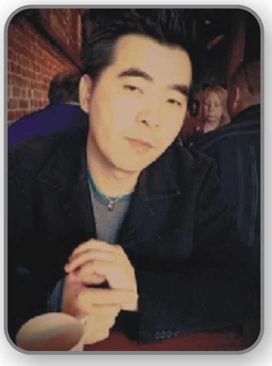

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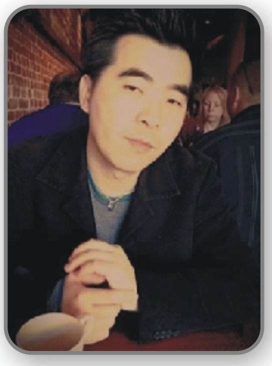
研究興趣

果蠅神經生物實驗室有兩個主要的研究目標：探討大腦老化及利用果蠅進行癌症研究。目前的研究認為生物老化與眾多疾病、行為模式改變、細胞層級的變化息息相關，實驗室利用果蠅模式生物研究與中樞神經系統衰老相關的分子機制和伴隨的老化特徵。由於果蠅相對於其他模式生物具有較短的壽命，因此被認為是研究老化的最佳動物模型之一。透過次世代基因定序分析老化的果蠅大腦，我們找到一系列的基因和微小核糖核酸在生物衰老的過程中具有特別的表現量差異，並希望能利用這些基因作為研究大腦老化的機制和探討生物老化指標。在這眾多的基因中，我們首先對於小熱休克蛋白（sHSPs）的基因家族特別感興趣，也證實了一些小熱休克蛋白具有調節果蠅壽命的能力，將來我們也希望能了解老化是如何在細胞層次上調節小熱休克蛋白的表達機制。此外，我們也對於神經元和神經膠細胞的老化感興趣，由於不同類型的腦細胞可能的衰老機制、速度並不相同，因此我們將探討不同細胞老化時的特徵型態。最後，我們發展了一種專門的老化測定法，使我們能夠有效地評估果蠅的認知狀態（腦功能指標）。透過這種測定法，我們能夠在不同的實驗條件下評估果蠅認知能力的變化，例如：在老年的果蠅或具有神經退行性疾病的果蠅。更重要的是，這種果蠅認知能力檢定平台將可以被應用於篩選或測試對神經退行性疾病有益的藥物與治療。

實驗室的另一個方向則是利用果蠅作為癌症研究模型。藉由在果蠅體內大量表現人類的致癌基因-表皮生長因子受體家族(ERBB/HER)，我們成功建立了人類多形性膠質母細胞瘤(GBM)的腫瘤模型。此模型除了可用於測定腫瘤的特徵和生理環境外，還可以用於探討幾項問題：第一，從臨床腫瘤樣本中找到的有關的基因突變後，可以利用果蠅快速地檢測及評估該突變對於腫瘤形成的影響。第二，我們可以利用果蠅來探討一個可能的致癌基因對於不同種類癌症的致病性。第三，大多數癌症的形成需要同時出現多個致癌基因突變，而利用果蠅我們能夠輕易地探討多個致癌基因突變之間的交互作用，使我們更能模擬腫瘤實際的基因背景。 最後我們希望能利用果蠅腫瘤模型帶來個人化醫療，創造出作為癌症病人替身的果蠅，讓這些果蠅帶有病人體內的多基因突變，成為抗癌藥物的篩檢或治療平台。



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Research Interests

The Drosophila Neurobiology Lab has two major research directions: the Aging Brain and the Drosophila Tumor Model. Current studies have linked a broad spectrum of cellular events, diseases, and behavioral traits with the aging of animals. My lab is interested in studying the phenotypes and molecular mechanisms associated with the aging process of central nervous system using the fruit fly model. Given the relatively short lifespan, Drosophila is considered one of best animal models for the aging studies. Through NGS analyses of the aging fly brains, we were able to identify a collection of genes and small RNA species showing differential expression patterns. These genes and small RNAs are potential candidates related to the brain aging machinery and markers. Particularly, we focused on the gene family of small heat shock proteins (sHSPs) and demonstrated some sSHPs have the capability to modulate the life expectancy of Drosophila. It will be interesting to learn what are the cellular events triggered by sHSPs and the mechanisms to regulate the expression levels of sHSPs as age progresses. Along with the NGS studies, we are also interested in the phenotypic analysis of aging neurons and glial cells. Specifically, distinct types of brain cells may employ specific aging mechanisms and degenerate with different paces. Lastly, at the level of organism aging, we formulated a specialized behavior assay that allows us to faithfully assess the cognitive status (an indicator of brain function) of Drosophila. With this robust behavior assay, we were able to explore the changes of Drosophila cognition under distinct experimental conditions, such as in the aged animals and animals with neurodegenerative symptoms. More importantly, this Drosophila cognition assessment platform will be used to screen/test drugs/treatments beneficial to neurodegenerative diseases.

The next direction in the lab is to establish the Drosophila Tumor Model. We have successfully built the human glioblastoma (GBM) model in fruit flies via the ectopic expression of oncogenic human ERBB/HER genes. Besides characterize the tumor phenotypes and physiology, we realized the Drosophila Tumor Model can be used to study several questions. First, the oncogenic capability (tumor driving force) of mutations identified from clinical tumor samples can be quickly assayed and evaluated. Second, the potential of a given oncogenic to induce multiple types of tumor can be explored using the Drosophila Tumor Model. Third, given the tumorigenesis usually depends on the interactions of multiple oncogenic mutations, it is much experimentally feasible to recreate similar genetic background in the fruit fly model. Therefore, with the Drosophila Tumor Model, we like to create Drosophila avatars bearing multiple genetic changes akin to those of a cancer patient. Most importantly, the genetically personalized fruit flies can be used to screen/test cancer drugs/treatments.