出國報告（出國類別：參加學術會議）

出席第十屆國際一氧化氮學術會議和第一屆歐洲生理學會學術會議 會議心得報告

服務機關：國防醫學院 藥理學科

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派赴國家：英國

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摘要

第十屆一氧化氮之生物化學及治療應用國際會議今年再度於英國牛津市召開，除了主辦國(英國)之外，尚有多個國家的學者約 280 人來參加，其中主要包括基礎醫學研究人員和臨床醫師以及部分藥廠或儀器商的研究人員。會議的內容包括至少 40 個研討會和自由討論會，壁報摘要有七十餘篇。會議的地點是牛津市的 Keble College 會議中心，該會議中心位於 Keble College Math Building 內，是一棟新建的建築物，被傳統的建築物包圍在其中，顯得格外的醒目。

會議的第一天（9 月 16 日）主要是報到和領取會議資料以及晚上的歡迎會和一場會演講，是由 1998 年諾貝爾醫學獎得主之一的 Professor Lou Ignarro 告訴大家 NO 發現的由來和有趣的歷史故事。這次第十屆一氧化氮之生物化學及治療應用國際會議恰好是接續第一屆歐洲生理學會議舉行，是在離倫敦約二小時車程的牛津市 Keble College。所以在 9/16 下午 15:30 歐洲生理學會議結束後，趕搭 X90 巴士到這個會議場地，可以說是馬不停蹄。然後隨即到牛津博物館參加大會所安排的大會特別演講和歡迎會，以及簡單的點心與飲料，並與前來參與的各國學者打招呼和寒喧。這次會議場地有 2 個，每天從 08:30 到 18:00，可見會議議程的緊湊性和充實性，直到 9 月 20 日 14:00 才結束。筆者隨即返回住宿處提取行李，並走路到市中心搭巴士前往倫敦 Heathrow 國際機場，趕搭 18:20 飛機返國。可以說是，一刻時間也都沒有浪費，整個行程的安排是充份的利用了！

第一屆歐洲生理學會學術會議今年首度於英國倫敦市召開，是由 The Physiological Society、Deutsche Physiologische Gesellschaft、Scandinavian Physiological Society 和 Federation of European Physiological Societies 四個學會聯合舉辦。隨後將於 2020 年在德國和 2022 年在瑞典舉辦，將會是一系列的雙年度會議。歐洲生理學會會議也將成為這幾年合作夥伴協會的主要會議。這次會議除了在地的英國學者之外，尚有歐洲多個國家的學者約 1,200 人來參加，其中主要包括基礎醫學研究人員和臨床醫師以及部分藥廠研究人員。會議的內容包括 5 個 plenary lectures、11 個 keynote lectures、20 個 symposia、

7 個 lunchtime sessions 和自由討論會，海報摘要有近二千篇。會議的地點是倫敦市的伊利莎白二世女皇國際會議中心– EQII center，就在英國國會大廈旁。交通非常容易到達的地方。該場地於 1986 年由 HM 女王開放，並在倫敦活動行業的中心慶祝成立 32 年。經過翻新的 QEII 中心是倫敦市中心最大的專用會議，活動和展覽空間。該場地位於 Westminster，提供世界一流的設施，可舉辦高級會議，會議，展覽，頒獎晚宴和企業活動，最多可容納 2,500 人。 該中心每年舉辦 400 多場國內和國際活動。

會議的第一天（9 月 14 日）除了報到和領取會議資料之外，馬上進行大會的專題演講和相關的會議議程。筆者本人 9 月 13 日一早由桃園國際機場出發，中途在香港轉機，最後抵達英國倫敦國際機場，轉搭乘地鐵到市區的 Princes Gardens 旅館，已是當地晚上 22:00。隔日(9 月 14 日)早上搭乘地鐵前往會議中心報到和張貼報告的海報，然後隨即參加大會所安排的大會演講。這次會議場地共有七個，不但會議議程緊湊，海報的展覽也是充滿人海，甚至有時擠得寸步難行，真是熱鬧非凡且充實，會議直到 9 月 16 日下午 17:00 才結束。因為繼續參加會後在牛津召開的第十屆一氧化氮國際學術會議，所以 15:30 先行離開會場去搭 X90 巴士到牛津的 Keble College。

（參加國際一氧化氮學術會議）

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壹、會議緣起

這次國際一氧化氮學術會議的特色是繼續四年前所整合，與一氧化碳及硫化氫學會所共同舉辦，而國際一氧化氮學術會議的緣起是擬藉助參與會議的過程中來激發從事生物醫學和生命醫學的科學家或臨床人員經由會議的報告、認識和討論彼此的研究主題，互相激盪出新觀念或想法，或是找尋共同合作的機會或交流，以提升研究的品質，達到互利和良性互動。

貳、參加目的

這次三種氣體的學術會議之主要目的在於呈現當今學者對整體一氧化氮、一氧化碳及硫化氫的生理、化學和治療應用之巨觀，甚至更深一層從其合成酶和代謝物的分子和細胞層次以及調控機制之微觀，如訊號傳遞路徑和分子作用機轉，甚至基因的參與等。譬如：這次有許多學者用 NO 的開發產品其實際的應用之研究探討，是這次讓筆者印象最深刻的部份之一。另外，比較學理上的研究包括 NO 作用的標的 soluble guanylyl cyclase 的蛋白質結構修飾和藥物研發，也做了很深入的探討，甚至包括其 kinetic 的變化，可以說是非常的細膩。這次會議甚至邀請了微生物免疫學家一起來參與，使會議更加多元化和周衍。這次我參加幾次一氧化氮學術會議所不曾遇見的，也顯示出 NO 在人類身體上的各種角色及其重要性。甚致有些是延續以往的熱門研究就是以 nitrite 或 nitrate 作為探討的對象，然後將這些已知的知識再度反推回一氧化氮在人體器官所扮演的角色，讓研究人體或體內微生物在不正常時所引發相關疾病的科學家們，更能精準地掌控一氧化氮其生理學和疾病形成間的關係。

叁、會議過程

會議在第一天下午 16:00 開始辦理報到，接著晚上 19:00 由地主的二位英國教授 Mark Crabtree 和 Philip James 致歡迎詞揭開會議的序幕，緊接著由美國教授 Jack Lancaster 介紹大會特別演講人，1998 年諾貝爾醫學獎得主之一的 Lou Ignarro 做專題演

講；隨後在博物館內舉行簡單的酒會和小點心，讓與會人士透過簡單的交談以彼此認識，也巧遇了好友 Dr. Brant Isakson 和他的研究團隊，到 20:30 結束。在歡迎會上也見到這次會議的籌備委員，舊識英國 Amrita Ahluwalia 教授，倍極愉悅！返回住宿處後，就趕快盥洗就寢！因為隔天會議是早上 8:30 開始，有另一位 1998 年諾貝爾醫學獎得主 Ferid Murad 教授做另一場大會特別演講；另外，我需要提早到會場去張貼我的報告海報。這次 Plenary lectures 的演講人有 Lou Ignarro 教授 (UCLA School of Medicine, USA)、Ferid Murad 教授 (Stamfor University, USA)、Tim Billiar 教授 (University of Pittsburgh) 和 Carol A. Colton 教授 (Duke University Medical Center)。這四天會議是從早上 8:30 到晚上 18:00 結束(除了最後一天到 14:00)，所以不能太晚睡，睡眠充足才能全神貫注全程參與這四天的會議議程！

我在這次會議的報告時間是 9/17、9/18、9/19 三天中午 12:45~14:00 都要在同一時段報告，報告的內容是 SPAK 在內毒素性鼠的血管低反應性和一氧化氮生成的角色。由於血管低反應性會導致敗血性休克時嚴重低血壓、組織灌流不良和多重器官衰竭，而且一氧化氮過量的產生常扮演內毒素誘導血管低反應性的一個重要角色。預發炎細胞激素和誘導型一氧化氮生成酶的生成和一氧化氮的過量產生有關。在敗血性休克中，抗發炎的治療可以減弱一氧化氮的生成和血管低反應性的產生。SPAK 已經被證實會活化 mitogen 活化的蛋白激酶，導致腸子發炎。因此，我們檢視 SPAK 在內毒素性鼠的血管低反應性和一氧化氮生成的角色。採用雄性野生型和 SPAK 缺乏型小鼠經由腹腔注射 *Escherichia coli* 內毒素(LPS, 50 毫克/公斤) 偵測實驗過程中的收縮壓和血中一氧化氮代謝物濃度的變化。活體實驗結束後，取出胸主動脈測定血管張力和 SPAK 的表現。本研究中，小鼠經 LPS 處理後，產生嚴重低血壓和血管對血清素、PE 和 ACh 產生低反應性。內毒素性休克鼠的磷酸化 SPAK 表現和血中一氧化氮濃度都顯著的增加。有趣的是，剔除 SPAK 後不只減少一氧化氮增加量，也改善內毒素性鼠血管對血清素和 PE 的低反應性。因此，我們推論 SPAK 會導致內毒素性休克時，一氧化氮過量產生和血管對血管收縮劑的低反應性；所以，抑制 SPAK 可能會是改善內毒素誘發一氧化氮過量生成導致

血管低反應性的另類治療方法。

三天的報告過程中，雖有幾位有興趣的學者來觀看我的海報，但幾乎都沒有給我很特別的建議，倒是有位四年在這會上認識的學者 Dr. Nadeem Wajih (Wake Forest University, USA)，因為他的海報就在我的海報附近，所以這三天都來跟我談他在美國做的研究，因為他的研究重心是在醫材方面的研究和開發，所以互為打氣加油！同時也認識了二未來自中國的學者，目前在瑞典工作，跟著他們的教授一起來做海報的報告。因為他們的海報也在我的附近，所以也彼此認識交流研究心得。

肆、會議心得

將此次參加會議，比較有興趣的主題摘錄如下：

(1) Nitric Oxide: A Truly Remarkable Molecule (Professor Lou Ignarro, USA)

An excellent example of the application of basic information learned about NO has been the development of selective phophodiesterase-5 inhibitors, which has revolutionized the treatment of erectile dysfunction. Other examples include drugs that act as NO donors or stimulate the production of NO, which leads to vasodilation and decreased blood pressure. There are undoubtedly many as yet unknown functions of NO. This allows for the opportunity to develop novel drugs for diagnosis, prevention and treatment of a multitude of cardiovascular and other disorders.

(2) Discovery of Nitric Oxide and Cyclic GMP in Cell Signalling and Their Role in Drug Development (Professor Ferid Murad, USA)

Professor Murad's key research demonstrated that nitroglycerin and related drugs worked by releasing NO into the body, which relaxed smooth muscle by elevating intracellular cyclic GMP. The missing steps in the signaling process were filled in by Robert F. Furchgott and Louis J. Ignarro of UCLA. A review of the discovery of NO and cyclic GMP in

cell signaling and their application in some biological and medical areas for drug discovery and development. These messengers first described in the 1970's have led to about 150,000 research publications in a variety of areas in biology and medicine and numerous therapies have been and will continue to be developed.

(3) Arginase and NOS2 – Immune Regulated "Gateway" Enzymes in the Brain (Professor Carol A. Colton, USA)

Two immune regulated enzymes – Arginase and NOS2 play a particularly important role by serving as "gateway" enzymes, directing use of arginine to multiple metabolic pathways. This is particular important in the brain where the presence of the blood brain barrier produces a restricted tissue compartment. Professor Colton show their work on Alzheimer's disease (AD) using both human tissue and animal models of AD have discovered imprints of arginine mediated-metabolic changes that lead to brain pathology. The use of "omic" tools have allowed them to begin to decipher which metabolic pathways in the brain may inappropriately dominate and have provided specific sites in the pathways where interventions may permit a return to a more physiological state.

(4) Regulation of eNOS by Protein-Protein Interactions (William Sessa, USA)

eNOS activity can be regulated via its subcellular localization, phosphorylation and regulated protein-protein interaction. To explore the nature of regulated protein-protein interactions with eNOS in an unbiased manner, SILAQ labeled endothelial cells were cultured under "basal" verus "stimulated" conditions and eNOS immunoisolated. A series of proteins were bound to eNOS under basal conditions and additional proteins were recruited by serum/growth factor stimulation. Data describing these results will be presented with a specific focus on an unusual pathway of eNOS regulation by plasminogen activation inhibitor-1 (PAI-1).

(5) Regulation of Vascular Tone and Blood Pressure in Inflammation by Indoleamine

2,3-dioxygenase-mediated formation of singlet oxygen (Professor Roland Stocker, Australia)

Singlet molecular oxygen has well-established roles in photosynthetic plants, bacteria and fungi, but not in mammals. Under inflammatory conditions, this heme-containing enzyme becomes expressed in arterial endothelial cells, where it contributes to the regulation of blood pressure. Professor Stoker show that arterial indoleamine 2,3-dioxygenase 1 regulates blood pressure via formation of singlet molecular oxygen. They observed that in the presence of hydrogen peroxide, the enzyme generates singlet molecular oxygen and that this is associated with the stereoselective oxidation of L-tryptophan to a tricyclic hydroperoxide via a previously unrecognized oxidative activation fo the dioxygenase activity. The tryptophan-derived bydroperoxide acts as a hitherto undiscovered signaling molecule in vivo, which induces arterial relaxation and decreases blood pressure dependent on cysteine residue 42 of protein kinase G1. They suggest that a pathophysiological role for singlet molecular oxygen in mammals through formation of an amino acid-derived hydroperoxide that regulates vascular tone and blood pressure in inflammatory conditions.

(6) Cell-specific effects of Nox2 on blood pressure and cardiovascular remodeling (Professor Ajay M. Shah, UK)

Professor Shah found that myeloid cell Nox2 modulates basal blood pressure in healthy mice through interaction with NO-mediated vasodilatation of resistance arteries. In contrast, endothelial cell Nox2 has no effect on basal blood pressure but contributes to angiotensin II-induced hypertension. They also reveal that an important role of Nox2 in regulatory T cells (Tregs) in modulating angiotensin II-induced hypertension and remodeling. This involves an altered tissue balance between effector T cells (Teffs) that promote remodeling and Tregs that inhibit this process, Professor Shah concludes that Nox2 has a pivotal but cell-promising therapeutic target in angiotensin II-induced hypertension and cardiovascular remodeling.

(7) Role of Neuronal NO in Cardiovascular Regulation (Professor Phil Chowienczyk, UK)

Endogenous release of NO was regarded to be derived mainly from endothelial NO synthase (eNOS), recent experiments in humans with a specific neuronal NO synthase (nNOS) inhibitor suggest that nNOS-derived NO is an equally or more important source of basal NO production, regulating coronary and systemic vascular nNOS-derived NO is dependent on the degree of mental activation and is stimulated by acute mental stress. Basal regulation of nNOS appears to be influenced by functional coupling of the a1-adrenergic receptor to nNOS in vascular/perivascular tissue , possibly mediated through the a1-syntrophin PDZ domain and downstream effects of nNOS-derived NO are limited by phosphodiesterase activity. Little is known about nNOS dysfunction in disease states; indirect evidence suggests eNOS and nNOS function are differentially affected by risk factors and disease states and that mechanisms of dysfunction of nNOS are likely to differ from those of eNOS. However, differing mechanisms of nNOS/eNOS dysfunction may explain the lack of therapeutic efficacy of interventions targeting eNOS dysfunction whereas those targeting nNOS dysfunction remain to be explored.

(8) A New Model for Mild Traumatic Brain Injury: NO Protection (Dr. Greg Thatcher, USA)

Recent reports link traumatic brain injury (TBI) and multiple concussions to dementia. However, the connection between TBI and the depletion of "cognitive reserve" underlying progression to dementia is still unknown. A pre-clinical model of mild TBI (mTBI) would allow rapid assessment of disease-modifying strategies, in particular, if these can be related to later development of dementia. The deletion of mitochondrial ALDH2 in Aldh2-/- mice in conjunction with a closed head injury mTBI model led to cognitive deficits, neuroinflammatory pathology, and phospholipid dysregulation. Single hit, mTBI led to

cytokine surge, neuronal and synaptic pathology, and post-concussive syndrome 1-day post-injury, in contrast to WT littermates. ALDH2 detoxifies lipid peroxidation products, providing a weaker protection against oxidative stress. Pharmacological agents activating NO/cGMP signaling were effective after mTBI in attenuating cytokine surge and alleviating concussive amnesia. Further work is needed to link these benefits to delayed progression to dementia.

(9) Dysregulation of NO and Redox Signaling Underlies Synaptic Dysfunction in Neurodegeneration (Professor Joern R Steinert, UK)

Their data suggest that suppressing NO production during early disease stages has positive impacts on glutamatergic synaptic transmission and neuronal function, thereby slowing prion disease progression. Our findings further indicate that NO-signalling is closely linked to protein glycation and thus suppression of aberrant NO production can diminish both, direct NO toxicity and secondary generation of AGE. As both signalling routes can mediate cell death and are evident in several neuropathologies, indicating that targeting NO-AGE interactions might represent a beneficial disease modifying approach to slow neuronal degeneration.

國際一氧化氮學術會議是研究一氧化氮科學家們的重要會議。筆者從這次會議中獲得不少有關 NO一系列訊號傳遞和相關疾病之醫學研究新知和其相關生技產品應用的新觀念。參加這類國際型會議，除了懷著多多學習的態度和吸收新知之外；也借由會議交流的方式認識國際上的著名學者，相信這將有助於仲引國防醫學院在國際學術舞台上的連結以及張顯本校的研究成果。然而此次筆者之所以能夠順利成行，全仰仗國防部核予公假和科技部的經費補助，在此深表感謝！

伍、建議事項

回顧這次參與國際一氧化氮學術會議人士中，發現代表台灣出席參加這次會議的人員只有本人應一位！

另外，筆者也觀察到這次參加會議的中國人在歐美各國工作的人數不在少數，外國人中，有少數幾位是來自蘇俄、印度、東歐，甚至還有非洲國家，其所從事的基礎醫學研究或醫療機構的研究工作都做得不錯！因此，警惕我自己要多思考未來的研究深度！尤其近年來各國的競爭力日益增大，反觀我們台灣目前各方面常常是內耗或是停滯不前，導致社會和教育出現嚴重的兩極化現象，過去我們的優勢也隨著時間而漸漸流失，心中的感受真是百感交集，惟有再三的告訴自己，更應盡心盡力，至少讓外國人看見我們台灣人是努力的！

期待當前政府對教育與科技研究的政策制定上需多下點功夫琢磨和努力，也期待在未來類似的國際會議上能多看到台灣的論文報告和參與者，相信這將有助於台灣的國際研究地位和競爭力之提升。

（參加歐洲生理學會學術會議）

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壹、會議緣起

歐洲生理學會學術會議的會議緣起於今年首度在英國倫敦市舉辦，往後將是每二年舉辦一次，隨後將於2020年在德國和2022年在瑞典舉辦。歐洲生理學會議也將成為這幾年合作夥伴協會的主要會議。合作協會主席評論說：「我們對這一歷史性舉措感到高興和興奮，這一舉措將歐洲三大生理學會和歐洲生理學會聯合會以這種協作方式匯集在一起。科學應該是無國界的，我們希望這一點共識不僅會吸引我們各自社團的成員，也會吸引更廣泛的國際生理學會成員。」會議的緣起是擬藉助各國科學家參與會議的過程中，來激發從事生物和醫學的科學家或臨床人員透過會議的報告，認識和討論彼此的研究主題，誘發出新觀念或想法，或是找尋共同合作的機會或學術交流，以提升研究的品質，達到互利和良性互動。

貳、參加目的

參加這個會議的主要目的在於呈現當今學者對整體現代生物的生理、生病理和治療應用之巨觀，甚至更深一層從細胞的酶和代謝物之細胞和分子層次以及調控機制的微觀(如訊號傳遞路徑和分子作用機轉，甚至基因的參與等)。所以涵蓋各種研究的主題面非常廣，所使用的會議場地之多，也是筆者有幸參加國際會議以來見證第一次學術會議的首次會議！筆者也是台灣來參加並報告的唯一台灣人。雖然會場的規劃動線不甚清楚，但隨時有服務人員適時提供會議場地的資訊，基本上都可以在五分鐘內到達所欲聆聽的會議場地。而且每場會議的主持人也都能確實的掌控時間，不致於有過度拖延的情況發生。其次是推動人類的科學和技術進步、經濟振興和社會的發展，這將一方面促使生理科學技術和經濟同步化，另一方面也是促進社會進步重要的力量，因為可以加強國際彼此間的學術交流與合作機會。

叁、會議過程

這次會議在英國英格蘭的倫敦市的 QEII (伊莉莎白二世)國際會議中心舉行，QEII

中心距離大本鐘(Big Ben)和泰晤士河(Thames River)有不到 5 分鐘的步行路程，位於威斯敏斯特(Westminster)教堂對面，距離皇家公園有 2 分鐘的步行路程。該中心擁有出色的交通連接，方便與會人士前往城市的所有景點，距離倫敦國際機場約一小時十分鐘的車程。由於時差和飛機座位狹窄的關係，在飛機上睡眠嚴重不足！只能在到達旅館後，稍做盥洗就趕快就寢，以備隔日開始的連續七天聆聽大會演講，不致於因精神不濟而打瞌睡，錯過演講的內容！

我在這次會議的報告時間是 9/14 下午 16:45~18:30，報告的內容是 Levosimendan 對內毒素引起的彌漫性血管內凝集大鼠的作用，探討瀰漫性血管內凝血反應是敗血症常見的併發症之一，會導致重症病患產生多重器官衰竭（multiple organ failure）與死亡。敗血症時期大量的細胞激素（如 tumor necrosis factor (TNF)-α 與 interleukin (IL)-6）分泌，會藉由刺激細胞表現 tissue factor 導致血液凝集系統的活化。Levosimendan 為一鈣離子增敏劑同時具有血管擴張作用，研究發現 levosimendan 具有抗發炎作用，在給予心臟衰竭病患後可以降低血中細胞激素的濃度。同時最近也發現 levosimendan 對於動物的敗血症實驗模式具有療效。在本實驗中，我們嘗試去探討 levosimendan 對於內毒素誘發瀰漫性血管內凝血反應是否具有效果，且利用血栓彈力計數儀（thrombelastography, TEG）來觀察凝血反應的變化。將 Wistar 大鼠分為四組：(1) 控制組，(2) 給藥（levosimendan）控制組，(3) 內毒素組，和 (4) 給藥內毒素組。引發內毒素血症的內毒素劑量為 4 mg/kg。而 levosimendan 則是先給與一個起始劑量（24 μg/kg）再開始連續注射 4 小時（0.6 μg/kg/min）。在實驗開始前、注射內毒素後一個半小時與四個小時分別採血以 TEG 分析凝血反應的變化，同時測量血小板數目、fibrinogen 含量、IL-6 與生化參數（lactate dehydrogenase、alanine transaminase 以及 creatinine）。實驗結果發現，給予內毒素後成功誘發大鼠產生瀰漫性血管內凝血反應；早期呈現凝血活化，晚期則是發生消耗性凝血功能異常。同時發現 levosimendan 具有降低 IL-6 分泌、避免過度消耗血小板與 fibrinogen 以及維持器官功能等效用。由本實

驗可知，使用 levosimendan 治療敗血症的另一好處：可以減輕瀰漫性血管內凝血反應與消耗性凝血功能異常的嚴重程度，避免出血。

由於我做的研究題目比較偏臨床醫師有興趣的研究主題，所以大家只是看看，並沒有人特別問我問題。會議在第一天早上 07:30 開始辦理報到，緊接著就是大會特別演講，會後晚上有個簡單的歡迎會。接下來每天的會議是從每天早上從 09:00 開始就有 keynote lectures，而且議程滿滿，所以每天會議 19:30 結束後，在回旅館途中隨意的買個晚餐回旅館吃，然後把隔日的議程看過後，就趕快盥洗就寢，以免太晚睡導致睡眠不足時，就無法全神貫注的全程參與這七天的學術會議！特別是有鑑於以前出國開會時曾因休息不足，遇到脖子無法轉動的痛苦經驗，所以現在出國開會時，都會隨時提醒自己，要有充分的休息，才有充足的體力來應付每天滿滿的議程！

肆、會議心得

將此次參加會議的幾個主題摘錄如下：

(1) Sweetness and Light: Impaired regulation of insulin secretion in diabetes (Frances Ashcroft, University of Oxford, UK)

Her research centers on how changes in blood glucose levels regulate insulin secretion from the pancreatic beta-cell and how this process is impaired in diabetes. She discovered that the ATP-sensitive potassium (K_{ATP}) channel serves as the molecular link between glucose elevation and insulin secretion. Mutations in K_{ATP} channel genes cause a rare inherited form of diabetes (neonatal diabetes), and her work with Professor Hattersley has enabled patients with this disorder to switch from insulin injections to drug therapy. Her current focus is on beta-cell metabolism and the metabolic regulation of beta-cell ion channels.

(2) From mountains to the bedside: Lessons learnt from Everest (Daniel Martin, Royal Free Hospital, University College London, UK)

Professor Martin is a critical care physician with research interests that include human

adaptation to hypoxia, microcirculatory blood flow, mitochondrial function and oxidative stress biology. He has been conducting research at altitude for over a decade and is part of the Xtreme Everest team. When he summited Mount Everest in May 2007 as part of large-scale research expedition measurements of arterial blood taken near the summit revealed him to have the lowest level of oxygen ever reported in a human. Professor Martin is also the critical care lead for the High Level Isolation Unit at the Royal Free hospital, responsible for patients with viral hemorrhage fever.

(3) The glymphatic system (Maiken Nedergaard, University of Copenhagen, Denmark)

Her multiple interests range from basic research on neuron-glia interactions to their role in aging, small vessel disease, seizure disorders and cerebral blood flow. Forefront amongst her discovery is the identification of the glymphatic system, a brain equivalent of the lymphatic system within which cerebrospinal fluid diffuses rapidly and mixes with interstitial fluids, thereby filtering metabolic byproducts that accumulate due to neuronal activity. The glymphatic system dramatically expands during sleep compared to waking – brain cleaning and detoxification is thus greatly facilitated during sleep, providing a novel and direct explanation for what we all generally consider sleep's restorative effect.

(4) Elucidation of oxygen sensing pathways in human and animal cells: Implications for physiology (Peter Ratcliffe, University of Oxford, UK)

After studying the physiology of renal circulation, Professor Ratcliffe became interested in the regulation of the hematopoietic growth factor erythropoietin, which is produced by the kidneys in response to reduced blood oxygen availability, and in 1989, he set up the Hypoxia Biology Laboratory at Oxford. His work on oxygen sensing has won a number of awards including the Louis-Jeantet Prize in Medicine, the Canada Gairdner International Award, and the Lasker Award for Basic Biomedical Research.

(5) Skeletal muscle mediators and exercise-induced adaptations governing insulin

sensitivity in type 2 diabetes (Juleen Zierath, Karolinska Institute, Sweden)

Professor Zierath is a member of the Royal Swedish Academy of Sciences and the Nobel Assembly. She was Chair of the Nobel Committee at Karolinska Institutet between 2013 and 2015 and is currently a member of this Committee. Professor Zierath's research has provided evidence for the physiological regulation of insulin signaling pathways in skeletal muscle, revealing key steps are impaired in diabetic patients. As an exercise physiologist, she has a long-standing interest in the health promoting benefits of physical exercise. The ultimate goal of her work is to identify and validate molecular candidates to prevent or treat insulin resistance in type 2 diabetes. Improving insulin sensitivity should alleviate diabetic complications and enrich the quality of life for the diabetic patient.

(6) Therapeutic potential of vascular growth factors (Kari Alitalo, University of Helsinki, Finland)

Professor Alitalo discovered and characterized novel growth factors that regulate lymphangiogenesis, their receptors and signalling mechanisms. He isolated and characterized several tyrosine kinases including the endothelial receptor tyrosine kinase Tie1, which is related to the Tie2 receptor for angiopoietins and is implicated in tumor angiogenesis. He cloned the vascular endothelial growth factor (VEGF) receptor-3, purified and cloned its ligand VEGF-C, and showed that the VEGF-C/VEGFR-3 pathway is required for angiogenesis and lymphangiogenesis. He was also central in the cloning and characterization of the VEGF-B in collaboration with Dr. Ulf Eriksson. Studies in his laboratory have demonstrated VEGF-C induced tumor angiogenesis and lymphangiogenesis, intralymphatic tumor growth, and VEGF-C association with tumor metastasis and its inhibition by blocking the VEGFR-3 signal transduction pathway. The inhibitors of these pathways from his laboratory have undergone phase I clinical trials and he has also developed growth factor therapy for lymphedema, which is now in phase I clinical trial.

(7) Tuning the heart beat through cytoskeletal regulation (Benjamin Prosser, University of Pennsylvania, USA)

Dr. Prosser started his own group at the University of Pennsylvania Perelman School of Medicine in 2014, where he is now an Assistant Professor of Physiology. His lab focuses on the mechanobiology of the heart – the mechanisms that regulate the ability of the heart cell to generate force, and how external forces in turn feedback to influence myocyte physiology and pathology. His lab leverages super-resolution imaging, cellular biophysics and bioengineering to tackle fundamental questions of mechanics and mechanosensing, with a particular focus on the cardiac cytoskeleton. In recognition of the lab's early work, Dr. Prosser was named the Outstanding Early Career Investigator by the American Heart Association and the Outstanding Young Investigator of the Penn School of Medicine in 2017.

總括來說，歐洲生理學會學術會議是歐洲多國研究動植物科學家們的重要會議。筆者有幸參加他們的創始會議，更具有歷史性的意義。筆者從這次會議中獲得不少有關血管訊號傳遞和相關的分子機轉之醫學研究的新知識。參加國際級會議主要除了懷著學習的態度和吸收學術上的新知之外；也借由會議交流的方式認識著名的國際學者，以邀請其來台講學，相信將來有助於國內和國防醫學院與國際上的相關研究接軌。然而筆者這次之所以能夠順利成行，全仰仗國防部核予公假和科技部的研究計畫經費補助，在此深表感謝！

伍、建議事項

回顧這次參與歐洲生理學會學術會議人士中，我是代表台灣出席參加這次會議有做報告的唯一一位學者！本人在這次會議中的最後一天巧遇來自高雄長庚醫院的陳慶鏗和華瑜教授夫婦，他們是代表國際生理學會來參與首屆的歐洲生理學會會議，因為華瑜教授是國際生理學會的理事長。

另外，筆者也觀察到這次參加會議的人士中，也有少數幾位來自北非突尼西亞和中亞土耳其以及東亞日本的學者！而且有些研究成果都做得很不錯！因此，提醒我自己不得不多思考未來的研究競爭力！尤其近年來我們台灣的情勢常常是內耗或是停滯不前，導致社會和教育出現嚴重的兩極化現象，而台灣的優勢也一再隨著時間而流失，心中的感受真是百感交集、至為無力！只能告訴自己，要靠著自己努力不斷的做到，讓外國人也能夠看見台灣人的努力！因為這將有助於台灣國際研究地位的能見度和競爭力的提升。