Chapter 10
Nanotechnology for the Management of Respiratory Disease

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ABSTRACT

Respiratory infections are among the leading causes of medical presentation in the United States. The most common respiratory viruses that affect humans are influenza virus, parainfluenza, and Respiratory Syncytial Virus (RSV). Among these, RSV is the leading cause of lower respiratory tract infections in infants, young children, elderly, and immune-compromised populations. Hence, there is an urgent need for the development of a safe yet potent alternative to conventional antiviral therapies. Nanotechnology is a multidisciplinary field that covers a vast and diverse array of devices derived from engineering, physics, chemistry, and biology. In nanotechnology, materials and devices that are designed to interact with the body at molecular level with a high degree of specificity are utilized. Hence, specific clinical applications can be designed to achieve maximal therapeutic efficacy with minimal side effects. In this chapter, detection and therapeutic application of nanotechnology in conjunction to RSV are discussed.

INTRODUCTION

Pulmonary diseases affect mainly the respiratory system and any of their structure and organs which is related to breathing. Pulmonary tract includes, nasal cavities, the pharynx (or throat), the larynx, the trachea (or windpipe), the bronchi and bronchioles, the tissues of the lungs, and the respiratory muscles of the chest cage. Among many pulmonary diseases, Respiratory Syncytial Virus (RSV) is the leading cause of lower respiratory tract infection in infants, older adults and immune compromised individuals (Collins et al., 1996; Dowell et al., 1996; Falsey et al., 2005; Hall et al., 1986). Worldwide, there are reportedly about 12 million severe and 3 million very severe cases of lower respiratory tract infection (LRTI) in children (Nair et al., 2010). Severe RSV infection spreads to the lower respiratory tract and can cause bronchiolitis and pneumonia. This virus has the capacity to repeatedly infect humans throughout their life. In the tropical regions of the world, RSV incidence peaks in winter with a wide ranging persistence depending on the geographical topology (Fraga et al., 2013). RSV is prevalent in both developed and developing countries. The

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major countries which are affected by RSV are India, USA, Brazil, Canada, Cambodia, Mexico, Uruguay, Peru, France, Finland, Norway, Sweden, Latvia, Denmark, Germany, Netherlands, Ireland, Italy, Turkey, Iran, Saudi Arabia, Australia, New Zealand, China, Korea, Hong Kong, Japan, Columbia, Bangladesh, Nepal, Taiwan, Vietnam, Myanmar, Thailand, Kenya, Zambia, Nigeria, and Pakistan,. An estimate of more than 2.4 billion US dollars per year is the economic cost of viral lower respiratory tract infection in children (Tran et al., 2013).

Hence, RSV infections pose significant global health challenge, especially in view of the fact that traditional methods utilized for virus detection are typically labor intensive and require several days to successfully confirm infection. Nanoparticles are at the leading edge of the rapidly developing field of material science in nanotechnology with many potential applications in clinical medicine and research (Gronberg et al., 2006). The unique size of the nanoparticles paves a way to utilize them for developing both diagnostic tools as well as therapeutic agents. Nanoparticle-based detection strategies have been employed in an effort to develop detection assays that are both sensitive and expedient. The development of these nanoparticle-based detection strategies holds the potential to be a powerful method to quickly and easily confirm respiratory virus infection (Halfpenny et al, 2010).

RSV infection incepts in the upper respiratory tract, and then spreads to the lower respiratory tract. The immune response is initiated in the upper respiratory tract while cells and tissues in the lower respiratory tract are destroys leading to bronchitis, bronchiolitis, and pneumonia, which is occasionally fatal. Therefore, there is need for the development of a safe yet a potent alternative to conventional antiviral therapies. Nanoparticles have emerged and have been employed as antiviral agents due to their attractive properties especially in relation to their physical and chemical properties. Nanotechnology enables scientists to use these nano-scale materials which have created new therapeutic horizons. The ability to incorporate drugs into nano-systems displays a new paradigm in pharmacotherapy that could be used for cell-targeted drug delivery. Non-targeted nano-systems such as nano-carriers that are coated with polymers or albumin and solid lipid particles have been used to transport a large number of compounds (Pison et al., 2006). Therapies utilizing nanoparticles vaccine in which antigenic components have been incorporated has proven to stimulate mucosal and systemic immune responses, which can prevent the spread of infection to the lower respiratory tract (Adair, 2009). The encapsulation of viral proteins within nanoparticles may also facilitate production of respiratory vaccines which are efficacious in infants, where presence of maternally derived antibodies can reduce vaccine efficacy (Adair, 2009). This chapter mainly focuses on detection of RSV using nanoparticles as well as nanoparticles vaccines against RSV.

BACKGROUND

Respiratory Syncytial Virus

Respiratory Syncytial Virus (RSV) is a member of the genus *Pneumovirus* that belongs to the family *Paramyxoviridae.* There is no licensed vaccine available to prevent RSV, in spite of its clinical relevance (Zeng et al., 2007). Formalin-inactivated RSV (FI-RSV), once used as a vaccine, not only failed to protect but exacerbated pulmonary disease and resulted in death upon subsequent infection with wild type RSV (Kim et al., 1969). In mice infected with RSV, the inactivated vaccine augmented lung disease which was attributed to an unbalanced Th_2 immune response (Zeng et al., 2007).

The genome of the RSV is a single-stranded, negative-sense RNA genome that codes for ten genes and is translated into eleven proteins (Collins et al., 2001). It is an enveloped virus. The genome of RSV include nonstructural proteins NS1 and NS2 (type I interferon inhibitors), L (RNA polymerase), N (nucleoprotein), P (Phospho-protein

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