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## Optical regulation of stem-cell differentiation by femtosecond-laser photostimulation

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Stem-cell therapy is showing great potential in regenerative medicine because of their inherent ability to self-renew and differentiate. Biochemical and genetic methods and 3D materials/structures have been developed and making great progresses on controlling the development and differentiation of stem cells. One of the major remaining concerns is the invasion of those technologies. In this study, we demonstrate an all-optical and noninvasive approach to precisely induce the differentiation of mesenchymal stem cells (MSCs) and cerebellar granule neuron progenitor (GNP) cells. We show that the single-time fast-flash of photostimulation by a tightly-focused femtosecond laser, without any optogenetics, can activate endogenous signaling pathways for stem-cell differentiation directly by multiphoton excitation. The significant upregulation of differentiation regulator RUNX2 and Osterix in MSCs 7 days after photostimulation indicates the osteogenic differentiation of MSCs. The differentiation was finally confirmed by Alizarin Red staining 28 days after photostimulation. The differentiation of GNP cells *in vitro* and *in vivo* can also be induced by this method. This noninvasive optical technology hence provides an encouraging advance in activation of signaling pathways in cells and alternative to classic biochemical methods for stem-cell differentiation. This result also provides an optical choice with promising potential for clinical regenerative applications.

### **Short Bio:**

**Dr. Hao He** is a full-time professor at Shanghai Jiao Tong University. He got the B.S. in the University of Science and Technology of China in 2006 and the PhD degree in the Chinese University of Hong Kong in 2010 respectively. Since 2011, he worked as an associate professor in the Ultrafast laser Laboratory at Tianjin University. Since 2014, he joined the School of Biomedical Engineering at SJTU. His research focuses on the precise stimulation and modulation of cellular signaling and functions by femtosecond lasers. Currently he has published more than 30 SCI papers as the first or corresponding author, two on Nature Photonics and two highlighted by Nature Photonics. His research was supported by the

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