Addenbrooke's Charitable Trust
Registered charity number: 1048868

Fostering the future leaders of clinical research

Summary of the evaluation of the Cambridge Clinical Research Fellowship Scheme, August 2014

Introduction

Building clinical academic research capacity to advance medical knowledge and improve patient care

A clinical academic is defined as a doctor or other healthcare professional who engages in both clinical practice and research. Clinical academics with their patient experience, coupled with research skills and knowledge, are well positioned to pursue innovation, to build a research-led environment and ensure that patient needs inform research. Teaching, education and knowledge sharing are also key activities. This interplay ensures evidence based practice and continued improvements in healthcare.

The recognised value and shortage of clinical academics in the UK[1] has been partially relieved by national 'fellowship' training schemes provided by major funders such as the National Institute of Health Research (NIHR), Medical Research Council (MRC) and the Wellcome Trust. However, competition for such fellowships is high.

1 'Building clinical academic capacity and the allocation of resources across academic specialities' Academy of Medical Sciences 2009

'Developing the role of the clinical academic researcher in the nursing, midwifery and allied health professions' Department of Health, 2012

'Response to the Shape of Training Review' Academy of Medical Sciences 2013

'Shape of training call for evidence: joint submission from supporters and funders of health research' Association of Medical Research Charities 2013

'Securing the Future of Excellent Patient Care' Final report of the independent review led by David Greenway 2013 www.shapeoftraining.co.uk

NB: The full evaluation of the Cambridge Clinical Research Fellowship scheme can be downloaded at www.act4addenbrookes.org.uk/ResearchFellowships

Addenbrooke's Charitable Trust leading the way

Cambridge Clinical Research Fellowships: strategic positioning

Addenbrooke's Charitable Trust (ACT) funds clinical academic research fellowships which are positioned at the entry point of the clinical academic training pathway and strategically provide trainees with early stage support (one year or less) and access to experienced mentorship and supervision. This allows Cambridge Clinical Research Fellows to compete effectively in national fellowship schemes.

An independent evaluation of the impact of the Cambridge Clinical Research Fellowships awarded between 2007 and 2012 showed the scheme as successful in training a clinical academic workforce and building capacity in fuelling the training pathway with the most talented young doctors.

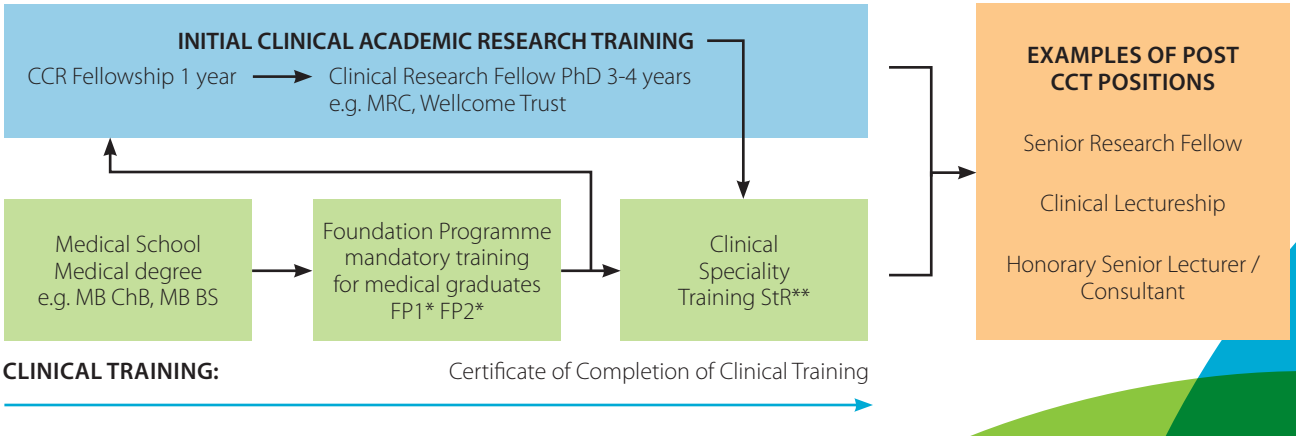
Cambridge at the heart

Cambridge Clinical Research Fellowships are awarded annually through open competition. Applications are scrutinised by the Cambridge University Hospitals NHS Foundation Trust (CUH) Research Advisory Committee ('RAC', chaired by Dr John Bradley, Consultant Physician and Nephrologist and Director of the NIHR Cambridge Biomedical Research Centre), based on the calibre and dedication of the candidate, scientific merit of the proposed research and quality of supervision and mentorship. Typically, fellowship candidates have existing Cambridge connections and are retained in Cambridge on completion of the fellowship.

> 'Dream run' is how one fellow described a Cambridge Clinical Research Fellowship and as a good grounding for a successful single external fellowship application

The CUH environment is the bedrock of the Cambridge Clinical Research Fellowship scheme, providing high calibre clinical academic training opportunities within a well resourced environment, where research and clinical expertise are fully integrated. Indeed, CUH is recognised internationally as a centre of excellence where ideas created in the laboratory are translated into patient benefits.

Typical integrated clinical training path: strategic positioning of Cambridge Clinical Research Fellowships



* previously called pre-registration House Officer/Senior House Officer
** previously called Senior House Officer / Speciality Registrar

Fellowship scope

Fellowships awarded

Between 2007 and 2012, ACT awarded 18 fellowships, to a value of £822,586*. These were made up of :

Cancer – 10 fellowships:
blood, bowel, brain, breast, ovary, paediatric, renal, thyroid

Dermatology – 3 fellowships:
These are Maxwell Charnley fellowships, in whose memory they are named

Other areas of medicine – 5 fellowships:
cardiovascular, hepatology, immunology, transplantation, underpinning biology

Fourteen of the 18 Cambridge Clinical Research Fellows participated in the independent evaluation which used a number of recognised criteria to assess outputs and impact. The fellows also provided their own recommendations for supporting similar training opportunities in the future. The information gathered has been used to develop a fundraising strategy so that ACT may continue to support and extend clinical academic training at CUH.

'... my Cambridge Clinical Research Fellowship kicked in at the right time ...'

* including partial co-funding from NIHR Cambridge BRC

Knowledge sharing

Ten fellows published abstracts and gave presentations at scientific meetings, received travel bursaries, awards and prizes for research excellence.

Despite Cambridge Clinical Research Fellowships being short duration and early stage, six fellows published research articles in peer reviewed journals.

'... fantastic opportunity to get started in research and supported my formal PhD funding application ...'

Abby MacBeth received a fellowship award in 2012

Demonstrating benefit

Next steps

The success of the fellows with awards, prizes and follow-on funding serves testament to their high calibre, dedication to clinical academic training and the quality of the research and mentorship.

With external follow-on funding, 10 Fellows continued their research towards a PhD qualification.

Sources of follow-on funding

Research charities (2):

Crohn's in Childhood Research Association (CICRA)

Kay Kendall Leukaemia Fund

Institutional (2):

NIHR Cambridge BRC

Princess Alexandra Research Fellowship and University of Queensland Research Scholarship

National schemes (6):

MRC / Royal College of Radiologists
Wellcome Trust

Benefits to patients

The research the fellows have undertaken helped to:

- better understand disease mechanisms
- develop and refine models to study the disease in the laboratory
- design clinical trials
- develop new ways to diagnose cancers, assess and predict responsiveness to treatment
- progress understanding on how to tailor existing therapies to individual patient needs.

The realisation of research findings leading to tangible patient benefits often lies in the future, however, the immediate impact of the fellows' research is exemplified in their comments:

'... clearly see how the area of research feeds into clinical application ...'

'... better understanding of cancer biology and the rationale behind the treatment approaches ...'

'... better able to explain treatment options to patients ...'

NB: The full evaluation of the Cambridge Clinical Research Fellowship scheme, along with the fundraising case for support can be downloaded at www.act4addenbrookes.org.uk/ResearchFellowships

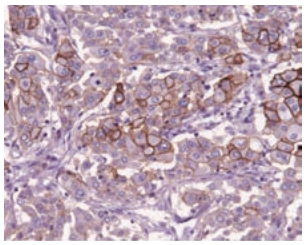
Examples of Cambridge Clinical Research Fellows

Dr Hamid Raza Ali (2009)

Digital morphometric analysis of cancer stem cells in breast carcinoma

Raza used state of the art computational techniques to develop new methods for use in pathology laboratories to classify breast cancer.

The fellowship formed Year 1 of Raza's PhD, with Years 2 and 3 supported by the NIHR Cambridge BRC. Raza published high profile research papers and participated in press and TV interviews. Recently Raza received further ACT support to strengthen an innovative collaboration with the University of Cambridge's Institute of Astronomy and was appointed as Clinical Lecturer in the Department of Pathology.



Highly magnified image of breast cancer cells. The brown staining shows some cells express unusually high levels of a protein called integrin alpha-6 (ITGA6) which together with other proteins may serve as a 'marker' to identify patients at higher risk of the cancer returning.

Dr Helen Benham (2009)

IL-22 producing lymphocytes in the pathogenesis of psoriasis and psoriatic arthritis – Maxwell Charnley Fellowship

This project formed Year 1 of Helen's PhD on understanding disease mechanisms in psoriasis and psoriatic arthritis and may help design new therapies.

Helen returned to Australia as a Consultant Rheumatologist and to complete her PhD at The University of Queensland Diamantina Institute but maintains links with Professor Hill Gaston in Cambridge. In 2013 Helen was a finalist for the 'New Investigator Award' by the Australian Rheumatology Association.

IMAGE Courtesy of The University of Queensland Diamantina Institute

Dr John Gounaris (2010)

ARID1A in endometrial proliferation, endometriosis and ovarian cancer pathogenesis

John's research focused on better understanding the biology of endometrial and ovarian cancer and in developing disease models for use in the laboratory. This has potential to provide new methods for screening and early diagnosis of ovarian cancer in women at risk. John secured an MRC Clinical Research Training Fellowship.

Dr Abby MacBeth (2012)

Understanding lupus: interferon-alpha related pathways and optimising therapy - Maxwell Charnley Fellowship

Abby's project focused on how currently used medicines work in treating systemic lupus erythematous and provides insights into developing new treatments. Abby established a research collaboration with King's College London and provided training to colleagues on 'Out of Programme Research'.

Dr Richard Mair (2012)

Stratifying anti-angiogenic response in glioblastoma

Glioblastoma is a vascular and angiogenic tumour and is the most common brain cancer with an average survival of 14 months. Some improvements in patient survival have been shown using medicines that block tumour blood vessel growth. Richard's project focused on whether new methods of brain scanning can detect changes in the tumour after this type of treatment and, at an early stage, identify which patients respond to treatment and those who do not.

Dr Lukas Niederreiter (2011)

Epithelium intrinsic role of XBPI in colitis associated cancer

Lukas investigated the genetic risk factors for inflammatory bowel disease that predisposes for intestinal inflammation and tumour formation. This project formed Year 1 of Lukas' PhD, with Years 2 and 3 being funded by the Crohn's in Childhood Research Association. Lukas presented his research at several conferences and in 2012 received a Certificate of Excellence from the United European Gastroenterology Society.

Dr Fotis Sampaziotis (2012)

In vitro modelling of cholestasis associated with cystic fibrosis

Cystic fibrosis (CF) is one of the commonest, potentially lethal, inherited diseases. Some but not all patients develop liver damage starting in biliary epithelial cells (BEC), a type of cell lining the hepatobiliary tract, i.e. the tubes that transfer bile from the liver to the bowel. Fotis' work focuses on BECs from skin samples obtained from CF patients and creating a model system for studying the disease in the laboratory.

Dr Elizabeth Wallin (2011)

Lymphocyte analysis in health and autoimmunity

Elizabeth's research focused on how cell biology is altered in autoimmune diseases and generated new knowledge to predict prognosis and the best ways of using existing therapies. On completing the fellowship, Elizabeth returned to clinical duties and then secured a MRC Clinical Research Training Fellowship for a PhD in renal immunology at the University of Oxford. Elizabeth continues to collaborate with Cambridge researchers.

'... first steps in the transition into research in a fertile ground for interactions between researchers and clinicians ...'

'... only possible to achieve such research in Cambridge which provides opportunities for clinical study and a unique environment with technological and biological resources ...'

'... the Cambridge Clinical Research Fellowship was useful in building confidence and training. At interview (for an external follow-on fellowship) being in receipt of funding was viewed positively ...'

Summary of Cambridge Clinical Research Fellowships 2007-2012

Fellow (and mentor; *indicates Fellow of the Academy of Medical Sciences)		About the research	Where now (Feb 2014)
2007	**Marie-Louise Daly** (Prof David Lomas*)	**Molecular pathways in the regulation of PERK and its involvement in ER-stress** UNDERPINNING BIOLOGY	Clinical Fellow (Dermatology) King's College Hospital
2007	**Emma Gudgin** (Dr Brian Huntly)	**Transcriptional control of the CDX-HOX pathway in acute myeloid leukaemia** CANCER (BLOOD)	Cambridge Institute of Stem Cell Research
2008	**Ines Harper** (Dr Gavin Pettigrew)	**Humoral autoimmunity and allograft vasculopathy** TRANSPLANTATION	Clinical Research Fellow University of Cambridge
2008 (co-funded with Gates Foundation)	**Rao Kondapally Seshasai** (Prof John Danesh)	**Quantifying the impact of glycaemic control on the risk of coronary heart disease: analysis of case-control data of 5,000 participants from the Pakistan Risk of Myocardial Infarction Study (PROMIS)** CARDIOVASCULAR	Clinical Lecturer (Cardiology) St George's Hospital, London
2008	**Soo Yeun Teo** (Prof V Peter Collins*)	**Biological and clinical significance of alterations in chromosome 1 in paediatric medulloblastoma** CANCER (PAEDIATRIC)	Unknown
2009	**Helen Benham** Maxwell Charnley Fellowship (Prof Hill Gaston*)	**The role of IL-22 producing lymphocytes in the pathogenesis of psoriasis and psoriatic arthritis** DERMATOLOGY/RHEUMATOLOGY	University of Queensland Diamantina Institute; Consultant Rheumatologist at Princess Alexandra Hospital Brisbane
2009	**Nicholas Matheson** (Prof Paul J Lehner*)	**Characterisation and functional analysis of the TRC8 tumour suppressor gene, a novel ubiquitin E3 ligase** CANCER (RENAL)	Clinical Research Fellow University of Cambridge
2009	**Hamid Raza Ali** (Prof Carlos Caldas*)	**Digital morphometric analysis of cancer stem cells in breast carcinoma** CANCER (BREAST)	Clinical Lecturer (Pathology) University of Cambridge
2010	**John Gounaris** (Dr James Brenton)	**Examination of the role of ARID1A in endometrial proliferation, endometriosis and endometriosis-associated ovarian cancer pathogenesis** CANCER (OVARY)	MRC Clinical Research Fellow Cambridge Cancer Research Institute
2010	**Thomas Booth** (Prof Kevin Brindle*)	**The development of new imaging methods for detecting brain tumour response to treatment** CANCER (BRAIN)	National Hospital for Neurology and Neurosurgery, London
2010	**Shaun Flint** (Prof Kenneth Smith*)	**Analysis of gene expression in purified leukocyte subsets and correlation with clinical outcomes for patients with active Systemic Lupus Erythematosus (SLE)** IMMUNOLOGY	Clinical Research Fellow University of Cambridge
2011	**Nicholas Grigoropoulos** (Prof Ming-Qing Du)	**The genetic basis of diffuse large B-cell lymphoma refractory to R-CHOP treatment** CANCER (BLOOD)	Clinical Research Fellow University of Cambridge

Summary of Cambridge Clinical Research Fellowships 2007-2012

	Fellow (and mentor; *indicates Fellow of the Academy of Medical Sciences)	About the research	Where now (Feb 2014)
2011	**Lukas Niederreiter** (Prof Arthur Kaser)	**Epithelium intrinsic role of XBP1 in colitis associated with cancer** CANCER (BOWEL)	Clinical Research Fellow University of Cambridge
2011	**Nicholas Rabey** Maxwell Charnley Fellowship (Prof Fiona M Watt*)	**Fibroblast gene expression in hypertrophic scars and cutaneous squamous cell carcinoma** DERMATOLOGY / CANCER	Specialist Registrar (Plastic & Reconstructive Surgery) Queen Alexandra Hospital, Portsmouth
2011	**Elizabeth Wallin** (Dr David Jayne*)	**Lymphocyte analysis in health and autoimmunity** IMMUNOLOGY	Clinical Research Fellow University of Oxford
2012	**Abby MacBeth** Maxwell Charnley Fellowship (Dr David Jayne*)	**Systemic lupus erythematosus- Anti-interferon-alpha monoclonal antibody as a therapeutic tool to a greater understanding** DERMATOLOGY	Clinical Research Fellow in post
2012	**Richard Mair** (Prof Kevin Brindle*)	**Stratifying anti-angiogenic response in glioblastoma** CANCER (BRAIN)	Clinical Fellow Cancer Research UK Cambridge Institute
2012	**Fotis Sampaziotis** (Dr Ludovic Vallier)	**In vitro modelling of cholestasis associated with cystic fibrosis** HEPATOLOGY	Clinical Research Fellow in post

Research publications

Adolph TE, Tomczak MF, Niederreiter L* et al. Paneth cells as a site of origin for intestinal inflammation. Nature 2013; 503: 272-76 (*Joint lead author).

Ali HR, Dawson SJ, Blows FM, Provenzano E, Pharoah PD, Caldas C. Aurora kinase A outperforms Ki67 as a prognostic marker in ER-positive breast cancer. British Journal of Cancer 2012; 106: 1798-806.

Benham H, Norris P, Goodall J, Wechalekar MD, Fitzgerald O, Szentpetery A, Smith M, Thomas R, Gaston H. Th17 and Th22 cells in psoriasis and psoriatic arthritis. Arthritis Research & Therapy 2013; 15: R136.

Gounaris I, Charnock-Jones DS, Brenton JD. Ovarian clear cell carcinoma -- bad endometriosis or bad endometrium? Journal of Pathololgy 2011; 225: 157-60.

Malzer E, Daly M-L, Moloney A, Sendall TJ, Thomas SE, Ryder E, Don Ryoo H, Crowther DC, Lomas DA, Marciniak SJ. Impaired tissue growth is mediated by checkpoint kinase 1 (CHK1) in the integrated stress response. Journal of Cell Science 2010; 123: 2892–900.

Niederreiter L, Fritz TM, Adolph TE et al. ER stress transcription factor Xbp1 suppresses intestinal tumorigenesis and directs intestinal stem cells. Journal of Experimental Medicine 2013; 210: 2041-56.

Ali HR, Dawson S-J, Blows FM, Provenzano E, Pharoah PD, Caldas C. Cancer stem cell markers in breast cancer: pathological, clinical and prognostic significance. Breast Cancer Research 2011; 13: R118.

Sarwar N, Aspelund T, Eiriksdottir G, Gobin R, Seshasai SRK, Forouhi NG, Sigurdsson G, Danesh J, Gudnason V. Markers of dysglycaemia and risk of coronary heart disease in people without diabetes: Reykjavik prospective study and systematic review. PLoS Medicine 2010; 7: e1000278.

Yuan Y, Failmezger H, Rueda OM, Ali HR et al. Quantitative image analysis of cellular heterogeneity in breast tumors complements genomic profiling. Science Translational Medicine 2012; 4: 157ra143

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