姚季光

中央研究院生物化學研究所副研究員

代表著作：

- Jhan-Jie Peng, Shih-Han Lin, Yu-Tzu Liu, Hsin-Chieh Lin, Tsai-Ning Li, **Chi-Kuang Yao***, 2019, “A Circuit-Dependent ROS Feedback Loop Mediates Glutamate Excitotoxicity to Sculpt the *Drosophila* Motor System”, *eLife*, 8, e47372.
- **Chi-Kuang Yao***, Yu-Tzu Liu, , I-Chi Lee, You-Tung Wang, Ping-Yen Wu, 2017, “A Ca^{2+} Channel Differentially Regulates Clathrin-mediated and Activity-Dependent Bulk Endocytosis”, *PLoS Biology*, 15(4), e2000931.

簡評：

姚博士的兩篇代表作是有關神經科學的研究。2017 年的 PLOS Biology 論文在探討神經細胞如何在長期刺激下維持突觸囊泡的衡定，姚博士的研究成果為突觸囊泡的釋放與循環間的平衡提供了重要的機制，並有助我們了解快速有效的突觸傳遞。2019 的 eLife 論文研究成果在於闡述穀胺酸（L-glutamate）的興奮毒性（excitotoxicity）如何造成神經系統功能障礙，姚博士提出經由活性氧化物質與神經迴路的作用模型。雖然兩篇論文方向並不相同，但都是非常完整且具份量的研究。姚博士是這兩篇論文的通訊作者。這些成果顯示姚博士是一位傑出的神經科學家，他的研究具有新穎性、原創性與科學影響力。

簡歷：

姚季光博士於 1999 年畢業於成功大學生物系，求學期間因接觸了分子生物與遺傳學等課程後燃起對科學研究的好奇，之後進入李益謙教授實驗室開啟了研究之路。因對科研的熱愛而甄試就讀陽明大學遺傳所，受孫以瀚教授研究風格及題材所吸引而加入他的團隊，透過果蠅模式生物系統中優化的研究技術闡釋了調控組織分化的機轉，於 2005 年取得博士學位。為了擴展研究的視野及張力，2006 年進入 Hugo Bellen 教授位於德州休士頓貝勒醫學院的實驗室，從事神經細胞傳導之相關研究；2011 年底起任職中研院生物化學所，主要研究方向為探索大腦神經細胞能緊密互通的分子機制，也致力於解開導致神經退化疾病的成因，目標為能了解人類大腦精密運作的奧妙以及開發治療神經系統相關疾病的方法。

代表作簡介：

Synaptic Transmission in Health and Disease

Background:

Functional robustness of the human brain relies on complicated yet extremely coordinated communications among tons of neurons. Neurons communicate via synapses in which fast exocytosis of the synaptic vesicle (SV) in response to nervous stimuli releases chemical neurotransmitters, such as glutamate, thereby governing all human behaviors. Repetitive SV exocytosis however would eventually deplete SVs and disorganize presynaptic plasma membrane architecture. To overcome such burdens, SV endocytosis immediately occurs after exocytosis. However, the key outstanding questions are “how is exocytosis tightly coupled with endocytosis?” and “What factor initiates endocytosis?”

Glutamate is the major excitatory neurotransmitter. A tight balance between glutamate release and reuptake is therefore critical for keeping extracellular glutamate low. In a variety of acute and chronic neurological diseases, accumulation of extrasynaptic glutamate has been known to result in “glutamate-mediated excitotoxicity” to the nervous system. Yet it has remained largely

unclear how glutamate-mediated excitotoxicity can influence the integrity of neural circuits and cause nervous system dysfunction.

Approach:

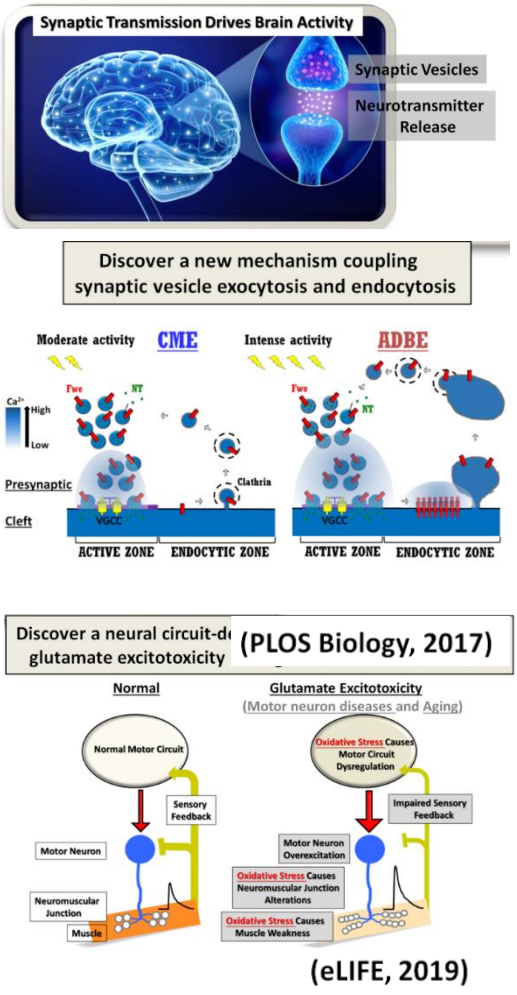
To tackle these puzzles, the group led by Dr. Chi-Kuang Yao took advantage of the *Drosophila* system, e.g. comprehensive genetic tools, and combined it with a variety of microscopies, live imaging, and electrophysiology.

Outcome and Significance:

Dr. Yao's team has discovered:

(1) A SV-associated Ca^{2+} channel, called Flower (Fwe), initiates SV endocytosis and therefore couples exocytosis and endocytosis, which has provided a conceptual breakthrough for synaptic vesicle cycling. Future investigations on understanding spatiotemporal regulation of activity and localization of the Flower channel will be expected to advance our knowledge of fast and efficient synaptic transmission underlying brain computation.

(2) In motor system, glutamate-mediated excitotoxicity can induce a circuit-dependent reactive oxygen species (ROS) feedback loop to impair proper activities of the locomotor circuit and muscles, ultimately leading to motor neuron over-excitation, aberrant neuromuscular junction growth and strength, and compromised motor function (the model depicted in right panel of figure), . This finding has therefore opened a new window for investigating the impacts of excitotoxicity and ROS on the nervous system. In addition, our fly system will be a good animal-based platform for excitotoxicity and ROS-related research.



得獎感言：

如果研究工作是一段漫長艱辛的旅程，那麼這個獎項就像是座加油站，肯定了我們研究團隊的努力，也為我們加了滿滿的油讓接下來的研究可繼續勇往直前。很感謝中研院及科技部在研究資源上的支持，也感謝中研院的導師們與同事的協助與激勵，更要感謝在實驗室中一起日以繼夜努力的年輕夥伴們。最後特別要感謝家人對我全力的支持，讓我能全心做研究。期許不僅能繼續培育出優秀的科研新血，也能有更多重要的研究成果貢獻於社會健康醫療。