



St Hilda's College
UNIVERSITY OF OXFORD



NDORMS
NUFFIELD DEPARTMENT OF ORTHOPAEDICS,
RHEUMATOLOGY AND MUSCULOSKELETAL SCIENCES
Medical Sciences Division



Climax Professorship of Clinical Therapeutics

University of Oxford

Annual Review 2019-2020



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The focus on Clinical Therapeutics in Oxford originated in discussions between Professor John Climax, Professor Sir John Bell and Professor Sir Gordon Duff. A year has now passed since the initiative was launched and we are delighted to document in this report the successes that have been achieved in that time. We look forward to seeing what more can be accomplished in this important field of medicine in the future.”

Professor John Climax, Professor Sir John Bell and Professor Sir Gordon Duff

INTRODUCTION

In February 2019, the University of Oxford and St Hilda's College were delighted to welcome Oxford's first Climax Chair of Clinical Therapeutics, Professor Duncan Richards.

This report provides a summary of the work that has been undertaken so far under the leadership of Professor Richards and sets out our vision for the future of Clinical Therapeutics and Pharmacology within the University and beyond.

The work of the Climax Professor of Clinical Therapeutics falls under three strategic objectives: research; education; and outreach. This report is structured around those objectives.

RESEARCH

New Centre for Clinical Therapeutics

A priority for Professor Richards over the last eighteen months has been the development of a new Centre for Clinical Therapeutics within the Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences (NDORMS). The new Centre will work with biomedical researchers and with industry to drive new drug treatments through early phase clinical trials. The objectives of the new Centre are to:

- Build clinical translational expertise in the University of Oxford, Oxford University Hospitals and Oxford Health NHS Trusts;
- Have a positive impact on the UK Life Science sector by improving the probability of success for therapeutic development projects; and to
- Provide a means to advance internally generated therapeutics projects by providing funding for activities in support of clinical translation.

Progress has been rapid; the following research programmes have been established, each demonstrating collaboration across different departments and divisions:

1) Based on Internal (Oxford University) assets

Nanobubbles

The nanobubble project with Professor Eleanor Stride (Department of Biomedical Engineering) is aimed at establishing clinical proof of the potential therapeutic mechanism of nanobubbles in joint hypoxia associated with inflammatory arthritis.

£60,000 of external funding from the UKSPINE has been secured to support the laboratory aspects of this investigation. A clinical study is planned to start as soon as possible subject to COVID-19 restrictions.

Novel Calcilytic drugs

A collaboration with Professor Rajesh Thakker (Radcliffe Department of Medicine) has identified a potential opportunity for a novel calcilytic drug for a rare disease. We have submitted a proposal to the Harrington Network and have opened discussions with a venture capital start up based in San Francisco.

2) Based on external assets

Bromodomain (BET) inhibitors for pancreatic neuroendocrine tumours (PNETs)

Successful completion of preliminary work by Clinical Research Fellow, Dr Omair Shariq, has led to an expanded collaboration with GSK to explore the potential of this mechanism in PNETs.

A novel target for inflammatory bowel disease (IBD)

Our first medicine vision workshop examining the potential for a novel asset in IBD has led to a Material Transfer Agreement for collaborative work in Professor Paul Klenerman's laboratory, examining the role of the target in the immune system. Ongoing work is mapping the clinical translational path.

Novel antibody targeting immune system

Following preliminary discussions with MiroBio, Dr James Fullerton, our new Associate Professor, is developing an INNOVATE UK application to support demonstration of clinical proof of mechanism using a novel human immune challenge model.

Future Focus of the new Centre for Clinical Therapeutics

The new Centre is working closely with the Arthritis Therapy Acceleration Programme (A-TAP). A specific focus of this approach is the use of single cell technology to inform indication selection by examining the cellular basis of disease. We anticipate this will be the basis of future studies and are in discussion with several companies to conduct clinical proof of mechanism studies.

Oxford Clinical Research Facility

A new clinical research facility (CRF) within NDORMS will provide capability for the first time in Oxford for overnight patient and volunteer stays in a dedicated unit. Coupled with endoscopy/ bronchoscopy facilities and a procedure room, the new CRF is expected to transform the capability for conducting experimental medicine studies in Oxford. A core feature of this new unit is that it will be cross-divisional, facilitating collaboration between different groups in the exploration of novel therapies. The project has experienced some delay owing to COVID-19 but is expected to open in mid-2021.

Response to COVID-19

Since the start of the COVID-19 outbreak, Oxford has been at the forefront of global efforts to understand and tackle the virus.

Professor Richards leads Oxford's COVID Clinical Trial Planning Group. This multidisciplinary group includes both academic disease area experts and those responsible for delivering and coordinating care on the front line. This coordination has ensured that those admitted to Oxford hospitals are able to participate in the widest range of clinical research without competition between studies. In particular, the group has supported the local conduct of the national RECOVERY trial. This study was the first to show that dexamethasone has reduced mortality in those with severe disease.

The Centre is also contributing to the evaluation of novel therapies. Professor Richards is arm lead for the infliximab arm of CATALYST, the nationally prioritized phase 2 study in COVID-19. In addition, he is Chief Investigator for the AVID-CC study of adalimumab in care home residents. This latter study has secured substantial (£1.5 million) funding from the Wellcome Trust.

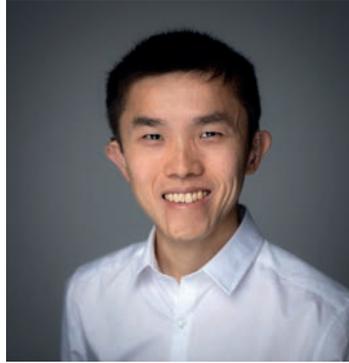
Professor Richards has also been appointed to the UK COVID-19 Therapeutics Advisory Panel (UK-CTAP), an independent national advisory group within UK Research and Innovation (UKRI). UK-CTAP reviews proposals for novel therapies for COVID-19 and has been charged by the Chief Medical Officer for England to provide advice to the nationally prioritised intervention studies.

EDUCATION

Fellows



Clinical Research Fellow, Dr Omair Shariq, began a DPhil in Surgical Sciences in October 2019. Dr Shariq's work is focused on novel epigenetic therapies for pancreatic neuroendocrine tumours.



Clinical Research Fellow, Dr Shing (Tom) Law, began a DPhil in Molecular and Cellular Medicine in October 2020. Dr Law is working with Professor Eleanor Stride to study the effects of nanobubbles in arthritic joints.



Dr James Fullerton took up the post of Associate Professor of Clinical Therapeutics in September 2020. Dr Fullerton has a particular interest in human immune challenge models and is developing plans to make the new CRF a centre of excellence for these types of study which have utility across multiple drug targets.

Dr Shariq and Dr Fullerton are affiliated to St Hilda's, while Dr Law has secured a prize studentship at University College. The strengthening of an intellectual capability in Clinical Therapeutics within St Hilda's represents a key objective in the College's 2019-24 Strategic Plan. In the immediate term, St Hilda's is planning to appoint a new Professor of Medical Statistics. This appointment has been delayed as a result of COVID-19 but will take place as soon as the University recruitment restrictions are lifted.

Clinical Pharmacology training

The University already offers a wide range of MSc courses, several of which include a focus on novel therapeutics. Professor Richards has delivered modules on several of these courses:

- The preclinical package required to support first-in-human studies
- Safety monitoring in clinical trials
- The role of experimental medicine in drug development
- A workshop on designing first in human studies

Dr Fullerton will strengthen teaching in clinical pharmacology, focusing on the delivery of practical clinical pharmacology skills to clinical medical students on the wards.

OUTREACH

Establishment of the Centre for Therapeutic Innovation at St Hilda's

 Plans to establish the Centre for Therapeutic Innovation, under the direction of Professor Duncan Richards, supported by Ms Emma Campbell, have had a flying start with excellent workshops and lectures from leaders such as Sir Michael Rawlins and Dr Nick Cammack. Sadly, the advent of the pandemic meant that subsequent events had to be put on hold.

However, the time has not been lost, and useful learnings have been made from Professor Richards' role in coordinating clinical trials in COVID patients, in Oxford and further afield. We have also had a chance to reflect on practical preparedness for future emergencies.

We look forward to better times when we can meet once again and debate the cross-disciplinary challenges of much-needed therapeutic innovation in a rigorous, yet convivial, setting.”

Professor Sir Gordon Duff, Chair of the Climax Professorship of Clinical Therapeutics Steering Group

In parallel with the development of the new Centre for Clinical Therapeutics within NDORMS, Professor Richards is also leading plans to establish a new multidisciplinary and patient-centric research centre at St Hilda's – the Centre for Therapeutic Innovation at St Hilda's¹.

By 2024, the St Hilda's Centre intends to achieve the following:

- To have identified those areas of drug development that can be most impacted by the work of the Centre and to have established a research agenda around these themes with specific objectives.
- To have established a termly programme of events that is recognised as impactful, pragmatic and innovative as measured by high and diverse attendance and by participant feedback.
- To have conducted at least one event bringing together leaders from outside Oxford University to address a topic of international importance.
- To be informing and influencing the national and international debate on the key topics through the Centre's outputs, which will include peer-reviewed publications.
- To have forged a diverse community around the new Centre, a multidisciplinary forum of scholars, practitioners and lay-people that seeks to advance patient-centric approaches to the development of novel medicines. This will include the appointment of at least two new Fellows at St Hilda's.

¹ This is a working title for the new Centre

- To have established partnerships with other national and international academic and professional institutions, supporting the training of clinical scientists across the world.
- To have the work of the Centre on a sound financial footing with secured medium to long term core funding.
- To be generating income for St Hilda's College.
- To be raising the profile of St Hilda's through the Centre's world-leading research activities.
- To be making a significant contribution to the re-establishment of the UK as a leader in therapeutic development and to be reinforcing traditional collaborations with European colleagues.

Research

An important and unique element of the Centre's approach will be to involve patients in a meaningful way in the design and planning of research. As a first step, the Centre commissioned original research examining key success factors for the involvement of patients in the design and conduct of clinical studies. This research was completed at the end of 2019 and a paper for publication in a peer-reviewed journal is in preparation.

Workshops and seminars

The Centre's first workshop, which took place in June 2019, brought together patients, philosophers, engineers, national regulators and physicians to explore important questions regarding the role of patients in planning clinical research. As a direct result of this event, we have established an ongoing relationship with the National Institute for Health Research (NIHR).

Following the workshop, we were honoured to welcome Professor Sir Michael Rawlins, Chair of the Medicines and Healthcare products Regulatory Agency (MHRA), to deliver the Centre's inaugural lecture. On the back of this event, we have begun to develop relationships with regulatory agencies such as the MHRA and the US Food and Drug Administration (FDA).

In March 2020, we hosted a public lecture by Dr Nick Cammack, who leads the Wellcome Trust's ambitious £80 million snakebite programme. Dr Cammack presented the case for therapeutic innovation in this greatly underrecognised healthcare emergency.

Our next project (originally scheduled for April 2020 but postponed due to COVID-19) is a series of workshops, developed in collaboration with the Oxford Centre for Triple Value Healthcare, aimed at addressing the challenge of healthcare resource allocation. Professor Stephen Powis, National Medical Director of NHS England, and Julian Kelly, Chief Financial Officer for NHS England and NHS Improvement, have both agreed to participate. The first workshop will be followed by a public lecture by Professor Sir Muir Gray, who has held a number of senior positions in population health screening, public health, information management and value in healthcare. We have secured £4,000 in funding from UKSPINE to support these events, which will take place as soon as the public health situation allows.

Future work of the Centre for Therapeutic Innovation

Professor Richards' work to support the University's and the UK's efforts to tackle COVID-19, has provided him with a direct insight into the practical and intellectual challenges of testing novel therapies at pace in a pandemic environment. Clinical pharmacological skills are vital in these settings but are often overlooked; we would like to develop this theme as part of the ongoing work of the St Hilda's Centre.

We are also keen to focus on what is known as 'Regulatory Science', where COVID-19 has highlighted the critical need for a more innovative approach to regulation. As the pandemic subsides, the unique value of the St Hilda's Centre – with its offer of multidisciplinary input, patient participation, and free discussion under the

Chatham House Rule – will be all the more significant in bringing new insights to thinking about the future of medicines development.

The establishment of the new Centre comes at an auspicious time as St Hilda's comes to the end of the first phase of a transformational building project, which will increase significantly the quality and capacity of the College's facilities and spaces.

Collaboration

In addition to the extensive network of relationships that we are developing with industry, patient, regulatory and government partners, we are also establishing formal associations with other academic institutions, medical institutions and professional societies. To this end, 2019-20 saw the signing of two Memoranda of Understanding (MOU): the first between St Hilda's, the Medical Sciences Division and the University of British Columbia (UBC), signed in October 2019; and the second between St Hilda's and the Faculty of Pharmaceutical Medicine (FPM), signed in June 2020.

The MOU between St Hilda's, the Medical Sciences Division and UBC will form the basis of a programme of training exchanges for early and mid-career clinical scientists (eg UBC's Sultan Karim Clinical Pharmacology Fellows), providing them with the opportunity to develop their theoretical and practical expertise at both Oxford and UBC. This programme will be hosted by the new Centre for Therapeutic Innovation at St Hilda's.

Similarly, the MOU between St Hilda's and the FPM underpins a number of areas of collaboration between the two institutions, including supporting training for physicians and scientists enrolled on FPM specialist training programmes. This relationship between St Hilda's and the FPM has been reinforced through the appointment of the Climax Chair of Clinical Therapeutics to FPM's Advisory Committee on training for first-in-human study physician training.



Building the Future: Academic facilities for the Centre for Therapeutic Innovation at St Hilda's College, Oxford

GOVERNANCE

The work of the Chair of Clinical Therapeutics is overseen by the Climax Professorship of Clinical Therapeutics Steering Group, which meets once a term. The members of the Steering Group are:

- Professor Sir Gordon Duff (Chair) – Principal of St Hilda's College and Pro-Vice-Chancellor, University of Oxford
- Professor Sir John Bell – Regius Chair of Medicine, University of Oxford
- Professor Gavin Screatton – Head of the Medical Sciences Division, University of Oxford
- Professor Andrew Carr – Nuffield Professor of Orthopaedic Surgery, Head of the Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, and Director of the Botnar Research Centre, University of Oxford
- Professor John Climax
- Professor Duncan Richards – Climax Professor of Clinical Therapeutics, University of Oxford
- Dr Sarah Norman – Senior Tutor, St Hilda's College, University of Oxford
- Professor Dermot Kelleher – Dean, Faculty of Medicine and Vice-President, Health, University of British Columbia
- In attendance: Ms Emma Campbell, Strategic Projects Director, St Hilda's College, University of Oxford

PUBLICATIONS

Feldmann M, Maini RN, Woody JN, Holgate ST, Winter G, Rowland M, Richards D, Hussell T. Trials of anti-tumour necrosis factor therapy for COVID-19 are urgently needed. *The Lancet*. Volume 395, Issue 10234, P1407-1409, 2 May 2020.

Robinson PC, Richards, D, Tanner HL, Feldmann M. Accumulating evidence suggests anti-TNF therapy needs to be given trial priority in COVID-19 treatment. *The Lancet Rheumatology*. Published online 4 September 2020.