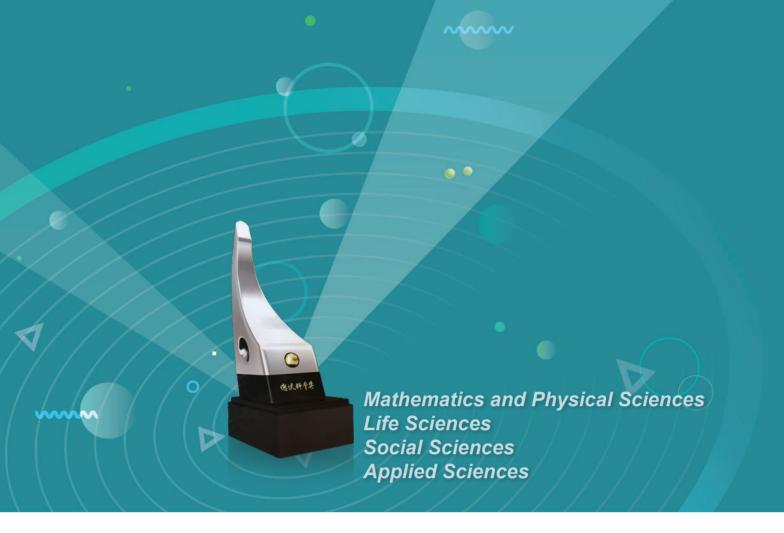
2021 總統科學獎表揚實錄 PRESIDENTIAL SCIENCE PRIZE

愧诀科ギ栗

Award Ceremony Program



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總統科學獎設立於 2001 年,今年已經邁入第 11 屆; 象徵國內學術研究最高榮譽的總統科學獎,由中央研究院 院長邀集相關部會首長,以及專家學者共 15 人組成「總 統科學獎委員會」籌劃總統科學獎項,並於 2001 年起, 每 2 年頒發一次,以獎勵國內在數理科學、生命科學、社 會科學與應用科學領域,有重大貢獻的基礎學術研究者, 並提升臺灣之國際學術聲譽。

總統科學獎得獎人的產生,係由中央研究院院士或總統科學獎得主,或總統科學獎委員會得邀請學術、研發單 位或團體及社會賢達人士提名,分由4組遴選小組推薦候 選人,再經聯席會議審議遴選得獎人。本屆總統科學獎歷 經縝密的推薦及遴選程序,計遴選出1位得獎人,為數理 科學組陳長謙院士。

藉由總統科學獎的頒發,表達國人對科學前景崇高的 冀望、對人才培育的重視與對知識份子的無限尊崇,除了 彰顯得獎人的崇高學術地位之外,更期盼將科學的精髓發 揚光大,裨益民生。





<u>4___________</u>成就事蹟

數理科學組— 陳長 謙 院士 破解甲烷氧化奥秘 發明分子催化劑 熱愛科學 醉心人文關懷 陳長謙啟發無數學子

在一甲子的學術生涯中,中央研究院(簡稱中研院) 院士陳長謙投入物理化學(physical chemistry)、化學物理學 (chemical physics)、生物物理學(biophysics)等多個領域, 他的研究範疇既深且廣,專門破解基礎科學的「黑盒子」, 於不同研究階段均在全新領域創造出突破性科學成就。

陳長謙率先以創新的光譜學及生物化學法,探討最基礎的問題,包括膜蛋白結構與作用、核酸鹼基與蛋白質的關係,其中尤以膜蛋白與金屬蛋白在生物學的重要性 (biological importance)最受囑目。對一般大眾來說,這些 深奧的名詞或顯陌生,但他的研究成果,就像火炬一樣, 點亮了基礎科學尚未了解的面向,也替全球許多基礎及應 用科學的重大發現,開啟了契機。

核磁共振光譜法

探討核酸鹼基平面間的「垂直」作用力

1960 年代初期,他運用核磁共振(NMR)光譜法,來 探討水溶液中核酸鹼基的排列,當時科學界仍在辯論,核 酸鹼基的「水平」氫鍵的交互作用,是否就足夠解釋 DNA 雙螺旋,在室溫下的結構穩定性。陳長謙院士發現,DNA 中的核酸鹼基,在處於水溶液環境時,存在著強大的「垂 直」作用力,因而確認了支撐核酸分子的結構,主要憑藉 分子內,在水中具有相互聚集的特性,亦即後來大家所熟 知的「疏水效應」,也一舉終結了科學界的辯論:華生-克里克鹼基對為何及如何在水中成形的謎題。



破解細胞色素 c 氧化酶的結構與作用: 氧化還原質子泵

陳院士最重要的科學貢獻,是採用創新的光 譜法及生物物理方式來探測膜蛋白,特別是膜結 合的金屬酶,以了解這些重要分子機器的結構、 功能及動態行為(dynamic behavior)。他在「牛 心臟粒腺體的細胞色素 c 氧化酶」的研究成果極 具原創性,既獨到又簡明;1970年代晚期,陳 院士成為這個領域的世界權威,他的實驗室也因 為闡明「牛心臟粒腺體的細胞色素 c 氧化酶」這 個複雜又重要的酵素系統的架構及功能,聞名全 球。

細胞色素 c 氧化酶對於建立粒腺體中 ATP 合成所需的原動力非常重要,但當時仍是「黑盒 子」,科學界只知其重要性,對於其結構和作用 仍十分陌生。陳院士帶領研究團隊,在 1980 年 代早期,進行了決定性的實驗:描繪金屬輔因子 的配體結構,因此確定了在質子泵送過程中,如 何透過金屬輔因子和蛋白質基質之間的氧化還原 閥,動態地控制電子和質子的流動。

發現甲烷變甲醇的催化機制:三銅簇

1990 年代初期,陳院士再度投入全新的研 究領域,探討微粒型單加氧酶 (pMMO) 如何以高 度效率將甲烷轉化為甲醇。2000 年之後,他的 臺灣團隊以創新技術,找到單加氧酶中的銅金屬 簇,因此發現了甲烷轉為甲醇的催化機制,即獨 特的三銅簇。近幾年,陳院士與中研院及國立 臺灣大學(簡稱臺大)化學系的同仁攜手合作, 開發出全球首個分子催化劑,能夠在室溫下利用 氧氣將甲烷轉化為甲醇,可說是甲烷氧化領域的 重大突破。尤其在當今全球淨零減碳的趨勢下, 「減甲烷」有助阻止氣候暖化,也讓陳長謙院士

的這個發現更顯重要。

陳院士的研究興趣廣泛,近年又成就另一 創舉,他投入蛋白質折疊的基礎研究。蛋白質折 疊是生物體十分重要的作用,可形成肌肉、荷爾 蒙、酵素等,但其過程仍是一大謎團。陳院士運 用籠狀化合物,研究在沒有變性劑的情況下,蛋 白折疊的最早期作用;這項最新研究闡明動力學 的途徑在蛋白折疊過程中的重要性。

除了專業領域的傑出表現,少年時立志從事 神職的他,在科學界獲得世界肯定後,毅然以傳 教士精神,放棄加州理工學院這個美國頂級學術 殿堂的光環與豐沛資源,來到臺灣,替國內先進 學研建立嚴謹的基礎設施及研究系統。他在中研 院副院長任內策劃的「中央研究院基因體研究中 心」,以及與前行政院國家科學委員會(現今科 技部)合作的「基因體醫學國家型科技計畫」, 替國內應用醫學研究及生技產業的發展,奠定堅 實的基礎。

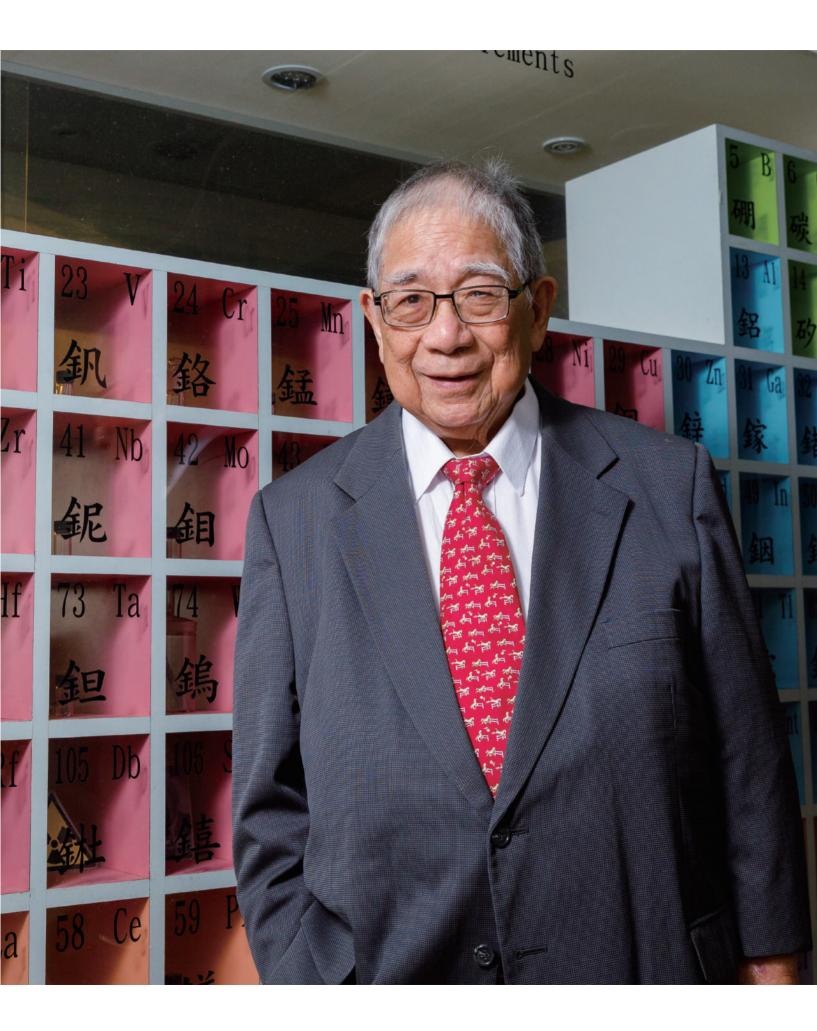
此外,陳院士也在中研院創辦了國際研究 生學程 (Taiwan International Graduate Program, TIGP),目的是充實中研院的研究人力,吸引全 球頂尖學術菁英前來,接受碩博士研究訓練;該 學程已有 20 年歷史,迄今仍是中研院最成功的 計畫之一。

陳院士運用豐沛的國際人脈,邀請頂尖學者 來臺輪流擔任 TIGP 講座,大大提升臺灣的國際 能見度及研究能量。多年來,他曾主辦多場國際 研討會,探討下列領域最先進的研究主題:化學 生物學(chemical biology)、生物催化與化學催化 (biocatalysis and chemical catalysis)、能源、燃 料、環境永續等。陳院士是眼光前瞻的學者,對 於科學界的未來發展方向,始終具有敏銳的洞察 力。

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陳院士最為同儕欽佩的特質,是他無私地培養許多後進人才, 他將他在美國的研究,移轉深耕在臺灣,至今大約23年的光景, 所教導授課的博士研究學者、大學部學生及碩博士生,已達數百 人以上;其中至少有25位他的臺灣學生,目前任職於國際知名的 學術機構,例如美國俄亥俄州大學、德國馬克思普朗克研究院等。 即便十年前已自中研院退休,陳院士仍持續貫徹身為科學家及教 育家的使命;直到今天,國內外許多青年菁英,依然受到他的鼓 舞與啟發,陳院士將其研究成果、方法與精神不斷傳承,造福未 來世代。

8 國家桂冠故事



科學家也是教育家 傳教上精神無私播種 改變中央研究院成為世界一流學術機構

陳長謙院士出身美國社會的弱勢族群,憑藉對科學的好奇、熱 情及天分,他在生物物理、生物化學等多個領域,創造了重大成就。 曾想成為「第一位華人教宗」,但一頭栽進科研,更讓他快樂與滿足; 儘管早己在膜蛋白及嗜甲烷菌領域建立世界級名聲,但他不愛鎂光 燈、也不看重科研成果的商業化;他總是牽著研究團隊的手,一起 享受追尋知識的美好歷程,並教會不同世代最重要的課題:做學問 的方法。

陳長謙院士策劃中研院基因體研究中心而不求「成功在我」, 他貢獻自己的國際人脈, 替國內學術界建立方法論和研究系統, 現 今中研院能成為世界一流的學術機構, 陳院士扮演了關鍵角色。不 論學術研究或行政工作, 他就像傳教士般播種耕耘, 這樣一個世界 級學者,將後半生貢獻在這片土地, 是臺灣的榮幸。

中研院院士陳長謙在美國成長,父親於 1920 年代從中國南方移 居加州,屬於第一代移民,父母親並未接受正規教育,都在 Levis 牛 仔褲工廠工作,工時極長,是上個世紀典型的「血汗勞工」。陳院 士在並不富裕的中國城社區長大,屬於文化和社會地位上相對弱勢 的族群。

在他的成長過程中,身邊沒有學者、科學家或專業人士可做為 仿效的榜樣;陳院士是家族中第一個上大學、獲博士學位的成員。 「我能走到今天,可說是一趟奇妙旅程,完全無法事先安排!」 9

10 國家桂冠故事



出身平凡 想做第一位華人教宗

小學畢業,陳長謙院士已成為標準的「香蕉人」,外表黃皮膚, 內涵卻是道地美國作風;父親覺得這個兒子需要理解文化的根源, 便在二次世界大戰結束後的1948年,將他獨自送進香港的中學。年 僅12歲的他,完全不懂中文,連「英文」課裡講的中文他都鴨子聽雷; 想當然爾,第一個學期就全部當掉。他笑說,「真是很丟臉的經驗, 還好沒造成永久的心理創傷。」

後來他轉到由愛爾蘭耶穌會士 (Irish Jesuits)所主持,以英語授課的另一所香港中學,遇到了很棒的數學和科學老師,從此點燃他對學術研究的熱情。

1953年秋天,陳院士回到加州,進入舊金山大學(USF),帶著 滿腔熱血,想要擔任神職及科學老師,「我為自己訂了一個目標: 要成為第一位華人教宗。」不過青春期的雄心壯志並沒有實現,也 還好如此,否則這個世界便少了一名頂尖的科學家和教育家。天主 教神父的養成生涯,在生活上有諸多限制,對一位未滿17歲、對世 界充滿好奇的青少年來說,實在太具挑戰。父母親對他的期待也不 一樣;「母親要我做醫生,但大一上解剖學時殺青蛙,我實在不喜歡; 父親希望我做工程師,未來要建設新中國;」折衷之下,他轉往加 州大學柏克萊分校,攻讀化工。

「對當時的我來說,柏克萊是很困難的環境。」課程相當吃重, 但還好他遇到了兩位好老師,George Pimentel 教授對於化學平衡 (chemical equilibrium)這門課程的生動解說,激發出他的學習興趣; Andrew Acrivos 教授則教會他應用數學及動力學,並幫助他找到自學 及獨立研究的方式。到了大四,陳長謙已懂得運用課外資源來學習、 去旁聽不在課表上的學科。

陳長謙在柏克萊繼續攻讀博士,並從化工轉往物理化學領域, 博士論文主題是以微波光譜研究小分子結構;不到三年的時間,他 便拿到博士學位,許多產業界的高薪工作向他招手;「那是 1960 年 代初期,麻省理工學院的林肯實驗室、軍火商洛克希德馬丁、通用 電氣、IBM,都提供我很好的職位。」

<u>12</u> 國家桂冠故事

放棄產業高薪 赴哈佛進行博士後研究

不過,指導教授對他卻有不同的規劃。「老師堅持我申請 NSF(美國國家科學基金會)的博士後獎學金,到哈佛大學物理系跟隨 Norman Ramsey教授(1989年獲得諾貝爾物理學獎)。」高解析的核磁共振光譜學(NMR, Nuclear Magnetic Resonance),當時正在發展,有人建議他可以善用博士論文在微波頻譜的研究基礎,投入 NMR 的小分子研究。

其實,陳長謙院士申請 NSF 獎學金,只是為 了不讓老師不開心,沒想到申請通過,他反倒猶 豫了起來。最終他還是決定前往哈佛,老師很滿 意,父親可不然。陳長謙居然放棄通用和 IBM 的 高薪,去領區區 4,500 美元的獎學金,老爸失望 地說:「兒子,我沒有博士學位,但我賺的錢比 你多很多。」

1960年9月,陳長謙在哈佛展開博士後生涯, 醉心研究的同時,也近身觀察許多資深學者的丰 采。有一天,他在實驗室有了重大發現,剛好也 在現場的一位知名教授,Dr. J. H. van Vleck(1977 年獲得諾貝爾物理學獎),立刻援引相關微擾理論 (perturbation theory)來向團隊說明,讓身為菜鳥科 學家的陳長謙印象深刻,震懾於知識的力量,心 裡也慶幸,放棄高薪來到哈佛是正確的選擇。

1961年,加州大學河濱分校邀請陳院士擔任 助理教授,這是他的第一份教職。該校的化學所 剛成立不久,「我覺得我可以幫忙打造健全的教 學環境和研究系統。」在河濱分校期間,陳長謙 對教學的熱情更進一步發展,也對指導學生產生 高度的興趣。

「柏克萊和哈佛的經驗讓我體會到,若要鼓 勵年輕人發揮潛力,讓他們成為創新又獨立的科 學家,『研究訓練(research training)』」很重要!」 陳長謙因此確定了目標:既要成為優秀的學者、 也要做一名能夠激勵學生的老師;那年他 25 歲。

人生志向底定:做學問、激勵學生

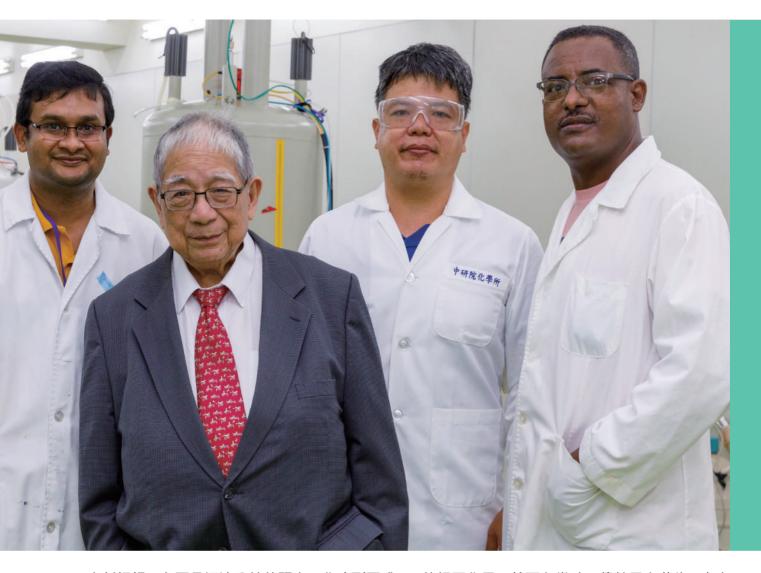
儘管人生志向已經確定,但在河濱分校要做 什麼研究主題,卻尚未成形。「我不想再繼續做 NMR 的分子束研究,這種光譜學和微波一樣,已



經逐漸成熟,不太可能發展出新概念或新突破。」

陳院士說,訓練研究生必須「以『發現』為 導向」,有了好奇心的驅使,年輕人才能積極學 會如何定義科學問題、發展研究計畫、形成假說、 設計驗證方法;而這一系列紮實的過程才是完整 的科研系統。為了達到這個目標,陳長謙決定在 河濱分校嘗試他自己也陌生的題目,帶領學生一 起前進,包括:用 NMR 研究溶液中過渡金屬錯 合物的結構、嘌呤(purine)和嘧啶(pyrimidine)的 核磁共振研究、高濃度鹼金屬氨溶液的電子順磁 共振(EPR, Electron Paramagnetic Resonance)研 究。

他在河濱分校的歲月十分短暫。事實上,剛 到河濱分校不久,加州理工學院便邀他參加該校 的研討會,並發表一場演講。「沒想到,隔一個 星期,他們就寄信來要我加入化學系。」陳長謙



立刻拒絕,主要是河濱分校的研究工作才剛要成 形,「而且加州理工學院是極具影響力的學術殿 堂,我有些卻步」。

加州理工學院請他再多想想,同一時間,耶 魯大學的化學系也來信,提供類似的職務給陳長 謙;「這似乎在告訴我,必須重新思考未來。」 加州理工學院擁有世界級的學者、研究生素質更 是一等一,整個學術環境只有「高品質」可以形 容;於是,陳長謙便從河濱分校搬到了城市另一 頭的加州理工學院,而且一待就是 40 年。

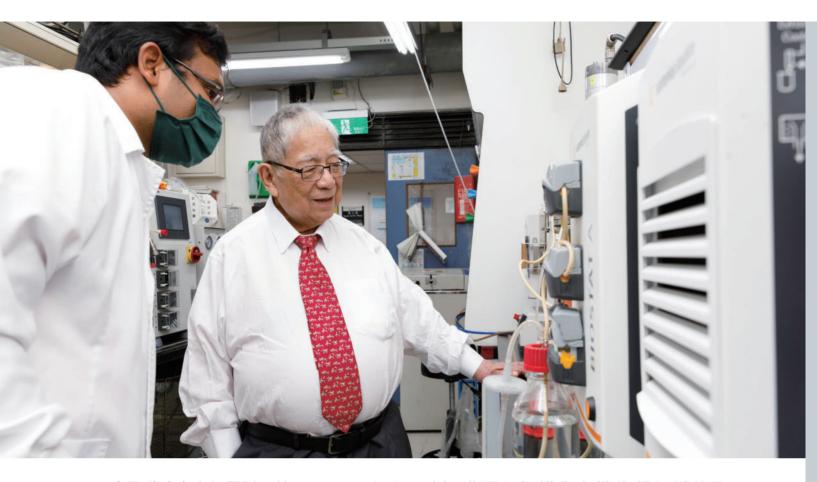
進入加州理工學院 首度投入生物物理領域

在加州理工學院,他首度投入生物物理領 域(學士是化工、博士是物理化學、博士後是物 理),運用核磁共振(NMR)光譜法來探討水溶液 中核酸鹼基的排列。如今科學界已了解鹼基排列 的相互作用,然而在當時,儘管已有華生-克立 克(Watson-Crick) A-T與G-C鹼基對的研究,但 科學界仍在爭論,核酸鹼基的「水平」氫鍵的交 互作用,是否就足夠解釋DNA 雙螺旋,在室溫 下的結構穩定性。

「我朝著生物物理這個全新的研究領域出 發,心裡並不知道,過去在物理化學的背景, 竟然對現在的研究有莫大幫助。」他說,他從未 接受過生物學的正規訓練,看起來似乎是一大弱 勢,其實恰好相反。

「對我來說,投入新領域,比較大的障礙是 如何先找出已知和未知、然後定義哪些問題須待 解決、以及該利用什麼工具直搗問題的核心。」 以往在物理學的背景和訓練,讓他擁有足夠的創 見,在研究之初就提出複雜的問題,並加以分 析。

<u>14</u> 國家桂冠故事



陳長謙院士率領團隊,於1962-1964年發 現,DNA(及RNA)中的核酸鹼基,在處於水溶 液環境時,存在著強大的「垂直」作用力。因而 確認了支撐核酸分子的結構,主要憑藉分子內, 在水中具有相互聚集的特性,亦即後來大家所熟 知的「疏水效應」,也一舉終結了科學界有關辯 論,解開 Watson-Crick A-T 與 G-C 鹼基對為何及 如何在水中成形的謎題。

1968 年,他進一步以核磁光譜法來探測磷 脂雙層膜(phospholipid bilayer membrane),結果 發現,磷脂雙層膜既非固態也非液態,而磷脂分 子在雙層膜內僅能作有限度的分子運動,運動時 間從皮秒到毫秒;此一發現也開啟了科學界今天 對生物膜動態結構的認知。

有了這個突破之後,陳院士繼續研究膽固 醇、兩親性胜肽和膜蛋白對液體雙層膜結構的影 響,這些分子會影響雙分子層內分子的相行為、 協作域大小、集體運動的相關長度、彈性、表面 曲率和橫向擴散。他還研究脂蛋白相互作用如何 影響蛋白質的行為,以及如何產生脂質介導的膜 內蛋白-蛋白作用力。

破解膜蛋白架構與有機化學領域的聖 杯議題 細胞色素 *c* 氧化酶與甲烷單加 氧酶世界權威

細胞內的膜蛋白新知一個個被發現,相關成 果不斷累積,陳院士在1970年代晚期,將他的 注意力轉向揭示活體細胞內分子機器的結構及功 能,這些分子機器大多屬於膜蛋白,極度難以分 離及純化,也因此無法深入研究。當時,陳院士 的研究團體成功地將細胞色素 c 氧化酶純化至均 質,這是細胞胞器,粒腺體內一系列氧化呼吸電 子傳遞鏈中的末端酵素,對於細胞完成其活動來 產生能量至關重要。

然而,細胞色素 c 氧化酶在當時仍是不為人 知的「黑盒子」。在陳院士的指導下,他的學生 及博士後團隊有系統地研究了其內負責調節電子 傳遞的金屬輔因子結構、探討金屬輔因子之間的 電子流動順序、以及氧分子如何裂解以形成所需 的高氧化還原電位的蛋白質中間體,因而驅動了 質子的易位(細胞色素 c 氧化酶事實上是一種質 子泵!)。這些研究讓陳長謙實驗室得以預測不同 金屬輔因子的化學結構以及它們在酵素整體功能中 扮演的可能作用。在所有進行相關研究的學者當 中,陳院士最早將哺乳動物細胞內的細胞色素 c 氧 化酶研究,推動至分子層次的解析,他對該系統的 了解,遠早於 1990 年代初期被解析的相關蛋白質 晶體結構。也因此,陳院士成為該領域的世界權 威。

1992年,他再度投入全新的研究領域,探討 微粒型單加氧酶 (pMMO) 如何以高度效率的方式, 將甲烷轉化為甲醇。在進入中研院任職前,他在加 州理工學院即已成功分離出嗜甲烷菌中的單加氧 酶,並將之純化至均質的狀態。2000年之後,他 的臺灣團隊發現了甲烷生物氧化的催化機制「三銅 簇」,這個活性中心,利用來自分子氧(O₂)的單 線態氧,輕易地將氧原子直接插入 C-H 鍵內。這 種新穎的化學反應,闡明了大自然是如何利用金屬 簇,生成高效能的甲烷氧化催化試劑,同時具可回 收,不易失活等優點。甲烷轉化為甲醇是一種氣、 液態轉換的過程,屬於極其困難的化學反應,主因 是甲烷中的 C-H 鍵在有機物中,具有最高的鍵能。 因此,該轉化路徑,一直是有機化學領域的"聖杯" 議題之一。陳院士破解甲烷氧化的奧義之後,近年 更攜手中研院及臺大化學系的同仁,開發出全球首 個分子催化劑,能夠在室溫下利用氫氣將甲烷轉化 為甲醇,是甲烷氧化的另一重大發明。

在加州理工學院的 40 載歲月,陳長謙因為闡 明了「牛心臟粒腺體的細胞色素c氧化酶」以及「嗜 甲烷菌中甲烷氧化的銅單加氧酶」這兩大標竿系統 而揚名國際。

擔任 800 人舍監 與毒販在校園內對峙

然而帶給他滿足的,不只是科學的探究,還有 與學生的互動。「我曾經擔任加州理工學院學生宿 舍的舍監,是很特別的經驗!」加州理工學院的學 生宿舍有 800 名學生,有一年,舍監任期已滿, 校方擇定的繼任人選,學生不喜歡,當時兼任大一 化學課的陳長謙,備受愛戴。1980 年 5 月的某一 天,一群學生下課後跑來問陳長謙,願不願意接下 這個工作。「其實我不清楚舍監是什麼,工作內容 有哪些。」陳長謙去問了一位同事的意見,這位同



事是比他年長的華人、也是臺灣的院士「他說如 果我接下這個工作,將是第一個在加州理工學院 擔任行政職的華人,意義重大。」在這樣微妙的 壓力下,陳長謙同意了,並不知道未來的工作會 面臨什麼挑戰。

為了這個新職,他舉家搬遷,住到了宿舍 旁,每個週末辦活動、請學生吃飯、照顧這群青 年學子的日常生活,還要提供心理諮商。身為宿 舍的總舵頭,他既要保護學生的安全,也得解決 各種疑難雜症。那是嬉皮年代的後期,校園裡依 然毒品泛濫,毒販進到校內兜售毒品,是稀鬆平 常的事。有一次,毒販被他發現,於是上前制 止,對方不從,掏出槍來對峙;「面對這樣的威 嚇,我也只能跟他說,你再不離開,就請警察來 處理。」還好毒販識趣的離開,讓這段危險插曲 有了平安的結果。

擔任舍監的四年期間,幫助了許多學生, 有些因為課業壓力而憂鬱甚至有自殺傾向、有些 在感情、性別認同或家庭關係上出現問題。他說 「年輕的生命歷程,經常遇到困難,學生願意在 受挫時來找我,而他們需要時我也能幫得上忙, 是令人滿足的事。」

陳院士在美國期間,一直積極參與社區和 公共服務,他是華裔教授協會(Chinese American Faculty Association)的創始成員並擔任兩屆主 席,該協會致力為南加州的華裔學者謀求福利。 他也曾擔任加州理工學院Y學會主席(1992-93) 和華美化學學會理事(1988-98)。自1970年以 來,陳院士一直是美國國家衛生研究院(NIH)的 常任顧問,並曾任職 NIH 旗下多個諮詢委員會, 包括:生物物理和生物物理化學研究組(1970-1974)、物理生物化學研究組(1989-1993/主席 1992-1993);美國國家癌症研究所審核委員會 (1996-1997)和小型企業創新研究部門(1992-2002)。此外,他也是美國和國際間眾多科學諮 詢委員會的成員。

移居臺灣 轟動全球學術圈

1988年,陳長謙獲選為中研院院士,1997 年,他接受中研院李遠哲院長的邀請,從加州理 工學院退休,來到臺灣的中研院任職。「這在當 時是很大的新聞,轟動學術圈;」中研院院士、 臺大化學系名譽教授彭旭明說,陳長謙是世界 頂尖一流的教授,願意放下美國的光環,來到臺 灣,「我想跟他父親從小灌輸給他的人文情懷, 很有關係。」

陳院士的父親希望他在華人地區發光發熱, 初中送他到香港念書,就是要他不能忘了文化的 根。他在學術界逐漸嶄露頭角,父親也時時提 醒,必須將所學貢獻給華人圈。陳長謙因此決定 接受李遠哲院長的邀請,移居臺灣,幫助中研院 化學所及整個中研院成為世界一流且現代化的研 究中心。

來到臺灣,他先擔任中研院化學所所長, 那一年的耶誕晚會,他扮成耶誕老公公來娛樂大 家。彭旭明教授說,「他的性格和體型都像聖誕 老公公的翻版,待人親和客氣、隨時樂意協助; 我們常笑他的身材是圓形的s軌域(原子物理學 中最穩定的原子軌域)」。

陳院士是科學家,也是美食家,更是呼朋 引伴的性情中人。1989 年第一次來到臺灣兼任 中研院分子生物所代理所長時,就親自烤了火



▲ 2018 年 12 月榮獲 TASCO 化學終身成就獎

雞,邀請同事們一起吃感恩節大餐;1997年來 臺定居後,不到兩三年,臺北所有好吃的餐廳, 都被陳長謙吃遍了。六條通的龍都、仁愛路的錢 唐村,至今仍有「陳副院長的專屬菜單」。今年 的85歲生日,他在內湖設宴款待了一群好友; 他的老同事,加州理工學院化學系教授 Harry Gray,偶爾也會專程飛來臺灣參加陳長謙的生日 宴。

創立國際研究生學程與基因體研究中心

1999年7月,他出任中研院學術副院長, 在這個新職位上,陳院士負責全院的學術和研 究發展。擔任副院長四年期間,他最重要的貢 獻有兩項。首先是創設中研院國際研究生學程 (Taiwan International Graduate Program, TIGP), 以全英文授課,目的是吸引各國最頂尖的研究 生來臺參與中研院的計畫,藉此充實中研院的 研究人力;更運用長年累積的國際人脈,邀請 世界級學者來臺,輪流擔任講座,大大提升臺 灣的國際能見度,因此讓更多年輕學子願意來 到臺灣,形成了良性的循環,讓中研院得以充 實人力並建立世界級的聲譽。 陳副院長任內的另一項重要貢獻,是一手 策劃「中研院基因體研究中心」,協調中研院 內生命科學的研究;另一方面,他也與前行政 院國家科學委員會(現今科技部)合作,展開 「基因體醫學國家型科技計畫」,全面建立國 內先進學研的體系架構及方法論(paradigm), 兩項計畫為臺灣生技產業及應用醫學的發展, 打下深厚的基礎。

「當初來到臺灣,我的目標就是幫助中研 院成為亞洲第一、世界一流的研究機構;經過 二十多年,我想這個目標已經達成。」他認為, 與日本、新加坡、中國的頂尖機構相比,如今 的中研院在學術水準上已更勝一籌。

無私提攜後進 是科學家也是教育家

「我最佩服他的一點,是提攜後進的精神; 他是科學家、也是教育家。」彭旭明教授說,他 不止訓練年輕學者有系統地從事研究,還經常幫 忙修改論文;英文是他的熟悉語言,只要改幾個 字,論文的表述就變得很有質感。

多年下來,曾經參與陳院士實驗室工作的 各國學生、博士後研究學者及訪問學人超過 200 人,這個數字,在冷門的基礎研究領域,並不多 見。在加州理工學院的最後十年,他已在微粒型 單加氧酶 (pMMO)將甲烷轉為甲醇的領域取得初 步成果;他將這個研究移轉深耕至臺灣,近年有 了重大突破及發明。對陳院士來說,最重要的是 這些突破及發明,是他在臺灣的學生及博士後研 究學者努力不懈而獲得的成果。也正因如此,幾 位跟隨他的國內年輕學者,逐漸在國際上綻放光 采,在陳長謙的助力下,準備飛得更高更遠。

在臺灣,陳院士也是一位人人景仰的老師, 他所指導的臺灣學生中,至少有 25 位目前任 職於國際知名的學術機構,包括美國俄亥俄州 立大學、德國馬克思普朗克研究院(Max Plank Institute)等,另有將近 10 位在中研院及國內大 學擔任學術研究工作。他在加州理工學院所訓練 的學生及博士後研究學者,許多都在全球各個知 名大學任職。另外,陳院士的學生也在產業界有



▲ 1997 年 7 月擔任中央研究院學術副院長

傑出的表現,例如太景生技創辦人許明珠便於 1970年代初期跟隨他在加州理工學院進行博士 後研究,臺灣生技產業在20年前起飛,許明珠 便是最成功的第一代創業家之一。10年前,陳 院士從中研院退休,但直到今天仍孜孜不倦地履 行他作為科學家和教育家的使命,不斷激勵海內 外更多青年學子,將他的成果傳承給未來世代。

即便從加州理工學院退休,來到臺灣擔任 行政職,陳院士對學術研究的熱情絲毫未減,他 再度投入一個全新領域:蛋白質折疊的基礎研 究。他說這是「化繁歸簡」,「為了替自己的科 學生涯劃下美好的句點,我決定回歸簡單的研 究主題。」蛋白質折疊是生物體十分重要的作 用,可形成肌肉、荷爾蒙、酵素等,但其過程仍 是一大謎團。近幾年,他運用籠狀化合物(caged compounds),研究在沒有變性劑的情況下,蛋白 折疊的最早期作用,因而闡明了動力學途徑在蛋 白折疊過程中的重要性。

回顧過往,陳院士說,「我的生涯充滿了驚 奇,這一路的旅程帶我走進膜蛋白的世界,是全 然無法事先規劃的;但另一方面看來,其實也是 很有邏輯的發展。」從最早期他對簡單系統的化 學物理研究、磷質雙層膜到膜蛋白的作用架構、 以至於膜蛋白的離子遷移,最後進展到數個膜蛋 白系統的架構功能。

<u>18</u> 國家桂冠故事

當研究的生物系統變得更複雜時,他學會了 如何妥善管理研究的流程、如何從零開始,在幾 乎一無所知的情況下,定義出一系列有待解決的 複雜問題、以及如何制定研究策略來解密這些問 題。「我發現,科研上最複雜的問題若要取得進 展,必須仰賴代代相傳和演進,前一代的實驗成 果才能造就下一代的突破。」例如嗜甲烷菌的題 目,就是他與跨世代的同僚們一起努力,才有了 收穫。「基礎科學的研究資源往往是有限的,無 法像產業界組成龐大的團隊並在短時間解決問題; 但是只要一步一腳印,並且善用新興科技,也能 夠加速基礎科學的進展」。

打造臺灣學研更開放的環境

陳院士在加州理工學院時,其膜蛋白的研究, 曾獲得美國國家衛生研究院的計畫資金長達 30 年,他說,這樣的資金規模確實較能涵蓋所有研 究支出,但無法添購新設備或替設備升級。來到 中研院之後,研究經費不如美國國衛院,卻有足 夠的預算來建置先進儀器設備,對於他在科學工 作上的進展,很有幫助。

他認為,臺灣在先進學研上,無論是經費或 研究設備,與世界級機構相比,並不算差,但整 個學術環境,應該可以更開放。「在追求知識和 科學真理的漫長道路上,年輕人需要動力及熱情, 他們對知識的渴求必須被激發出來,才能擁有創 造力,而不是按照教科書或期刊上的東西來學 習」。

「發展自己的『科學判斷』能力也很重要, 但這必須靠經驗。」他把科研歸納為三大類:(1) 探索式研究(或開創性研究)、(2)主流科研(如 材料化學、水分解、新藥研發、機器學習、量子 運算)以及(3)成熟科研(已被大量理解的領域)。 其中探索式研究是陳長謙最為醉心的領域,這是 針對前人尚未了解或知之甚少的面向,提出科學 上的疑問;他說,就像哥倫布出發探險時,憑的 是直覺,並不知道向西會發現美洲大陸,只是問 自己:「那裡有什麼?」

他認為,探索式研究是想像力的發揮、是對 未知的渴求。「當你出發踏上旅程時,什麼都沒 有,只有手上的一個黑盒子,盒子裡藏著什麼,



完全不知道。這不代表前人沒問過相同的問題, 只是沒找到答案,或者太難破解。」

也因此,探索式研究是高風險又長期的投 資,它需要高度的知識含量,卻可能只有極低的 產出。他說自己是「隨機走入了研究主題,很幸 運這些題目在不同的時代都成為主流。」

但幸運不足以說明他的成就。做學問對他 來說,並不是拿經費、得獎項、拼論文數,而 是純然對知識的好奇。「我從小就喜歡問問題, 想了解週遭的一切,包括大自然、人的行為。」 他並不熱愛鎂光燈,也不享受與人競爭、更不追 求高人一等的感覺;「我只是個教育者、科學人, 或知識分子」。

熱愛知識追求 更甚於商業化

如果當初踏入其他領域,或許也能成功; 「母親要我做醫生,我試了但放棄;父親要我做 工程師,拯救中國脫離貧窮,因此我去柏克萊念



了化工。但我發現,我更感興趣的是『想法』而非 『應用』。」他說也可以像家族的表兄弟姐妹,擔 任美國華人最常做的工作:銀行行員、郵局櫃檯、 雜貨店員工、甚至肉販,過著平凡快樂的生活;「我 做一名高中科學老師也可以樂在其中。」

陳院士 50 歲時(已經是知名學者),父親希 望他接下家裡的生意。「真的接了應該會是一場惡 夢。商業上的算計、講條件、討價還價甚至勾心鬥 角,並不是我的風格。」

對於這點,他的好友彭旭明院士深表贊同。 「有些學者的研究目的是為了做可以進入市場的產 品,例如新藥或疫苗;陳院士不一樣,他熱愛基礎 科學、享受和團隊彼此激盪共同發現的旅程,因此 他全心投入訓練研究生及博士後人才;他並不那麼 商業化。」

陳院士說,自己並不排斥過更富裕的生活,也 可以選擇賺大錢、開公司,「但我還是決定做科學, 這是出於自私的理由,因為做科學讓我更滿足。」 ▲ 出席第 15 屆 TIGP 頒贈儀式 (第一排中央位)

陳長謙經常接到演講邀約,早期他大多談與 研究主題相關的深奧內容,近年他開始到校園分 享自己的科學人生,希望激勵更多學子。對於熱 愛學術研究的學子,他提醒大家,做研究就是不 斷的找答案,需要紀律、耐心、決心和辛勤工作, 還要有一點頑固的精神,因此並不是每個人都適 合學術研究這條路。

儘管自己專注基礎科研,但他的思維更為宏 觀。以化學這門學科為例,他說,「我們訓練化 學家,不只是為了產業界或學術界,還有更多職 業都需要,例如公共政策、風險分析、化學安全、 環境保護、環保法規、智財權等。」

他在美國化學教育期刊(Chemical Education Journal)中,曾以「化學教育的創新機會」為題, 暢談化學科研在過去一百年的重大突破,例如新 元素的發現、分子的形成、分子間的交互作用、 在實驗室以人工合成新分子。

然而化學對於人類生活及產業的貢獻,現

已甚少被提及,主要是過去五十年各種污染造成 的悲劇事件如 DDT 及戴奧辛對健康及生態的衝 擊、含鉛汽油中的四乙基鉛(tetraethyllead)導致 神經性中毒、印度農藥工廠異氰酸甲酯(Methyl Isocyanate)外洩造成的重大傷亡,以及佛利昂 (Freon)化合物破壞臭氧層等,都導致了「化學」 這門學科被污名化。

媒體在報導基因定序、疫苗、降膽固醇藥物、 二型糖尿病藥等生技領域的重大成果時,從不提 到它們是源自於化學。「換言之,我們應該提升 大眾對化學的認知,它的基礎科研還是很蓬勃, 也很有貢獻」!

陳院士認為,這個世界本來就需要多元的人 才,「我的學生和研究團隊,有很多後來走入了 其他領域,我認為這很自然,我也以他們為榮」。 不過,對他來說,破解大自然的奧秘,仍是 最迷人的事。「不論問題有多麼難解,在窮盡一 切努力之後,總會找到一個簡單的答案;自然界 是如此單純且複雜,而透過已知的物理及化學法 則來探索並觸釋生物系統的運作,又是如此樂趣 無窮。」

與其說陳長謙院士是一名世界級學者、無私 的教育家;對臺灣而言,他就像來到中研院第一 年所扮演的聖誕老公公,為這片土地帶來了制度 改革與學術躍進的贈禮。不過,他更像一名探險 家,帶著智慧踏上未曾開拓的道路,為眾人領航 走向真理,並激勵新世代一同前進。正因如此, 世界才有了不一樣的風貌。



▲ 2015 年 4 月 24 日成為臺灣永久居民(特殊貢獻梅花卡)

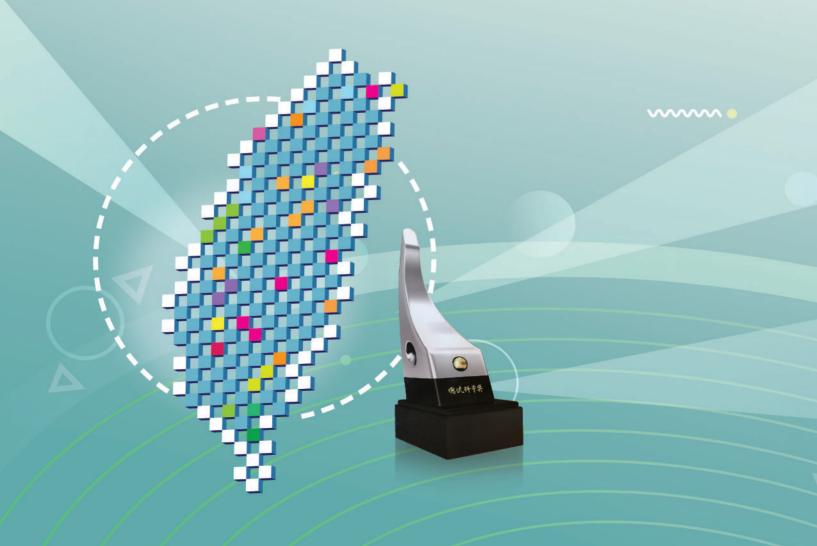


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由眾多傑出的候選人中, 遴選出我國最優秀的科學研究學者, 今年膺選的總統 科學獎得獎人數理科學組陳長謙院士, 其學術研究領域具高度專業、貢獻非凡, 且 在臺灣所打造與國際交流之學術研究環境, 吸引外籍人才的投入; 所培養之國際學 術研究人才, 在國際上也展現出亮眼成績, 同時建立臺灣學術環境「自由、大膽、 包容」的風氣, 是位在國際科學界備受肯定的傑出學者。

多年來,其對研究工作長期的專注與堅持,對科學研究的無盡付出與無私奉獻, 讓臺灣在國際科學研究上能與先進國家齊驅並進,同步發展,不僅對臺灣及國人同 胞有著莫大的助益,對於全人類的福祉更有著深遠的影響。

將來,還需要我們持續耕耘這一方科學園地,共同探求科學的極致光華,在國際科學上,展開更燦爛輝煌的未來。



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(任期 2020 - 2021)

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Established in 2001 and presented every two years, this is the 11th Presidential Science Prize. This prize symbolizes in the highest academic honor to pay respect to the most outstanding scientists in the Republic of China (ROC).

To promote Taiwan's position in the international science community, the Office of the President has established the Presidential Science Prize to recognize innovative researchers who have made monumental contributions to international research in the fields of Mathematics and Physical Sciences, Life Sciences, Social Sciences, Applied Sciences, especially those scholars whose works have had major impact on the development and applications of these fields in Taiwan.

To implement the selection and award of this prize, the President of Academia Sinica has convened a steering committee of fifteen distinguished scientists and related cabinet ministers. Nominees for the Presidential Science Prize are only taken into consideration when

(1) they are nominated by academicians of Academia Sinica and/or Presidential Science Prize awardees;

例,依科养檗

(2) they are nominated by academic and research institutions and associations and leaders of the community invited by the Presidential Science Prize Steering Committee.

After nomination, four selection committees in the abovementioned fields perform nominee screening tasks. This year, through a careful nomination and selection process, the three awardees of this prestigious honor have been chosen as: Mathematics and Physical Sciences Category-Dr. Sunney I. Chan.

Conferred by the head of state, the Presidential Science Prize gives recognition to those scientists for their long-term efforts at conducting scientific research and cultivating young researchers. This prize also aims to pay respect to outstanding scholars who have made top-notch academic achievements and to have scientific R&D fully benefit people's livelihood.





26 A Track Record of Achievements

Mathematics and Physical Science Category — Sunney I. Chan Cracking the Mystery of Methane Oxidation in a Membrane Protein and Inventing a Molecular Catalyst

Sunney Chan Has Inspired Countless Talented Minds for the Love of Science and Humanity

In the 60 years of his scientific research career, Sunney I. Chan has navigated the fields of physical chemistry, chemical physics and biophysics. His research achievements are as broad as they are essential, cracking one black box after another in basic science. Every 20 years, he would come up with a ground-breaking discovery that takes the study of biological systems to a new epoch.

Sunney Chan is best known for developing and applying innovative spectroscopic and biophysical methods to solve fundamental problems on the structure and dynamics of membranes, nucleic acids and proteins, especially membrane proteins and metalloproteins of biological importance. To the general public, these terms may appear abstruse and unfamiliar, but his findings are like torches illuminating the dark, unknown territories, and paving the way to many more important discoveries in basic and applied science.

Ended Scientific Debate by Discovering 'Vertical Interactions' between Nucleic Acid Bases

In the early 1960s, Sunney Chan used nuclear magnetic resonance (NMR) spectroscopy to study the stacking of nucleic acid bases in aqueous solution. At that time, scientists around the world were still debating whether or not 'horizontal' interactions of hydrogen bonds in nucleic acid were sufficient to account for the stability of the structure of the DNA double helix at room temperature. In pioneering NMR experiments undertaken during 1962-64, Sunney Chan established that in a water solution, there exist strong 'vertical' interactions between the nucleic acid bases in DNA, and the nucleic acid bases stack in water in order to minimize the disruption of the hydrogenbonded network structure of the water, now commonly referred to as the 'hydrophobic effect'. Consequently, this discovery of his brought to an end the scientific debate on why and how the Watson-Crick A-T and G-C base pairs can be formed in water.





Cracking the Myth of Cytochrome *c* Oxidase: A Redox-Linked Proton Pump

One of Sunney Chan's most significant scientific researches is his probing of membrane proteins, particularly membrane-bound metalloenzymes, using novel biophysical methods to unravel the structures, functions, and kinetic behavior of these important molecular machines. His work on cytochrome *c* oxidase from bovine heart mitochondria was pioneering and elegant. In the late 1970s, Sunney Chan became the world authority in this field and his laboratory was particularly well known for the many original and insightful contributions elucidating the structure and function of this complex and important enzyme system.

Cytochrome c oxidase is an electron-driven proton pump, important for establishing the protomotive force obligatory for ATP synthesis in the mitochondrion. However, cytochrome c oxidase was a 'black box' for scientists at that time. Sunney Chan's laboratory carried out decisive experiments during the early 1980s to delineate the ligand structures of the metal cofactors. With this structural information, Sunney Chan and his students established the rules on how the electrons and protons must be gated by redox linkage between the metal cofactors and the protein scaffold during proton pumping in order to kinetically control the flow of electrons and the coupled movement of the protons uphill against the protomotive force across the inner membrane of the mitochondrion.

How pMMO Converts Methane into Methanol: A Tripcopper Cluster at the Catalytic Center

In the early 1990s, Sunney Chan initiated a new venture directed toward understanding how methane is converted into methanol with high efficiency by the particulate monooxygenase (pMMO). Before moving to Academia Sinica in Taiwan, his laboratory at Caltech had succeeded in isolating and purifying the pMMO to homogeneity. He continued this research in Taiwan. During the 2000s, Sunney Chan's Taiwan team developed novel methods to characterize the enzyme in depth and established the nature and identity of the copper cofactors in the protein, and discovered that a tricopper cluster is the critical element in the catalytic mechanism. This discovery is regarded one of the holy grails in organic chemistry. In recent years, Sunney

Chan's team at Academia Sinica and National Taiwan University has successfully developed the first molecular catalyst capable of efficient conversion of methane into methanol by O_2 at room temperature. This marks a breakthrough milestone in methane oxidation. Today, with net zero carbon and decarbonization becoming the world's most urgent mission, reducing methane emissions will help slow down global warming, and Sunney Chan's discovery is more significant than ever.

As further evidence of his broad interests and research activities, Sunney Chan also devoted several years to understanding protein folding, an essential process in biosystems that creates muscles, hormones, enzymes, etc. It was one of biology's biggest mysteries to be solved. Sunney Chan developed the use of caged compounds to study the very early events in protein folding initiated in the absence of denaturants. This work has demonstrated the importance of kinetic channeling in protein folding.

On top of his academic brilliance, Sunney Chan's career is also marked by his love of humanity. As a teenager, he once vowed to join the priesthood. After gaining world-class recognition as a scientist, he stepped out of American science from one of the world's most prestigious research institution-Caltech, and came to Taiwan to devote himself to building paradigms and infrastructures of advanced research for the then still-developing Academia Sinica. He was like a missionary spreading his faith. During his tenure as Vice President of Academia Sinica, he formulated a roadmap for the Genomics Research Center; he also worked with the National Science Council of Taiwan in creating the National Research Program in Genomics Medicine. Both have laid solid foundation for the booming of Taiwan's applied medicine and biotechnology industry.

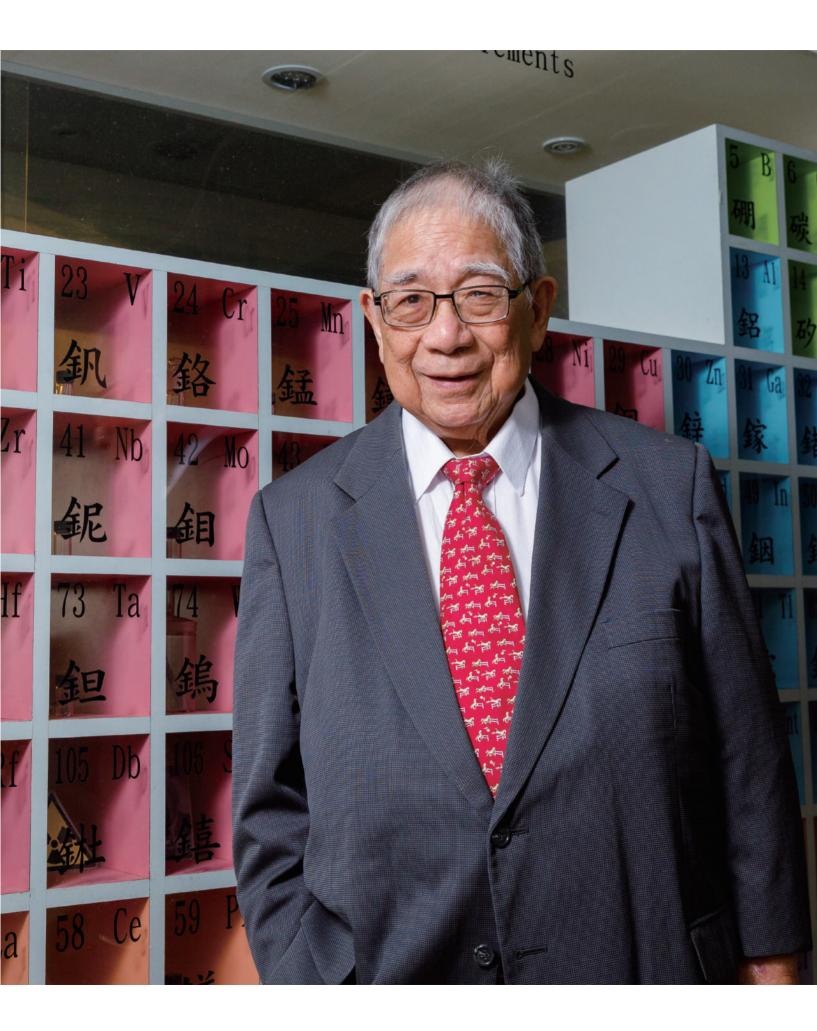
The TIGP (Taiwan International Graduate Program) in Academia Sinica was founded by Sunney Chan with an aim to attract global talents to undertake their graduate training in Taiwan. TIGP was established 20 years ago and it remains one of the most successful programs in Academia Sinica for the diversity and enrichment it has brought.

Leveraging his academic connections, Sunney Chan invited internationally-recognized researchers to lecture in Taiwan, significantly elevating Taiwan's worldwide visibility and academic strengths. Over

the years, he has organized many international symposia on cutting edge research in the frontiers of many fields, including chemical biology, biocatalysis and chemical catalysis, and energy, fuels, and sustainability. He is a visionary scientist with a keen sense of the directions that science is moving toward.

Sunney Chan was applauded by his fellow academicians for his selfless devotion in training young talents. He moved his research projects to Taiwan two decades ago and have since mentored hundreds of students: postdocs, graduate and undergraduate students. Among them, at least 25 from Taiwan are currently working in academic and research institutions, such as Ohio State University in the US and Max Planck Institute of Molecular Biology in Freiburg, Germany. Sunney Chan retired 10 years ago and still carries on his mission as a scientist and an educator. To this date, he continues to inspire many young minds in Taiwan and abroad, passing on his inheritance as valuable assets for generations to come.

<u>30</u> The Story of a Champion





A Scientist, an Educator and an Adventurer, Planting Seeds without Asking for Harvest

Sunney Chan Turned Academia Sinica into a World-class Institution

Coming from a humble background, Sunney Chan invented his own legend with curiosity, passion and intellectual giftedness in science. Vowed to become the first Asian Pope as a teenager, he dived into scientific research instead, finding more joy and fulfillment and reaching groundbreaking accomplishments in biological physics and biological chemistry. As a world-renowned scholar, he doesn't like the limelight . He didn't pursue science for personal or financial gains. He enjoyed the journey of discovery with fellow researchers and guiding the way forward for young talented minds. He has taught different generations of his students one valuable thing: how to do science.

Sunney Chan engineered the establishment of the Genomics Research Center for Academia Sinica without taking credits. His contribution in introducing solid paradigms and system architecture for Taiwan's advanced research is pivotal to the transformation of Academia Sinica into a premier research institute today, outshining its peer institutions in Asia. He plants seeds of hope like a missionary. It is simply Taiwan's privilege to have such a world-class scholar dedicating his best years in this land.

Sunney Chan was brought up in the US. His parents were firstgeneration immigrants from southern China to California. Both of them didn't have any formal education and worked long hours as 'sweatshop laborer' in a denim factory for Levi Strauss & Co. Sunney Chan grew up in the Chinatown ghetto, a socially and culturally disadvantaged environment.

As a teenager, he had no family members to emulate as role models, scholars or scientists. He became the first in his family to attend university and obtain a PhD degree. "How I ever got to where I ended up makes for an interesting saga. It was not by design or program," Chan said.

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The Boy in the Ghetto Wanted to Become the First Asian Pope

By the time he finished sixth-grade, Sunney Chan was a typical "banana", an Asian American who is yellow outside and white inside. His father decided that he needed to understand his Chinese heritage and sent him to a Chinese-speaking middle school in Hong Kong. He had just turned 12 and didn't understand a single word of Chinese, not even what was taught in the "English" class. Not surprisingly, he flunked out at the end of the term. "It was a socially humiliating experience, if not a psychological trauma that took many years to shake off," Sunney Chan recalled.

Chan was then transferred to an English-speaking school run by the Irish Jesuits, where his interests in academics were kindled by a number of excellent math and science teachers.

In the fall of 1953, he returned to California and entered the University of San Francisco with the intention of joining the priesthood and becoming a science teacher. "My career aspiration at the time was to be the first Asian Pope." This ambition did not take shape since the rigid lifestyle of a Jesuit priest was too much for a 16-year-old who was set to explore the world and curious about everything in his surroundings, and fortunately so or the world would have one less outstanding scientist and passionate educator. His parents have different expectations to him, too. "My mother wanted me to be a medical doctor. I did try and dropped out. Dissecting a frog in pre-med class was an experience I didn't enjoy. My father wanted me to be an engineer and return to China to rebuild the country out of poverty."

Sunney Chan transferred to U.C. Berkeley to study chemical engineering for a bachelor degree. "U.C. Berkeley was a difficult school for me," he said. The rigorous curriculum was intimidating for a transfer student; it also took some efforts for Sunney to build up confidence in the new environment. Luckily, two professors at Berkeley were inspirational to him: Professor George Pimentel's lucid lectures on chemical equilibrium stimulated his interest of learning; Professor Andrew Acrivos taught him applied mathematics and kinetics as well as introducing him to the process of self-study and independent research. By the senior year, he was prepared to learn from sources outside the classroom and auditing courses not on the formal curriculum.

Sunney Chan stayed at Berkeley for a PhD in physical chemistry. His PhD thesis was on the microwave spectrum of oxetane and its molecular structure. In less than three years, he obtained the PhD degree with lucrative job offers awaiting him. "By the early spring of 1960, I had lined up attractive positions at MIT Lincoln Laboratories, Lockheed, General Electric and IBM."

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Giving up High-paying Positions for a Post - doc at Harvard

Sunney's PhD mentor, however, had a different plan for him. "He insisted that I apply for an NSF Postdoctoral Fellowship to work with Professor Norman Ramsey (1989 Nobel laureate in Physics) in the department of physics at Harvard University," Chan said. High-resolution solution NMR was developing at the time; he was suggested to enter the field leveraging his background in microwave spectroscopy of gases to study the NMR of small molecules in molecular beams.

Just to keep peace with his professor, Sunney Chan filed an application for a National Science Foundation postdoctoral fellowship. When the word came that he had won the fellowship, he was taken aback. Ultimately, he accepted to go to Harvard; the professor was pleased but his father was disappointed that he rather took the \$4500 fellowship instead of the much-higher-paying positions at General Electric and IBM. "My father said to me, 'Son, I don't have a PhD, but I make much more money than you do'," Sunney Chan remembered.

In September 1960, Sunney arrived at Harvard and began his postdoc research. While deeply engrossed in research, he was fascinated by the intellectual power of savvy scholars at Harvard. One day, he had made a significant discovery in the lab, and J. H. van Vleck (1977 Nobel laureate in physics) happened to be there. The next morning, Dr. van Vleck reappeared in the lab and explained the observation using "perturbation theory" on the chalk board. To a novice scientist, it was an impressive demonstration of real intellectual power. It left a deep and lasting impression on Sunney Chan; he was reinforced that he had made the right decision to do his postdoctoral study at Harvard.

In 1961, he was offered a position as an assistant professor at the University of California at Riverside (UCR), his first teaching job. The graduate program in chemistry at UCR had just started, "I thought I could contribute to building a high-quality program," he said. It was here that Sunney Chan's original interest in science teaching began to take shape.

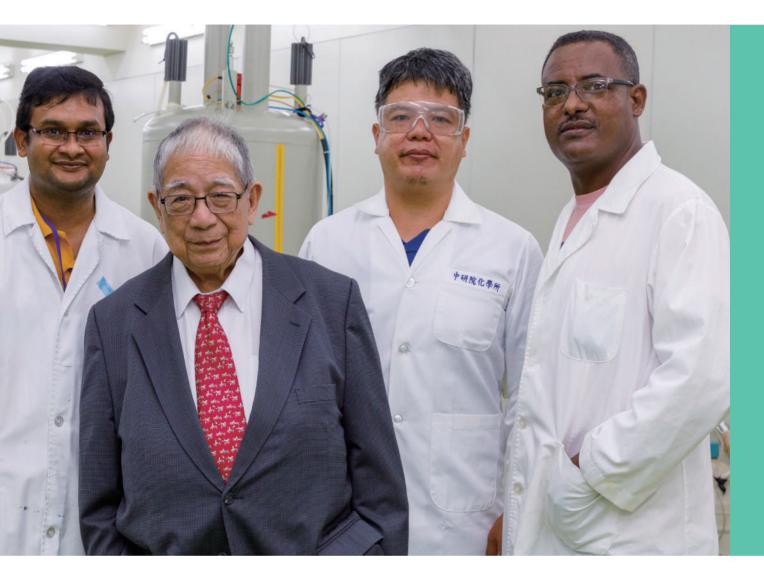
"My graduate training at Berkeley and postdoctoral experience at Harvard had convinced me that research training was a great way to encourage young people to develop their potentials to become



original and independent research scientists." Sunney Chan decided to become an academic scholar as well as a teacher who can stimulate students in learning. He was about to turn 25.

His career goal was settled, but his research plans at UCR was far from crystallized. Sunney Chan didn't want to continue in NMR of molecular beams which, like microwave spectroscopy, was maturing and becoming less likely to generate new concepts or breakthroughs.

"To train students, I felt that the research they worked on had to be 'discovery' driven," Chan said. With curiosity as an impetus, young people could learn to define the science question, develop the research plan, formulate the hypotheses to be tested, and design the experiments to test them. To him, this solid set of system was the way to do science. So he decided to try a number of research areas that were new to him, including the structure of transition metal complexes in solution by NMR,



NMR of purine and pyrimidine bases, and EPR of concentrated alkali metal ammonia solutions.

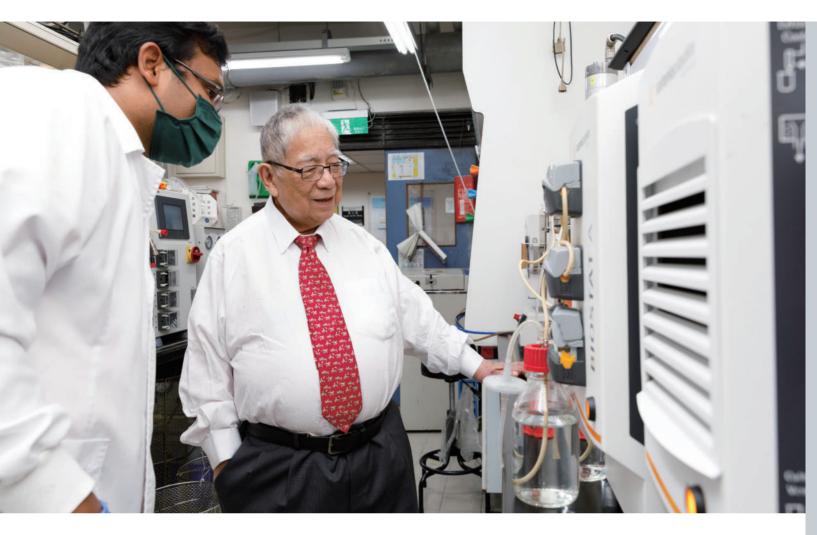
Sunney Chan's stay at UCR was very brief. He was invited to present at a seminar at Caltech shortly after he arrived UCR. "To my surprise, I was offered to join the Caltech chemistry faculty the following week." He turned down the offer immediately, mainly because his research program at UCR was about to gel. "Caltech was such a high-power place. I wasn't sure that I was up to the challenge," he added.

Caltech asked him to reconsider. At the same time, a similar offer was extended to him from the chemistry department at Yale. "Perhaps it was telling me that I should consider the long-term impact of a stimulating environment and high-quality graduate students on the development of my research career." Caltech has world-class scholars, its graduate students are firstrate, all the way around, there is quality. So Sunney Chan moved across town from UCR to Caltech and stayed there for 40 years.

Early Years in Caltech: From Physical Chemistry to Biophysics

In Caltech, Sunney Chan embarked on his first research in biophysics: base-stacking of nucleic acids in aqueous solution. He focused on the application of NMR to address the structure of biological molecules and their interactions in solutions. The base-stacking interaction is now commonly known by scientists but at that time, while molecular biology was centered on the structures of the Watson-Crick A-T and G-C base pairs, there was a debate as to whether or not these 'horizontal' interactions were in fact sufficient to account for the stability of the structure of the DNA double helix in water at room temperature.

"As I began to embark on the new field of biophysics, little did I know that my background in chemical physics would serve me well in my future endeavors," Sunney Chan said. "It seemed a major handicap to have no formal training in biochemistry



or biology, but it turned out to be quite the opposite. Molecular biophysics was a relatively virgin field, and not knowing too much was a blessing in disguise."

"To me the more serious hurdle was finding out what was known and what was unknown, as well as identifying the scientific questions that needed to be solved and the tools that would get me to the heart of the matter." Sunney Chan's background in physics gave him the insights to formulate and analyze complex problems rigorously from the outset.

In pioneering NMR experiments undertaken during 1962-64, Sunney Chan's laboratory showed that in water solution, there exist strong "vertical" interactions between the nucleic acid bases in DNA (and RNA), and the nucleic acid bases stack in water in order to minimize the disruption of the hydrogen-bonded network structure of the water, now commonly referred to as the "hydrophobic effect." Consequently, this discovery brought to an end the scientific debate on why and how the Watson-Crick A-T and G-C base pairs can be formed in water. In 1968, his lab began to probe the phospholipid bilayer membrane with NMR and discovered that the membrane is neither a solid nor a liquid and could undergo only restricted molecular motions with a hierarchy of timescales from picoseconds to nanoseconds to microseconds and to milliseconds. This uncovered the picture of the dynamic structure of the biological membrane that we have come to know today.

Following this seminal work, Sunney Chan moved on to study the effects of cholesterol, amphipathic peptides and membrane proteins on the structure of the fluid bilayer membrane. These molecules affect the cooperative domain size of the bilayer membrane, the correlation length of the collective motions, the surface curvature, the elasticity, lateral diffusion of the phospholipid molecules within each leaflet of the bilayer, the exchange of the lipid molecules between the two leaflets, and the phase behavior of mixtures of phospholipids in the membrane. He also studied on lipid-protein interactions and lipid-mediated protein-protein forces.

Cracking the Mystery of Cytochrome *c* Oxidase and the Holy Grail of Organic Chemistry

With so many membrane proteins in cells and so many discoveries made in research on membrane proteins, Sunney Chan turned his attention to unraveling the structure and function of molecular machines within living cells in the late 1970s. Many of these molecular machines are membrane proteins, which are extremely difficult to isolate and purify for in-depth study. His group was able to purify the cytochrome c oxidase, the terminal enzyme in the mitochondrial respiratory chain, which is crucial to generate energy for cells to complete their activities.

However, cytochrome c oxidase was a black box at that time. Under Sunney Chan's leadership, his student and postdocs systematically worked out the structure of the metal cofactors that mediate the electron transfer, the sequence of electron flow between metal cofactors, and details of how the dioxygen molecule is cleaved to form the high potential redox intermediates required to drive the proton translocation (cytochrome c oxidase is a proton pump!). These studies allowed them to predict the chemical structures of the various metal cofactors and their possible role in the overall function of the enzyme. Sunney Chan became the world authority in this field, and his early papers on the mammalian cytochrome c oxidase were among the first to place the understanding of this important enzyme on the molecular level, well before the X-ray structures of the cytochrome c oxidase became available in the early 1990s.

In 1992, Chan initiated a new venture toward understanding how methane is converted into methanol with high efficiency by the particulate methane monooxygenase (pMMO). Before moving to Academia Sinica in Taiwan, Sunney Chan's laboratory at Caltech had succeeded in isolating and purifying the pMMO to homogeneity. During the 2000s, his Taiwan team elucidated the catalytic mechanism of biological methane oxidation. The mechanism is based on the deployment of a tricopper cluster to harness a singlet oxene from molecular oxygen (O_2) for facile direct O-atom insertion across the C-H bond. This chemistry is novel, and beautifully illustrates how nature exploits metal clusters to catalyze difficult chemistry with a powerful oxidant without self-



destruction of the catalyst itself. The conversion of methane into methanol, a gas-to-liquid process, is extremely difficult chemistry because the C-H bond in methane has the highest bond energy among organic substrates. For this reason, the process has been one of the "holy grails" in the field of organic chemistry. Recently, Sunney Chan and coworkers in the Institute of Chemistry at Academia Sinica and the Department of Chemistry at National Taiwan University, have developed the first molecular catalyst capable of efficient conversion of methane into methanol by O_2 at room temperature. This is yet another ground-breaking invention in the field of methane oxidation.

During the 40 years at Caltech, Sunney Chan became world-renown because of his groundbreaking discoveries in two benchmark systems: "bovine cytochrome c oxidase" and "pMMO in methane oxidation."

House Master for 800 Students, Confronting Drug Dealers

What brings fulfillment to Sunney Chan is not just scientific adventure, but also his interaction with

students. "I was the Master of Student Houses at Caltech. It was quite an experience." There were 800 students in the school's dormitories, or Houses. The term of office of the previous master was about to expire, and students were not very fond of the candidate suggested as successor by the Caltech Administration. Sunney Chan taught freshman chemistry at the time and was loved by students. One morning in May 1980, a group of students approached Sunney Chan after class and asked if he was willing to take the job. "I had no idea what a house master is and what the master does or needs to do." Sunney Chan sought advice from a fellow colleague on campus, an elder Chinese and academician of Taiwan, who noted that "if I take the job, I'll be the first Chinese American to assume an administrative role at Caltech. It will be a milestone." With this subtle pressure, Sunney Chan decided to consider the position and the unforeseen challenges that came with it.

For this concurrent position, Chan and family moved to the neighborhood of the student houses. He organized extracurricular activities every weekend and cooked dinners for students. He became a caretaker/counselor for these brilliant young people. As the students' "gang lord", Sunney Chan undertook the responsibility of making sure they were out of harm's way and standing with them in the face of knotty problems. It was the end of the Hippie era, but narcotics abuse was still rampant in the school campus. One day, a drug dealer was peddling drugs on the campus and spotted by Sunney Chan. Sunney stopped the drug dealer and asked him to leave. The drug dealer refused to go and took out a gun to intimidate Chan. "In the face of such a menace, I could only say to him, 'please go away or I will call the police.' Luckily, the drug dealer backed down, ending this daunting episode without any mishap."

During the four years of the House Master's tenure, Sunney Chan helped many students: those with depression and were suicidal because of pressure from schoolwork, those who had relationship and gender identity issues or family problems. "We all encounter problems when we are growing up. These students were willing to come to me and I was able to provide them with a helping hand. That was the most rewarding thing."

Over the years in the US, Sunney Chan has also been active in community and public service. He



TASCO award ceremony with President Wu on Dec 2018

was a founding member of the Chinese-American Faculty Association (CAFA), a service organization devoted to the welfare of academics of Chinese descent working within the Southern California community. He served two terms as the CAFA President. He has also chaired the Caltech Y Board of Directors (1992-1993) and the Board of the Chinese-American Chemical Society (1988-98). Chan has been a regular consultant of the National Institute of Health (NIH) in Bethesda since 1970, and has served on many NIH Advisory Committees, including the Biophysics and Biophysical Chemistry Study Section (1970-74), the Physical Biochemistry Study Section (1989-93; chair, 92-93), the National Cancer Institute Review Board (1996-97), and Study section on Small Business Innovation Research (1992-2002). In addition, he is a member of many scientific advisory committees in the US and abroad.

In 1988, Sunney Chan was elected as the Academician by Academia Sinica in Taiwan. In 1997, he was invited by Lee Yuan Tseh, the then President of Academia Sinica, to move to Taiwan and help modernize the institution. "This was certainly a big news at that time. Sunney's decision



to retire from Caltech and move to Taiwan made quite a splash in the academic circle," Shie-ming Peng, Academia Sinica Academician and Honorary Professor at the Department of Chemistry, National Taiwan University recalled. Peng said that Sunney Chan was already a top scientist in the world and willing to give up the fame and resources at Caltech for an entirely new beginning, "I think it has a lot to do with his father. He always wanted Sunney to contribute more to humanity."

Sunney Chan's father had great expectation for him, more than making big money or achievements. He always told Chan to cherish what he has and contribute to the global Chinese community. That is why Chan was sent to Hong Kong for middle school education—to not forget his cultural origins.

In 1997, Sunney Chan accepted the invitation of Lee Yuan Tseh, then President of Academia Sinica in Taiwan, and came to Taiwan with a goal: to transform the Institute of Chemistry and the entire Academia Sinica into a modern, world-class research center.

In Academia Sinica, he began with the position as Director of the Institute of Chemistry. In the Christmas party that year, Sunney Chan put on a Santa Claus costume to entertain the faculty. Professor Peng recalled, "his figure and temperament are exactly like Santa, always willing to help and always kind and nice. We'd use to call him "s-orbital", the most stable orbital in atomic physics."

Chan is as much a gastronome as a scientist, and he is well known for his hospitality. When he first came to Taiwan as acting director of the Institute of



Sunney was promoted to become Vice President of Research, Academia Sinica on July 1997

Molecular Biology at Academia Sinica in 1989, he roasted a turkey to celebrate Thanksgiving with his colleagues. In 1997, he relocated to Taiwan; within two years, he had visited all the gourmet restaurants in Taipei. The Dragon Restaurant, the must-go place for authentic roast duck and exquisite dim-sum. The ChianTangTsuen, named after a scenic river in the east coast of China and offered Shanghai delicacy, and several other restaurants he visited regularly, still have "Sunney Chan's menu" today. In his 85th birthday this year, he will host a banquet at The Dragon Restaurant, Neihu for friends and colleagues. Harry Gray, Professor of Chemistry at Caltech would on occasions fly to Taipei just to attend Chan's birthday parties.

TIGP Elevated Taiwan's International Visibility

Chan was appointed the Academic Vice President of Academia Sinica, steering the direction of research development and academic standards for the entire institution. Over the four years in this capacity, he led the effort to establish the Taiwan International Graduate Program (TIGP) at Academia Sinica, an English-speaking program to attract international graduate students to participate in Academia

Sinica's research projects. Sunney Chan leveraged his connection in the global academic circle and invited world-class scientists to give lectures in Taiwan, which significantly elevated Taiwan's international visibility, and therefore attracting more young talents, creating a mechanism for Academia Sinica to strengthen its human resources and establish its global reputation.

During the tenure as Academic Vice President of Academia Sinica, Sunney Chan has another epochmaking contribution for Taiwan. He formulated a roadmap for the Genomics Research Center; he also worked with the National Science Council of Taiwan in creating the National Research Program in Genomics Medicine. Both have laid solid foundation for the booming of Taiwan's applied medicine and biotechnology industry.

A Scientist and an Educator, Generations of Young Talents Are Nurtured

"What I really admire him is his selflessness in mentoring generations of young talents. He is a scientist and an educator." Professor Peng said, Sunney Chan systematically trained his students and research team members to do science properly. Sometimes he also helped them with the literature of the thesis; with English being Chan's native language, a slight modification of a word or two will turn the academic expression neat and elegant.

Over the years, more than 200 graduate students, postdocs and visitors have the privilege to take part in Chan'sresearch ventures. This number is quite rare in the basic sciences. During the last ten years at Caltech, Chan made breakthroughs in the role of pMMO in methane oxidation into methanol. He then moved this project to Taiwan, and in recent years has made major discoveries and inventions. What is most important to Sunney Chan is that these discoveries and inventions have been made by students and postdocs working in Taiwan. Thanks to that, a number of young Taiwanese scholars in his team have now stepped onto the international stage, ready to fly higher with Sunney Chan as the wind beneath their wings.

Among his students, at least 25 from Taiwan are currently working in academic and research institutions, including Ohio State University in the US and Max Planck Institute of Molecular Biology in Freiburg, Germany, and almost 10 hold academic



and research positions at Academia Sinica and the National Universities in Taiwan. Many of his students and postdocs trained at Caltech have also taken on academic positions in major universities throughout the world. Some of his students have achieved success in industry. For example, Ming-Chu Hsu, founder of Taigen Biotechnology was in Chan's lab at Caltech for postdoctoral training during the early 1970s. She's among the first generation of successful biotech entrepreneurs in Taiwan after the local biotech industry took off 20 years ago. Sunney Chan retired from Academia Sinica 10 years ago and still carries on his mission as a scientist and an educator. To this date, he continues to inspire many young minds in Taiwan and abroad, passing on his inheritance as valuable assets for generations to come.



Sunney Chan's zeal for scientific research did not wane after his retirement from Caltech. He devoted himself in yet another unrevealed frontier: protein folding. In his own words, "To close out my scientific career, I decided to return to a simpler issue." Protein folding is an important mechanism in living science since with this process, muscles, hormones and enzymes are formed. However, how it works was still a mystery some 20 years ago. Sunney Chan developed the use of "caged" compounds to study the very early events in protein folding initiated in the absence of denaturants. In this work, Chan has demonstrated the importance of kinetic channeling in protein folding.

In retrospect, Sunney Chan said, "I have had an exciting career. The journey that ultimately led me to the world of membrane proteins was hardly programmed. It evolved serendipitously (although

 15th Taiwan International Graduate Program (TIGP) certificate conferral ceremony

logically) from the chemical physics of simpler systems, from the dynamic structure of the lipid bilayer to lipid-protein interactions, to membrane biophysics of ion transport, and culminated in the structure and function of several membrane protein systems."

As the systems he studied became more complex, Chan said, he learned how to manage the research undertaking, how to define a myriad of complex biological problems from scratch without knowing much about them, and how to formulate research strategies to approach the various issues. "A problem like pMMO is so complex that it transcends generations of coworkers, with the next generation of experiments building on the outcome of earlier ones." He noted that in academia, with



limited research resources, it's not possible to build a large team and solve problems in a short amount of time as is done in industry. "However, with a more deliberate pace, it is possible to take advantage of emerging technologies as they develop," Chan said.

Shaping an Open Environment for Taiwan's Academia

While at Caltech, the bulk of Chan's membrane research was supported by the National Institute of General Medical Sciences of NIH and he was able to sustain NIH funding for more than 30 years. He said that the level of support was adequate to cover most research expenditures, with the exception of upgrades of research instrumentation or the purchases of major pieces of equipment. In contrast, after he moved to Taiwan, his research program was funded by Academia Sinica. Although the level of support was not as high, Academia Sinica did provide funds for upgrade of research facilities and the acquisition of state-of-the-art instrumentation as justified by the research. This capability greatly accelerated the progress of his work in Taiwan.

"In Taiwan, resources (funding and research facilities) are not too bad, but the research

 William A. Rose Award from the American Society of Biochemistry and Molecular Biology in 2004

environment could be more open." Chan believed that along the long, exhausting journey of pursuing scientific truth, young people need to be motivated by passion and intellectual inquiry. "It is intellectual curiosity that fosters creativity. Not just learning textbook or journal science."

In Chan's opinion, developing one's "scientific judgement" is also important in science, but that requires experience. He categorized science into three different kinds: (1) discovery science (or exploratory science); (2) mainstream science (popular areas actively pursued such as materials chemistry, water splitting, new drug development, machine learning or quantum computing); and (3) mature science (issues largely defined but need fine-tuning). Among them, discovery science is most fascinating to Chan. "This is an area that nobody knows anything or much about it, so you need to ask questions and find the answers from scratch. It was like Christopher Columbus embarking on his journey to the west. He had a hunch. He didn't know he would discover the new continent. He simply asked himself: what is out there?"

To Chan, discovery science is about stretching one's imagination, groping in the dark and probing the unknown. "When you hit the road, you have nothing but a black box in hand, without any clues about what is in the box. This doesn't mean nobody has never asked the question before. But nobody has found the answer yet. Or the nut was too hard to crack."

In this manner, discovery science is a high-risk and long-term investment, with high intellectual content but low productivity, at least at the beginning, Chan said. "I was fortunate enough to have randomwalked into scientific issues that later became mainstream."

Act of fortune, however, does not explain his accomplishment. To him, science is not about research grants, research publications or awards; it's all about intellectual curiosity. "I have always wanted to understand my surroundings, about nature and human behavior." He doesn't like the limelight. He doesn't enjoy competing with others nor into oneups-man-ship. "After all, I am just an educator, or a scientist, a thinker or an intellectual at best," Chan said.

Loves Intellectual Discovery More than its Commercial Value

If Chan chose a different career, he supposed he could have succeeded, too. "My mother wanted me to be a medical doctor. My father wanted me to be an engineer. But I discovered that I was more interested in ideas than applications." Chan said that he could have ended up like many of his cousins as a teller in the bank, a post office clerk, a grocery checker or a butcher, and be happy about it. This was the typical career path for a young Chinese Americans of his generation grown up in San Francisco Chinatown. "I could have been a high school science teacher and enjoyed it, however."

When Chan turned 50, already an established scholar, his father wanted him to take over the family business. "That would have been a nightmare for me. I do not like wheeling and dealing. I would have been bored my entire life."

Professor Shie-Ming Peng, a good friend of Chan's, agreed. "Some scholars dedicate in research to find a marketable solution or product, such as new drugs or vaccines. Sunney is not like that. He loves basic science. He enjoys discovering the unknown in a stimulating environment with his teams. That is why he spares no efforts in teaching and training young people. He is not commercial-minded at all."

Chan is often invited to give lectures. In earlier days, he spoke mostly about the profound topics of his scientific researches. In recent years, he started to share his scientific career in school campuses, hoping to inspire more students. His advice to young people who are passionate about academic studies: "Research is about searching and searching until you are intellectually satisfied with the answer; it takes hard work, discipline, patience and a degree of stubbornness. Therefore, it's not for everyone."

Although basic science research is definitely for him, Chan has broader perspective. Citing the science of chemistry as an example, he said, "we train chemists not only for industry and academia, but a multitude of other professions: public policy, risk analysis, chemical safety, environment protection, environmental law, patent law, etc."

In his article titled "Opportunities for Innovation in Chemical Science" published in the Chemical Education Journal, Chan talked about the breakthroughs in chemistry over the past one hundred years: discovery of the elements, how molecules are formed, how molecules react to form new molecules and how to synthesize molecules in the laboratory.

The field of chemistry is moving on but it's also experiencing some sort of an identity crisis. The contribution of chemistry to human life and industry is no longer mentioned, mainly because a series a tragic incidents caused by serious pollution such as



Sunney discussing the structure and mechanism of enzymes mediating methane oxidation with British microbiologist Sir Howard Dalton at C1 Meeting, Magdalen College, Oxford in August 2006.

the impacts of DDT and dioxin on ecology and human health, the use of tetraethyl lead in gasoline causing neurotoxicity, the methyl isocyanate leak resulting in serious casualties in India, and the contribution of freons to the depletion of ozone. These tragic events have tarnished the image of chemistry as a science.

Today, when the news media discuss sequencing of genomes, vaccines, cholesterol-lowering statins, a new drug for type II diabetes, chemistry is never mentioned. But the truth is, these breakthroughs all involve chemistry. "In other words, we need to make the general public more related to chemistry. The basic research of chemistry is still very vibrant and contributive to human life," Chan said.

The world needs diversified talents, and Sunney Chan is cultivating them for the world. "Many of my students have gone into new territories. I think it's only natural. And I'm proud of them." But for Chan himself, cracking the mystery of nature is still the most charming task. "No matter how complicated biological problems may appear to be, there is a simple answer to the outcome when all is said and done. In my view, nature is intrinsically simple, and it is fun to discover how the behavior of a complex biological system is explicable in terms of the law and physics and chemistry as we now understand them to be."

Sunney Chan is more than a world-class scientific researcher or a selfless educator. For Taiwan, he's like the Santa he dressed up to be in his first year in Academia Sinica, bringing to this island the gift of system reform and academic leap. But ultimately, he is just an adventurer who took to the untrodden route with insight, navigated the path to truth with strategy and patience, and inspired bright young gangs to march ahead together. And that has made all the difference.

Sunney became a permanent resident of Taiwan in April 24.2015



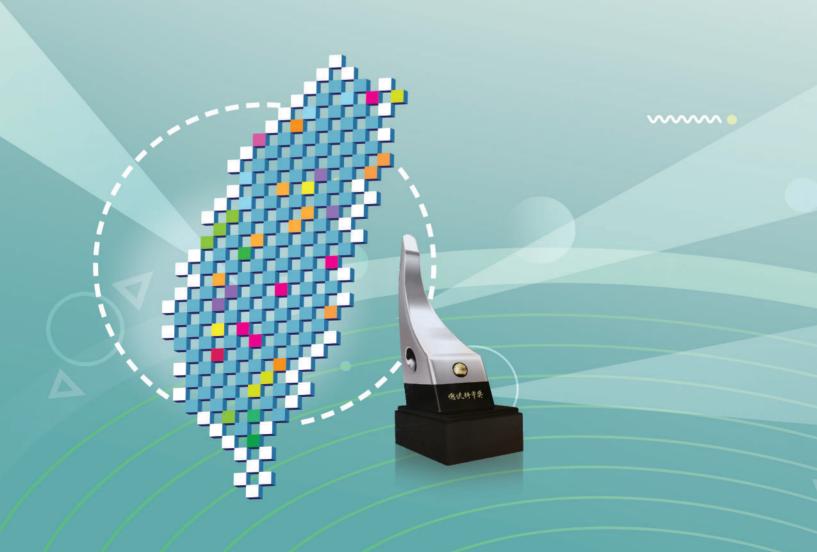
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- "Effects of structural defects in sonicated phospholipid vesicles on fusion and ion permeability", Růdiger Lawaczeck, Masatsune Kainosho, Jean-Luc Girardet and Sunney I. Chan*, Nature 256, 584-586 (1975).
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- "Efficient oxidation of methane to methanol by dioxygen mediated by tricopper clusters", Sunney I. Chan*, Yu-Jhang Lu, Penumaka Nagababu, Suman Maji, Mu-Cheng Hung, Marianne M. Lee, I-Jui Hsu, Pham Dinh Minh, Jeff C.-H. Lai, Kok Yoah Ng, Sridevi Ramalingam, Steve S.-F. Yu,* and Michael K. Chan*, Angew. Chem. Int. Ed. 52, 3731–3735 (2013).
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Chosen from a number of excellent candidates, the three awardees of the 2020-2021 Presidential Science Prize - Dr. Sunney I. Chan of the Mathematics and Physical Sciences Category is the most outstanding and internationally-recognized scholars who has achieved great contributions in scientific R&D.

Indeed, for decades, they have distinguished themselves in various fields of research with selfless attitude and a sincere spirit of inquiry. Thanks to their dedicated endeavors, Taiwan now can stand side-by-side with advanced countries in various fields of scientific research. Moreover, their research achievements have not only benefited people in this country but also had far-reaching influence on the prosperity of all mankind.

Looking toward the future, scientific development still requires persistent efforts of all scientists around the world. Working hand-in-hand, we will be able to make even greater breakthroughs in science and usher in a new era of international scientific cooperation.



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