Nanohybrid Biomaterial Interfaces for Surface Mediated Gene Delivery

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Gene expression within a cell population can be directly altered through gene delivery approaches, which have tremendous potential for therapeutic uses, such as gene therapy or tissue engineering, or in research and diagnostic applications. However, inefficient gene delivery is a critical factor limiting the development of these applications. The adaptation of controlled release technologies to the delivery of DNA (typically complexed with cationic polymers or lipids) has the potential to overcome extracellular barriers that limit gene transfer, including aggregation of complexes, degradation of complexes, and in particular mass transport limitations that result in low concentration of DNA at the cell surface. Substrate-mediated delivery, also termed solid phase delivery, describes the immobilization of plasmid DNA or DNA complexed with nonviral vectors, to a biomaterial or substrate through specific or nonspecific interactions. In this delivery system, DNA complexes are immobilized to a substrate or biomaterial that supports cell adhesion, thus placing the DNA directly in the cellular microenvironment and increasing its local concentration. In this proposal we hypothesize that substrate-mediated gene delivery can be improved using novel nanohybrid surfaces, prepared using glancing angle deposition (GLAD) technqiues, with the capability to modulate cell function and increase surface loading of DNA complexes to maximize DNA transfer. The goal of this project is to develop a system to load exogenous genetic material (i.e. DNA complexes) into nanostructured surfaces and subsequently deliver these complexes to cells adhered to the surfaces. *GLAD nanostructures will serve two purposes in the proposed application, first to "prime" adhered cells for optimal uptake of delivered DNA as a result of nanotopographical influence, and second to deliver DNA in a controlled and enhanced fashion.* **This goal of the project will be accomplished by two objectives: 1) Design and characterize GLAD nanostructures that optimally load and release DNA complexes; and 2) Characterize transfection profiles and cellular attributes on GLAD nanostructures.** The proposed exploratory project focuses on the Center for Functional Nanohybrid Materials (CFNM) Research Clusters (1, 2, and 3), and intersects with many of CFNM's current interests including 3-D ordered nanostructures, chemical/biochemical sensing, nanohybrid characterization, polymer matrix inclusion, and the study of interactions of various materials with nanohybrid substrates. The results of this project wil impact the medical and biotechnological communities, including applications in gene therapy, tissue engineering, and diagnostics. For instance, surface nanohybrid structures, loaded with DNA, could be used in biomaterial implants, providing for genetic modification of cells interacting with the implants (e.g. hip implants, stents for restenosis, or bone fixation screws), which could promote healing and decease inflammation., or for tissue engineering scaffolds that promote tissue regeneration or cell cutlutre sbustrates used in bitochnolical assays.