for respiratory syncytial virus infection-induced lung diseases

Shyam S Mohapatra

Abstract

The respiratory syncytial virus (RSV), is an important pathogen that infects an estimated 64 million people and causes ~200,000 deaths globally every year. Despite progress in the biology of RSV, there is no effective treatment or vaccine against RSV infection. Currently, only high-risk infants receive antibody-based prophylaxis, which is expensive and moderately effective in reducing hospitalization. Therefore, a broadly applicable, effective and inexpensive approach to prevent or treat RSV-bronchiolitis or pneumonia remains an urgent unmet need. We have been investigating nanomedical approaches against RSV infection and have reported on a variety of different strategies including genome vaccine, and siRNA based nanoparticles. More recently, we have developed a novel prophylaxis and/or therapy against RSV infection was inspired by the following discoveries: (1) A platform of phospholipid micellar nanoparticles (PMN) was developed, which when given intranasally delivers payload predominantly to the lung, (2) A decoy short heptad repeat (HR)2 peptide was identified, which effectively inhibits the RSV-cell fusion. iii) Human mesenchymal cells were found to be highly susceptible to RSV. The latter aided in establishing a novel 3D scaffold for anti-RSV drug screens, which consisted of creating a completely naked mouse lung scaffold (nMLS) by completely decellularizing and recellularizing the nMLS with desired human cells such as including hMSCs and epithelial cells and then infecting the cells in scaffold with RSV with or without drugs. (4) A robust immunocompromised mouse model was created by combining cyclophosphamide treatment with infection by a highly mucogenic strain, RSV-L19F. These developments have led to the hypothesis that a RSV-targeted PMN (RTPMN), combining HR2D anti-fusion peptide and plasmid encoded siRNAs against RSV-NS1 can provide a safe, effective and inexpensive anti-RSV prophylaxis and/or therapy. The completion of preclinical formulation of anti-RSV PMN-based prophylactics and therapeutics is expected to pave the way to IND-driven studies and clinical trials.

Respiratory syncytial virus (RSV), conjointly referred to as human metabolic process syncytial virus (hRSV) and human orthopneumovirus, could be a quite common, contagious virus that causes infections of the tract. it's a negative-sense, fibre polymer virus, and its name comes from the massive syncytia that kind once infected cells fuse along. whereas RSV is that the single most typical reason behind metabolic process hospitalization in infants, reinfection remains common throughout the period and it's a very important infective agent altogether age teams. Infection rates ar generally higher throughout the cold winter months, inflicting bronchitis in infants, common colds in adults, and additional serious metabolic process diseases like respiratory disease within the old and upset. RSV is unfold through contaminated air droplets and may cause outbreaks each within the community and in hospital settings. Following vaccination of the eyes or nose, the virus can infect the animal tissue cells of the higher and lower airway, inflicting inflammation, cell injury, and airway obstruction. a range of strategies ar accessible for microorganism detection and designation of RSV as well as matter testing, molecular testing, and microorganism culture.

A nanocarrier is nanomaterial being used as a transport module for an additional substance, like a drug. Normally used nanocarriers embody micelles, polymers, carbon-based materials, liposomes and different substances. Nanocarriers are presently being studied for their use in drug delivery and their distinctive characteristics demonstrate potential use in therapy. Nanocarriers discovered up to now embody chemical compound conjugates, compound nanoparticles, lipid-based carriers, dendrimers, carbon nanotubes, and gold nanoparticles. Lipid-based carriers embody each liposomes and micelles. samples of gold nanoparticles area unit gold nanoshells and nanocages. differing types of nanomaterial being employed in nanocarriers permits for hydrophobic and hydrophilic medication to be delivered throughout the body. Since the body contains principally water, the power to deliver hydrophobic medication effectively in humans could be a major therapeutic good thing about nanocarriers. Micelles area unit ready to contain either hydrophilic or hydrophobic medication counting on the orientation of the lipoid molecules. Some nanocarriers contain carbon nanotube arrays permitting them to contain each hydrophobic and hydrophilic medication.

One potential downside with nanocarriers is unwanted

Shyam S Mohapatra
University of South Florida, USA, E-mail: smohapat@health.usf.edu

toxicity from the kind of nanomaterial being employed. Inorganic nanomaterial can even be unhealthful to the body if it accumulates in bound cell organelles. References 1. Cheung M B, et al. (2016) Respiratory syncytial virus-infected mesenchymal stem cells regulate immunity via interferon beta and Indoleamine-2,3-Dioxygenase. PLoS One.; 11(10): e0163709. 2. Bird G H, et al. (2014) Mucosal delivery of a double-stapled RSV peptide prevents nasopulmonary infection. J Clin Invest.; 124(5): 2113-24. 3. Wong T M, et al. (2014) Respiratory syncytial virus (RSV) infection in elderly mice results in altered antiviral gene expression and enhanced pathology. PLoS One.; 9(2): e88764. 4. Boyapalle S, et al. (2012) Respiratory syncytial virus NS1 protein colocalizes withmitochondrial antiviral signaling protein MAVS following infection. PLoS One; 7(2): e29386. 5. San-Juan-Vergara H, et al. (2012) Cholesterol-rich micro domains as docking platforms for respiratory syncytial virus in normal human bronchial epithelial cells. J Virol.; 86(3): 1832-43.

This work is partly presented at 17th International Conference and Exhibition on Nanomedicine & Nanotechnology in Healthcare November 23-24, 2017 | Melbourne, Australia.

Shyam S Mohapatra
University of South Florida, USA, E-mail: smohapat@health.usf.edu