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Intracellular molecular manipulation by femtosecond laser triggering

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Regulation of cell signaling is a very attractive challenge to life science which provides good potential for better understanding of cellular processes, cell development, and cell physiology, as well as potential application for gene therapy, economical metabolic engineering and biopharmaceutical production. A lot of approaches have been developed for specific stimulation of cell molecules, signaling pathways, functions. But most of those approaches are based on biochemical techniques, for example, optogenetics and introducing some signaling proteins to cells. Hence usually such techniques are invasive and complicated. In this report, we present series of all-optical methods to modulate cell signaling and processes simply by photostimulation. Cellular Ca^{2+} store and reactive oxygen species (ROS) can be released and regulated by a short flash of femtosecond laser irradiation. The opening of Ca^{2+} channel in cell membrane and mitochondrial release of ROS can be controlled. Therefore we developed an optical method to regulate gene expression since some transcription factors can be activated by this optical treatment, by which some specific differentiation regulators in mesenchymal stem cells are upregulated for potential induced differentiation. The tightly focused femtosecond laser can further induce precise insult and oxidative flashes in single mitochondria. Mitochondrial fragmentation and swelling can be induced with no perturbing to surroundings, but the membrane potential and permeability transition pores are influenced. Localized translocation of Bax and cytochrome C can be precisely controlled by this optical method. Hence we propose that femotosecond laser has a promising application potential in cell research, mitochondrial diseases, gene therapy, and stem-cell medicine.