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Optogenetics-Mediated Ca^{2+} Signaling in Regulation of Ca^{2+}- Dependent Transcription Factor Activation

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The ability of a simple ion such as Ca^{2+} to play an highly versatile intracellular signal results from the facility that cells have to shape Ca^{2+} signals in the dimensions of space, time and amplitude. Thus, spatial and temporal changes in intracellular Ca^{2+} concentration is important to determinate the cell fate. Optogenetics is the combination of genetics and optics to control well-defined events within specific cells of living tissue in real time. Optogenetic stimulation approach that uses channelrhodopsin-2 (ChR2) related proteins has been developed for providing more precise and targeted stimulation effect on cells *in vivo* and *in vitro*. We aimed to pose the formerly unaddressed fundamental question of how Ca^{2+} signals regulate transcription factor activation by manipulating intracellular Ca^{2+} through using optogenetic strategies. Three Ca^{2+}-dependent transcription factors, NFAT, NFkB and CREB, were examined in this study. We found that (1) elevation of intracellular Ca^{2+} levels that correspond with the power, frequency and duty cycle of light illumination in a dose-dependent manner; (2) activation of Ca^{2+}-dependent transcription factors is depends on Ca^{2+} oscillations with different frequency and amplitude in ChR2 overexpressed cells. Moreover, activation of NFκB required low-frequency and low-amplitude Ca^{2+} oscillations, whereas high-frequency and high-amplitude Ca^{2+} oscillations tended to activate NFAT. On the other hand, CREB activation occurred regardless of the frequency and amplitude of Ca^{2+} oscillations. In summary, the delicate regulation and precise control of transcription factor activation can be achieved under the optogenetic platform. It will enable us to be confident in applying this advanced technique to manipulate the expression patterns of genes by desire. Such a process would be a potential platform in study of cell development and cancer.

Biography:

Dr. Wen-Tai Chiu received the Bachelor's, Master's and Ph.D. degrees from National Cheng Kung University, Taiwan in 1997, 1999 and 2007, respectively. He has been a postdoctoral fellow at the University of Texas MD Anderson Cancer Center from 2008 to 2010. Prof. Chiu is currently an associate professor in the Department of Biomedical Engineering at National Cheng Kung University. His research interests lie in the area of Ca^{2+} signaling and molecular imaging of cancers. Much of his work has been on improving the understanding, design and performance of Ca^{2+} in focal adhesion dynamics, cell migration, metastasis and chemoresistance.