# How will nanotechnology lead to better control of asthma?

**Bumhee Yang[1#], Hayoung Choi[2#], Sang-Heon Kim[3], Ho Joo Yoon[3], Hyun Lee[3]**

[1]Division of Pulmonology, Center of Lung Cancer, National Cancer Center, Goyang, Korea; [2]Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Internal Medicine, Hallym University Kangnam Sacred Heart Hospital, Seoul, Korea; [3]Division of Pulmonary Medicine and Allergy, Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea

[#]These authors contributed equally to this work.

*Correspondence to:* Hyun Lee. Division of Pulmonary Medicine and Allergy, Department of Internal Medicine, Hanyang University College of Medicine, 222-1, Wangsimni-ro, Seongdong-gu, Seoul 04763, Korea. Email: namuhanayeyo@naver.com.

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Asthma is a common inflammatory disease of the lungs characterized by reversible airway obstruction, bronchial hyper-responsiveness, and chronic airway inflammation (1). The most widely used therapies for asthma include inhaled corticosteroids and bronchodilators (short- or long-acting $\beta_2$-adrenergic agonists or muscarinic antagonists). Although most patients with asthma respond well to inhaled corticosteroids, asthma control is poor in some patients who require maximal dosages (2). These patients rely on chronic oral corticosteroid use which can result in many serious side effects (3-8) and increased mortality (9). Although biologics have been shown to effectively reduce the use of systemic corticosteroid use (10), their use is associated with a higher socioeconomic burden, which limits the availability of these drugs. Thus, there is an urgent need to develop novel drugs or improve the delivery of current inhaled drugs which can enhance their bioavailability and effectiveness. From this perspective, an article by Wang and colleagues in *Annals of Translational Medicine* provides an important review on nanotechnology as a promising weapon against asthma (11).

Nanotechnology is a new interdisciplinary science which can revolutionize clinical practice in terms of improvement of current therapeutics as well as the development of new therapeutic strategies for respiratory diseases (12). The most advanced areas for nanotechnology research currently applied to asthma are related to drug delivery, which produce better effects, improved patient compliance, and optimal therapeutic safety compared to traditional drug administration (1,13). The anti-inflammatory and bronchodilator drugs used for asthma (e.g., glucocorticoids and $\beta_2$-agonists) are known to be more advantageous for topical use in respiratory organs than systemic routes (14-16). Since the importance of local drug delivery in asthma is already known, nanotechnology has been employed to enhance drug delivery. A previous study reported that nanoparticle dry powder inhalation enhanced inhalation delivery as well as deeper lung permeability (14). Also, Matsuo *et al.* showed that a steroid encapsulated in biocompatible blended nanoparticles produced prolonged and greater benefits at the site of airway inflammation compared to free steroids in a murine model of asthma (17). Nanoparticles enhance the therapeutic effect by facilitating the delivery of the drug to the target tissue, thereby improving the deposition of the drug in the lungs.

Along with facilitating the delivery of drugs, another use of nanotechnology in asthma is the application of brand new nano-drugs. A nanocarrier can carry various biologically active compounds such as DNA, RNA, and drugs in its internal nuclei and various molecules such as antibodies and drugs on its surfaces. It can easily enter cells by cellular uptake, providing safe and effective drugs and gene therapies. Several studies have shown that gene therapy using nanoparticles can be an effective alternative treatment. Kumar *et al.* showed that Chitosan-IFN-γ pDNA nanoparticles (CIN) could effectively reduce airway hyperresponsiveness (18), reduce proinflammatory ovalbumin-specific CD8+ T cells, and decrease the number and activity of dendritic cells in an ovalbumin-induced asthma model using BALB/c mice (19). Nanoparticle-based immunotherapy against specific antigens which induce asthma is also a promising field. Joshi *et al*. and Salem *et al*. reported the development of a nanoparticle-based vaccine for protection and treatment against dust mite allergies. These studies showed that the size of nanoparticles used for vaccination played a major role in the prevention of house dust mite-induced allergies (20,21).

Contrary to the promising aspects of nanotechnology, there is also concern regarding the accumulation of nanoparticles in the lung. As an example, in the case of nanoparticles which are persistent, not readily excreted or metabolized, or reside in lung tissues for extended periods of time, it is reasonable to expect adverse effects of accumulated material (22). In addition, when nanoparticles less than 100 nm are inhaled, the nanomaterials may induce pulmonary inflammation and oxidative stress (23). Thus, the establishment of manufacturing and test procedures is required to address the safety issues of nanotechnology. From this perspective, we need to understand potential benefits as well as safety issues in its clinical use for patients with asthma.

Nanotechnology for asthma treatment has been extensively studied and it has already been found that there are many advantages in drug delivery and vaccination. Asthma is a highly complex chronic airway inflammatory disease involving a variety of cells and cellular components. Therefore, asthma has many potential molecular targets which can be delivered together with drugs through nanoparticles. Wang and colleagues reviewed the potential benefits of nanotechnology and nano-drugs for asthmatic patients (11). Considering that uncontrolled asthma is a substantial burden to individuals and public health, we hope that nanotechnology is utilized for difficult to treat asthma cases as in the story of David and Goliath.

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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