

Development of Nanoparticulates Capable of Penetrating Physiological Barriers and the In Vitro Systems Used for Their Analysis

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Despite the fact that nanoparticulate systems have been widely used in biomedical applications such as drug delivery over the past several decades, their implementation and success has largely been limited. Central to this obstacle are that the interactions between nanoparticles and their biological surroundings are often overlooked during the design process. Physiological barriers that are known to hinder nanoparticle transport include mucosal layers present in organs such as the lungs or cervix, tumor parenchyma (bulk), and the blood-brain barrier. The ongoing research in my group seeks to address these challenges in order to bridge the gaps in knowledge that restrict the success of nanoparticle therapeutics. The development of novel nanoparticle systems and/or the use of specific penetrating agents can lead to effective delivery of a therapeutic payload to a target site in the body which would otherwise not be easily reached. Thus, our research focuses on the rational design of nanoparticulates by modifying their penetration properties via surface modification or the application of nanocomposites. In particular, this currently involves systems such as mucus-penetrating dry powder aerosol nanocomposite microparticles used for the treatment of pulmonary diseases such as cystic fibrosis and pulmonary hypertension. We have successfully generated and characterized the nanoparticles involved in these systems and are currently working to finalize this work through their *in vitro* characterization. Unfortunately, the *in vitro* systems used to characterize drug delivery vehicles, in particular those for aerosol lung cancer therapeutics, are not physiologically representative. As a result, we are developing *in vitro* methods involving air-grown multicellular tumor spheroids to overcome this constraint. The overarching goal of this research is to provide nanoparticle systems and tools for the development of intelligently designed therapeutics capable of targeting and penetrating physiological barriers of several types.