

# **Nanomedicine for non-invasive drug delivery across epithelial barriers – intestines, skin and lung**

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Between the intended site of action of a drug and the site of its administration to the patient, there are always some biological barriers. For non-invasive (“needle-free”) administration, the body’s outer epithelia - intestines, skin and lungs – are of particular importance. In the context of inflammatory and infectious diseases, they might even represent relevant therapeutic targets by themselves. This presentation will highlight some of our recent work in this area, both concerning the development of new in-vitro models or of new drug carriers systems, for which the nano-size often has turned out to be advantageous.

For the treatment of inflammatory bowel diseases (IBD) we could demonstrate an improved efficacy of anti-inflammatory drugs, paralleled by a reduction of adverse side effects due to systemic drug absorption, both in various preclinical animal models as well as in some advanced human cell culture models. In colitis patients, a significantly increased particle accumulation in inflamed mucosal areas could be confirmed by confocal laser endoscopy, correlating with the diagnosed degree of the inflammation.

Based on the finding that nanoparticles applied to the skin do not penetrate the stratum corneum but accumulate in hair follicles, we hypothesized that this route could possibly allow the non-invasive delivery of antigens. By encapsulating a model antigen (ovalbumin) along with some innovative adjuvant in biodegradable polymer nanoparticles and applying such formulation to the back of shaved mice, we found encouraging evidence that transfollicular immunization through the intact skin is possible, thereby stimulating antigen-specific T cells without the need of using any needles, chemical or physical penetration enhancers.

While the lung is a most attractive route for both local and systemic drug delivery by way of inhalation, its peculiar cellular and non-cellular barriers ask for a thorough understanding of the relevant nano-bio interactions. Besides cellular uptake and penetration, the interaction with bronchotracheal mucus and alveolar surfactant has implication for designing the shape and surface properties of aerosolized nanocarriers. Encouraging examples include the improved delivery of novel anti-infectives to reach intracellular bacteria, as well as of nuclease-encoding mRNA for genome editing in Sp-B deficient mice