出國報告

# 天然物醫藥保健產業之合作交流平台

服務機關：國防醫學院
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出國期間：102 年 11 月 9 日 至 11 月 15 日
報告日期：102 年 12 月 12 日

# 摘要

英國 Norwich 科學園區 (Norwich Research Park; NRP)與國防醫學院 (National Defense Medical Center; NDMC) 之研發專才之間達成一個持續性與高度協同性的研發夥伴關係，進而以雙方之實質合作為基礎，規劃近期能通過歐盟科技計畫之申請與執行為主要目的。因此，本計畫之重點　就是擷取雙方專業與技術之精華，以互補與高度協同之方式，針對”開發利用天然物 (Natural Products)成為醫療保健食品或藥物之候選項目(What makes a natural product a good candidate for nutritional or therapeutic exploitation?)”進行評估，並完成共同開發之構想與步驟。

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## 一、 參加目的

依國科會執行計畫(天然物醫藥保健產業之合作交流平台; NSC 102-2911-1-016-501)之規定，我們一行人於 102 年 11 月 9 日自台北出發首先抵達英國 Norwich 市接著抵達 Norwich 研發園區展開一系列之拜訪與交流活動。市接著抵達 Norwich 研發園區展開一系列之拜訪與學術交流活動。

## 二、 會議過程

在為期五天學術交流活動中，於 102 年 11 月 9 日自台北出發 102 年 11 月 10 日抵達英國後與 Rob Field 教授以及其研發團隊成員在英國 Norwich 研發園區展開學術交流活動，102 年 11 月 11 日及 12 日由英方成員介紹目前進行中之研究主題、研發興趣、成果、與未來合作方向，接著由我方計畫主持人陳安教授重點闡述之研發優勢，說明非常適合進行雙方國際型合作，接著再由本研發團隊其他成員分別報告研發興趣與目前研發狀況，並進行學術面的討論，102 年 11 月 13 日由 Rob Field 教授率領我方同仁拜訪劍橋大學 Dr. Andreas Bender 教授，特別針對中草植物藥純化物之製備與療效預測分析方面進行學術討論，102 年 11 月 14 日搭機離開英國，102 年 11 月 15 日抵達台北。

# 三、心得及建議

首先,本研發團隊所有參訪同仁衷心要向(1)國防醫學院總務 (人事李少校)、研發室、主計室、教務處各級業管單位、長官、院長司徒將軍與(2)軍醫局各承辦/業管之長官表達最高之感謝，使得本次台英計畫我方參訪英方之任務得以順利完成。

依本執行計畫(天然物醫藥保健產業之合作交流平台; NSC 102-2911-1-016-501) (請參閱附件 1)之規定，我們一行人於 102 年 11 月 9 日自台北出發首先抵達英國 Norwich 市接著抵達 Norwich 研發園區展開一系列之拜訪與交流活動。首日先與 Rob Field 教授以及其研發團隊成員，包括：Dr. Mark Searcey、Dr. Paul O'Maille、Dr. Colin Kay、Dr. Ganesan、Dr. Grant Wheeler、Dr. Andreas Bender 等主要成員。

在雙方簡報中，首先由英方成員分別介紹自己與目前進行中之研究主題，最後再由 Rob Field 教授總結該研究團隊之重點研發興趣、成果、與未來之國外研發合作方向。接著由我方進行簡報，先由計畫主持人陳安教授以國防醫學院最新版本之英文版介紹國防醫學中心(含三軍總醫院)，重點闡述本校之研發優勢，已公開發表之研發成果與高度有效之行政服務,並說明非常適合與英國在各大學、研發中心、生物醫學/製藥中心進行雙方互補之國際型合作。接著由本研發團隊成員(醫科所蕭嘉陽教授、神經外科部/電腦刀中心洪東源主任、航太暨海底醫學研究所賈淑敏老師、醫科所李孟璋博士生、財團法人生技中心張嘉銘副所長及莊士賢研究員)分別報告研發興趣與目前研發狀況，並進行學術面的討論(請參閱附件 2)。

次日，再度進行第二階段之雙方研討，主要針對下列事項取得共識與預做安排：

1. 希望在下一年度(按：本計畫第二年期互補計畫)能形成相對應之實質研發規劃，以利未來雙方能共提歐洲聯盟之重點長期型合作研發計畫。
2.討論明年英方來訪之人員組成與時程,以及在台灣的訪視點,已達成雙方快速、互補、實質合作之目的。

此外，雖然 Rob Field 教授等人安排我方三總同仁多次參訪該研發區之各項硬體、軟體、高效率之基礎及轉譯醫學/藥學研究單位。其間並與各研究室現場之研發人員交流取得雙方在研究實驗方面比較實質面之了解,以利未來各項相關合作計畫之準備與申請。

由於有一位成員 Dr. Andreas Bender 之工作地點在英國劍橋大學( University of Cambridge)之國王學院，Rob Field 教授也特別安排一天的時間率領我方同仁由 Norwich 搭乘火車至劍橋大學拜訪 Dr. Bender。並由 Dr. Bender 率同其研發團隊成員特別針對中草植物藥純化物之製備與療效預測分析之新策略發表數項演說,並與本團隊成員充分討論學術面之議題以及未來擴大雙方互補合作之準備工作，成果頗佳。

茲摘錄本次赴英參訪互補之成果如下：

1. 本研發團隊成員與英國 Rob Field 教授成員達成 Rob Field 教授充分面對而交流並在研發等略之理念方面獲得極佳之共識，有利於未來擴展進階實質合作，並爭取大型國際合作型(例如歐盟計畫)共同執行之機會。
2. 傳統中草植物(自製物)藥之開發在英國與歐洲多國之醫藥界是重點項目，雖然該國明顯在基礎研究方面較強，但在臨床前期之轉譯醫學端較弱。而本研發團隊在轉譯端正好是強項，因此未來與英方發展實質互補合作開發傳統中草植物藥成為新藥之契機已衍然成形，對我方是一大利基。
3. 英方在軟、硬體設備方面，尤其是儀器系統的維持與運轉均配備專人管理及/或執行，因此有極佳之橫向分工，對研發之進度掌握與品質之保證皆可有一定之信譽，可做為未來我方研發執行面與策略面之參考。
4. 英方大學校園內有較多之自由活動與餐飲等供應中心，對研究生與研發人員可比較方便交談及自由思考研究之方向，對本研發團隊同仁是一項新的體會。
5. 在離英前，已近一步談妥明確擴增一項雙方之交流研發互補計畫，由本團隊成員航太暨海底所之賈淑敏老師擔任我方之計畫主持人，同時由英方之 Simon Carding 教授擔任英方之主持人，針對老化(Ageing)之生病機轉與藥物開發之主題向國科會共提下一年度二年期之互訪計畫，以利能快速有效的擴充本次互訪之成果(請參閱附件 3)。

# 四、附件資料

**國科會與英國生物技術暨生物科學研究委員會國際夥伴關係建立暨交流計畫**

**(NSC--BBSRC International Partnering Award)**

**天然物醫藥保健產業之合作交流平台**

**Taiwan-NRP: Natural Product Bioactives**

John Innes Centre

| YEAR ONE | | | | YEAR TWO | | | |
|---|---|---|---|---|---|---|---|
| Apr - June | July - Sept | Oct-Dec | Jan - Mar | Apr - June | July - Sept | Oct-Dec | Jan - Mar |
| Field to Taiwan | | | | | | | |
| | 3 day Workshop | | 4 day Workshop | | 3 day Workshop | | 4 day Workshop |
| | | PhD/Postdocs to Taiwan | | PhD/Postdocs to Norwich | | PhD/Postdocs to Taiwan | |
| | | PhD/Postdocs to Norwich | | PhD/Postdocs to Taiwan | | PhD/Postdocs to Norwich | |
| << Skype/Teleconference communication throughout >> | | | | | | | |

**Period: 2013/4/1 – 2015/3/31**

**Taiwan PI: Prof Ann Chen, MD, PhD**
Department of Pathology, Tri-Service General Hospital; Academy of Medicine, National Defense Medical Center, Taipei, Taiwan, ROC

**Taiwan Co-PI: Prof Chia-Yang Shiau, PhD**
Graduate Institute of Medical Sciences, National Defense Medical Center, Taipei, Taiwan, ROC

**Taiwan Co-PI: Dr Jia-Ming Chang, PhD**
Development Center for Biotechnology, Taipei, Taiwan, ROC

**Taiwan Co-PI: Dr Shuk-Man Ka, PhD**
Academy of Medicine, National Defense Medical Center, Taipei, Taiwan, ROC

**Taiwan Co-PI: Dr Dueng-Yuan Hueng, MD, PhD**
Department of Neurological Surgery, Tri-Service General Hospital; Department of Biochemistry, National Defense

Medical Center, Taipei, Taiwan, ROC

**Taiwan Co-PI: Dr Shih-Hsien Chuang, PhD**

Development Center for Biotechnology, Taipei, Taiwan, ROC

**Taiwan Co-PI: Prof Shih-Hua Lin, MD**

Division of Nephrology, Department of Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, ROC

**UK PI: Prof Rob Field, PhD**

John Innes Center, Norwich, UK

**UK Co-PI: Dr Paul O'Maille, PhD**

Institute of Food Research/John Innes Center, Norwich, UK

**UK Co-PI: Dr Colin Kay, PhD**

Department of Nutrition, Norwich Medical School, University of East Anglia, Norwich, UK

**UK Co-PI: Prof Mark Searcey, PhD**

School of Pharmacy, University of East Anglia, Norwich, UK

**UK Co-PI: Prof A Ganesan, PhD**

Chair of Chemical Biology, School of Pharmacy, University of East Anglia, Norwich, UK

**UK Co-PI: Dr Grant Wheeler, PhD**

School of Biological Science, University of East Anglia, Norwich, UK

**UK Co-PI: Dr Andreas Bender, PhD**

Centre for Molecular Science Informatics, Department of Chemistry, University of Cambridge, Cambridge, UK

**國科會與英國生物技術暨生物科學研究委員會國際夥伴關係建立暨交流計畫**
**(NSC--BBSRC International Partnering Awards)**

**天然物醫藥保健產業之合作交流平台**

**Taiwan-NRP: Natural Product Bioactives**

## 中文摘要


**本台英計畫之中心目標是藉由一個整合性的運作將英國 Norwich 科學園區(Norwich Research Park; NRP)與國防醫學院(National Defense Medical Center; NDMC)之研發專才之間達成一個持續性與高度協同性的研發夥伴關係，進而以雙方之實質合作為基礎，規劃近期能通過歐盟科技計畫之申請與執行為主要目的。**因此，本計畫之重點就是擷取雙方專業與技術之精華，以互補與高度協同之方式，針對"開發利用天然物(Natural Products)成為醫療保健食品或藥物之候選項目(What makes a natural product a good candidate for nutritional or therapeutic exploitation?)"進行評估，並完成共同開發之構想與步驟。

英方之NRP科學園區下轄John Innes Center (JIC)、Institute of Food Research(IFR)、University of East Anglia (UEA)、Norwich and Norfolk University Hospital 與Genome Analysis Center。而該園區之研發代表已組成一核心團隊與本學院相關之研發專才(包含與本學院已長期進行研究合作之生醫製藥重點研發單位—生物技術開發中心[Development Center for Biotechnology]之研發伙伴)進行實質合作。**而NRP科學園區之團隊目前正進行一項由英方BBSRC支持之重點計畫—〝Understanding and exploiting plant and microbial metabolism〞，總研發經費達每年 5 百萬英鎊(NT$ 233,630,000/年)共計 5 年，包含了植物與微生物之天然物之基礎生化學與合成，將啟動新穎化合物之開發案。因此，生物活性物(Bioactives)之分析與相關應用是該計畫最需要的核心技術與研發策略。**而本夥伴型研發計畫之英方主持人Rob Field 教授就是基於擔任該大型計劃之執行者之優勢，與本學院之研發團隊合作，欲透過共同執行由我們國科會支持之NSC-BBSRC Program，建立長期穩定之研發伙伴關係。雖然，英國目前極欲重點推動轉譯研究(Translational Research)並鼓勵產品導向之產官學研發主題，但是相關機制與平台尚未完全建立(比較不成比例)。而我方的強項就在轉譯端(驗證[validation]與應用規劃)，正好符合與英方互補的需求，是我們切入之最佳時機。**這可由本團隊已執行下列 3 項分別獲得國科會與經濟部支持之生醫製藥與先期台英雙方核心計畫為佐證，包括:(1) 國科會之台灣與英國頂尖大學前期合作研究計畫(Pathogenic role of KLF2 in the development of diabetic nephropathy-NSC101-2911-1-016-001 ) ;(2) 國科會之NRPB計畫 (Core Service platform Project for Animal Pharmacology [AM4]-NSC-100-2325-B-169-001);(3) 經濟部科專計畫(Development of biomarkers and kidney-protective components for high risk chronic disease -100-EC-17-A-19-S1-161)。**

因此，本台英計畫將進行雙方之:

1. 定期互訪，並以舉辦討論會之方式進行相關專題之討論(包含雙方研發興趣、主題與衍生之合作機會)。

2. 年輕而有潛力之研究人員(博士生、博士後研究員、研發專員)之互動交流。
3. 運用 Skype 系統之便利性與高效率性，雙方針對管理與技術層次之確切聯繫與討論。
4. 分享雙方在開發商業化產品或產品導向之生物活性物(Bioactives)在法規面與實際執行面的現況與規劃之心得。
5. 研討由雙方共同在天然物與生物活性物申請國際型合作開發計畫，成功獲取相關經費之規劃(包含進入歐盟科技主題計畫)。

# Collaboration Letter

John Innes Centre

**BIOLOGICAL CHEMISTRY**
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14 January 2013

To whom it may concern

**Taiwan-UK International Partnering Award Bid – *Taiwan-NRP: Natural Product Bioactives***

On behalf of our colleagues, we write to express our great enthusiasm for the opportunity to establish collaborative links between the Norwich Research Park, the National Defence Medical Centre and the Development Centre for Biotechnology in Taiwan. The collective and complementary expertise by the teams concerned spans synthetic and chemical biology through phytochemistry and medicinal chemistry to pharmacology and toxicology. The key question being addressed relates to determination of the features of natural products that make them suitable for use as dietary supplements and therapeutic leads.

At the centre of the NRP part of this bid are:

- the **JIC *Understanding and Exploiting Metabolism* ISP** (BB/J004561/1)
- the **IFR *Food and Health* ISP** (BB/I015345/1)
- a range of **supporting BBSRC project grants**

The Taiwan partners have an established record of achievement in the evaluation and development of natural product bioactives for health benefit; in addition, they have ongoing collaborative links with UK academia, as exemplified by the following representative projects:

- **Initiative Research Cooperation among Top Universities between UK and Taiwan,** entitled "Pathogenic role of KLF2 in the development of diabetic nephropathy" sponsored by NSC, Taiwan, ROC. (Govt approval number: NSC 101-2911-1-016-001). Collaboration with Dr. Simon Satchell, Dept of Internal Medicine, University of Bristol.
- **Core Service Platform Project for Animal Pharmacology (AM4),** sponsored by NSC Program for Pharmaceuticals Program (Govt approval number: NSC 100-2325-B-169-001)
- **Development of biomarkers and kidney-protective components for high risk chronic kidney disease,** sponsored by the Ministry of Economic Affairs, Taiwan, ROC. (Govt approval number:100-EC-17-A-19-S1-161)

To complement funds sought from BBSRC, the NRP will also contribute to the partnership by:

- Support and access to conference and teleconferencing facilities
- Opportunity to bid for seed-corn funds to support projects through the JIC Institute Development Grant, the JIC KEC and UEA 'Proof of Concept' Innovation Funds
- Opportunity to bid for PhD studentship support directly from the NRP, and also from the BBSRC-supported NRP Doctoral Training Centre.

We trust that out case for support meets the criteria and strategic needs of BBSRC and we look forward to hearing from you in due course.

Sincerely

R. A. Field

Professor Robert A. Field, JIC, Norwich

Professor Ann Chen, NDMC, Taipei

Director, Professor Dale Sanders FRS





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# Taiwan-NRP: Natural Product Bioactives

NDMC - National Defense Medical Center, Taipei, Taiwan - http://www.ndmctsgh.edu.tw
DCB – Development Center for Biotechnology, Taipei, Taiwan - http://www.dcb.org.tw
NRP – Norwich Research Park, Norwich, UK - http://www.norwichresearchpark.com
JIC – John Innes Center, Norwich, UK - http://www.jic.ac.uk
IFR – Institute of Food Research, Norwich, UK - http://www.ifr.ac.uk
UEA – University of East Anglia, Norwich, UK - https://www.uea.ac.uk

## Summary of the Main Scientific Objectives

The role of food components in maintaining health is increasingly seen as a practical and cost-effective alternative (or at least complement) to drug prescription. Many academic labs world-wide are working on the premise that, since nature has had millennia to evolve small molecules to interact with biological systems, natural products remain a rich source of novel molecules for investigation, whether as drugs or dietary components. The purpose of this collaboration is to explore how the diverse chemical space covered by natural products maps onto biological space of relevance to the maintenance, or recovery, of human health. This will be underpinned by studies on the production of natural products (industrial biotechnology) and the generation of new-to-nature molecules by chemical biological means (chemical/synthetic biology), coupled to synergistic studies on the assessment, cataloguing and prediction of therapeutic potential and toxicity (chemical informatics). Projecting beyond the purely academic, a key further area for consideration therefore concerns mechanisms for the translation of natural product leads into genuine commercial entities. Hence the programme is based around three goal-oriented topics:

- Natural product (and analogue) generation
- Assessment of bioactives
- Development of lead compounds

## The Taiwan and UK Partner Organizations

The Taiwan partners are from the NDMC and the DCB. The UK partner is the Norwich Research Park, consisting of the JIC, IFR, UEA and the Norwich and Norfolk University Hospital, and the Genome Analysis Centre. Representatives from Taiwan will form the core team to facilitate interaction more widely between Taiwan and partners from NRP institutions. Core partnership members are as follows:

|  **Taiwan Team** |  **NRP Team** |
|---|---|
| **PI:** Prof Ann Chen - NDMC<br>*Pharmacology/Drug Evaluation Platform* | **PI:** Prof Robert A Field - JIC<br>*Natural products and chemical genomics* |
| Prof Chia-Yang Shiau - NDMC<br>*Natural products and medical biochemistry* | Dr Paul O'Maille - IFR/JIC<br>*Terpene diversity and anti-microbial activity* |
| Dr Jia-Ming Chang - DCB<br>*Preclinical assessment platform and toxicology* | Dr Colin Kay - Norwich Medical School<br>*Dietary flavonoids and health* |
| Dr Shuk-Man Ka - NDMC<br>*Animal models for chronic disease* | Prof Mark Searcey - UEA Pharmacy<br>*Natural product anti-cancer agents* |
| Dr Dueng-Yuan Hueng - NDMC<br>*Animal models for cancers* | Prof A Ganesan - UEA Pharmacy<br>*Natural product epigenetic regulators* |
| Dr Shih-Hsien Chuang - DCB<br>*Medicinal chemistry* | Dr Grant Wheeler - UEA Biol Sci<br>*Developmental chemical genetics* |
| Prof Shih-Hua Lin - NDMC<br>*Cell models for major chronic disease* | Dr Andreas Bender - Cambridge Chemistry<br>*Chemical informatics* |

## Summary of previous contacts

Professor's Chia-Yang Shiau and Robert A Field were contemporaries at the University of Oxford in the early 90s, working together on aspects of penicillin biosynthesis. While they have not previously collaborated since establishing independent positions, their (re)converging interests in bioactive natural products provides a timely opportunity to support the development of Taipei-NRP links. Professor's Chia-Yang Shiau and Robert A Field will serve as the key coordinators for the partnership, facilitating day-to-day connectivity.

## Action Plans

The partnership will:

- Meet alternately in Norwich and Taipei to discuss, in workshop format, interests and opportunities for collaboration
- Exchange early-stage researchers (PhD students and postdocs) to conduct exploratory studies
- Adopt Skype communication as a practical means of regular contact between partners, both at a managerial and a technical level,
- Share best practice in relation to the development and commercialisation or natural product–based bioactives
- Consider prospects for securing joint research funding in the area of natural product bioactives

| YEAR ONE | | | | YEAR TWO | | | |
|---|---|---|---|---|---|---|---|
| **Apr - June** | **July - Sept** | **Oct-Dec** | **Jan - Mar** | **Apr - June** | **July - Sept** | **Oct-Dec** | **Jan - Mar** |
| **Field to Taiwan**  | | | | | | | |
| | **3 day Workshop**  | | **4 day Workshop**  | | **3 day Workshop**  | | **4 day Workshop**  |
| | | **PhD/Postdocs to Taiwan**  | | **PhD/Postdocs to Norwich**  | | **PhD/Postdocs to Taiwan**  | |
| | | **PhD/Postdocs to Norwich**  | | **PhD/Postdocs to Taiwan**  | | **PhD/Postdocs to Norwich**  | |
| **<< Skype/Teleconference communication throughout >>** | | | | | | | |

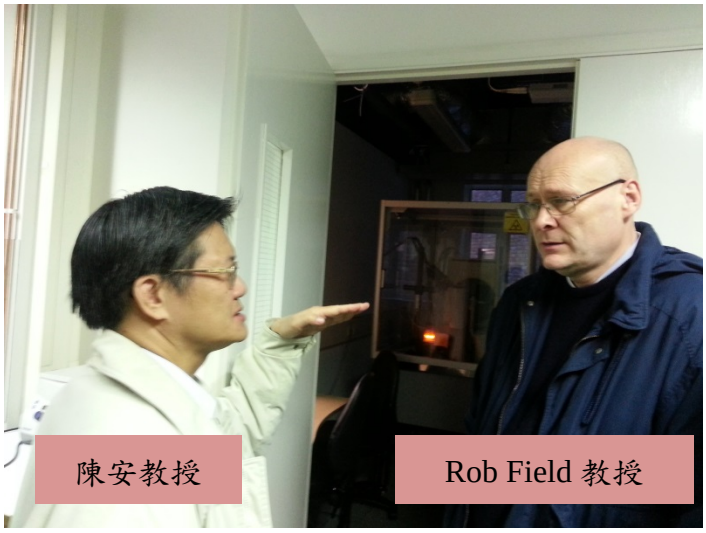
台灣研發團隊與 Rob Field 教授研發團隊於 University of East Anglia

台灣研發團隊與 Rob Field 教授研發團隊於英國 Norwich 研發園區

(1)


(2)

計畫主持人陳安教授與 Rob Field 教授研發團隊於英國 Norwich 研發園區進行學術討論 (1)(2)





台灣研發團隊參訪 University of East Anglia

# 國科會與英國生物技術暨生物科學研究委員會國際夥伴關係建立暨交流計畫

**(NSC-BBSRC International Partnering Award)**

## 建置一台英雙方研究老化致病機制之整合型平台

Taiwan-Norwich (UK): Development of an integrated platform for the study of mechanisms underlying ageing

**Period: 2014/4/1 – 2016/3/31**

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## 建置一台英雙方研究老化致病機制之整合型平台

Taiwan-Norwich (UK): Development of an integrated platform for the study of mechanisms underlying ageing

## 中文摘要

本研究團隊成員長期對異常之發炎反應、高度之氧化壓力(Oxidative stress)與凋亡(Apoptosis) 等所引起之細胞與組織之變性與損傷 (Li HF, *et al.*, ***J Am Soc Nephrol***, 2012；Klaiber M *et al.*, ***Proc. Natl. Acad. Sci.* USA**, 2011；Tsai PY, *et al.*, ***Arthritis Rheum***, 2012；Yang SM, *et al.*, ***Diabetologia***, 2013；Ka SM *et al.*, ***Diabetologia***, 2013；Lan YF *et al.*, ***J Am Soc Nephrol,*** 2012；Fuchs Y, *et al.*, ***Developmental Cell***, 2012；Lin YC, *et al.*, ***J. Cell Sci***, 2013；Yang SM, *et al.*, ***Free Radic Biol Med,*** 2013；Hua HF, *et al.*, ***PLoS ONE***, 2013)，以及在臨床上對老化相關之罹病狀況與合併症（新陳代謝科洪乙仁主任與腎臟科許育瑞醫師）投入研發，**期盼獲得投入國科會目前重點推動之台灣－英國生物技術暨生物科學研究委員會國際夥伴關係建立暨交流計畫（NSC-BBSRC International Partnering Awards），欲在短時間內就能以台英雙方整合的方式，針對老化 (Ageing) 相關之健康問題，搶先投入歐洲研發聯盟研發計畫之申請與執行之機會**。

特別一提的是，本研發計畫之英方主持人Simon Carding教授目前主持三項該國BBSRC重點支持大型計畫之總經費高達3千4百餘萬英鎊（£34,170,735）；主要針對（1）Gut health and food safety strategic programme；（2）Commercialization of a live bacteria drug delivery technology for the treatment of gastrointestinal inflammation；與（3）Dynamic modelling of the intestinal villus 等方面之研發，利用基於擔任大型計畫執行者之優勢，欲與本研發團隊合作，透過共同執行由我國國科會支持之NSC-BBSRC International Partnering Awards，建立長期穩定而互補之研發伙伴關係。**故而，本台英計畫之中心目標是藉由一個整合性的策略，欲將國防醫學院（National Defense Medical Center；NDMC）與英國UEA大學（University of East Anglia）之研發專才之間達成一個持續性與高度協同性的國際研發夥伴關係，進而以雙方之實質合作為基礎，規劃近期能通過歐盟科技計畫之申請與執行為主要目標**。因此，本計畫之重點就是擷取雙方專業與技術之精華，以互補與高度協同之方式，針對”建置一研究台英雙方老化致病機制之整合型平台

（Development of an integrated platform for the study of mechanisms underlying ageing）”進行雙方之快速磨合，有效完成共同推動之構想與實際開發之步驟。英方之UEA大學與Institute of Food Research（IFR）、John Innes Center（JIC）、與NRP科學園區有聯合互助之加強機制。而該大學之研發代表已組成一核心團隊欲與本學院重點相關之研發專才，包含：（1）本學院已長期進行研究合作之生醫製藥重點研發單位—財團法人生物技術開發中心〔Development Center for Biotechnology；DCB；Taiwan〕之研發伙伴、（2）中央研究院生醫所、與（3）台北醫學大學進行實質研發合作。雖然英國目前極欲重點推動轉譯研究（Translational research），並鼓勵產品導向之產官學研發主題，但是相關機制與平台尚未完全建立（現況為明顯不成比例）。而我方的強項就在轉譯端（驗證〔validation）與產品導向之應用規劃），正好符合與英方缺口的需求。故而，此刻是我們在老化相關之生物醫學與製藥之主題切入之最佳時機。

**此外，正好本研發團隊之主持人國防醫學院醫學系賈淑敏老師曾擔任：（1）國科會之台灣與英國頂尖大學前期合作研究計畫（Pathogenic role of KLF2 in the development of diabetic nephropathy-NSC101-2911-1-016-001）之共同主持人，並在國科會相關之支助下，赴英國布里斯托大學醫院客座兩個月（2013年5月28日至2013年7月24日），並完成針對人類腎臟內皮細胞KLF2轉錄因子在慢性腎臟病之護腎角色之雙方合作研究，目前正整理研究結果準備由雙方共同發表中；（2）經濟部三年期科專計畫（Development of biomarkers and kidney-protective components for high risk chronic disease 100-EC-17-A-19-S1-161）之第一分項篩選護腎成分之主持人，已獲得數項相關之美國專利與技轉成果。**


因此，本台英交流計畫將進行雙方之：

1. 深度之定期互訪，並舉辦討論會進行相關專題之討論；特別包含雙方研發興趣、亮點主題與衍生之合作機會，為長期擴大雙方研發合作之準備。

2. 每年推薦兩位本研究研發團隊年輕而有潛力之研究人員（博士生、博士後研究員、研發專員）隨赴英國進行互動交流，以利擴大長期雙方之研發合作。

3. 有效分享雙方在發炎、氧化壓力與細胞凋亡等重點老化相關致病路徑分析，開發商業化產品或產品導向在法規面與實際執行面的現況與規劃之心得，並具體共同提出最佳之深度研發策略。

4. 儘快由雙方共同申請國際型合作開發計畫，成功獲取相關經費之規劃（特別以進入歐盟科技主題計畫為優先）。

Institute of Food Research
Norwich Research Park
Colney
Norwich NR4 7UA
UK
www.ifr.ac.uk

To whom it may concern 25th November 2013

**Re: Taiwan-UK International Partnership Awards**
***"Taiwan-Norwich: Development of an integrated platform for the study of mechanisms underlying ageing"***

We are delighted to have this opportunity to establish collaborative research links between institutions in the Norwich Research Park, UK and the National Defense Medical Center, Development Center for Biotechnology, and Taipei Medical University in Taiwan. This brings together a multidisciplinary group of scientists with complementary research fields in which to pursue a much more comprehensive understanding of the mechanisms that underlie the decline in immune, gastrointestinal, cardiovascular and neurological tissue function as we age. In addition, with complementary expertise in plant bioactive compounds (dietary-derived compounds from Norwich and traditional medicinal herbs and plants from Taiwan), this will provide an opportunity to identify and investigate anti-ageing plant bioactives, using a much more in-depth approach. The ultimate goal will be to identify plant compounds as future nutraceuticals to prevent age-related tissue decline and therapeutics for the treatment of age-related illnesses. We trust that this fits with the strategic requirements of BBSRC.

The Norwich partner is supported by the IFR-UEA "Gut Health and Food Safety" and "Plant Natural Products and Health" ISPs and BBSRC project grants, in addition to other awarding bodies. Further support by the Norwich partner will be provided in terms of access to conference, audiovisual and teleconferencing facilities and opportunities to bid for seed-corn funds at the Institute of Food Research and the University of East Anglia. The Taiwan partners have previous collaborations with UK academic institutions and have extensive publications, grant funding, technology transfer and patents in plant bioactives for health, using an extensive cell and animal model platform.

If you require any further information, please do not hesitate to contact us. We look forward to hearing from you in due course.

Yours Sincerely

Professor Simon R. Carding
Leader, Gut Health and
Food Safety Programme
Institute of Food Research

Assistant Professor Shuk-Man Ka
Academy of Medicine,
National Defense Medical Center,
Minquan E. Rd., Nei-Hu, 114
Taipei, Taiwan

# Taiwan-Norwich: Development of an integrated platform for the study of mechanisms underlying ageing

NRP - Norwich Research Park, http://www.norwichresearchpark.com
IFR - Institute of Food Research, Norwich, http://www.ifr.ac.uk
UEA – University of East Anglia, Norwich, https://www.uea.ac.uk
NDMC – National Defense Medical Centre, Taipei, http://www.ndmctsgh.edu.tw
TSGH-Tri-Service General Hospital, Taipei, www.tsgh.ndmctsgh.edu.tw
DCB-Development Centre for Biotechnology, Taipei, http://www.dcb.org.tw
Taipei Medical University, Taipei, http://:www.tmu.edu.tw
Academia Sinica, Taipei, http://www.sinica.edu.tw

## Summary of the Main Scientific Objectives

Ageing results in the decline in function of various body systems, including the immune, nervous, cardiovascular and gastrointestinal systems. Currently, the dramatic worldwide increases in life expectancy are not being matched by healthy life expectancy and a delay in the ageing process is key to reducing the global burden of age-related chronic diseases. Although reactive oxygen species (ROS) and inflammation are important components of signalling pathways and innate immunity respectively, a chronic low grade generation of ROS and pro-inflammatory mediators are key drivers of the ageing process and the development of age-related illness. In addition, many cell membrane proteins and signalling pathways are important in ageing and the development of age-related illnesses, including G protein-coupled receptors, purine receptors, Toll-like receptors, Klotho and the Nrf2 and NF-κB transcription factor pathways.

Plants contain a wealth of bioactive molecules that may delay ageing by preserving tissue function. Human epidemiological evidence and findings from a limited number of randomised controlled trials (RCT) indicate that an increased intake of such components, either as natural whole foods, functional foods or supplements (nutraceuticals), may be highly effective in the prevention or treatment of a wide range of chronic age-related illnesses. Many of these compounds have yet to be discovered and the mechanisms of action of those that are known are still unclear. However, for select plant-derived bioactives such as vitamin C and flavonoids, anti-oxidant and anti-inflammatory properties have been demonstrated.

The purpose of this proposal is to bring together a consortium of plant and animal biologists, chemists, nutritionists, pharmacologists and immunologists to investigate signalling pathways underlying ageing and to explore the efficacy (with respect to gastrointestinal, cardiovascular, cognitive and immune health) and mechanism of action of select plant-derived bioactive compounds.

The specific aims of the proposal are:

- Investigation of membrane proteins and receptor signalling pathways in age-related decline of tissue function
- Investigation of ROS and inflammation-activated signalling pathways involved in age-related decline of tissue function
- Identification and mechanism of action of potential plant bioactive molecules in cell and animal models of age-related tissue function decline.

## The Partner Organizations

The UK partner is the Norwich Research Park, which comprises IFR, John Innes Centre, UEA, Norfolk and Norwich University Hospital and The Genome Analysis Centre. Representatives from the Institute of Food Research and the UEA School of Pharmacy will form the core team and will facilitate interactions across the institutions and with members of the Taiwan team. The Taiwan partners are from the NDMC, TSGH, DCB, and Taipei Medical University. Core members of each of the partner's teams are as follows:

***Norwich (UK) Team***

PI – Professor Simon Carding - IFR

*Gut health, microbiology and immune function*

Dr Maria O'Connell – UEA Pharmacy

*Dietary bioactives, Nrf2, NF- B, and inflammation*

Professor Anne Marie Minihane- UEA Medicine

*Diet and cognitive function*

Dr Jelena Gavrilovic – UEA Biological Sciences

*Metalloproteinases, wound healing and cardiovascular function*

Dr Julie Sanderson – UEA Pharmacy

*Purine receptors and retinal function*

Dr Peter McCormick – UEA Pharmacy

*GPCRs in neurological function*

***Taiwan Team***

PI – Dr Shuk-Man Ka - NDMC

*ROS signalling pathways, Pathology and animal models for chronic age-related diseases*

Dr. Yu-Juei Hsu – TSGH Medicine

*Renal pathophysiology and Klotho pathway*

Dr. Yi-Jen Hung – TSGH Medicine

*Metabolic syndrome and cell metabolism*

Dr. Hui-Ling Chen – DCB Institute for Drug Evaluation Platform IND core team,

*Traditional Chinese Medicine and drug evaluation platform, experimental brain pathology*

Dr. Heng Lin –Taipei Medical University, Department of Physiology

*Vascular pathophysiology and inflammatory processes*

Dr. Ruey-Bing Yang- Academia Sinica, Institute of Biomedical Sciences

*Cell biology and endothelial cell injury*

## Summary of Previous Contacts

Professor Carding has no previous contacts with the NDMC or DCB. Dr. O'Connell does not have any collaborations with the Taiwan applicants, but has met Dr. Ka once, while she was on a recent visit to the UK. None of the other co-applicants has previous contact with any of the Taiwan departments.


## Action Plan

The partnership will:

- Hold workshops in Norwich and Taipei to discuss interests and opportunities for collaboration.
- Have regular contact (through teleconferencing, Skype and email) to ensure that progressions that are established will progress within the partnership.
- Permit exchange of early stage researchers (PhD student and post-docs) to conduct initial studies in partner labs.
- Develop joint research proposals that investigate tissue decline in ageing and the protective effects and mechanisms of action of bioactive plant compounds in cell and animal models of age-related disorders.
- Share best practice with regards to the further development and commercialisation of bioactive plant compounds.

| YEAR ONE | | | | YEAR TWO | | | |
|---|---|---|---|---|---|---|---|
| **Apr-Jun 2014** | **Jul-Sep 2014** | **Oct-Dec 2014** | **Jan-Mar 2015** | **Apr-Jun 2015** | **Jul-Sep 2015** | **Oct-Dec 2015** | **Jan-Mar 2016** |
| Joint PI meeting in Taiwan | | | | | | | |
| | Joint Workshop (Norwich) | | Joint Workshop (Taipei) | | Joint Workshop (Norwich) | Early careers | Joint Workshop (Taipei) |
| | | Early careers | Early careers | Early careers | | Early careers | |