

**Institution:** University of Cambridge

**Unit of Assessment:** 1

**a. Context**

Our approach to delivering impact on UK health and wealth is fundamentally based on the 2006 Cooksey Report which seeks to optimise the potential of UK biomedical research to deliver benefit to patients, the National Health Service (NHS) and the wider healthcare economy. Our UoA1 departments, institutions and staff follow this approach and also deliver impact to society via public engagement. For UoA1, the University partnership with our associated NHS institutions, especially through our National Institute for Health Research Biomedical Research Centre (NIHR-BRC; Director, John **Bradley**, Cat C); Scientific Director, Sir Stephen **O’Rahilly** – returned staff in bold, Cat A unless stated), remains key to our translational research and to producing impact. We have excellent relationships with major pharmaceutical companies notably GSK, Astra Zeneca and Pfizer, as well as strong relationships with local biotech companies, including spin-outs. All of this is within the context of a strong culture of supporting technology transfer and establishing spin out companies in the University of Cambridge. This is reflected in the University being at the heart of one of the most productive technology clusters in the world. The 1,500 companies in the cluster have a combined annual turnover of £11.8 billion and employ more than 53,000 people. The vast majority of these companies are connected to the University in some way. Overall impact in UoA1 is seen in the improved classification and diagnosis of disease, new therapeutic and diagnostic approaches, quality of patient care, effects on national clinical guidelines published by the National Institute of Health and Care Excellence (NICE) and social policy, as well as the development of spin out companies, effects on the working practices of major Pharma and public engagement through broadcasting, science festivals and other activities. Our main non-academic user groups and beneficiaries include the NHS, big Pharma companies, biotech companies, patients and the general public both in the UK and internationally. The staff returned in this UoA1 submission are members of seven Research Groups that have similar impact and map on to strategic research themes of the School of Clinical Medicine (SCM) and School of Biological Sciences (SBS): Cancer; Infection and Immunity; Systems Medicine-Metabolic and Related Diseases; - Cardio-Respiratory Medicine; - Reproductive Biology and Medicine; Genomics, Structural and Cell Biology and their application to Medicine and Stem Cell Biology and Medicine. All of these themes have similar diversity of impact and the 20 submitted impact case studies are spread across all themes.

**b. Approach to impact**

The University of Cambridge aims to pursue the highest quality biological and biomedical research, to connect this with the highest quality clinical science and epidemiological studies, and to translate the research into improved therapies, disease management, healthcare and preventive strategies at the population level. Throughout the SCM and in all the departments with staff returned in UoA1, our strategy is to: 1. accelerate the transition between discovery and translational research; 2. accelerate translation into application and clinical practice; 3. engage with major pharmaceutical and biotechnology companies; 4. train the next generation of translational researchers; and 5. utilize support provided through the University’s technology transfer services. Public engagement and dissemination activities are encouraged and occur across each of these activities. In this way, and through a variety of outlets, we aim to make an impact on society with national and international reach in improvements in health care, policy development, education and the public understanding of science. Our strategy to deliver impact is completely aligned with that of our NHS partners facilitated by NIHR structures, especially the NIHR-BRC to address the ‘first gap in translation’ between discovery and early clinical trials and the NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC), to address the ‘second gap in translation’ between health technology assessment and knowledge management. In addition to the highly specialized University/NHS/Industrial partnerships outlined below to facilitate translational activities, our researchers receive strong central support to develop impact through dedicated bodies such as Cambridge Enterprise, the Communications Office and the Public Engagement Team. Non-academic impact is recognised in several ways within the University, including the academic promotions exercise, where commercialisation of research, policy development and outreach activities are rewarded. Impacts arising from researchers returned in UoA1 are also highlighted in the SCM monthly newsletter, thus creating a culture whereby these activities are valued and

celebrated.

**Acceleration of transition between discovery and translational research.** The partnership between the University and associated NHS institutions is fundamental to our strategy for producing translational research and impact. The success of our NIHR-BRC, renewed from April 2012 with an uplift in funding (to ~£120M over a 5 year period) reflects the strength of the partnership between the University and Cambridge University Hospitals Foundation Trust (CUHFT), and we work closely with a broader group of regional hospitals through Cambridge University Health Partners (CUHP; one of only 5 designated Academic Health Sciences Centres in the UK). The CUHP Clinical Trials Unit, which opened in 2011 and received full accreditation in 2013, is an essential vehicle for accelerating our discovery science through to clinical evaluation. All staff in the SCM and the Department of Pathology are actively encouraged to seek support both for early stage translational feasibility studies and for larger translational awards from major funding bodies. Staff in UoA1 have taken full advantage of the MRC Confidence in Concept award to the University of Cambridge in 2012. This award (£600k), matched with University funding (£200k), is designed to accelerate the transition from discovery research to translational development projects by supporting preliminary work and feasibility studies to establish the viability of an approach. In the first year of this award, five projects led by UoA1 Cat A staff were competitively selected for support. These five projects, which, together, received funding of £240k, include a discovery platform for approved drugs to aid therapeutic delivery of lysosomal enzymes in clinical application (**Cox**), the reversal of immune suppression in pancreatic ductal adenocarcinoma (**Fearon**), closed-loop insulin delivery in the general ward (**Hovorka**), a screen for novel autophagy-modulatory kinase inhibitors (**Rubinsztein**) and new transcriptome-based biomarkers for autoimmune disease (**Smith K**). Two of these projects also benefit from being located alongside GSK in the Stevenage Bioscience Catalyst (SBC; see below). UoA1 staff have also won awards from major translational funding initiatives. Currently totalling ~£12m, these include grants for the diagnosis of childhood cancers (**Coleman**, SPARKS), whole genome sequencing to detect nosocomial infections (**Peacock**, Health Innovation Challenge Fund, Wellcome Trust/NHS), (**Smith K**, Wellcome Trust Seeding Drug Discovery), a *Bacillus subtilis* whole-cell arsenic biosensor for field use (**Ajioka**, Wellcome Trust Translation Award), real-time, continuous monitoring in neonatal intensive care (**Beardsall**, NIHR Efficacy and Mechanism Evaluation award) new therapeutics to treat liver disease resulting from alpha-1 antitrypsin deficiency (Lomas, at UCL from 2013, GSK's Discovery Partnerships with Academia initiative award), and gene therapy for Tay-Sachs and Sandhoff diseases (**Cox**, MRC DPFS award).

**Translation into Clinical Practice.** Translation into clinical practice is managed in particular through an NHS/University partnership, to which the University attaches the highest strategic importance. The development of the Cambridge Biomedical Campus has been especially facilitative for translational research, with co-location of world class research (often in Institutes) and the hospital enabling both cross-fertilisation between the clinic and the laboratory bench, as well as space for biotech/business ventures. The effectiveness of the NHS/University partnership was formally recognised by the Department of Health in 2009, with the designation of Cambridge University Health Partners (CUHP), as one of five UK Academic Health Science Centres. The partnership between the University and CUHFT was awarded one of five comprehensive NIHR-BRCs, in recognition of a track record of translating basic science discovery into 'first in human' clinical studies, and on into patient benefit. The NIHR-BRC also provides a mechanism whereby unmet needs identified in clinical practice can influence research questions. The NIHR-BRC was reviewed by an international panel in 2011, which concluded that the partnership represented the UK's primary academic resource in biomedical research, and resulted in renewal of the NIHR-BRC with a 40% increase in funding (to ~£120M). The NIHR Cambridge Experimental Cancer Medicine Centre is complementary to the NIHR-BRC and aims to develop molecular prognostic and diagnostic tests to aid treatment decisions, focusing on genetic predisposition to cancer and the identification of high-risk groups. Critical to the success of early phase clinical research is the Wellcome Trust Clinical Research Facility (CRF; Director, **Chatterjee**) - one of the Wellcome Trust's original five 'Millennial' CRFs. The CRF is co-located with the GSK Clinical Unit Cambridge (CUC, see below) and forms part of the Addenbrooke's Clinical Research Centre (ACRC) operating 24h /7days with overnight accommodation with revenue funding from NIHR, together with a daytime / 5 days Clinical Investigation Ward (CIW), together supporting well over 100 experimental medicine studies p.a. (including Phase I and early Phase II clinical trials). The ACRC

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operates at 70-80% occupancy, reflecting marked growth in experimental medicine studies on campus following the advent of the BRC, and a £17M 6-storey extension is planned for completion in 2015 to accommodate the expected increase in translational research across the campus. The CRF is a key stakeholder, co-grant holder and founding member of the UK Clinical Research Facility (UK CRF) Network. This Network, funded by Department of Health, delivers support to CRFs nationally and engages with other NIHR infrastructure e.g. Experimental Cancer Medicine Centres, BRCs, NIHR Biomedical Research Units and Research Networks. Workstreams dedicated to unifying, streamlining and sharing good practice in the operational management of CRFs have been established. Outputs include a national Research Nurse Competency Framework, a Study Intensity Tool for assessing study workload that is used extensively across CRFs and Comprehensive Local Research Networks, training and education initiatives, including an annual CRF Conference hosted in Cambridge in 2009, and a repository of core documents, SOPs accessed via a portal hosted on the NIHR website. The Cambridge CRF represents the UK CRF Network as a member of the Academy of Nursing, Midwifery and Health Visiting.

Other initiatives and activities supported by the SCM to create an environment conducive to translation into clinical practice involving Cat A and Cat C staff in UoA1 include: 1. a Clinical Trials Unit (directed by **Wilkinson**) established under the auspices of CUHP and which was accredited ahead of schedule under the UKCRC scheme in 2013. This promotes and facilitates trials, and is linked to developmental work on trial methodology in the MRC Biostatistics Unit Trials Hub; 2. CUHFT hosts the West Anglia Comprehensive Local Research Network, the West Anglia Cancer Research Network, and the Eastern England Diabetes Research Network, and is a partner in the East Anglia Dementia, Neurodegenerative Diseases Research Network, Medicines for Children Network and the Thames Stroke Research Network; 3. Cambridge has led the development of a national NIHR BioResource, built on the success of the Cambridge BioResource (see below). It provides a national cohort of volunteers from the general population and patients who are well genotyped and phenotyped, thus allowing the study of well characterised subpopulations; 4. the Rare Diseases Translational Research Collaboration that links existing research infrastructure nationally to deliver greater impact of translational research into rare diseases than would be possible by the individual parts; 5. CUHFT is a partner in the NIHR Health Informatics Collaborative (led by Oxford University Hospitals NHS Trust), which enables an environment where the NHS, academia, industry and patients work collaboratively to make the most of existing assets to contribute to improvements to the health and wealth of the nation; and 6. the NIHR Translational Research Partnership in Joint and Related Inflammatory Disease in which the NIHR-BRC is a partner. Effective translation is also supported by the East of England CLAHRC that is developing research capacity and leadership to optimise the use of research evidence in the NHS and by NIHR Research for Patient Benefit awards in Cancer, including end of life care, Imaging, and Medicines Management; NIHR Programme Grants in Diabetes (Reducing the burden of Type 2 diabetes: translating epidemiology and behavioural science into preventive action; £1m), and Transplantation (Access to Transplantation and Transplant Outcome Measures; £2.1m).

Several staff returned in UoA1 influence Clinical Guidelines and Public Policy nationally and internationally. These include **Smith GL** who has chaired the WHO Advisory Committee on Smallpox since 2004 and is a Member of the WHO committee on Viral Infections, **Neal** who is the Chair of the Prostate Cancer Advisory Group, Dept of Health and a member of NICE Prostate Cancer Guideline Development Group, **Collins** who chairs the Pathology Committee of the National Cancer Intelligence Network, **Rintoul** (Cat C) who has been a member of NICE Lung Cancer Quality Standards and Guidelines Development groups, and **Compston** who has chaired the National Osteoporosis Guidelines group and been a member of several NICE committees evaluating the treatment and prevention of osteoporosis.

**Engagement with major pharmaceutical companies.** UoA1 strongly encourages and continues to build mutually beneficial partnerships between the academic Clinical Medicine community, the pharmaceutical and biotech industry, and the NHS. A key partnership that has been driven forward in recent years is with GSK. This is directly manifested in the existence of the GSK Clinical Unit Cambridge (CUC) since 1999 and the programme of open collaboration established in 2012. The CUC is a clinical research facility embedded in the University Hospital. The Unit specialises in innovative Phase 1 and early Phase 2 studies across a broad range of therapeutic areas, exemplified by recent studies on atherosclerosis, Type 2 diabetes, obesity, cognitive impairment, together with various aspects of inflammation and enables staff in UoA1 to overcome a key hurdle

in translation. The relationship between GSK and CUHFT, which provides CUC with access to resuscitation and intensive care facilities, was key to the GSK CUC gaining accreditation as a Phase 1 Clinical Trials Unit. The GSK CUC team maintains an extensive network of contacts in the Cambridge clinical and academic community, which benefits all parties. This means that the Unit can offer the benefits of engaging local academic talent in an environment that ensures high standards of regulatory compliance for early Phase studies. In 2012 the University of Cambridge expanded its links to GSK, embarking on a programme of scientific open collaboration to advance drug discovery and the development of new medicines. The programme includes the co-location of relevant University researchers with members of the GSK Scinovo team at the SBC in Stevenage, thus providing University researchers with uncomplicated access through Scinovo to GSK drug discovery and development know-how, project management expertise, outsourcing options at preferential rates and commercial assistance with market definition and assessment. Cambridge Enterprise (the University's technology transfer office - see below) facilitates this programme.

In 2012 the Pfizer-Cambridge Centre for Cardiovascular Genomics was established with support from Pfizer, the British Heart Foundation (BHF), and the MRC (through its CASE industrial scheme, including the provision of PhD studentships), and the NIHR-BRC. The objective of the Pfizer-Cambridge-Centre is to identify and validate potential therapeutic targets for cardiovascular disease through the focused application of population science approaches.

In 2013 AstraZeneca announced that it would develop a new global R&D centre and re-locate its corporate headquarters to 11 acres of the Cambridge Biomedical Campus by 2016 at a cost of £330M. This is in recognition of the global significance of the Cambridge Biomedical Campus and reflects access to scientific talent and clinical expertise. Pascal Soriot, Chief Executive Officer of AstraZeneca said of the move that: "Cambridge competes on the global stage as a respected innovation hub for life sciences and our choice of site puts us at the heart of this important ecosystem, providing valuable collaboration opportunities. Moving to the Cambridge Biomedical Campus means our people will be able to rub shoulders with some of the world's best scientists and clinicians carrying out some of the world's leading research – that's a really exciting prospect." The new R&D centre will become the company's largest for oncology research as well as hosting scientists focused on cardiovascular and metabolic diseases, respiratory, inflammation and autoimmune diseases and conditions of the central nervous system.

Also in 2013 AstraZeneca entered into a 2 year agreement with the University of Cambridge to work with researchers in the CRUK Cambridge Institute and the Department of Oncology to develop monitoring of tumour activity by examining tumour DNA in blood and to test AstraZeneca drugs in pre-clinical prostate cancer models and in early phase trials.

**Training the next generation of translational researchers.** Training of clinical translational researchers is supported through the Centre in Translational Medicine and Therapeutics (TMAT) awarded by the Wellcome Trust in 2012 to the SCM with GSK as its industry partner. The £2.75M TMAT MPhil programme trains clinical academics, from MB PhD students to clinical lecturers, using a modular MPhil followed, in some cases, by a PhD, in a wide range of translational and pharmacological skills. In partnership with the Eastern Deanery and NIHR-BRC, the ACRC has developed a "Research Skills for Clinicians" course that covers methodological aspects (e.g. design, ethical approval, good clinical practice, analysis & presentation) of clinical research for medical and other trainees.

**Technology Transfer.** The University provides strong support for technology transfer through Cambridge Enterprise (CE), a wholly owned subsidiary of the University of Cambridge, that provides technology transfer, consultancy and seed-fund services to support researchers, inventors and entrepreneurs. CE works within the University's Intellectual Property Policy, which provides flexibility in approaches to commercial exploitation, including the option to exploit advances independent of CE. The policy includes generous returns to inventors (e.g., 90% of income up to £100,000 goes to the inventor), providing incentives for entrepreneurial activities. CE is also supporting Cambridge Innovation Capital (CIC), a new £50 million investment business launched to provide long-term finance that will support the development of University spin-outs. CE staff whose major responsibilities are in biomedicine/the SCM provide frequent drop-in 'surgeries' for researchers in cross-departmental institutes and departments to advise on all aspects of commercialisation, including IP advice, licensing and the development of spin out companies. A network of 'Enterprise Champions' are based within institutes and departments and include Maria Adams (Institute of Metabolic Science), **Charnock-Jones** (Obs & Gynae), Emily Clement

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(Pathology), **Davenport** (Clinical Pharmacology), Anna Davies (Cambridge Infectious Diseases), **Rubinsztein** (Cambridge Institute for Medical Research) and Tennie Videler (Cambridge Immunology Network), who are well networked to facilitate the reach of CE.

Companies (other than those reported in individual impact case studies), at different stages of spin out from research by academic staff returned in UoA1 or staff who have left the University but were in UoA1 departments/research groups include :

- Chroma Therapeutics, founded in 2000 by **Kouzarides** with the help of Cambridge University and Cancer Research UK to develop epigenetic drugs against cancer. To date it has raised over £60million of venture capital to finance the development of clinical trials to assess small molecule therapies for cancer and inflammation, including the completion of a Series D financing round of £15m in 2009 and has received undisclosed milestone payments from GSK with whom it entered a collaboration in 2009 to identify small molecule therapeutics. (See impact case study entitled "Epigenetic pathways: from basics to cancer treatment").
- Funxional Therapeutics Ltd, founded in 2005 by David Grainger (a Principal Investigator in the Department of Medicine until December 2011) to exploit the anti-inflammatory effects of stable mimetics of C-terminal lactam peptides (somatostatins). The lead molecule, FX125L, received Investigational New Drug approval in 2009 from the US Food and Drug Administration and in 2010 Funxional Therapeutics Ltd raised 10million Euros in a private Series B financing round allowing FX125L to enter Phase 2 trials in asthma, RA, chronic obstructive pulmonary disease and psoriasis. In July 2012 this programme was sold to the German-based global pharmaceutical company Boehringer Ingelheim for an undisclosed sum.
- XO1 Ltd, a new company spun out from the University of Cambridge and Addenbrooke's Hospital in 2013, that has raised \$11million in funding to develop a new anticoagulant drug ichorcumab, a synthetic antibody developed by **Huntington** and **Baglin** (Cat C), which targets thrombin, the enzyme responsible for blood clotting. The company will operate in virtual mode, without offices or labs, using out-sourced drug development expertise from across the globe and expects to expect to begin trials in human volunteers within two years. Ichorcumab has been licensed to XO1 by Cambridge Enterprise.

**Public engagement.** A wide range of outreach and public engagement activities are undertaken to raise awareness of research in UoA1, involve the general public in our scientific research and/or increase general interest in science. This includes school visits by our researchers and their teams, Open Days to showcase departments and institutes and their research, and participation in monthly Café Scientifiques that take place in local bars and theatres. The 'Rising Stars' course offers younger researchers training in public engagement and educational outreach, and encourages participants to offer unusual, engaging activities rather than straight-forward talks.

Notable recent outreach activities include:

- The Cambridge BioResource (<http://www.cambridgebioresource.org.uk/>) led by **Todd** to involve the public actively in statistically robust investigations of the molecular genetic basis of common diseases. Cambridge BioResource is a panel of over 12,000 members of the local population who have agreed to participate in medical research. Over 2,000 have taken part in more than 45 studies. The BioResource allows recall by genotype facilitating stratified medicine approaches. The success of this programme has led directly to the development of a national NIHR BioResource described above.
- NIHR-BRC Public/Patient Panel to involve members of the public in research.
- The Naked Scientists, a multimedia initiative that includes the award-winning, live, weekly one-hour, audience-interactive "Naked Scientists" radio programme broadcast by the BBC Eastern Region (also syndicated on 5Live). The Naked Scientists project operates as an outreach initiative at the Cambridge University Pathology Department where it is staffed by a dedicated team led by Clinical Lecturer Chris Smith. The Naked Scientists programme is syndicated internationally by national networks in several countries including Australia (on the ABC) and South Africa, reaching a combined live weekly radio audience of over 1 million people. The programme is also distributed globally via the intranet with over 22 million downloads in the past 4 years and it has won many prizes including the Society for General Microbiology's Peter Wildy Prize 2008, the Royal Society Kohn Award for 2008, the Best Radio Show Award at the Population Institute's 29th Global Media Awards, 2008, the European Podcast Award for UK Non-Profit podcast, the inaugural Royal College of Pathologists Furness Prize for science communication 2010 and the Society of Biology Science Communication Prize 2012.

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- Press releases to inform media and public about significant advances, as well as contributions to TV and radio programmes, all aided by support from the University's Office for External Communication.
- Contributions by many UoA1 scientists including individual presentations including public lectures and demonstrations at the Cambridge Science Festival, the UK's largest free science festival. The science festival, which takes place each March, attracts over 35,000 attendees each year.

The Bugs Battles card game, devised by **Peacock** and aimed at educating young people about infectious disease, was successfully piloted at the Cambridge Science Festival in 2013, <http://www.cam.ac.uk/sciencefestival/files/2013/03/Bug-Battles-Info-Collection.pdf>

**c. Strategy and plans**

Our strategy over the next five years is to maximise the potential for our research to lead to benefit for patients in the developed and the developing world and/or to lead to economic benefits. To this end we will increase our partnerships with biotechnology and pharmaceutical companies, and increase encouragement to investigators to embark on translational studies, generate IP and consider spin outs. We will have a greater focus on obtaining funding from translational funding schemes including the MRC's Developmental Pathway and Developmental Clinical Studies Funding schemes and the Wellcome Trust's Seeding Drug Discovery initiative. Whilst there is a significant amount of activity ongoing, we recognise that there is still real untapped potential, e.g. the demand for MRC Confidence in concept funding within Cambridge has out-stripped available supply by a ratio of 4:1. We have applied to renew our MRC Confidence in Concept funding scheme, since this is a critical early step on the translational pathway. Other specific plans currently being enacted to enhance the likelihood that scientific discoveries leading to patient or economic benefits include: (i) establishing in October 2013 in the SCM a translational research office in partnership with the BRC and CE. Three FTE staff will be appointed by the end of 2014 to assist investigators with the interactions with ethics, CUHFT R&D, CE, funding bodies and industrial partners and they will assemble and maintain a portfolio of projects suitable for industrial partnerships; (ii) expanding the Cambridge Biomedical Campus including the re-location of the Papworth Hospital and with it the establishment of the Heart and Lung Research Institute; (iii) establishing on the Cambridge Biomedical Campus by December 2013 a location for IdeaSpace, a University of Cambridge hub for early stage open innovation. This will follow the successful model that already provides space and resources to a flourishing community of innovators, entrepreneurs and advisors on the University's west Cambridge and central campuses, <http://www.ideaspace.cam.ac.uk/>.

**d. Relationship to case studies**

Many of the 20 submitted case studies from across all of our Research Groups have had more than one type of impact on health, welfare and/or other impacts. The submitted case studies include 11 in which there have been impacts on the diagnosis, classification and screening of disease, 3 in which new therapeutic approaches have resulted, 9 with direct effects on the management and quality of patient care, 10 with effects on national and/or international clinical guidelines, 2 resulting in/influencing the development of spin out companies, 4 resulting in the sale of new products, 1 having an effect on the working practices of major pharmaceutical companies, 4 influencing public debate and 5 affecting the education and training of medical professionals.

The 20 case studies submitted relate to our Research Groups as follows : Cancer (7); Infection and Immunity (5); Systems Medicine – Metabolic and Related Diseases (3); -Cardiovascular and Respiratory Disease (2); -Reproductive Biology and Medicine (1); Genomics, Structural and Cell Biology and their application to Medicine (2).