157d Multilayered Polyelectrolyte Films for the Localized Delivery of DNA to Cells

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New materials and principles that provide control over the morphology, packaging, and presentation of DNA at surfaces will contribute to the development of localized gene therapies and advances in other areas of biotechnical research. We demonstrate here that multilayered polyelectrolyte films fabricated from alternating layers of plasmid DNA and a hydrolytically degradable synthetic polycation can be used to direct the spatially localized transfection of cells in culture without the aid of a secondary transfection agent. Multilayered assemblies 100 nm thick consisting of alternating layers of a synthetic degradable polyamine and plasmid DNA encoding for enhanced green fluorescent protein (EGFP) were deposited on quartz substrates using a layer-by-layer fabrication procedure. Placing film-coated slides in contact with COS-7 cells growing in serum-containing culture medium resulted in gene expression in cells localized under the film-coated portion of the slides. The average percentage of cells expressing EGFP relative to the total number of cells ranged from 4.6% to 37.9%, with an average of 18.6% +/- 8.2%, as determined by fluorescence microscopy. In addition to providing a mechanism for the immobilization of DNA at the cell/surface interface, the characterization of film topography by atomic force microscopy (AFM) demonstrated that these films, while initially smooth, undergo significant structural and topological rearrangements upon exposure to physiological media to present condensed plasmid DNA nanoparticles at the surfaces of coated substrates. These data suggest that the cationic polymer in these materials may, in addition to serving as a structural component of these films, also contribute to the condensation, internalization, and expression of plasmid in cells. The materials and procedures used here permit the deposition of erodible polyelectrolyte films onto a variety of clinically relevant surfaces. Prospects for these assemblies as a framework for the localized delivery of DNA from implantable materials will be discussed.