2008 年中央研究院「年輕學者研究著作獎」得獎人簡介

姓名：吳素幸 	學歷： 加州大學戴維斯分校 博士 1992-1997 台灣大學植物學研究所 碩士 1989-1992 台灣大學植物學系 學士 1985-1989 現職及經歷： 中研院植微所助研究員 2001 迄今 史丹福大學 博士後研究 1999-2001 加州大學戴維斯分校 博士後研究 1997-1999 台灣大學植物學系 助教 1990-1992

得獎著作名稱：（請以申請時之格式填入）

1. Lin, J.F. and S.H. Wu, *Molecular events in senescing Arabidopsis leaves.* Plant J, 2004. **39**(4): p. 612-28.
2. Buchanan-Wollaston, V., et al., *Comparative transcriptome analysis reveals significant differences in gene expression and signalling pathways between developmental and dark/starvation-induced senescence in Arabidopsis.* Plant J, 2005. **42**(4): p. 567-85.
3. Chen, H.M., Y.H. Li, and S.H. Wu, *Bioinformatic prediction and experimental validation of a microRNA-directed tandem trans-acting siRNA cascade in Arabidopsis.* Proc Natl Acad Sci U S A, 2007. **104**(9): p. 3318-23.

得獎著作簡介: （2000 字左右）

基因表現如何調控植物的型態形成是許多植物學家探索的課題，我們著重在研究影響植物生長和發育的基因調控網路，以系統生物學研究法來鑽研這個研究領域。

一、 阿拉伯芥光訊息傳導分子機制之研究

由於植物無法自由遷徒，所以在生長過程中，經常需要調控體內基因表現，來因應周遭環境的變遷，以達成最適合的生長和發育狀態。「光」是所有環境因子中影響植物生長與發育最明顯的一項。在植物內已發現有多種光受體，這些光受體的存在使植物能夠感應環境中的光訊息，以進行生長發育。例如，適當的光照能夠使植物由土壤中長出幼苗、躲開其他植物樹冠的陰影，並在每年特定季節開花，甚至可以影響植物老化的過程等。我們的研究著重於了解植物如何藉由訊息傳導機制來調整生理生化特性，以適切回應外在環境「光」的訊息。

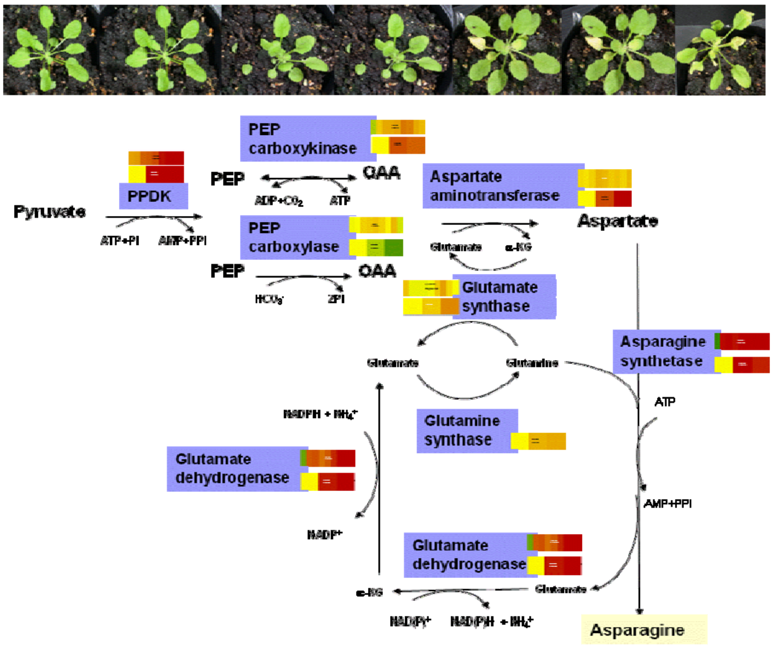
在探討外在光環境如何影響植物葉片老化的研究中，我們結合基因表現圖譜

分析與資料庫分析，探索在此過程中生化代謝途徑之調整、細胞大分子降解之分子機制與轉錄因子之調控；研究結果亦引導我們建立一個全新與氮循環利用相關的代謝路徑（圖一）。這個研究報告並促成一多國合作計畫，對各種影響植物葉片老化的內生型因子與外在環境調控因子進行比較基因體研究，使我們得以一窺此過程中之複雜的分子交互作用網路。這二篇文獻中的研究模式與成果在植物系統生物學領域中廣為引用。

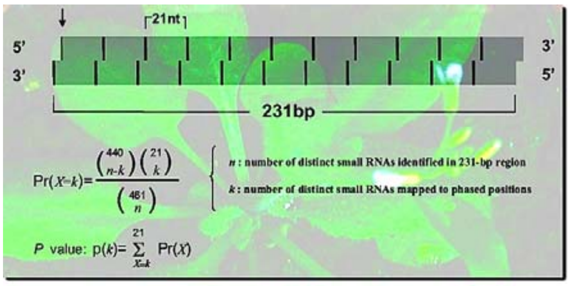
二、 生物資訊導向研究

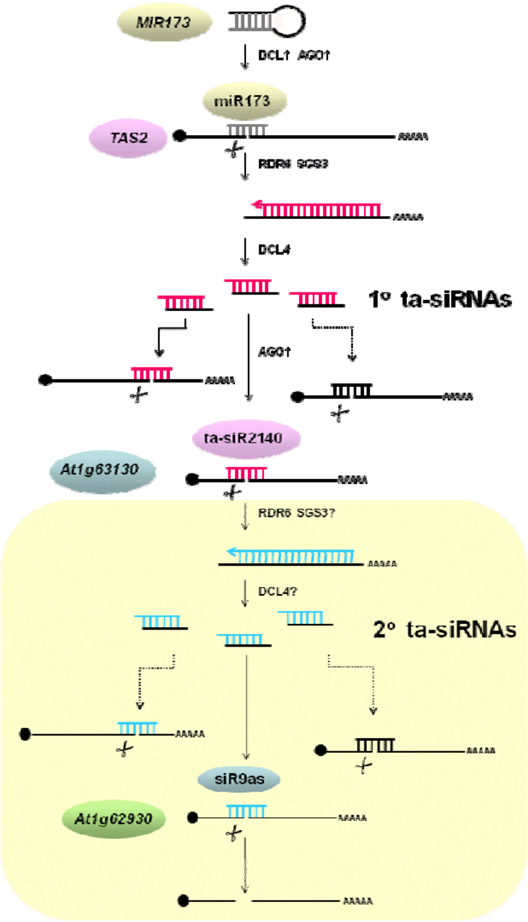
隨著研究技術日新月異的進步，生物相關資料庫所涵蓋的資訊也以幾何速度增加，這些資訊提供給生物學家一個前所未有的機會，去以一個全新的角度研究已知的生物問題，甚或去發掘一個未曾探討過的生命現象；在發掘更多新基因的同時，生物學家也發現：除了過去數十年眾所皆知的轉錄 (transcription) 與轉譯 (translation) 機制外，生物中的小型核醣核酸 (small regulatory RNA) 也在調控基因表現的過程中，扮演很重要的角色。

Trans-acting 小型干擾核醣核酸 (trans-acting small interfering RNA; ta-siRNA) 屬於一種新型的小型核醣核酸，對於植物正常的生長發育有舉足輕重的影響力；為發掘新的 trans-acting 小型干擾核醣核酸基因，我們根據 trans-acting 小型干擾核醣核酸已知的特質，發展出一個融合統計概念的生物資訊演算法，並成功的利用此生物資訊演算法，找出許多新的 trans-acting 小型干擾核醣核酸基因，並進一步藉由生物學實驗證實這些基因的確會產生前所未知的 trans-acting 小型干擾核醣核酸。我們的研究結果發現了一條前所未知的 trans-acting 小型核醣核酸之連鎖生成途徑 (圖二)，這個途徑顯示單一小型核醣核酸對調控基因表現會以連鎖反應方式呈現，對下游基因表現的影響可能以幾何級數方式擴增，相關研究成果不但增進目前小型核醣核酸生合成途徑的知識，也讓我們得以重新評估對 trans-acting 小型干擾核醣核酸對基因表現的潛在影響力。



圖一：我們藉由 DNA 微矩陣實驗探討植物葉片老化過程中之基因調控，以分析基因表現圖譜作為基礎提出假說，支持 PPDK 參與一個合成 asparagine 的全新生化途徑，使植物葉片在老化的過程中得以有效循環可再利用之氮源。





圖二：生物資訊演算法與小型核醣核酸之連鎖生成途徑的模式圖。

評審簡評：

吳博士擅長於以多層次研究法專研植物學重要基本課題：她於 2004 年首度報導由黑暗誘導老化之阿拉伯芥葉片的基因表現圖譜(Plant J.)，並於 2005 年與跨國團隊整合發表植物葉片老化分子機制的探討(Plant J.)，這兩篇文獻在植物學領域有極高引用率，並獲頒”Thomson Scientific Citation Laureate Award”，顯示其研究成果甚受推崇。吳博士並於 2007 年報導一個嶄新小型調節性核酸生合成途徑(PNAS)，該研究成功結合資料庫分析與實驗驗證，擴展了現今對小型干擾核醣核酸的瞭解。

吳博士的研究成果具深度、原創性與重要性，使得她在這相當競爭的研究領域中備受國際重視，並且有大幅揮灑空間，值得肯定並鼓勵其再接再勵。

2008 Academia Sinica Research Award for Junior Research Investigators

Name: Shu-Hsing Wu 	Education: University of California, Davis, PhD, 1992-1999 National Taiwan University, MS, 1989-1992 National Taiwan University, BS, 1985-1989 Employer(s)/Job Title(s): Assistant Research Fellow, Institute of Plant and Microbial Biology, Academia Sinica, 2001-present Postdoctoral Fellow, Stanford University, 1999-2001 Postdoctoral Fellow, UC Davis, 1997-1999 Teaching Assistant, National Taiwan University, 1990-1992

Award publications：

1. Lin, J.F. and S.H. Wu, *Molecular events in senescing Arabidopsis leaves.* Plant J, 2004. **39**(4): p. 612-28.
2. Buchanan-Wollaston, V., et al., *Comparative transcriptome analysis reveals significant differences in gene expression and signalling pathways between developmental and dark/starvation-induced senescence in Arabidopsis.* Plant J, 2005. **42**(4): p. 567-85.
3. Chen, H.M., Y.H. Li, and S.H. Wu, *Bioinformatic prediction and experimental validation of a microRNA-directed tandem trans-acting siRNA cascade in Arabidopsis.* Proc Natl Acad Sci U S A, 2007. **104**(9): p. 3318-23.

Summary of the Award publications（around 2000 words）：

The research emphasis of my laboratory is to understand the gene regulation networks underlying the morphogenesis processes in plants. We adopt the innovative concepts and state-of-art approaches for the pursuit of this goal.

The two papers published in Plant Journal presented two genome-wide investigations of the molecular events during Arabidopsis leaf senescence, a form of programmed cell death, which is of pivotal importance in many aspects of plant development. My laboratory described the first molecular portrait of dark-induced senescing Arabidopsis leaves via transcriptome analyses [1]. An innovative biochemical pathway for nitrogen remobilization in dark-treated leaves was also revealed (Figure 1). The approach of integrating transcriptome, biochemical pathway and gene ontology data has been broadly adopted by other plant research groups of diverse disciplines.

The above work laid a foundation for a multi-nation collaboration on comparative genomics analyses of Arabidopsis leaf senescence [2]. We were able to assign specific biochemical or phytohormone pathways to various routes leading to the senescence process. These two consecutive articles are highly perceived and have both been highly cited by the research community.

One other paper we published in PNAS is a fine example for the elegant integration of bioinformatic prediction and experimental validation in revealing novel information in the highly competitive microRNA field [3]. This paper has two major impacts. First, it presented a novel algorithm combining computational and statistical analyses for the prediction of a unique class of small RNA (trans-acting siRNA, ta-siRNA) via analyzing any given small RNA databases. With the advancement of large scale sequencing methodologies, this algorithm could serve as a powerful tool for the discovery of small RNAs with special characteristics. Second, it reported the existence of a miRNA-directed tandem production of small interfering RNAs in Arabidopsis (Figure 2). This discovery expands our current knowledge of small RNA biogenesis pathway in Arabidopsis. It also broadens our appreciation for the impact of small regulatory RNAs in plants.

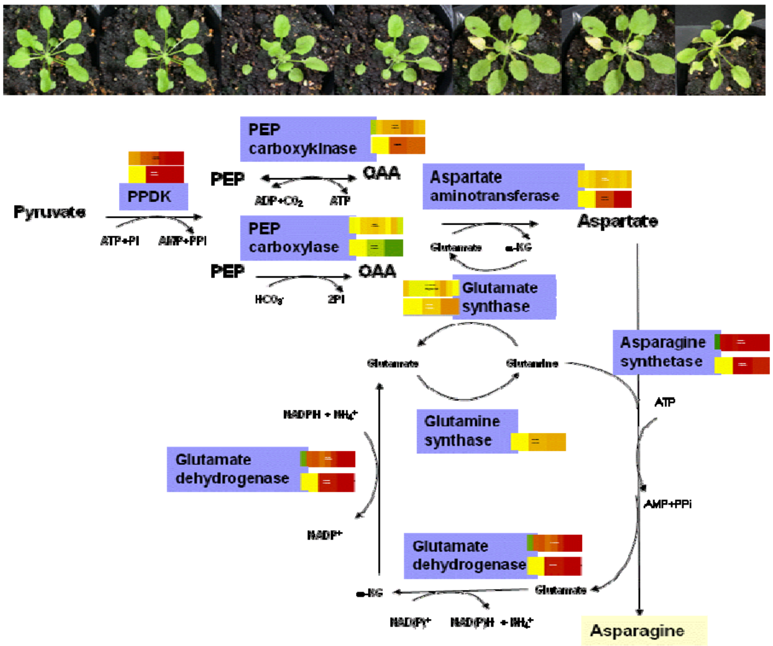


Figure 1: Gene expression profiling studies revealed a novel biochemical pathway. The up-regulation of pyruvate orthophosphate dikinase (PPDK) might contribute to the production of metabolic precursors for the synthesis of asparagine, believed to be the nitrogen carrier for nitrogen remobilization during senescence. The amount of free asparagines increased significantly in leaves experiencing senescence process triggered by darkness.

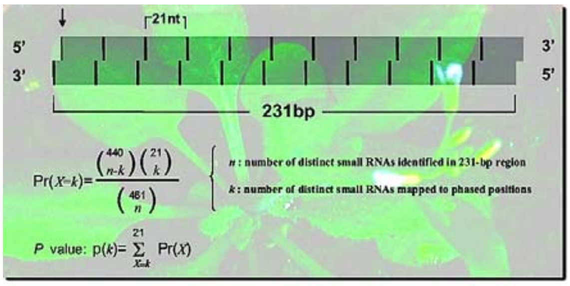


Figure 2:

Bioinformatic algorithm and a model representing a tandem small RNA cascade initiated by the miR173-targeted cleavage.