Laser-activated Plasmonic Intracellular Delivery: Using Micropyramids to Deliver CRISPR-Cas9 to Hematopoietic Stem Cells (HSCs)

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We propose 1) to investigate how our laser-activated intracellular delivery technique affects living cells and 2) to deliver genome-editing biomolecules to living cells for human health-care applications. The safe and efficient delivery of macromolecules to living cells is crucial for advancing health care. No currently available intracellular delivery method concurrently offers the characteristics necessary for successful therapy: high efficiency, viability, and throughput; delivery of diverse cargo into diverse cell types; spatial selectivity; and scalability. We pioneered the use of laser-activated micropyramids that absorb light and generate microbubbles to porate the cell membrane, allowing membrane-impermeable macromolecules to diffuse into the cell. Our competitive non-viral intracellular delivery technique simultaneously offers all desirable features: preliminary results show 90% delivery efficiency, 97% viability and 10,000 cells/s throughput with HeLa cells. Our team has the requisite expertise in nanofabrication, laser physics, and cell biology to propel our technology to positively impact biomedical and human heath-care research. The Catalyst grant will enable us to combine our current nanofabrication and cell culture research at CNS with advanced imaging at HCBI to investigate cellular response and to deliver genome-editing tools to living cells using our technique. With the support of the Catalyst team, we will develop our technique as a first step towards creating treatments for genetic diseases.