國立清華大學第 21 屆新進人員研究獎得獎人簡介

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"發展精準控制細胞技術"

科學的進展往往藉由新技術的發明而有所突破。本團隊過去幾年來發展出利用加入化學小分子及照射超音波去精準控制細胞生理功能的嶄新技術。我們精準地控制活體細胞中微管骨架蛋白的後轉譯修飾，這些研究首次揭露微管如何藉由後轉譯修飾在細胞中特定位置調控細胞結構及功能(Hone *et al.*, Nat Commun, 2018)，更是發展治療與微管缺失有關人類疾病的重要基石。除此之外，超音波因為高穿透性、高安全性及可聚焦等特性，被廣泛運用在醫療診斷上。為了要建立非侵入式地調控深層組織生理作用，我們結合了超音波照射技術與化學生物學兩系統，建立一個嶄新技術(SonoCID)，其可利用聚焦超音波照射來快速地調控目標細胞內的特定生理機制(Fan *et al.*, ACS Synth Biol, 2017)。除了現有已發展的技術外，我們近期更在自然界中，一些能感受超音波的物種如蝙蝠、鯨魚、海豚等身上，發現一個超音波感應蛋白質，將其移植進人類細胞中能增加其超音波感受能力，希望能藉此了解生物感受超音波的分子機制，甚至加以利用，而來發展更多非侵入式醫用超音波操縱技術。很榮幸能獲得此獎項，非常感謝審查委員的肯定及校方、科技部於經費上的支持，並且感謝實驗內成員及合作團隊的大力協助，還要感謝家人一直以來的支持。

"Controlling cells precisely"

The development of approaches that control cellular activities has made it possible to dissect the underlying mechanisms of cellular events and to offer potential therapeutic applications. We recently have built a series of tools to manipulate molecular components and activities in living cells using various external stimuli such as chemicals or focused ultrasound. One of these tools, STRIP, overcomes a long-standing technical challenge in biology which spatiotemporally rewrites tubulin post-translational modifications (PTMs) in living cells (Hong et al., 2018, Nat Commun). With this new tool, we, for the first time, provided evidence of how tubulin spatiotemporally regulates cellular activities through its PTMs. Moreover, the ability of tubulin manipulation may offer far-reaching implications for the progression of various diseases caused by the deregulation of tubulin PTMs, including cancers, neurodegenerative diseases, and ciliopathies.

The focused ultrasound (FUS) has been globally used for diagnosis and non-invasive treatments due to its high spatiotemporal resolution with good penetration depth and low cost. To expend its applications, we established a new ultrasound-chemical hybrid system to remotely control cellular activities by FUS excitation and named it the SonoCID. Owing to the great penetration depth of FUS we used in SonoCID (~400 mm in depth), this system can be potentially applied to deep tissues in large animals like primates (Fan et al., ACS Syn Biol, 2017).

Very recently, with collaboration with Professor Chih-Kuang Yen's group in the Department of Biomedical Engineering and Environmental Sciences at NTHU, we identified an ultrasound sensing protein (USP). Heterogeneous expression of USP endows transfected human cells with ~11 folds better of ultrasound sensitivity compared to control cells. Ultrahigh sensitivity of USP makes it possible to remotely control cellular activities by a short pulse of FUS (as short as 3 seconds) under low acoustic pressure. We are developing a series of sonogenetics approaches to precisely manipulate cellular activities for various therapeutic applications.

It has been my great honor to obtain this prestigious research award. First, I would like to express my gratitude to the research award committee, National Tsing Hua University, and Ministry of Science and Technology for their great support. Moreover, I appreciate our lab members and collaborators for their excellent contribution to the research. Finally, big thanks for my family for their love and help in all aspects of life.