Using ultrasound to rapidly manipulate cellular activities

Yu-Chun Lin

Institute of Molecular Medicine, National Tsing Hua University, Taiwan

Developing tools to precisely control cellular activities has enabled people to dissect the underlying mechanism of cellular events and serves as potential therapeutic applications. Inducible protein dimerization by specific stimuli such as small chemical molecules and photons has been widely used to spatiotemporally regulate expression, location, and activities of proteins, accompanied with manipulating numerous cellular activities. Despite their significances, these approaches surfer from one inevitable drawback: it is challenging for the stimuli to access to target cells in deep tissue without any invasive surgical procedures. To circumvent these long-standing limitations, we attempt to use ultrasound, which is noninvasive, focused, and with great depth of penetration, to perturb cellular activities. Two distinct strategies were used to achieve our goals. Firstly, ultrasound-induced sonoporation was utilized to trigger the influx of membrane impermeable dimerizer into cells to induce protein dimerization as well as manipulating cellular activities. With this, we have successfully modulated lipid composition in living cells. Secondly, we have identified a genetically encoded ultrasound-sensing protein (USP) and found that expression of our USP endows mammalian cells with abilities to sense ultrasound stimulus and to trigger rapid calcium responses. The new approaches we developed will significantly improve the conventionally technical limitations and will extend the tool kit in the field. Most importantly, it will provide the possibility using ultrasound to locally and rapidly manipulate the specific cellular activities in deep tissues.