Chapter 67

Pulsed Laser-Activated Plasmonic Pyramids for Intracellular Delivery

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Abstract We use pulsed laser-activated plasmonic micropyramids to deliver molecules to living cells with high efficiency, viability, and throughput. Cellular therapy holds great promise for applications in gene therapy and fundamental biomedical research, and it is essential to develop a universal delivery platform that can safely deliver biomolecules to different cell types effectively. Such a platform would be an important stepping stone towards treatment of hematologic diseases such as leukemia and primary immunodeficiency disorder treatments. An idea molecular delivery platform would exhibit advantages such as high delivery efficiency, low toxicity, minimal immune reaction, and reusability. None of the currently available commercial methods, such as viral-based or electroporation, offer all desirable characteristics at once. We present a new optical method for molecular delivery that uses laser-activated microstructures. Our micropyramids produce a strong plasmonic effect under laser illumination by focusing energy in a small volume at the tip of each pyramid. This leads to the formation of microbubbles which temporarily porate the cell membrane and allow dye molecules and siRNA to diffuse into the cytoplasm. We fabricate large-area micropyramid arrays using photolithography, anisotropic etching of silicon, metal deposition, and template stripping. The silicon pyramid templates can be used repeatedly to fabricate gold pyramids. We optimize our laser parameters for high efficiency delivery of small dye molecules like calcein (>80 %) at high cell viability (>90 %). Alongside small dyes, we also deliver different-sized fluorescently labeled dextrans (70 kDa–2000 kDa) and fluorescent microspheres. Our method delivers molecules with high efficiency and high cell viability in different cell types, and our substrates can be reused for repeated high efficiency poration. Our scalable technique offers an innovative approach to delivering molecules to living cells for important applications in regenerative medicine.

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