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Modulating nanoparticle-cell interactions in the presence of biological molecules

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Nanoparticles (NPs) are used both pre-clinically and clinically, as vehicles for therapeutics to improve targeted drug delivery and imaging. Despite rapid pre-clinical work progresses, the NPs' translation into the clinical environment is challenging. A primary reason for limited therapeutic benefit is the complex biological environment, including tissue barriers and immune cells, which retain the NPs and limit their delivery to the target cells. A detailed understanding of endocytic mechanisms by which different cell types internalize and process NPs is critical for successful implementation of NPs in nanomedicine.
The thesis focuses on investigating endocytic mechanisms of NPs in the presence of biological molecules, which is essential to optimize cellular targeting and uptake of NPs. Four different approaches to modulate NPs endocytosis were investigated: (i) co-exposure of macrophages to micro- and nano-sized silica NPs in the presence of bacterial lipopolysaccharide, (ii) the effect of cholera toxin subunit B on the endocytosis of silica NPs in differentiated colon epithelial cells and macrophages, (iii) the influence of epidermal growth factor on silica and gold NPs endocytosis in lung epithelial cells and (iv) the impact of substrates possessing different physico-chemical properties on the internalization of adhered silica NPs by macrophages.
The main message of the thesis is that the cell interaction and response to external stimuli vary depending on the type of stimuli, cell type and surface receptor expression. Phenotypic changes caused by the cell interaction with different molecules can affect cell endocytic mechanisms and consequently the NPs uptake. In addition to chemical stimuli, mechanical cues can as well affect the degree of NPs clearance by cells.

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