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Nanomedicine for drug delivery across biological barriers: Intestines, skin and lung

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The focus of our research over the past ten years has been on the biological barriers of the gastro-intestinal tract, the skin and the lungs. This presentation will highlight some of our recent results or data of work in progress in these three areas, either concerning the development of new in-vitro models or new drug carriers systems, for which the nano-size often has turned out to be advantageous.

Inflammatory bowel diseases, such as Morbus Crohn or Colitis Ulcerosa, are painful for the patient and moreover difficult to treat due to the increased mucus production and the occurrence of diarrhea. We could demonstrate that the anti-inflammatory drug rolipram, when delivered by nanoparticles made of biodegradable PLGA, led to a prolonged alleviation of colitis syndromes in rats and a reduction of central nervous side effects, compared to the same dose of the drug administered as an aqueous solution. In order to study the mechanisms of this intriguing possibility of mucosal targeting, we have recently developed a 3D co-culture model of the inflamed intestinal mucosa and moreover started the clinical exploration of this concept in colitis patients.

With respect to skin drug delivery, there is an interesting new hypothesis that nanoparticles may penetrate along hair shafts and to thus accumulate in hair follicles. However, applying PLGA nanoparticles loaded with flufenamic acid, were mostly seen in the intercellular clefts between the keratinocytes. The observed enhancement of epidermal penetration may instead be explained by an acidic microclimate around the hydrolyzing polymer particles, leading to a reduced dissociation and higher lipophilicity/better penetration of flufenamic acid. This data points out that, besides of their small size, the chemical composition of such nanomaterials remains evenly important.

Due to their large surface area and excellent blood supply, the lungs are an attractive alternative route for drug delivery, both for local as well as for systemic action. By escaping mucociliary or macrophage clearance, inhaled nanopharmaceuticals could perhaps be used as platform for pulmonary sustained release delivery systems. In this context, we are working on a new in vitro modesl as well computational approaches to optimize particle deposition oc pulmnary cell culture systems, as well as to modulate their mucociliary clearance as well as the interaction with lung surfactant proteins. Finally, nanoplexes formed between biodegradable polymeric carriers and DNA/RNA-based drugs can be used to facilitate the transfection of cancer cells for the treatment and prevention of lung tumors.