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Self-Organization of Nanoparticles

Implications for Interface Biology

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ABSTRACT

Cells bind to their surroundings via proteins displayed on the cell surface. These interactions support the cells and are important for many cellular processes, e.g. cell migration during morphogenesis, wound healing and cancer metastasis. There is a yet unmet need for simple and robust *in vitro* models mirroring the complex molecular organization found in natural tissue. In this thesis, protein-sized gold nanoparticles were used to introduce morphological and biochemical nanopatterns on material surfaces via nanoparticle self-assembly. These surfaces were used to explore the effect of protein organization and other nanoscopic parameters on cell response.

In their simplest form, gold nanoparticles (in solution) are stabilized by negatively charged ions adsorbed onto their surfaces. It was shown that such nanoparticles, 10 nm in diameter, could self-organize on a dithiol modified gold surface under the influence of electrostatic double-layer forces. The distance between the adsorbed particles could be tuned by the ionic composition of the particle solution, which was described using classical DLVO-theory. A novel method to prepare surfaces with nanoparticle gradients, based on this mechanism, was introduced.

Prepared surfaces were used as templates for the assembly of nanopatterns of chemical entities and proteins, with a periodicity in the sub 100 nm regime, by site-specific grafting of different molecules to the particle surfaces. Patterns with specific cell-binding proteins and peptides as well as synthetic polymers were realized and characterized with SEM, imaging SPR, QCM-D and TOF-SIMS. Gradient patterns were also assembled with multiple ligands, e.g. RGD-peptides and heparin, allowing the investigation of synergistic cell stimuli.

Biochemical nanopatterns were evaluated in studies on human fibroblasts and endothelial cells, e.g. the cellular mobility was explored in response to different gradient stimuli. In a separate study, fimbria mediated adhesion of *E. coli* bacteria to nanoscopic adhesive domains was investigated. Surfaces decorated with gold nanoparticles were also shown to attenuate the complement protein cascade system via morphological alteration of adsorbed proteins. Altogether, concepts and methods presented in this thesis offer a route to systematically explore the interactions between biology and molecularly organized interfaces.

Keywords: Gold nanoparticles, self-organization, self-assembly, nanostructure, nanopatterns, cell surface interactions, chemical gradients.