出國報告（出國類別：進修）

台灣精準醫療種子人才訓練計畫

服務機關：衛生福利部臺北醫院
姓名職稱：王醫師怡人
派赴國家/地區：英國/牛津
期間：民國 111 年 7 月 3 日至民國 111 年 7 月 16 日
報告日期：民國 112 年 2 月 1 日

中文摘要

在 COVID-19 疫情之下，英國生物資料庫提供 2 萬名參與者及其親屬提供為期 6 個月的血液樣本，幫助瞭解感染程度並提供對病毒自然免疫力的理解，並確定誰曾感染過該病毒，瞭解 A 感染對健康的長期影響，並邀請個案參加二次影像追蹤，瞭解病毒對內臟器官的影響，此外英國近期將收 20 萬的新生兒，欲早期偵測出可治療的疾病，激發全球科研界的想像力，來改善人類健康。

基因體和表觀基因體資料的變異，往往不足以解釋疾病的發生和進程，因此環境成因必須考量，近來相關量測工具的進步，有暴露體學的運用，使用基因、環境及其交互作用，可以建置更精準的預測模型。以家族出生世代資料庫，有利於基因、環境交互作用的探討，可降低總個案數和成本，更快找到致病基因或環境成因，是臺灣地狹人稠、家庭凝聚力較大、總人口數較少之背景下，非常值得嘗試的世代建置方式。

近來癌症存活者人數增加，生命延長，許多癌症治療方式如標靶治療、賀爾蒙療法也都存在許多心毒性的風險，例如接受雄激素剝奪治療的前列腺癌患者，心血管疾病已成為第二大常見死因，再者運用個體化風險分層，可以識別高危人群以進行早期預防和治療建議，可避免併發症和改善臨床結果，也是未外來精準醫療必須納入的重點。

人工智慧(AI) 技術於精準醫療的運用已勢在必行，AI 已被視為「軟體醫材」，於臨床應用所面臨的挑戰包括「取代醫師」的誤解和不正確的期待，缺乏數據標準化，以及缺乏用於開發、驗證和優化 AI 模型的國家型準則，是以多管齊下，包括製造商、法規監管機構、醫療保險制度、預期用戶和臨床應用的目標族群，以及機器學習優良製造規範，這當中，各領域的合作是關鍵。

關鍵字: 精準醫療、人工智慧、生物資料庫、基因體學、暴露體、世代追蹤、癌症心血管風險

Abstract

Amid the COVID-19 pandemic, the U.K. Biobank has provided 20,000 participants and their relatives with blood samples over six months to help researchers understand the extent of infection and provide an understanding of natural immunity to the virus. The U.K. Biobank also plans to collect data on antibody test results to identify who had previously been infected with the virus to help understand the long-term health effects of the infection. With more information collected, cases were invited to participate in a secondary imaging follow-up to understand the virus's impact on internal organs. In addition, the U.K. will soon collect 200,000 newborns, and the early detection of treatable diseases will stimulate the imagination of the global scientific research community to improve human health.

Scientists have realized that variations of genomics and epigenomics data are often insufficient to explain the occurrence and progression of the disease. Therefore, environmental causes must be considered. Due to the recent fast advances in related measurement tools, we could utilize exposomics, which is the overall measurement of external environmental factors such as air, water, and food, to follow up on populations and observe the natural history of the disease. Further, the genetic, environmental, and interaction considerations of the two can build a more accurate prediction model. Using the family's birth cohort database is beneficial for discussing the interaction between genes and the environment, reducing the number of cases and costs, and finding diseases' genetic or environmental causes more quickly. The generational construction method is worth trying in a relatively small population. Although there are many advantages to a family-based birth cohort, many shortcomings must be considered and overcome in advance.

The number of cancer patients has recently increased, and cancer survival has improved vastly. However, cancer treatments such as targeted therapy and hormonal therapy also have many risks of cardiotoxicity. For example, cardiovascular disease has become the second largest cause of death in patients with prostate cancer receiving ani-androgenic therapy. Polygenic risk score (PRS) for individualized risk stratification can identify high-risk groups for early prevention and treatment recommendations, avoid complications and improve clinical outcomes. Thereby PRS is also a very worth adaptation in the practice of precision medicine.

Applying artificial intelligence (A.I.) technology in precision medicine is imperative. A.I. has been regarded as a "soft medical device". The challenges faced in the clinical application include misunderstandings and false expectations of "replace of the physician," lack of data standardization, and lack of national guidelines for developing, validating, and optimizing A.I. models, which involved fields including manufacturers, regulatory agencies, health insurance institutions, intended users and target groups for clinical applications, as well as Good Machine Learning Practice (GMLP), where collaboration in various fields is critical.

Keywords:
Precision medicine, Artificial intelligence, Biobank, Genomics, Exposome, Cohort follow-up, Cancer cardiotoxicity

目錄

壹、目的

瞭解如何運用精準醫學在疾病上進行臨床驗證。

瞭解環境表觀遺傳學、基因與環境的相互作用。

身為一名兒科醫生，這次培訓可幫助我瞭解罕見疾病及新生兒的產前篩查，早期發現早期治療。

在此次培訓後瞭解如何精準用藥，降低醫療花費。

藉由這次培訓，瞭解如何在醫院建立一個生物資料庫。

結合氣喘和過敏的大數據系統生物學（基因組、轉錄組、表觀基因組、微生物組和代謝組）的不斷進步，未來對疾病網絡模型的研究將更加準確地用於疾病預測和治療。

貳、行程簡介

DATE	DAY	TIME	ACTIVITIES
03/07	Sunday		Arrival at London Heathrow Airport; Transit to Oxford
		14:00	Check-in at the William Miller Building
		17:30	Orientation The William Miller Building
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall
04/07	Monday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	Welcome Remarks Prof. Kathy Willis, Principal Introduction to University of Oxford and Course Outline Prof. Chris Conlon, Course Director The Examination Schools, Lecture Room 6
		10:30-11:00	Tea / Coffee Break The Examination Schools, Lecture Room 7
		11:00-12:30	Towards personalised medicine using neuroimaging and neuromodulation Prof. Heidi Jansen-Berg The Examination Schools, Lecture Room 6
		12:30-13:15	Lunch The Wolfson Hall, St Edmund Hall
		14:00-15:30	Library Induction at St Edmund Hall Dr James Howarth
		15:30-17:30	Free Time
		18:00-19:30	Welcome Dinner Prof. John Knight & Prof. Chris Conlon The Old Dinning Hall, St Edmund Hall
05/07	Tuesday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	Characterising the peripheral determinants of response to checkpoint immunotherapy across a large patient cohort Dr Ben Fairfax The Examination Schools, Lecture Room 6

		10:30-11:00	Tea / Coffee Break The Examination Schools, Lecture Room 7
		11:00-12:30	New horizons in cellular therapy Prof. Ronjon Chakraverty The Examination Schools, Lecture Room 6
		12:30-13:15	Lunch The Wolfson Hall, St Edmund Hall
		14:00-18:00	Free Time
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall
06/07	Wednesday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	Autoantibody mediated diseases of the nervous system - a Q&A session Prof. Sarosh Irani The Examination Schools, Lecture Room 6
		10:30-11:00	Tea / Coffee Break The Examination Schools, Lecture Room 7
		11:00-12:30	How is Oxford changing the way we discover new medicines for patients? Prof. Chas Bountra The Examination Schools, Lecture Room 6
		12:30-13:15	Lunch The Wolfson Hall, St Edmund Hall
		14:30-16:30	Visit to the Peter Medawar Building (Pathogen Research and Immunology) South Parks Road Δ Prof. Susie Dunachie
		16:30-18:00	Free Time
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall
07/07	Thursday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	Applied clinical research: The PRINCIPLE and PANORAMIC adaptive platform trials of treatments for COVID-19 in the community Prof. Chris Butler The Examination Schools, Lecture Room 6
		10:30-11:00	Tea / Coffee Break The Examination Schools, Lecture Room 7

		11:00-12:30	Recent advances in the development of novel therapeutic approaches for Alzheimer's Disease Prof. John Davis The Examination Schools, Lecture Room 6
		12:30-13:15	Lunch The Wolfson Hall, St Edmund Hall
		14:30-16:30	Visit to the Target Discovery Institute, NDMRB Old Road Campus Δ Dr Margarida Ruas; or Visit to the Centre for Medicines Discovery South Parks Road Δ Dr Gamma Chi
		16:30-18:00	Free Time
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall
			Breakfast
08/07	Friday	08:00-08:30	The Wolfson Hall, St Edmund Hall
		09:00-10:30	The current and future role of AI and its limitations in the diagnosis of lung cancer Prof. Fergus Gleeson The Examination Schools, Lecture Room 6
		10:30-11:00	Tea / Coffee Break The Examination Schools, Lecture Room 7
		11:00-12:30	The metabolic consequences of obesity Prof. Leanne Hodson The Examination Schools, Lecture Room 6
		12:30-13:15	Lunch The Wolfson Hall, St Edmund Hall
		14:00-15:00	Song Rehearsal The Wolfson Hall, St Edmund Hall
		15:00-17:30	Free Time
		18:00-19:30	Dinner Sichuan Grand, the Old School, Gloucester Green

09/07	Saturday	08:00-09:00	Breakfast The Wolfson Hall, St Edmund Hall
		10:00	Visit to the Ashmolean Museum of Art and Archaeology (optional)
		12:30-13:00	Lunch (packed lunch)
		13:00-16:30	Visit to Bicester Village (optional)
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall
10/07	Sunday	08:00-09:00	Breakfast The Wolfson Hall, St Edmund Hall
		09:00 – 18:00	Free Time (packed lunch)
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall

11/07	Monday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	Stem cells and adaptive molecular phenotype in colorectal cancer Prof. Simon Leedham Lecture Theatre, the Oxford Martin School
		10:30-11:00	Tea / Coffee Break Lecture Theatre, the Oxford Martin School
		11:00-12:30	Evidence and Surgery – Can they be improved? Prof. Andrew Carr Lecture Theatre, the Oxford Martin School
		12:30-13:15	Lunch The Wolfson Hall, St Edmund Hall
		14:30-16:30	Lab Visit: Virology at the Dunn School of Pathology South Parks Road Δ Prof. William James
		16:30-18:00	Free Time
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall
12/07	Tuesday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	How genomics has provided insights into the immune response in severe infection due to COVID-19 and more generally the sepsis syndrome Prof. Julian Knight Lecture Theatre, the Oxford Martin School
		10:30-11:00	Tea / Coffee Break Lecture Theatre, the Oxford Martin School
		11:00-12:30	Pathogen whole-genome sequencing as a tool for molecular epidemiology and infection control Prof. David Eyre Lecture Theatre, the Oxford Martin School
		12:30-13:30	Lunch The Wolfson Hall, St Edmund Hall
		14:30-16:00	Visit to the Big Data Institute Old Road Campus Δ
			Prof. David Eyre
		16:00-18:00	Free Time
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall

13/07	Wednesday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	Biomarkers in obstructive airway diseases Prof. Ian Pavord Lecture Theatre, the Oxford Martin School
		10:30-11:00	Tea / Coffee Break Lecture Theatre, the Oxford Martin School
		11:00-12:30	The Road to a Vaccine for COVID-19 Prof. Dame Sarah Gilbert Lecture Theatre, the Oxford Martin School
		12:30-13:30	Lunch The Wolfson Hall, St Edmund Hall
		14:30-16:00	Visit to the Botnar Centre at the Nuffield Orthopaedic Centre (musculo-skeletal research) Δ Prof. Udo Oppermann
		16:00-18:00	Free Time
		18:00-19:30	Dinner Sichuan Grand, the Old School, Gloucester Green
14/07	Thursday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	Ethical considerations in genomic medicine and research Prof. Anneke Lucassen Lecture Theatre, the Oxford Martin School
		10:30-11:00	Tea / Coffee Break Lecture Theatre, the Oxford Martin School
		11:00-12:30	Clinical translation of gene therapy for rare lung diseases Prof. Deborah Gill Lecture Theatre, the Oxford Martin School
		12:30-13:30	Lunch The Wolfson Hall, St Edmund Hall
		13:30-17:30	COVID testing in preparation for travel
		18:00-19:30	Dinner Sichuan Grand, the Old School, Gloucester Green

15/07	Friday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	New directions in transplant organ preservation and repair Prof. Peter Friend Lecture Theatre, the Oxford Martin School
		10:30-11:00	Tea / Coffee Break Lecture Theatre, the Oxford Martin School
		11:00-12:30	Advances in understanding Inflammatory Bowel Disease Prof. Jack Satsangi Lecture Theatre, the Oxford Martin School
		12:30-13:15	Lunch The Wolfson Hall, St Edmund Hall
		13:30-14:00	Course Appraisal Prof. Chris Conlon St Edmund Hall
		15:00-16:00	Tea with the Principal Prof. Kathy Willis Senior Common Room, St Edmund Hall
		16:30-17:00	Group Photograph Session Prof. Kathy Willis The Front Quad, St Edmund Hall
		18:00-20:00	Farewell Dinner Prof. Kathy Willis The Old Dinning Hall, St Edmund Hall
16/07	Saturday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		10:00	Check-out from the William Miller Building
		13:30	Departure for London Heathrow Airport
		18:20	Departure for Taiwan

DATE	DAY	TIME	ACTIVITIES

03/07	Sunday		Arrival at London Heathrow Airport; Transit to Oxford
		14:00	Check-in at the William Miller Building
		17:30	Orientation The William Miller Building
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall
04/07	Monday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	Welcome Remarks Prof. Kathy Willis, Principal Introduction to University of Oxford and Course Outline Prof. Chris Conlon, Course Director The Examination Schools, Lecture Room 6
		10:30-11:00	Tea / Coffee Break The Examination Schools, Lecture Room 7
		11:00-12:30	Towards personalised medicine using neuroimaging and neuromodulation Prof. Heidi Jansen-Berg The Examination Schools, Lecture Room 6
		12:30-13:15	Lunch The Wolfson Hall, St Edmund Hall
		14:00-15:30	Library Induction at St Edmund Hall Dr James Howarth
		15:30-17:30	Free Time
		18:00-19:30	Welcome Dinner Prof. John Knight & Prof. Chris Conlon The Old Dinning Hall, St Edmund Hall
05/07	Tuesday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	Characterising the peripheral determinants of response to checkpoint immunotherapy across a large patient cohort Dr Ben Fairfax The Examination Schools, Lecture Room 6
		10:30-11:00	Tea / Coffee Break The Examination Schools, Lecture Room 7
		11:00-12:30	New horizons in cellular therapy Prof. Ronjon Chakraverty The Examination Schools, Lecture Room 6
		12:30-13:15	Lunch The Wolfson Hall, St Edmund Hall
		14:00-18:00	Free Time
		18:00-19:30	

			Dinner The Wolfson Hall, St Edmund Hall
06/07	Wednesday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	Autoantibody mediated diseases of the nervous system - a Q&A session Prof. Sarosh Irani The Examination Schools, Lecture Room 6
		10:30-11:00	Tea / Coffee Break The Examination Schools, Lecture Room 7
		11:00-12:30	How is Oxford changing the way we discover new medicines for patients? Prof. Chas Bountra The Examination Schools, Lecture Room 6
		12:30-13:15	Lunch The Wolfson Hall, St Edmund Hall
		14:30-16:30	Visit to the Peter Medawar Building (Pathogen Research and Immunology) South Parks Road Δ Prof. Susie Dunachie
		16:30-18:00	Free Time
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall
07/07	Thursday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	Applied clinical research: The PRINCIPLE and PANORAMIC adaptive platform trials of treatments for COVID-19 in the community Prof. Chris Butler The Examination Schools, Lecture Room 6
		10:30-11:00	Tea / Coffee Break The Examination Schools, Lecture Room 7

		11:00-12:30	Recent advances in the development of novel therapeutic approaches for Alzheimer's Disease Prof. John Davis The Examination Schools, Lecture Room 6
		12:30-13:15	Lunch The Wolfson Hall, St Edmund Hall
		14:30-16:30	Visit to the Target Discovery Institute, NDMRB Old Road Campus Δ Dr Margarida Ruas; or Visit to the Centre for Medicines Discovery South Parks Road Δ Dr Gamma Chi
		16:30-18:00	Free Time
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall
			Breakfast
08/07	Friday	08:00-08:30	The Wolfson Hall, St Edmund Hall
		09:00-10:30	The current and future role of AI and its limitations in the diagnosis of lung cancer Prof. Fergus Gleeson The Examination Schools, Lecture Room 6
		10:30-11:00	Tea / Coffee Break The Examination Schools, Lecture Room 7
		11:00-12:30	The metabolic consequences of obesity Prof. Leanne Hodson The Examination Schools, Lecture Room 6
		12:30-13:15	Lunch The Wolfson Hall, St Edmund Hall
		14:00-15:00	Song Rehearsal The Wolfson Hall, St Edmund Hall
		15:00-17:30	Free Time
		18:00-19:30	Dinner Sichuan Grand, the Old School, Gloucester Green

09/07	Saturday	08:00-09:00	Breakfast The Wolfson Hall, St Edmund Hall
		10:00	Visit to the Ashmolean Museum of Art and Archaeology (optional)
		12:30-13:00	Lunch (packed lunch)
		13:00-16:30	Visit to Bicester Village (optional)
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall
10/07	Sunday	08:00-09:00	Breakfast The Wolfson Hall, St Edmund Hall
		09:00 – 18:00	Free Time (packed lunch)
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall

11/07	Monday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	Stem cells and adaptive molecular phenotype in colorectal cancer Prof. Simon Leedham Lecture Theatre, the Oxford Martin School
		10:30-11:00	Tea / Coffee Break Lecture Theatre, the Oxford Martin School
		11:00-12:30	Evidence and Surgery – Can they be improved? Prof. Andrew Carr Lecture Theatre, the Oxford Martin School
		12:30-13:15	Lunch The Wolfson Hall, St Edmund Hall
		14:30-16:30	Lab Visit: Virology at the Dunn School of Pathology South Parks Road Δ Prof. William James
		16:30-18:00	Free Time
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall
12/07	Tuesday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	How genomics has provided insights into the immune response in severe infection due to COVID-19 and more generally the sepsis syndrome Prof. Julian Knight Lecture Theatre, the Oxford Martin School
		10:30-11:00	Tea / Coffee Break Lecture Theatre, the Oxford Martin School
		11:00-12:30	Pathogen whole-genome sequencing as a tool for molecular epidemiology and infection control Prof. David Eyre Lecture Theatre, the Oxford Martin School
		12:30-13:30	Lunch The Wolfson Hall, St Edmund Hall
		14:30-16:00	Visit to the Big Data Institute Old Road Campus Δ
			Prof. David Eyre
		16:00-18:00	Free Time
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall

13/07	Wednesday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		~~09:00-10:30~~ 10:30-11:00	Biomarkers in obstructive airway diseases Prof. Ian Pavord Lecture Theatre, the Oxford Martin School
		11:00-12:30	Tea / Coffee Break Lecture Theatre, the Oxford Martin School
			The Road to a Vaccine for COVID-19 Prof. Dame Sarah Gilbert Lecture Theatre, the Oxford Martin School
		12:30-13:30	Lunch The Wolfson Hall, St Edmund Hall
		14:30-16:00	Visit to the Botnar Centre at the Nuffield Orthopaedic Centre (musculo-skeletal research) Δ Prof. Udo Oppermann
		16:00-18:00	Free Time
		18:00-19:30	Dinner Sichuan Grand, the Old School, Gloucester Green
14/07	Thursday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	Ethical considerations in genomic medicine and research Prof. Anneke Lucassen Lecture Theatre, the Oxford Martin School
		10:30-11:00	Tea / Coffee Break Lecture Theatre, the Oxford Martin School
		11:00-12:30	Clinical translation of gene therapy for rare lung diseases Prof. Deborah Gill Lecture Theatre, the Oxford Martin School
		12:30-13:30	Lunch The Wolfson Hall, St Edmund Hall
		13:30-17:30	COVID testing in preparation for travel
		18:00-19:30	Dinner Sichuan Grand, the Old School, Gloucester Green
15/07	Friday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	New directions in transplant organ preservation and repair Prof. Peter Friend Lecture Theatre, the Oxford Martin School
		10:30-11:00	Tea / Coffee Break Lecture Theatre, the Oxford Martin School
		11:00-12:30	Advances in understanding Inflammatory Bowel Disease Prof. Jack Satsangi Lecture Theatre, the Oxford Martin School
		12:30-13:15	
		13:30-14:00	

			Lunch The Wolfson Hall, St Edmund Hall
			Course Appraisal Prof. Chris Conlon St Edmund Hall
			Tea with the Principal Prof. Kathy Willis Senior Common Room, St Edmund Hall
		16:30-17:00	Group Photograph Session Prof. Kathy Willis The Front Quad, St Edmund Hall
		18:00-20:00	Farewell Dinner Prof. Kathy Willis The Old Dinning Hall, St Edmund Hall

16/07	Saturday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		10:00	Check-out from the William Miller Building
		13:30	Departure for London Heathrow Airport
		18:20	Departure for Taiwan

Notes:

- ✓ Venues:
  The Examination Schools, 75 - 81 High Street, Oxford OX1 4BG;
  The Oxford Martin School, 34 Broad Street, Oxford OX1 3BD
- ✓ Each lecture session comprises up to one hour for the lecture and at least half an hour for discussion
- ✓ Lecturers are expected to use power-point presentations and lecture notes will be made available to the attendees after the Course
- ✓ Dress Smart
- ✓ Δ Wear Lab Coat
- ✓ Each attendee is required to compose a minimum 3,000-word essay, presenting his/her original arguable opinion about an academic issue of his/her choosing – typically related to a lecture of the Course. The essay can be in any format and should be submitted electronically to the Course Director c/o the administration at xiaowei.chen@seh.ox.ac.uk by 5pm on Tuesday 12th July 2022.

參、會議過程

Academic Medicine

Course Timetable

11/07	Monday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	Stem cells and adaptive molecular phenotype in colorectal cancer Prof. Simon Leedham Lecture Theatre, the Oxford Martin School
		10:30-11:00	Tea / Coffee Break Lecture Theatre, the Oxford Martin School
		11:00-12:30	Evidence and Surgery – Can they be improved? Prof. Andrew Carr Lecture Theatre, the Oxford Martin School
		12:30-13:15	Lunch The Wolfson Hall, St Edmund Hall
		14:30-16:30	Lab Visit: Virology at the Dunn School of Pathology South Parks Road Δ Prof. William James
		16:30-18:00	Free Time
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall

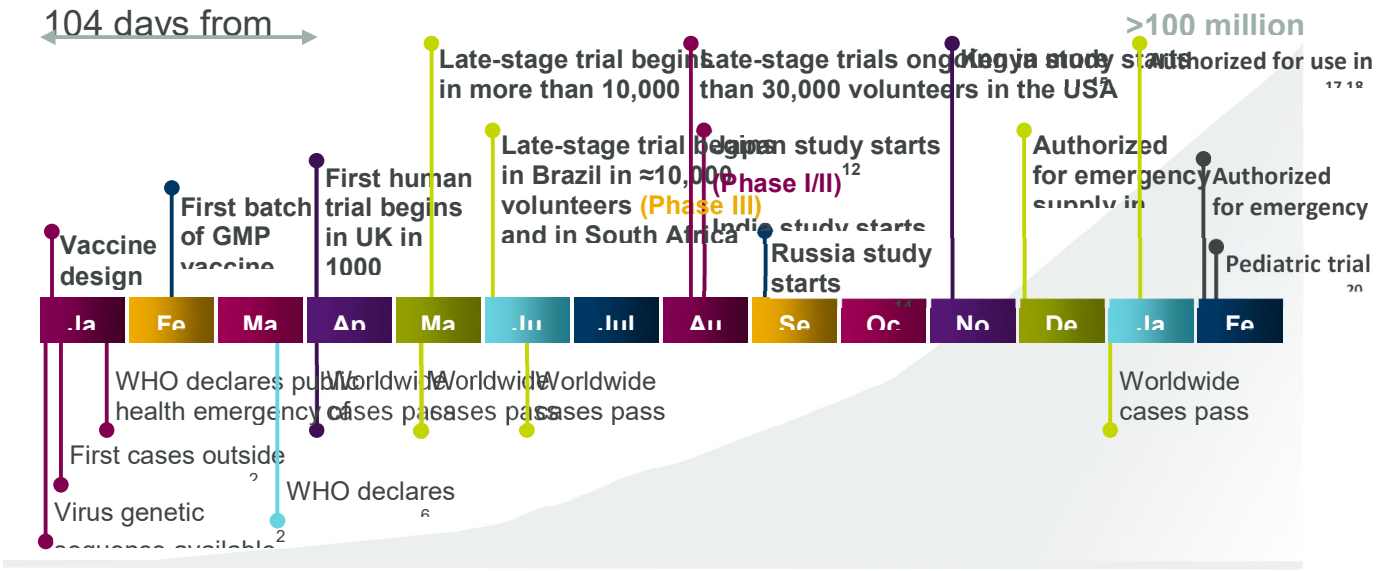
The Dunn School of Pathology

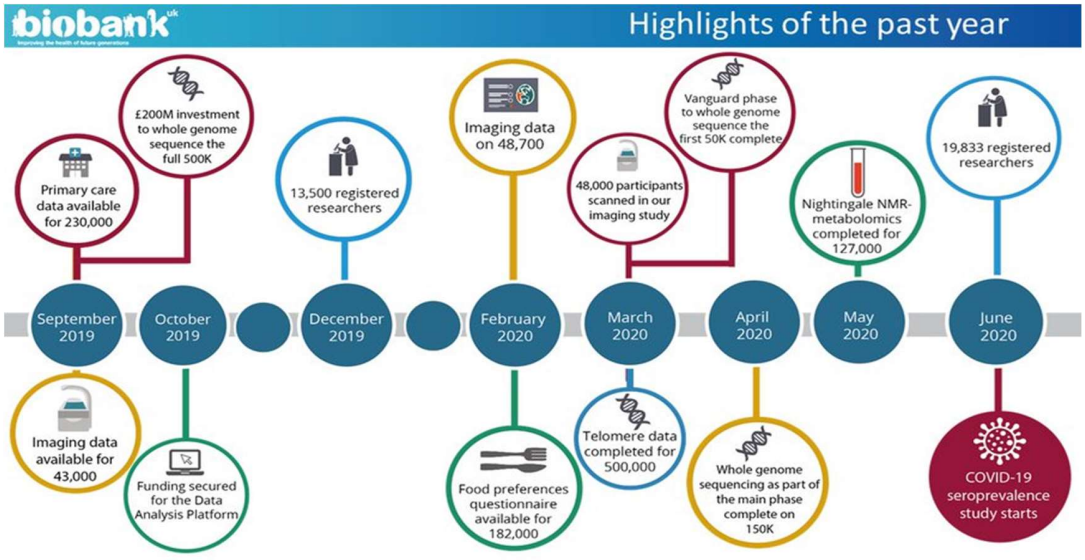
The Dunn School is a world-class biomedical research Department at the University of Oxford. Over 300 scientists from more than 30 countries aim to discover the molecular and cellular mechanisms that underlie human health and disease. Our research capitalises on outstanding facilities and addresses the full spectrum from fundamental biology to discovering medical advances.

13/07	Wednesday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	Biomarkers in obstructive airway diseases Prof. Ian Pavord Lecture Theatre, the Oxford Martin School
		10:30-11:00	Tea / Coffee Break Lecture Theatre, the Oxford Martin School
		11:00-12:30	The Road to a Vaccine for COVID-19 Prof. Dame Sarah Gilbert Lecture Theatre, the Oxford Martin School
		12:30-13:30	Lunch The Wolfson Hall, St Edmund Hall
		14:30-16:00	Visit to the Botnar Centre at the Nuffield Orthopaedic Centre (musculo-skeletal research) Δ Prof. Udo Oppermann
		16:00-18:00	Free Time
		18:00-19:30	Dinner Sichuan Grand, the Old School, Gloucester Green

From the ChAdOx1 platform to a vaccine candidate against COVID-19

Adapted from Sarah Gilbert





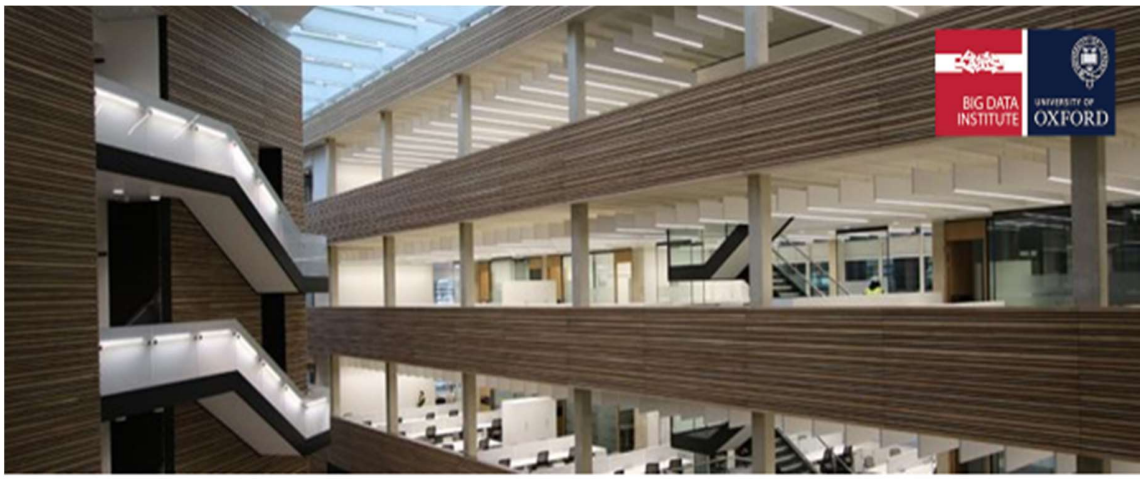
Adapted from UK biobank

Academic Medicine

Course Timetable

12/07	Tuesday	08:00-08:30	Breakfast The Wolfson Hall, St Edmund Hall
		09:00-10:30	How genomics has provided insights into the immune response in severe infection due to COVID-19 and more generally the sepsis syndrome Prof. Julian Knight Lecture Theatre, the Oxford Martin School
		10:30-11:00	Tea / Coffee Break Lecture Theatre, the Oxford Martin School
		11:00-12:30	Pathogen whole-genome sequencing as a tool for molecular epidemiology and infection control Prof. David Eyre Lecture Theatre, the Oxford Martin School
		12:30-13:30	Lunch The Wolfson Hall, St Edmund Hall
		14:30-16:00	Visit to the Big Data Institute Old Road Campus Δ Prof. David Eyre
		16:00-18:00	Free Time
		18:00-19:30	Dinner The Wolfson Hall, St Edmund Hall

The Big Data Institute



Interdisciplinary research institute
350 researchers in 35 research groups + 60 support staff

Big Data: large, complex, heterogeneous data sets
Research: causes, consequences, prevention and treatment of disease

Principal Prof. Kathy Willis

肆、心得與建議

人體生物資料庫運用於防疫和精準醫療

一、疫情期間如何立即建立人體生物資料庫？

台灣 TPMI 及人體生物資料庫是中研院與醫療中心之間的合作關係，旨在將遺傳信息帶入臨床。通過使用為台灣設計的一套遺傳標記對 **100 萬參與者進行分析**，旨在通過預防危險藥物副作用、對高危人群進行早期癌症篩查以及鼓勵高危人群改變生活方式。依年齡分組有兒童（出生至 17 歲）；成人（18-64 歲）；老年人（65 歲以上）。

至於英國人體生物資料庫，是由 37 至 73 歲的成年人組成的，在 2006 年至 2010 年受試者接受了醫學、社會人口學、心理健康和認知評估，並定期進行追蹤。近年, 英國即將收 **20 萬的新生兒**, 欲早期偵測出可治療的疾病, 激發全 球科研界的想像力，來改善人類健康。英國生物銀行在幫助全球 COVID-19 危機做出了很大貢獻。研究員定期從電子健康記錄（一般實作記錄、診斷測試數據、死亡、住院和影像學）中獲得數據. 此外，**2 萬名參與者及其親屬提供為期 6 個月的血液樣本，幫助研究員瞭解感染程度並提供對病毒自然免疫力的理解**。英國人體生物資料庫還計劃向所有 50 萬 名參與者發送抗體檢測試劑盒，以確定誰曾感染過該病毒，幫助了解感染對健康的長期影響。一些參與者被邀請參加第二次影像追蹤，瞭解病毒對內臟器官的影響。全球研究計劃，如 COVID-19 宿主遺傳學計劃，為科學家提供了合作、共享和分析數據的機會，瞭解 COVID-19 易感性、生活方式決定因素、嚴重程度和結果的遺傳決定因素。用生物信息工具來挖掘電子健康記錄中的數據，回顧患者數據與 COVID-19 結果進行比較。**隨著收集到更多 COVID-19 數據，機器學習可用於預測感染風險、傳播途徑和臨床結果**。

持續獲得資金對於生物資料庫的可持續發展至關重要。根據建立世代研究生物資料庫的成本考慮，包括與冷鏈供應鏈相關的設備投資、耗材和運輸成本。另一個主要挑戰是來自不同遺傳背景的人的數據不能一起分析，因為疾病易感性和藥物代謝受到種族差異的高度影響。與其他動物實驗或基礎研究相比，世代研究需要更多的投資。根據世代人體生物資料庫的前期實驗和項目投入資金，對樣本採集、保存等流程進行重新規劃。團隊合作需專注於國際融合的許多細節，**世代研究在正式開始之前進行試點前驅研究可能會對有限的資金做較好的利用**。

二、政府持有的健保生物資料庫資料如何才能開放用於學術研究？

英國是集中式的全國健康照護系統,生醫資料集中化程度高。在 COVID-19 疫情必須快速產生治療藥物的壓力以及脫歐後個資保護法制不必全然遵守 GDPR 後,英國對生醫資料治理有新的思維與法治發展。醫療與大數據在國內外的未來應用越來越重要。國際上知名的人體數據資料庫，例如目標收集百萬名美國人全基因體數據庫計畫 All of US、英國的 UK Biobank 等。**All of US 開放 9.86 萬筆全基因體定序，英國的 UK Biobank 是預計在明年以前釋放 50 萬筆 WGS**。海德堡大學早在 15 年前就建立了自己的人體生物資料庫 BioVU 並與 Illumina 合作，利用次世代定序平台來分析 BioVU 中約 300 萬筆人類 DNA 樣本。

在各醫療體系之間的數據合作與交換上，技術並不是困難點，最難的是心態。目前 Taiwan biobank 及 TPMI 仍存在各醫院數據合作與交換上仍有困難。然而,**英國的 UK Biobank 會將各醫院的資料收集起彙整後再給各醫院，讓每個醫院都可用到所有醫院的資料**。如何在開放、合理的平台上進行合作與交換，這或許需要政府透過法人單位再進行協調,才能物盡其用。大家在數據開放上能捨棄成見，才能大步向前。台灣對於個資保護上有許多不同的意見，目前健保資料庫的尚未宣布規則。在美國**只要是去識別化的數據便不屬於個人數據**，All of US 的創舉便是將研究人員帶到數據端，研究人員只能看到經過處理的數據，在安全性高的私有雲上進行數據分析，再將結果下載，期間並不會碰到原始資料，達到保護個資的目的。**並將遺傳基因結果，回饋給提供生物樣本用於研究的參與者，透過教育讓民眾了解醫療數據的重要性**。

三、台灣未來精準醫療研究

未來精準醫療有幾大趨勢需要關注，第一是 **AI 的運用以及影像組學資料庫**的建立。現在美國食品藥物管理局批准許多數位醫療 AI 軟體醫材，大多是用在影像辨識，因此醫療影像的數據庫建立十分重要。傳統的統計學家、醫師們都應該對於機器學習有大的接納程度，不僅大數據需要 AI 進行處理。**AI 不會取代醫師，但是醫師不能不會使用 AI**。

第二大趨勢為**全表型體關聯研究**，全表型體關聯研究與全基因體關聯研究正好相反。全表型體關聯研究是橫跨不同種疾病，找出與其關聯的基因表現型。好處在於可找到不同疾病共有的靶點，有利於老藥新用的發展。提出務實性平台臨床試驗設計(Pragmatic Platform Trial Design, PRINCIPLE, and PANORAMIC Adaptive Platform Trials of treatments for COVID-19 in the community 圖一)，這種靈活的臨床試驗方法，可降低試驗所需的患者總數，只要架設好平台，控制組與各種介入治療的組別可隨時加入平台，達到資源共享、加速臨床試驗。

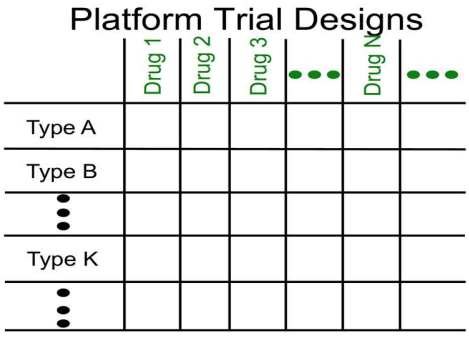


圖 3. Adapted from Chris Butler

隨著基因解碼不只遺傳性疾病有證據顯示一些慢性病如糖尿病高血壓癌症與基因息息相關。疾病的發生可分為先天遺傳基因，後天生活習慣與生活環境吸入空氣污染化學污染等。除了一些罕見的疾病和癌症的治療外，想要掌握健康可以透過基因的檢測進行疾病風險檢測。包括多種癌症與常見疾病不可逆的疾病，**有哪些特定基因的人比一般人罹患風險高，精準健康專門針對個人化的健康管理進行風險評估**,提早告知早期藉由飲食環境生活習慣來預防，才能享受生活品質及健康生活。

四、結語

英國收 20 萬的新生兒，欲早期偵測出可治療的疾病， 來改善人類健康。出生世代 資料庫，可降低總個案數和成本，更快找到致病基因或環境成因。 精準醫療除癌症外, 應更重視並投資在兒童上 做好早期預防。這次牛津精準醫療之行不僅是對個人研究生涯，也對各醫院、學校、甚至台灣的研究發展會有深遠的影響。期望未來國際及國內的交流及合作會開始向下紮根蓬勃發展，讓國衛院所撥的精準種子開花結果。

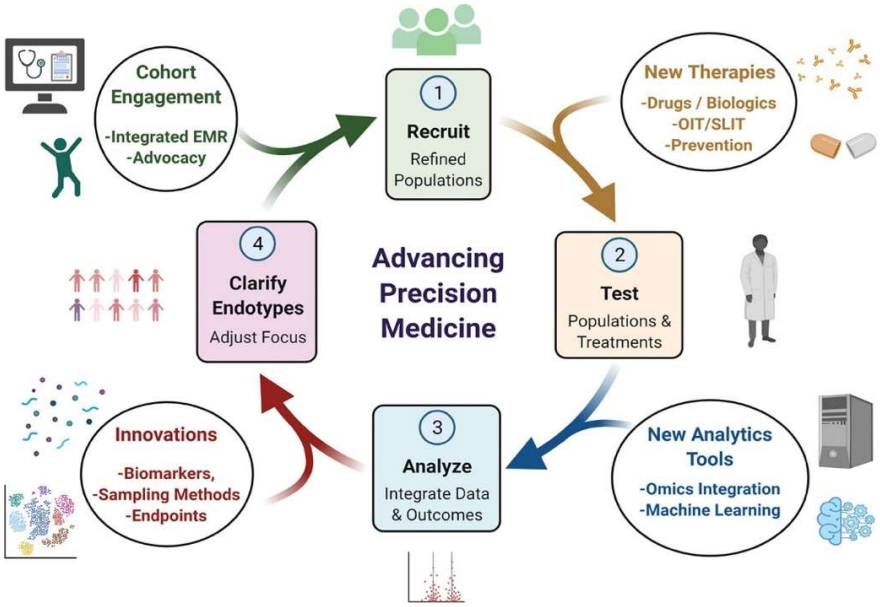


圖 4. Conceptual Cycle of Precision Medicine Advancement

(adapted from Frontiers in Immunology12:720746)

五、總結

這次牛津精準醫療之行不僅是對個人研究生涯，也對各醫院、學校、甚至台灣的研究發展會有深遠的影響。期望未來國際及國內的交流及合作會開始向下紮根蓬勃發展，讓國衛院所撥的精準種子開花結果。吾人進行了一個多世紀的癌症研究，應該有更多新的方法來預防和治療癌症等疾病，在各種分析工具突飛猛進的時刻，現在也是探討 DNA 表達產前編程的絕佳時機，是以出生世代結合基因體與暴露體，來探討複雜疾病的成因，是最低成本而有效的精準預防醫學措施。

在 COVID-19 疫情爆發初期，英國幾乎在一夜之間將老人的疫苗注射悉數完成，並且進行全年齡的優化（optimized）醫療照護，很快的恢復景氣和活絡經濟，著實有諸多相當值得學習的地方，尤其是法令規章的彈性和臨床試驗的靈活度，雖然在嚴密的民主監測體系下，藉著詳盡討論，在即短時間內制定完備諸多試驗和治療策略，而相關研究團隊也已經在進行下一波大流行的準備，包括病毒預測、疫苗和藥物研發等。

無論是在臨床實踐還是在研究中，精準醫學都是醫學未來的趨勢。在精準醫療時代，癌症治療前和治療期間的個體化心血管風險評估變得越來越重要。對於接受雄激素剝奪治療的前列腺癌患者，心血管疾病已成為第二大常見死因。由於動脈粥樣硬化是一種複雜的遺傳變異性疾病，因此需要結合基因組學數據和臨床因子數據的研究，來評估治療相關的心臟毒性。我們可以通過使用來自 TWB、TPMI、Cancer Moonshot、NHIRD 等資料庫 的大量深入基因組數據，並將其對照到其他國家級數據庫來進一步進行心血管事件準確預測的研究。而個體化風險分層，可以識別高危人群以進行早期預防和治療建議，這可以成為臨床實踐中的標準方法。

人工智慧為診斷、研究和教育目的的使用創造了機會和挑戰。政府、法規監管單位、智慧醫材製造商、臨床照護者、病人必須協作和溝通以製定標準，以確保數據的安全、保密和隱私。同時，目標用戶應了解 AI 的原理並接受相關的局限性，以更好地利用人工智慧技術來優化工作流程並提升醫療照護的品質。

牛津精神存在於終身學習追求卓越的使命感和榮譽感，William Hazlitt (1778-1830) 將牛津大學比擬為羅馬般神聖的學術聖殿，Lionel Johnson(1867-1902) 認為著名的 Radcliffe 圖書館圓頂就如同英國女皇的皇冠。一個轉角就是算出哈雷彗星軌道、或是發現生物克氏循環(Krebs cycle)的研究室，處處是改變歷史的科學發現地，與之而來的反思常令學生善感，甚至感到 intimidated，但老師們的風範與看待研究與知識的態度，能將高不可攀的智慧拉回地球表面，促使我們大膽假設、小心求證。透過這次的參訪，我們得以探索更深、更全面的知

識範疇。有幸我們目前所在的機構及醫院提供充足的支援與訓練，在不同主題的演講中均能與講者有豐富對談，並有基礎的合作聯繫。未來期待可以在教學、臨床、科研和其他領域長期有效對接牛津大學。

伍、參考文獻

Chia-Ling Kuo, Luke C Pilling,Janice L Atkins,Jane A H Masoli,João Delgado,George A Kuchel,David Melzer. (2020). APOE e4 genotype predicts severe COVID-19 in the U.K. Biobank community cohort. *J. Gerontol. A Biol. Sci. Med. Sci,* 75:2231-2232.

Lauring AS, Hodcroft EB. (2021) Genetic variants of SARS-CoV-2: what do they mean? *JAMA*, 325(6):529-531.

Karin Magnusson,Katrine Damgaard Skyrud,Pål Suren,Margrethe Greve-Isdahl,Ketil Størdal,Doris Tove Kristoffersen,Kjetil Telle. (2022). Healthcare use in 700 000 children and adolescents for six months after covid-19: before and after register based cohort study *BMJ*, 376.

Van der Made, C. I. (2020). Presence of genetic variants among young men with severe COVID-19. *JAMA,* 324:663-673.

AchievingPrecisionMedicineinAllergicDisease:ProgressandChallenges.

Proper SP, Azouz NP, Mersha TB. Front Immunol. 2021 Aug 18;12:720746.