Nanomaterials, Environment, Nanotoxicology & Health

MIM.3.031
Delivery of nanocarriers for pulmonary vaccination: recent advances and challenges

F Blank[1], P Stumbles[2,3,4], D Strickland[2], B Rothen-Rutishauser[5], P Holt[2], E Seydoux[1], Ch von Garnier[1]

[1]Respiratory Medicine, Bern University Hospital, Bern, Switzerland
[2]Telethon institute for Child Health Research, Perth, Australia,
[3]School of Veterinary and Biomedical Sciences, Faculty of Health Sciences, Murdoch University, Perth, Australia,
[4]Centre for Child Health Research University of Western Australia, Perth Australia
[5]Adolphe Merkle Institute, University of Fribourg, Fribourg, Switzerland

fabian.blank@dkf.unibe.ch
Keywords: nanocarriers, immunomodulation, antigen presenting cells cells

The respiratory tract is an attractive target for the delivery of vaccine antigens. Nano-sized carriers have been proposed as promising novel diagnostic, therapeutic, and vaccination approaches for a variety of human diseases. In particular, delivery of nano-sized carriers to the lung has been receiving increasing interest due to the large surface area provided by the gas exchange region, limited local proteolytic activity, non-invasiveness, and fine anatomical barriers for systemic access[1]. Pulmonary antigen presenting cells (APC) are considered as sentinels of the immune system due to their strategic localization, their phagocytic activity, and their ability to present antigen[2]. To improve efficiency of vaccination and develop new strategies, a well-founded knowledge about composition and characterization of APC populations throughout the respiratory tract is essential. In particular, respiratory tract dendritic cells, as key APC in the lung, constitute an ideal target for vaccine delivery[1]. Furthermore, carrier size is a key factor when designing new inhalable vaccines, as size determines not only deposition in different respiratory tract compartments, but also how an antigen and its carrier will interact with lung tissue components and immune cells[3]. Clarifying which APC / dendritic cell populations primarily interact with nano-sized carriers and traffic these from different respiratory tract compartments to lung draining lymph nodes is paramount to understanding related downstream inflammatory and immune responses. A very efficient approach to analyse particle-cell interactions in respiratory tissue is to combine flow cytometry and laser scanning microscopy in order to obtain profound quantitative (frequency of particle uptake, expression of APC surface markers) and qualitative data (in situ localisation of nanoparticles), respectively (Figure 1). Such data will be fundamental to rationally develop future novel particulate systems in the nano-size range for therapeutic or diagnostic applications in the respiratory tract.

Acknowledgements: Grant funding by the Swiss National Science Foundation and the Swiss Society for Pneumology

1. Blank F, Stumbles P, von Garnier C: Opportunities and challenges of the pulmonary route for vaccination, Expert Opin Drug Del 2011, 8:547-563
2. Blank F, von Garnier C, Obregon C, Rothen-Rutishauser B, Gehr P, Nicod L: Role of dendritic cells in the lung: in vitro models, animal models and human studies, Expert Rev Respir Med 2008, 2:215-233

3. Blank F, Stumbles PA, Seydoux E, Holt PG, Fink A, Rothen-Rutishauser B, Strickland DH, von Garnier C: Size-dependent uptake of particles by pulmonary antigen-presenting cell populations and trafficking to regional lymph nodes, Am J Respir Cell Mol Biol 2013, 49:67-77

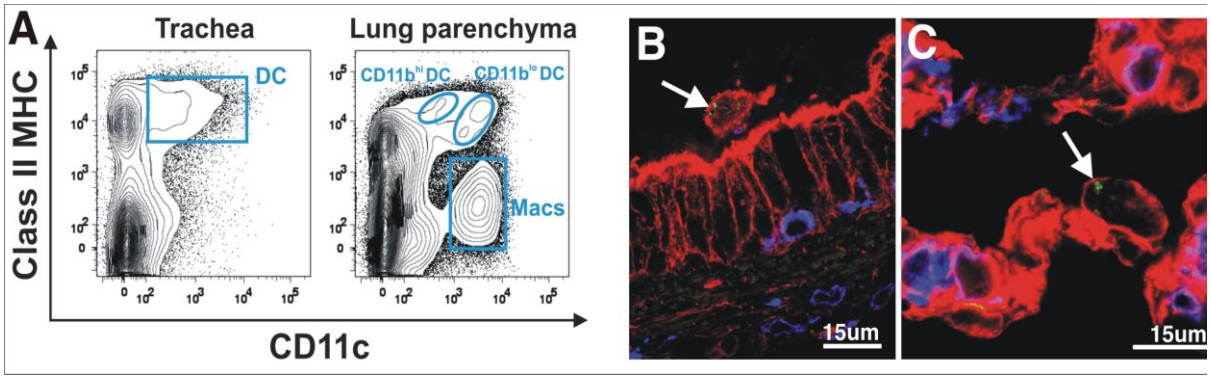

Figure 1. Analysis of nanoparticle trafficking in the respiratory tract using flow cytometry and laser scanning microscopy. Tissue from main conducting airways and lung parenchyma of mice was collected and processed for flow cytometry analysis (A) and confocal microscopy (B, C). A: Macrophages and different subsets of dendritic cells can be identified and analysed in airways and lung parenchyma. B, C: Localisation of nanoparticles (white arrows) in airways (B) and lung parenchyma (C). Particles: green; actin cytoskeleton: red; MHC class II: blue.