鄭珮琳

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得獎著作：

- Hsu, M.-T., C.-L. Guo, A.Y. Liou, T.-Y. Chang, M.-C. Ng, B. I. Florea, H. S. Overkleeft, Y.-L. Wu, J-C. Liao, and **P.-L. Cheng***, 2015, "Stage-Dependent Axon Transport of Proteasomes Contributes to Axon Development", *Developmental cell*, 35(4), 418-431.
- Ting-Ya Chang, Chen Chen, Min Lee, Ya-Chu Chang, Chi-Huan Lu Shao-Tzu Lu, De-Yao Wang, Aijun Wang, Chin-Lin Guo **Pei-Lin Cheng***, 2017, "Paxillin Facilitates Timely Neurite Initiation on Soft-Substrate Environments by Interacting with the Endocytic Machinery", *eLife*, 6, e31101.
- Guo, C.-L., and **P.-L. Cheng***, 2015, "Second Messenger Signaling for Neuronal Polarization: Cell Mechanics-Dependent Pattern Formation", *Developmental Neurobiology*, 75(4), 388-401.

得獎簡評：

鄭博士的三篇代表性著作是有關神經發育的研究。2015 年的 Developmental Cell 文章研究主要在證明神經軸突發育與 Proteasome gradient（蛋白酶體梯度）的逆相關性，該梯度是調控神經元極化（Neural polarization）所需的長程抑制機制。腦衍生神經因子（BDNF）造成 adaptor Ecm29 的磷酸化，可以促進蛋白酶體–動力蛋白（dynein）的結合，進而加強蛋白酶體的逆向運送。此結果證實了神經軸突的蛋白酶體運送可以決定

神經軸突的發育。2017 年的 eLife 文章研究成果在於闡述神經周圍環境的機械生物學，顯示 paxilin 在周邊軟硬受質的不同情況，可以經由細胞內吞作用或增強黏度而改變神經始突起（neurite initiation）的差異。第三篇論文發表在 Developmental Neurobiology，為鄭博士對神經極化的機轉，以次級訊息的觀點，綜合生化與力學的角度，提出一個模型來解說神經極化。鄭博士是這三篇論文的通訊作者。這三篇論文顯示鄭博士是一位傑出的神經科學家，她的研究具有原創性及科學影響力，有助於從生化與力學觀點瞭解神經軸突的發育。

得獎人簡歷：

Dr. Pei-Lin Cheng（鄭珮琳博士）is a cell biologist and neuroscientist. She received a Ph.D degree at NYMU, mentored by Dr. Yan-Hwa Wu Lee（吳妍華院士） from 1999-2004 for exploring roles of TGF-beta signaling pathway in hepatitis C virus infection. Then she researched neuronal polarization with Dr. Mu-Ming Poo（蒲慕明院士） at UC Berkeley from 2006-2011. Dr. Cheng joined the IMB, Academia Sinica(中研院分生所), in 2011. Dr. Cheng's primary research interests lie in the field of neuronal morphogenesis （神經元形態形成）, which defines how one of most functionally and mechanistically diverse structures, namely the brain and spinal cord, emerges. The strength of her lab has been the ability to implement advanced microscopy techniques, brain mimetic platforms, simple mathematical models, and conventional biochemistry/genetic methods to tackle fundamental questions relevant to mechanisms underlying neuronal development and physical principle of neuronal growth.

得獎著作簡介：

I. Proteasome transport in the nascent axon（新生神經元藉由蛋白質酶體的遠距輸送機制來決定軸突生長時序）

Background and Approach: The ubiquitin proteasome system

(UPS), which constitutes cellular machinery governing local protein turnover, also contributes to axon growth and guidance. It was previously known that inhibition of proteasomes, the major protein degradation machinery, by MG132 or lactacystin treatment promotes formation of multiple axons in standard cultures of rat hippocampal neurons. However, factors governing proteasome activities and distribution in neurons remain poorly understood. Using cultures of early rat hippocampal cells during the period in which axonal fate is determined, we have been able to detect endogenous proteasomes by monitoring accumulation of short half-life GFPu in neurons and analyzing mobility of MV151-labelled proteasomes.

Outcome and Significance:

Our findings reveal a developmental mechanism that causes a gradient of proteasome abundance from lowest at the axonal tip to highest near the soma in a single newborn neuron. The resulting gradient can serve as an efficient long-range inhibitory mechanism required for proper neuronal polarization, by which newly differentiated neurons ensure low and high protein turnover capacity in respective axon terminal and somatodendritic compartments. Accordingly, our work addresses the spatial dilemma of why and how other minor neurites do not succeed in becoming the "next axon," even if the first one, which stimulates lateral inhibition signals, extends several hundred micrometers away from the somata. Our study reporting these findings was published in Developmental Cell in 2015 (Hsu et al., 2015) and recommended by F1000Prime.

II. Soft tissue/substrate environments permit neurite initiation（極軟與極低黏附力的環境下，神經元方能快速啟動突觸生長）

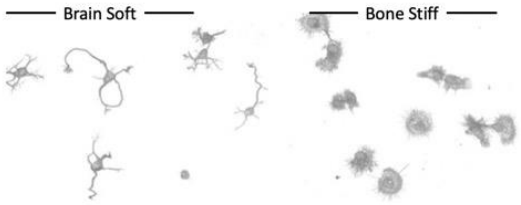
Background and Approach:

Both genetic programs and cell mechanics are required to execute neurite initiation in a timely manner under native physical environments in vivo. However, understanding how this occurs is not trivial, and to date many studies tackle the question using thin-glass or plastic cultures, in

which cells undergo aberrant activation of non-specific interactions through adhesion to solid substrata. We circumvented this limitation by using polymerized hydrogels of three elastic moduli—0.1, 1 and 20 kPa—verified by atomic force microscopy, and by functionalizing the surface with minimal laminin levels to investigate mechanisms driving neurite initiation on soft substrate environments.

Outcome and Significance:

Mechanobiology is an emerging field that embraces knowledge obtained from biophysics, biomaterial science, and physiology. We have used a mechanobiological approach to show that stiffness of a cellular environment strongly impacts cellular behavior. We also provided mechanistic insight linking stiffness with the adhesion and endocytosis machineries, opening a new avenue to study of how neurons adjust gene expression to membrane mechanics in different physical environments. Our study was published in eLIFE in 2017 (Chang et al., 2017) with the editorial comment: “This manuscript is one of the best in this young and growing field of mechano-tissue biology”



得獎感言：

謝謝中研院與評審委員們的肯定。在這就快跟“年輕”兩字告別的時間點，回頭看自己在科學研究上的起點，滿滿是家人與指導教授們無條件的給予與包容，學生助理及研究學者們的陪伴與激勵。我個人很享受這學術研究中所見的繁星點點，也相信這麼多的幸運與堅持，為的是讓現今覺得棘手的神經發育相關難題，終究在我們某個決定性的發現中得到答案。謝謝大家。