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Engineered particle surfaces to alter cell mechanotransduction and particle internalisation

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Engineering of materials for biomedical applications has enormous potential for advancing our ability to control and direct biological processes at biological interfaces and build nanostructures for improved therapeutic delivery. In order to explore the role of nanostructured surface features on cell-surface recognition and behaviour, interfaces bearing electrostatically stabilised colloidal particles were generated and assessed.

Polymeric particles were synthesised using poly(N-isopropylacrylamide) (PNIPAM) and designed to exhibit differential mechanical behaviour. Soft and stiff particles were subsequently attached to glass surfaces to investigate the role of particle stiffness and surface density on cell adhesion, migration and particle clearance. Stiffer particles were shown to be preferable for efficient uptake, while softer particles altered adhesion protein organisation in macrophages.

Contribution of cell mechanobiology to the uptake of freely suspended nanoparticles was assessed through the production of polydimethylsiloxane (PDMS) substrates with differing stiffness. The effect of substrate stiffness with and without a particle layer was assessed. Substrate characteristics were shown to influence nanoparticle uptake from suspension, cell adhesion and protein expression and offers a route to using the pathophysiology of diseased microenvironments to improve targeting of therapeutics.

Particle uptake from the surface holds enormous potential for local delivery and directed programming of cells at biointerfaces. Silica particles were functionalised with biopolymers such as poly(L-arginine) (PLA) and hyaluronic acid to encapsulate and deliver small interfering ribonucleic acid (siRNA) to cells from a decorated surface. Transfection and subsequent knockdown of protein expression suggest this paradigm would allow integration of genetic engineering of cells by biomaterial interfaces to improve integration.

Development of particle surfaces offers a highly tuneable landscape for the design of biomaterial interfaces. Physicochemical properties of particles can be engineered to introduce stimuli-responsive elements and improve selectivity to deliver agents to specific cell subpopulations. Moreover, it has been shown that potential synergises between mechanobiological cues arising from engineered materials and the native environment can be explored to improve treatment efficacy.

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