**Institution: University of Cambridge**

**Unit of Assessment: UoA1**

**a. Overview**

In this submission we combine the research of most of the departments of the School of Clinical Medicine (SCM) with that of the Department of Pathology in the School of Biological Sciences (SBS). Related work in other departments is being returned in UoAs 2 and 4 (SCM) and UoAs 4, 5 and 6 (SBS). This submission covers all areas submitted under UoA1-5 in RAE 2008. Although all staff returned in UoA1 are members of 'home' departments, many are now located within major cross-departmental research institutes, including the Cambridge Institute for Medical Research (CIMR) supported by a Strategic Award from the Wellcome Trust, the Wellcome Trust-MRC Institute of Metabolic Science (IMS) that includes the new MRC Metabolic Diseases Unit, the Cancer Research UK Cambridge Institute (CRUK-CI), the Wellcome Trust/MRC Cambridge Stem Cell Institute (including the Centre for Stem Cell Research and the Anne McLaren Laboratory for Regenerative Medicine), and the Wellcome Trust/CRUK Gurdon Institute. This return encompasses 198 (192.05 FTE) Category A and 16 Category C staff. Twelve eligible staff are not returned. Staff returned are members of seven Research Groups that map onto strategic research themes of the SCM and SBS (some staff are in more than one group): **Cancer** (58 Category A staff); **Infection and Immunity** (56); **Systems Medicine-Metabolic and Related Diseases** (36); **Cardio-Respiratory Medicine** (29); **Reproductive Biology and Medicine** (6); **Genomics, Structural and Cell Biology and their application to Medicine** (33); and **Stem Cell Biology and Medicine** (9).

**b. Research strategy**

Cambridge is renowned for the quality of its biomedical research as reflected in the awards of the 2010 and 2012 Nobel Prizes in Physiology or Medicine to Edwards and Gurdon, respectively. Our overall aim remains to pursue the highest quality basic biological and biomedical research and to connect this with the highest quality clinical science and epidemiological studies in order to translate our research into improved therapies, disease management, and healthcare and preventive strategies at the population level. Our strategy for achieving this goal has evolved progressively over the past 40 years. In the 1960s-70s the University initiated key programmes of clinically-related research based around distinguished investigators in areas such as Organ Transplantation (Calne FRS, Lasker Prize 2012), Diabetes (Hales FRS) and Haematology (Carrell FRS). The move of the MRC Laboratory of Molecular Biology (LMB) to the Addenbrooke's Hospital site in 1962 catalysed important collaborations that greatly strengthened these programmes. The pace of research in clinical medicine accelerated dramatically from the late 1970s with the establishment of the SCM and admission of the first clinical students. Whereas the initial focus was on the recruitment and development of high quality individual scientists and leaders, subsequent expansion has enabled us to concentrate on the development of critical mass in key thematic areas based on: 1. previously established strong leadership in areas such as Cancer, Neurosciences (UoA4) and Metabolism; and 2. providing the research infrastructure, often in the form of institutes, necessary to perform at the highest level. Since 2008 several important developments have strengthened the research environment. Many of these are detailed in the sections dealing with specific research themes, but examples include the incorporation of two existing and one new MRC Unit, and the CRUK-CI into the University, the award of £23M from the MRC and Wellcome Trust in 2013 to establish the Wellcome Trust-MRC Institute of Metabolic Science (IMS), the launch of the Wellcome Trust/MRC Cambridge Stem Cell Institute, including the Anne McLaren Laboratory of Regenerative Medicine, in the refurbished West Forvie Building that also houses new state of the art facilities for disease model phenotyping and imaging. Since January 2008, 18 Chairs have been filled/created, providing academic leadership in strategic topics that frequently bridge the interests of the sub-panels of Panel A.

Our research in Cancer and Metabolic Diseases (as well as that in Neurosciences UoA4 and Public Health UoA2) has reached a stage where its momentum is now well-sustained. We have made significant progress in other areas that were identified in 2008 as strategically important, including Stem Cell Medicine, Cardio-Respiratory Medicine and Immunity/Infection. Cambridge was recently one of six British Heart Foundation (BHF)-designated Centres of Excellence in

Cardiovascular Research, and, in a joint bid with Oxford, one of three BHF Centres for Regenerative Medicine. Relevant to our aspirations in Infection/Immunity, Cambridge was recently awarded one of five Centres for Global Health Research (CGHR) by the Wellcome Trust, with a major focus on parasitic and bacterial disease. The election of a new Chair of Medical Microbiology with strong links to the Sanger Institute has greatly enhanced our programme in applied bacterial genomics. A major recruitment drive in Immunity has already secured several key individuals, at least, in part by the attraction of University space in the new LMB (see below).

Partnership with our associated NHS institutions is central to our translational research. Of particular note is the success of our National Institute for Health Research Biomedical Research Centre (NIHR-BRC), which was renewed from April 2012 with a 40% uplift in funding (to~£120M over 5 years) compared to 2007. This success was a reflection of the strength of the partnership between the University and Cambridge University Hospitals Foundation Trust (CUHFT). We work closely with a broader group of regional hospitals through Cambridge University Health Partners (CUHP), one of only five 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. Links with the pharmaceutical industry have strengthened: in 2012 the University of Cambridge embarked on a programme of scientific, open collaboration with GlaxoSmithKline (GSK) to advance drug discovery and the development of new medicines. In 2013 AstraZeneca announced it would develop a new global R&D centre and relocate its corporate headquarters to 11 acres of the Cambridge Biomedical Campus by 2016 at a cost of £330M. This will become the company's largest R&D centre for oncology research as well as hosting scientists focused on cardiovascular and metabolic diseases, respiratory, inflammatory and autoimmune diseases, and conditions of the central nervous system. This provides a major, internationally significant boost to our strategy of promoting collaboration with industry and an extraordinary opportunity for translation.

Looking to the future, the two Schools (SCM and SBS) have recently undertaken a formal, joint, strategic review of biomedical science in the University that identified 10 broad research themes, each built on a foundation of internationally-recognised research expertise, connecting fundamental biological research with clinical application and fostering links with the physical sciences. Most components of seven of these research themes are returned under UoA1. Our strategic aims for the next 5 years, which have been informed by this review, include the full exploitation of the potential for inter-disciplinary research including disciplines outside the traditional bio-medical sciences (including, among others, Applied Mathematics, Engineering and Chemistry). We will also seek to maximise the value that comes from our geographical position at the heart of a remarkable and growing cluster of research institutes (including the Sanger and Babraham Institutes and the LMB), leading teaching hospitals and major industrial R&D facilities.

These activities will be facilitated by a series of large-scale, cross-school Strategic Initiatives and Networks recently established by the University that enable it to direct resource into strategic planning. Strategic Initiatives create a shared cross-School vision and development plan for building research capacity and partnerships over the medium to long-term, and Strategic Networks promote links and activities amongst a thematic cross-School academic community. Three of the eight current University Strategic Initiatives (Cancer, Infectious Diseases and Stem Cells) and two of the seven University Strategic Networks (Immunology and Metabolic Disorders) relate directly to this UoA1 return.

A specific, major, strategic aim for the next 5 years involves the further development of medical imaging science across the campus. While we have considerable individual strengths and excellent facilities, including radiochemistry and PET-CT, we wish to create a step-change in quality by better co-coordinating the elements and linking them with the strengths in Physical Sciences and Engineering in Cambridge. **Gilbert** has recently been recruited from Aberdeen to play a lead role in creating a Department of Medical Imaging Sciences that will bring together imaging scientists in the present Department of Radiology with those in the Wolfson Brain Imaging Centre.

In order to deliver these strategic aims, further infrastructure is needed. The next 5 years will see several relevant developments on the Cambridge Biomedical Campus. The MRC has recently completed construction of the new LMB (occupied from February 2013), which includes University space for Immunology and Infectious Disease research. The lease on the old LMB buildings will revert to the University from January 2014, providing interim laboratory space for recruitment and

opportunities for re-development. As part of the integration of the CRUK CI into the University there is a commitment to fit-out the third floor of the Li Ka Shing Centre (where the CRUK CI is based) at a project cost of ~£7.0M (including £2.4M from CRUK). There is also a University commitment to expand the Addenbrooke's Clinical Research Centre (ACRC) to provide five storeys of accommodation at an estimated cost of £17M (including £5M from the Wellcome Trust dedicated to metabolic disease research). In a programme to rationalise and develop biofacilities across the University, there is a University commitment to build a state of the art facility on the Cambridge Biomedical Campus for the study of model organisms (Translational Medicine and Technology Hub), with projected expenditure of up to £100m and completion by the end of 2016. The University is also committed to housing the whole of the Wellcome Trust/MRC Cambridge Stem Cell Institute in 8000m$^2$ of a new 16,000m$^2$ building (estimated cost £70M) that is planned for completion by 2016, thus physically bringing together basic and translational stem cell biology. Half of the remaining 8000m$^2$ will provide a new hub for Immunity and Infection research. In addition to these developments, plans are well advanced for the building of the new Papworth Hospital on the Cambridge Biomedical Campus and the associated Cambridge Heart and Lung Research Institute (estimated cost £40M).

The Strategy for each of the seven Research Groups/Themes is outlined below.

**1. Cancer**

**Progress since 2008.** The University has dramatically increased its commitment to Cancer Research. The Cancer Theme now includes 58 academic staff, this expansion resulting from the merger of existing University researchers with those from the CRUK CI and the MRC Cancer Cell Unit now the **Cancer Unit (CU).** The University has designated Cancer as one of its major Strategic Initiatives and the **Cambridge Cancer Centre** now links the SCM and CUHFT with researchers in other University Schools including Physical Sciences and in the other local biomedical research institutes. Several key developments have delivered the strategic objectives we set out in RAE 2008. With the opening of the third floor of the CRUK CI next year, we will have delivered our strategy in full. The CRUK CI (~£45M) opened in 2007 and now houses 22 Group Leaders whose work covers basic biology through to molecular imaging, computational biology and translational research. **Tavaré** FRS was appointed Director of the CRUK CI in 2013, replacing **Ponder** FRS. Tavaré has brought a strong focus on bioinformatics and computational biology to our cancer research, including leading a new, cross-institutional Wellcome Trust 4-yr PhD programme in Mathematical Genomics and Medicine. Cancer-related imaging has been strengthened. **Gallagher** with Brindle (Biochemistry and CRUK CI, UoA5) have brought novel $^{13}$C hyperpolarised MRI imaging to the clinic, funded by a £5.3M Wellcome Trust Award. **Gilbert**, recruited in 2011 has brought a strong breast imaging programme. **Griffiths J.** has developed MR spectroscopic techniques he developed pre-clinically to the differential diagnosis of brain tumours. We have established large bio-repositories of tumour and control samples and established a next-generation sequencing pipeline. The CRUK CI had a highly successful quinquennial review in 2011. **Venkitaraman** became the Director of the MRC Cancer Unit in 2010 and, in 2011, the MRC approved his proposal for a ~£25M, 5-year Unit programme. An early Phase I trials unit (led by **Jodrell**) has been established within CUHFT. Cambridge was approved as a CRUK Cancer Centre in 2010. In 2011, there was a successful renewal of the CRUK/DOH Experimental Cancer Medicine Centre (**Caldas**) and in 2012 'Cancer' was the largest theme in the renewed NIHR BRC. Plans for clinical research were supported by the appointments of **Jodrell** and **Eisen** and by the new Phase I clinical trials unit. The Cambridge Cancer Centre won recognition as a '**Comprehensive Cancer Centre**' (for excellence in research and clinical care) by the Organisation of European Cancer Institutes, and is the only Centre in Europe based in a general rather than a specialist hospital. We are consistently a leading **Regional Cancer Network** for accrual into recognized trials as a proportion of cancer incidence. In 2012 we were top ranked in the country with 7083 patients recruited representing 58% of incident cancers for all approved trials. In 2012, with Manchester, Cambridge became a **CRUK Imaging Centre**.

**Selected Research Highlights. Kouzarides** FRS described novel epigenetic changes in cancers that are amenable to small molecule drug therapy (*Nature* 2011). **Narita** discovered cellular senescence is a tumour suppressive phenotype (*Science* 2011). **Odom** discovered combinatorial binding of transcription factors is highly significant for genetic and evolutionary stability (*Science* 2010*; Cell* 2013). **Martins** demonstrated restoration of *TP53* function leads to the regression of non-small cell lung carcinomas (*Nature* 2010). **Venkitaraman** identified novel mechanisms that

maintain genome integrity during cell division (*Nature* 2008*; Cancer Cell* 2010). **Winton** defined the functional relationship between different candidate stem-cell populations and the repertoire of genes that drive intestinal tumorigenesis (*Science* 2010). **Jones** discovered a novel population of committed progenitor cells that maintains homeostasis in the epidermis and the oesophagus (*Science* 2012). **Shields** defined novel interactions between lymphatic vessels and the tumour stroma (*Science* 2010). **Carroll** discovered how transcription factors such as FOXA1 and GATA3 act as 'pioneer factors' to determine the genomic position of the oestrogen receptor in breast cancer (*Nature* 2008, 2012). **Caldas** identified 10 sub-types of breast cancer, with implications for stratifying risk (*Nature* 2012, 2013). **Neal** discovered novel mechanisms of castration resistance in prostate cancer (*Cancer Cell* 2013). **Rosenfeld** developed and applied new methods for detecting circulating tumour DNA (*Nature* 2013*; NEJM* 2013). **Fitzgerald** developed a novel lectin based technique for *in vivo* detection of pre-malignant change in Barrett's oesophagus (*Nat Med* 2012). **Griffiths J**. applied novel MRI and MRS methods to a range of cancer studies to include the discovery that inhibition of Hedgehog signalling enhances delivery of chemotherapy in pancreatic cancer (*Science* 2009). **Gallagher** imaged pH *in vivo* using hyperpolarised $^{13}$C-labelled bicarbonate MR (*Nature* 2008). **Markowetz** developed statistical methods to integrate complementary molecular data for cancer subtype identification and stem cell fate (*Nature* 2009). **Du** identified genes involved in MALT lymphoma (*Science* 2011).

**Future Strategy.** Our key strategic aim is to undertake research that will, ultimately, lead to improved patient outcomes through: 1) early detection and early, effective intervention; and 2) improved therapy of established cancers based on a better understanding of their biological heterogeneity. We will achieve these by catalysing interaction across scientific disciplines and across the laboratory-clinical interface, by creating the resources and pump-priming funds that will encourage new ideas to emerge and take root, and by working with CUHP to create the best clinical environment for true translational research and clinical innovation. Specifically, we will establish an **Integrative Cancer Medicine Programme** to address the following challenges: (i) **Earlier detection and intervention**. We will focus particularly on lung and oesophageal adenocarcinoma, because these are currently often diagnosed at advanced stages; we will harness our great strengths in basic laboratory science and computational biology to our world-class expertise in genetic epidemiology and Public Health (see UoA2) supported by a well-developed Primary Care Research Network; (ii) **Improving the targeting of therapy in invasive cancer**. This will exploit insights into molecular pathogenesis and drug resistance with the aim of accelerating pre-clinical and clinical drug development. We will achieve this through the integrated clinical application of genomics, molecular pathology and novel imaging approaches to improve cancer management decisions and by rational drug development based on understanding molecular mechanisms underlying cancer behaviour. The importance of computational biology to our strategy is emphasised by the appointment of **Tavaré** as Director of the CRUK CI emphasising our commitment to applying computational techniques in cancer research; (iii) **Bringing the full power of other disciplines in Cambridge to bear on cancer**, especially physical sciences, chemistry, biology and engineering. To do this we will establish an **Innovation Incubator Laboratory** that will integrate and exploit state-of-the-art thinking and technologies that can be used to detect, stratify and treat cancer. Cambridge has had prior success in the creation and clinical implementation of transformative technologies such as Illumina sequencing, bioinformatics, sequencing of epigenetic marks, molecular imaging using $^{13}$C-MRI/MRS, and the characterization of circulating tumour DNA as a liquid biopsy. This Incubator will also benefit from collaborative input from the Sanger, the Stem Cell Institute, the Cambridge-Manchester CRUK Imaging Centre, and the Network in Physical Biology. Other opportunities to deliver on our strategy will be provided by recruitment to the Li Ka Shing Chair of Oncology and the Chair of Surgical Oncology, the fitting out and opening of the 3$^{rd}$ floor of the CRUK CI building which will allow the recruitment of ~ 10 new research groups and the move of AstraZeneca to Cambridge.

**2. Infection and Immunity**

**Progress since 2008.** Infection and Immunity is a major strategic priority of the University, and is the second largest theme in UoA1, returning 56 Cat A staff. In RAE 2008 our strategic aims included ***enhanced integration of this discipline***, which is housed in different locations in the University (Depts of Medicine, Pathology, Medical Genetics and Surgery, CIMR and CRUK CI) with cognate work at the Babraham and Sanger Institutes. We achieved this through the formal establishment of the **Cambridge Infectious Diseases Strategic Initiative** and the **Cambridge**

**Immunology Strategic Network.** These nucleate their respective subjects through seminar series, websites, scientific meetings and training activities and help integrate the University research effort with outside bodies such as the Sanger and the Babraham Institutes. Joint appointments have assisted this (e.g. **Peacock** and **Bentley** with Sanger, **Randow** with LMB). We also emphasised the need for ***strategic recruitment in basic and applied immunology and infection*** and have made considerable progress in this regard. **Smith GL FRS** was recruited to lead the Dept of Pathology. **Goodfellow** obtained a Wellcome Trust Senior Research Fellowship to support his work on noroviruses and caliciviruses. **Weekes** and **Dolken** were appointed to University Lecturer positions with the aim of strengthening herpes research. Research in bacterial genomics has been catalysed by the appointment of **Peacock** (Professor of Clinical Microbiology) and **Bentley**. In immunology we recruited **Kaser** to a new Chair of Gastroenterology, **Jayne** to head the new Division of Experimental Medicine and Immunotherapeutics, and appointed **Clatworthy** to a University Lectureship. **James** (Wellcome Trust Career Development Award) and Modis (Wellcome Trust Senior Research Fellowship awarded; to commence 2014) have been recruited from UCSF and Yale to University space in the LMB. We have delivered major milestones on our aim to **build on our initiatives in Translational Immunology** with our programmes in Type 1 diabetes (**Todd, Wicker, Waldron-Lynch**), inflammatory bowel disease (**Kaser, Lee J**, **Parkes**, Category C), ANCA-Associated Vasculitis (**Jayne**, **Smith K.**) multiple sclerosis (Sawcer and Compston, UoA4) and tuberculosis (**Floto**, **Nejentsev**) This translational focus is supported by major collaborative initiatives with GSK and MedImmune, and recognised by the Theme's designation as a **Federation of Clinical Immunology Societies International Centre of Excellence**. The theme has been actively involved in plans for expansion of the ACRC and the creation of the new Division of Experimental Medicine and Immunotherapeutics. The decision of GSK to retain its Clinical Unit in Cambridge and to refocus its principal activity on Immuno-Inflammation with the appointment of an academic rheumatologist as its Director is of great significance for our research in this area. Our development of a Cell-Phenotyping Hub providing flow- and microscopic-based imaging for unscreened human samples, and advanced CL3 facilities allowing the study of tuberculosis are crucial developments underpinning this Theme The final strategic aim set out in 2008 was to enhance Cambridge's contribution to global health. Our success in this is exemplified by **Dunne** and **Peacock**'s successful application for a Wellcome Trust Centre for Global Health Research (WTCGHR). Translation in the area of infectious diseases includes a major award of $7.6m to **Lee H** to develop point-of-care diagnostics, and a Health Innovation Challenge Fund award of £4.5m to **Peacock** to bring molecular microbiology to the clinic.

**Selected Research Highlights.** ***Immunology*** Two new cell types have been discovered, the nuocyte (or ILCL2) (**McKenzie**, *Nature,* 2010, *Nat Imm,* 2012) and the T follicular regulatory cell (**Smith K**, *Nat Med* 2012). **Fearon** identified new pathways of CD8 T cell memory generation (*Science* 2009), and a sub-set of fibroblasts with major implications for cancer immunotherapy and metabolism (*Science* 2010) and cachexia (JEM 2013). **Randow** discovered novel mechanisms of intracellular pathogen resistance (*Nat Imm* 2009; *Mol Cell* 2011; *Nature* 2012). **Trowsdale** and **James L** (Cat C) showed that TRIM21 is a potent Fc receptor leading to the important new concept of antibody-dependent intracellular neutralisation (*Nat Imm* 2013). **Moffett** demonstrated how HLA class I molecules are involved in control of pregnancy as well as HIV (*Nat Gen* 2009). **Nathan** discovered immune-specific pathways of protein degradation (*Cell* 2013), **James J** new molecular mechanisms of TCR activation (*Nature* 2012), and **Nejentsev** has defined a new immunodeficiency syndrome (*Science* 2013). ***Autoimmunity*** In inflammatory bowel disease (IBD), **Kaser** discovered the role of the unfolded protein response (*Cell* 2008) and the key changes underlying IBD-associated malignancy (*Nature* 2013). **Lee J** and **Smith K** discovered a FOXO3-driven pathway that determines outcome in Crohn's Disease, and extended this to malaria and rheumatoid arthritis (*Cell* 2013). **Parkes** (Category C) continues to uncover the genetic underpinning of both Crohn's Disease and ulcerative colitis (*Nat Gen* 2008, 2010; *Nature* 2010). **Smith K** discovered biomarkers predicting outcome in vasculitis and SLE (*Nat Med* 2010) now entering clinical trials and **Jayne** demonstrated that Rituximab is an effective treatment for ANCA-Associated Vasculitis (*NEJM* 2008). **Cooke** developed stem cells from the NOD mouse (the best animal model of type-1 diabetes) (*Nat Med* 2009), and **Todd** continues to uncover the pathogenesis of Type 1 diabetes (*Nat Gen* 2008; *NEJM* 2008), including the role of rare variants (**Nejentsev** *Science* 2009) and, with **Wicker** and **Waldron-Lynch,** is pioneering novel therapeutic

approaches. ***Transplantation*** *w*ork has focussed on optimising organ donation (**Bradley A** *Lancet* 2010, 2012), and establishing an iPSC bank for HLA-matched transplantation (**Bolton** *Cell Stem Cell* 2012). ***Bacteriology and Parasitology*** A major new genomics initiative has examined bacterial evolution within outbreaks of pneumococcus (**Bentley** *Science* 2011), MRSA (**Bentley** *Science 2010*, **Peacock** *NEJM* 2012), Chlamydia trachomatis and Clostridium difficile (**Parkhill** Cat C, *Nat Gen* 2012,2013), Cholera (**Dougan** Cat C, *Nature* 2011), Tuberculosis (**Peacock** *NEJM* 2013) and other mycobacterial infections (**Floto**, *Lancet* 2013). ***Virology*** **Lehner, Weekes, Sinclair** have made key insights into CMV latency (*Science* 2013) and **Smith GL** into the rapid spread of viral infection (*Science* 2010).

**Future Strategy**. To enhance our delivery of research of global clinical relevance, we will develop a ***new institute focussed on translational immunity and infection.*** This will be housed in 4000m$^2$ of the new 16000m$^2$ building which will also contain the Stem Cell Institute. The Immunity and Infection component of this building will have two major sub-themes: 1) **Immunotherapeutics**, translating fundamental immune discoveries into patient benefit via detailed phenotypic analysis of patients and novel experimental medicine approaches. This will be closely linked to a new Division of Experimental Medicine and Immunotherapeutics and involve important industrial collaboration; and; 2) **Pathogen Control**, generating novel approaches to confront the global challenge caused by the spread of antibiotic resistance in pathogens. In both areas progressive development of our strategic relationship with the Sanger Institute will be a priority. We will exploit recruitment opportunities in the Dept of Pathology and in the new University space in the LMB to attract high quality young investigators. Opportunities for translational research in Transplantation will be enhanced by the move of Papworth Hospital to the Cambridge Biomedical Campus, which will become the largest solid organ transplant centre in the UK.

**Systems Medicine**

Many important medical problems involve disruption of the normal cross-talk between different organs and will be best tackled by taking an approach that involves integrating advances in molecular and cell biology with the study of the physiology of systems. In this regard we include three Systems Medicine 'subthemes', namely Metabolic and Related Diseases, Cardio-Respiratory Disease and Reproductive Medicine. In each of these subthemes, researchers from different departments increasingly interact through a range of mechanisms, including cross-departmental institutes and postgraduate training programmes e.g. 4-yr PhD programmes in Metabolic and Cardiovascular Disease and Mathematical Genomics and Medicine (both Wellcome Trust), and Cardiovascular Research (BHF).

**3. Metabolic and Related Diseases**

**Progress since 2008.** The University has increased its commitment to this subtheme (including the establishment of a Strategic Network in Metabolism), which now includes 36 Cat A staff. We have delivered our principal strategy of producing a body of world-leading research in basic and translation metabolic science through the development of a multidisciplinary research institute with excellent core facilities. In 2008, in partnership with the MRC and CUHFT, the University formally opened the Institute of Metabolic Science (IMS). The IMS, co-directed by **O'Rahilly** FRS and Wareham (UoA2) initially consisted of three entities: 1) The University of Cambridge Metabolic Research Laboratories (MRL) (Director **O'Rahilly**) devoted to laboratory-based and translational science; 2) The MRC Epidemiology Unit (now an MRC-University Unit, Director, Wareham) focused on population-based approaches to studying obesity and diabetes; and 3) CUHFT's ambulatory care facilities for endocrine and metabolic disease. In 2013 the Wellcome Trust and MRC provided a total of >£23M of new funding to establish the Wellcome Trust–MRC Institute of Metabolic Science. This includes capital for the construction of two clinical research floors devoted to metabolic disease, and funding to enhance core lab facilities (jointly with the CIMR) and to support collaborative work with the Sanger Institute. The MRC provided ~£10M to upgrade our existing MRC Centre to a MRC-University Unit (the Metabolic Diseases Unit) directed by **O'Rahilly**. A major aim of the IMS is to facilitate cross-disciplinary interactions between basic and clinical scientists, epidemiologists and clinicians to maximise the impact of research and improve the quality of patient care. Clinical research in metabolic disease in Cambridge also benefits greatly from our NIHR BRC. In Type 1 diabetes, research is focused on aetiology and early intervention based on immune mechanisms (**Todd, Wicker** and **Waldron-Lynch**). We have a strong programme of research in the artificial pancreas (**Hovorka, Evans, Dunger**, **Murphy**).

Research in the therapy of lysosomal disorders has been greatly strengthened by the recent award of major MRC Translational research grants totalling over £6.5M to **Cox** to 1) improve outcomes in Gaucher disease through disease stratification, and 2) build on successful trials in animal models to develop a clinical trial of gene therapy for neuronal Lysosomal Storage Disorders. Research in metabolic and related diseases has been greatly strengthened by recruitment, progression of early career scientists to independent fellowships, and the success of our scientists in obtaining large grants. Since 2008, **O'Rahilly, Chatterjee** and **Maxwell** have obtained Wellcome Trust Senior Investigator awards, **Ron** a Wellcome Trust Principal Research Fellowship, **Farooqi, Savage, Semple**, **Reddy, Gribble** Wellcome Trust Senior Fellowships (clinical) and **Volmer**, **Schoenmakers** and **O'Neill** (Cat C, now moved to LMB) Wellcome Career Development fellowships. **Constancia** (University Lecturer) and **Murphy** (NIHR Intermediate Fellow) have all been newly recruited. Importantly, a generous donation allowed us to establish the Bernard Wolfe Chair in Health Neurosciences (Fletcher UoA4) which forges a strong link between research in the neuroscience of human appetite and its disturbances in obesity.

**Selected Research Highlights. Farooqi, Barroso** and **O'Rahilly** defined novel mechanisms of severe, early-onset human obesity (*Cell* 2013*, Nature* 2011), including the first descriptions of copy number variation impacting on the risk of obesity (*Nature* 2010, *Nat Gen* 2013). **Semple, Barroso** and **O'Rahilly** defined a new class of disorder of constitutive activation of insulin signalling (*Science* 2011) and demonstrated that somatic mutations in PI3kinase catalytic subunits cause a syndrome of regional overgrowth (*Nat Gen* 2012) with that information now being translated into a therapeutic trial. **Savage, Semple, Barroso** and **O'Rahilly** discovered and characterised several novel human syndromes of insulin resistance (*NEJM* 2011, *Nat Gen* 2013). Highly productive collaboration with Wareham (UoA2) has identified common genetic variation in common metabolic disease (*Nat Gen* 2009, 2010, 2011, 2012, 2013). **Chatterjee** described the phenotype of humans with mutations in thyroid hormone receptor alpha, elucidating, for the first time, the human biology of this crucial receptor (*NEJM* 2012) and a novel cause of human central hypothyroidism (*Nat Gen* 2012). **Semple** and **O'Rahilly** established Neurokinin B as a regulator of the human reproductive axis (*Nat Gen* 2009). **Reddy** and **O'Neill** (Cat C) made paradigm-shifting observations regarding the non-transcriptional basis for metabolic circadian rhythms (*Nature* 2011, 2012). **Gribble** and **Reimann** were the first to transgenically label, isolate and study specific enteroendocrine cell populations of the gut (*Cell Metab* 2008), research which has generated extensive collaborations with industry. **Ron** established that endoplasmic reticulum thiol oxidase deficiency leads to ascorbic acid depletion and non-canonical scurvy in mice (*Mol Cell* 2012) **Vidal-Puig** discovered a novel regulator of brown fat development and activation (*Cell* 2012), and established the role of hypothalamic AMPK in the central effects of thyroid hormone on energy homeostasis (*Nat Med* 2010). **Hovorka, Evans, Dunger** and **Murphy** made major advances in the application of artificial pancreas technology to the treatment of adults, pregnant women and children with Type 1 diabetes (*BMJ* 2011*, Lancet* 2010).

**Future Strategy.** We will build on our multidisciplinary programme of research in obesity, diabetes and related endocrine and metabolic diseases with a tight link between basic and clinical science. The IMS, with its two embedded MRC-University Units will provide crucial infrastructure for our work. Our capacity to phenotype human participants will be greatly enhanced by the construction of new, dedicated facilities for clinical metabolic research in the ACRC. We will strengthen our research in the biology of appetite through enhanced links with the Wellcome-MRC Behavioural and Clinical Neurosciences Institute (BCNI, UoA4) in basic and clinical research. We will develop a new facility dedicated to the study of human eating behaviour. We will build on recent exciting discoveries in circadian biology (Reddy) to examine their relevance to human metabolic disease. With MRC support we will appoint two New Blood Fellows in Basic Metabolic Science, and anticipate that at least one of these will work in the area of hypothalamic function and appetite, and link with the BCNI. We will forge ever-closer links with the CIMR, facilitated initially through establishing shared core facilities in proteomics and cell imaging. We will build on existing extensive links with the Sanger Institute [**O'Rahilly** and **Vidal-Puig** are Associate Faculty and **Barroso** (Cat C), Joint Head of Human Genetics at Sanger, has a part-time position in the MRL] in the area of human genetics and more fully exploit the power of the Sanger in the area of model organisms. The creation of a Heart and Lung Institute adjacent to the IMS provides exciting opportunities for synergy between metabolic and cardiovascular research. We will build on our extensive and wide-ranging links with industry. In particular, we have a close relationship with

Medimmune, the 'biologics' division of AstraZeneca, and we will be key partners for AstraZeneca as they develop their major facility on campus. In addition to the work on the causes and consequences of obesity, we will continue to develop our internationally-leading programmes in the treatment of Type 1 diabetes, the genetics of thyroid disease and the therapy of lysosomal storage disorders, and will nurture our growing programme of research in metabolic bone disease in association with leading researchers in physical and engineering sciences.

**4. Cardiovascular and Respiratory Disease**

**Progress since 2008**. In light of growing synergies between cardiovascular and respiratory research, in this REF we have linked research from these two areas in a single subtheme, which is represented by 29 Cat A staff working across the Depts of Medicine, Haematology and Radiology. There are strong links with cardiovascular epidemiology, led by Danesh (UoA2) with research programmes in other Schools and with neighbouring research institutes. Strategic aims in our 2008 RAE submission included integrating cardiovascular biology, population sciences and functional genomics through the appointment of new senior scientists, establishing formal programmes of post-graduate training in cardio-respiratory research, and investment and recruitment in regenerative medicine. These objectives have been achieved through major research awards including the £3M BHF Centre for Research Excellence, the £2.5M BHF Oxbridge Centre for Cardiovascular Regenerative Medicine, BHF and Wellcome Trust (with Metabolism) 4-year PhD programmes (£2.5-5M each), 2 Chairs (**Morrell**, **Mallat**), 5 Senior Research Fellowships (**Wilkinson**, **Floto**, **Marciniak**, **Clarke**, **Sinha**), including 2 of only 5 Wellcome Trust or MRC Senior Clinical Fellows in Respiratory Medicine in the UK [a 3rd is under review (**Nathan**)], 1 HEFC Senior Lectureship (**Rudd)** and 6 Intermediate/Clinician Scientist Fellowships (**Foo**, **Clarke**, **Ghevert**, **Gorenne**, **Ormiston**, **Sinha**). In 2009, the combined Phenotyping and Imaging Centre and the Anne McLaren Laboratory for Regenerative Medicine were established utilising funds from SRIF (£8.4M), the BHF (£0.5M) and MRC (£2M), with dedicated research laboratories and state-of-the-art cardiovascular imaging and phenotyping cores for the study of model organisms This building also acts as the hub for the BHF 4-yr PhD programme in Cardiovascular Research. Cardiovascular Disease is one of eight research themes supported by the comprehensive NIHR BRC, with Respiratory Medicine receiving similar levels of support via the Infection and Immunology theme; **Wilkinson** heads the newly established and accredited CUHP Clinical Trials Unit which has transformed our ability to translate our research to the clinic.

**Selected Research Highlights. Ouwehand** identified 22 loci associated with eight haematological parameters (*Nat Gen* 2011), and genes that underlie the Vel blood group (*Nat Gen* 2013). **Brown** determined the optimum antihypertensive treatment in different patient groups, regimes incorporated into both national and international hypertension guidelines, and the role of new antihypertensive agents (*Lancet* 2011). **Mallat, Bennett** and **Clarke** established the fundamental role of innate and acquired immunity in atherosclerosis and aneurysm formation (*Nat Med* 2013; *Immunity* 2013). **Brown** and **Davenport** identified novel mutations and their function in Conn's syndrome (*Nat Gen* 2013). **Sinha** established induced pluripotent stem and human embryonic stem cells as models for inherited vascular disease and drug testing (*Nat Biotech* 2012). **Floto** demonstrated transmission of *Mycobacterium abscessus* between patients with cystic fibrosis (*Lancet* 2013). **Chilvers** conducted the first $^{99m}$Tc-labelled autologous eosinophil scans in humans (*Blood* 2012).

**Future Strategy**. We will capitalise on the major opportunities for basic and translational cardio-respiratory research provided by the new BHF Centre for Cardiovascular Research Excellence, the BHF Centre for Cardiovascular Regenerative Medicine and the relocation of Papworth Hospital to the Cambridge Biomedical Campus in 2015-2016. These initiatives will drive selective recruitment, improve career development and fostering of interdisciplinary research, enhance translation of research for patient benefit, and create an environment that will enable us to attract world-leading researchers. Our major goal will be to foster interdisciplinary research between cardiovascular and respiratory biologists, and to work with experts in population sciences, functional genomics and genetics to address major unanswered questions in this disease area. To this end we plan to create a new multi-disciplinary, University-wide Cambridge Cardiovascular Strategic Initiative, to harness the unique opportunities for synergies that exist across the University Schools and clinical landscape. Major themes will include defining the genetic architecture and gene-environment interactions in both common (e.g. atherothrombosis) and rare but important diseases (e.g. pulmonary arterial hypertension, bleeding and platelet disorders), exploiting next generation

sequencing and computational biology approaches, and strengthening links with the Sanger Institute, Institute of Public Health and the MRC Biostatistics Unit. BHF Centre funding will foster collaboration between cardiorespiratory biologists and researchers in developmental and stem cell biology to identify tractable mechanisms of disease and routes to regenerative medicine applications. We will exploit links with immunology (e.g. CIMR), metabolic sciences (e.g. IMS) and signalling (e.g. Babraham Institute) to define new treatment paradigms for atherosclerosis and inflammatory lung disease. We will pursue the development of new imaging techniques and biomarkers for the identification of vulnerable plaque and early lung disease. The University/Papworth Hospital partnership has committed to establishing a £41M Heart and Lung Research Institute configured to support wet laboratories for 12-15 PIs and their research groups, with a clinical trials unit, R&D offices and education space adjacent and linked to the new hospital. 40% of the planned laboratory space will be for recruitment of new investigators. This new Heart and Lung Research Institute will drive a step change in industrial and interdisciplinary collaborations.

**5. Reproductive Biology and Medicine**

**Progress since 2008.** We have succeeded in our aim of creating a critical mass of researchers in reproductive biology applied to medicine and return 6 Category A investigators. We have succeeded in delivering this through the growing success of **Constancia** (who co-leads a Programme in the new MRC Metabolic Diseases Unit), **Charnock-Jones** who, since 2008, has co-directed a Wellcome Trust programme with Burton (UoA5) to study maternal-fetal interaction and **Moffett** who has strengthened her programme of research in reproductive immunology and works closely with the recently recruited **Colucci.** Reproductive Medicine research has benefited greatly from the Centre for Trophoblast Research (CTR) which supports studentships and 'next-generation' fellowships. **Smith GC** has used funding from the NIHR BRC to develop a prospective study of human pregnancy and outcome of the offspring, involving deep phenotyping of pregnant woman. This provides a highly fruitful resource for translational research and is supporting a number of Wellcome Trust and MRC funded programmes

**Selected Research Highlights. Smith GC** demonstrated that the risk of Caesarean section for dysfunctional labour at term was closely related to the length of the cervix in mid-gestation (*NEJM* 2008) and an excess risk of neonatal death due to asphyxia during labour at term in births during evenings and weekends in Scotland (*BMJ* 2010). **Colucci** discovered molecular mechanisms of immunological recognition of melanoma by NK cells (*Science* 2010). **Moffett** showed that maternal activating KIRs protect against human reproductive failure mediated by foetal HLA-C2 (*JCI* 2010).

**Future Strategy.** We will develop our research examining placental dysfunction and its role in complicated pregnancy. Studies using our unique human cohort should identify novel mechanisms and pathways involved in adverse pregnancy outcomes, and we will exploit this to identify novel biomarkers for clinical application. Candidate molecules identified in the human studies will be evaluated *in vitro* and in animal models to refine our understanding of the pathophysiological cascades. Research in Reproductive Immunology will be developed further through the evolution of the work of **Colucci,** using the collaborative international networks that **Moffett** has established.

**6. Genomics, Structural and Cell Biology, and their application to Medicine**

**Progress since 2008.** Genomics, Structural and Cell Biology research that together underpins many modern advances in diagnosis and therapy is represented by 33 staff returned in UoA1. As proposed in RAE 2008 this research has developed strongly, centred on the critical mass of investigators in the CIMR (Director, **Griffiths** FRS) and the Depts of Pathology (Head of Department, **Smith GL** FRS) and Medical Genetics (Head of Department, **Maher**). The CIMR is a cross-departmental, inter-disciplinary institute that provides a unique interface between basic and clinical science, with a major focus on the molecular mechanisms of disease. A distinctive feature of the CIMR is that, since its foundation in 1998, over 40% of its PIs have been clinically active, enabling the CIMR to be effective in translating scientific discovery to patient benefit. The CIMR is a key element of the University's biomedical research vision and strategy, and currently has an annual grant spend of £21M, 60% funded by awards from the Wellcome Trust, including a Strategic Award (renewed in 2012, £4.7M over 5 years). Among awards from the Wellcome Trust, held by PIs returned in UoA1 under this theme, there are five PRFs (**Griffiths, Owen, Read, Robinson, Rubinsztein**), a Senior Investigator (**Maxwell**) and a Senior Clinical Research Fellow (**Reid**), as well as 3 MRC Senior Research Fellows [**Seaman, Siniossoglou** (basic) and

**Marciniak** (clinical)] and a Royal Society University Research Fellow (**Deane**) whose laboratories are in the CIMR. Research in the CIMR is focussed in three main areas: intracellular membrane traffic in health and disease; genetics of cell function and dysfunction in disease; and misfolded proteins and disease. These themes are strengthened by interactions with investigators housed outside the CIMR, especially in the Depts of Pathology and Medical Genetics. Members of the Dept of Medical Genetics play a leading role in the NIHR BRC cross-cutting research theme on Genomics, the NIHR supported Cambridge BioResource, which consists of thousands of volunteers who participate in research studies investigating the links between genes, the environment, health and disease, and were instrumental in establishing core genomics facilities that in 2013 was subsumed into the Genomics Core facility at the CRUK CI and the NIHR BRC Cambridge Translational Genomics laboratory.

**Selected Research Highlights.** ***Intracellular membrane traffic in health and disease*** **Owen** has shown how the major endocytic clathrin adaptor, the AP2 complex, is recruited to the plasma membrane and then selects for incorporation into endocytic CCVs cargoes that contain the most widely used trafficking motifs (*Nature* 2008; *Cell* 2010). **Owen, Luzio** and **Robinson** discovered that SNARE proteins, required for all membrane fusions, are actively trafficked by unique interactions with clathrin adaptor proteins and do not compete with cargo proteins employing the most widely used trafficking motifs (*Nature* 2007; *Cell* 2008, 2011; *Dev Cell* 2012). **Griffiths** identified the pathways controlling centrosome polarisation in cytotoxic T lymphocytes that regulate polarised secretion to destroy virally infected and tumorigenic cells (*Immunity* 2009). **Watson CJ** showed how Stat3 regulates lysosome mediated cell death in post-lactational regression of the mammary gland (*Nat Cell Biol* 2011), **Rubinsztein** made major contributions to understanding the origin of the autophagosome membrane, maturation of autophagosomes, fusion with lysosomes, and the relationship of autophagy to the ubiquitin-proteosome pathway (*Mol Cell* 2009; *Nat Cell Biol* 2010; *Cell* 2013), and **Buss** demonstrated the role of myosin motors in autophagy (*Nat Cell Biol* 2012). ***Genetics of cell function and dysfunction in disease*** **Woods** identified genes giving rise to autosomal recessive primary microcephaly, all of which encode centrosomal components required for centriole replication in the centrosome (*Nat Gen* 2010, 2011), **Raymond** discovered gene abnormalities that cause intellectual disability (*Nat Gen* 2010), **Sandford** identified new susceptibility loci for primary biliary cirrhosis (*Nat Get* 2012), and **Maher** discovered genetic causes of Wilm's tumour (*Nat Gen* 2012). ***Misfolded proteins and disease*** **Rubinsztein** showed that the toxicity of mutant proteins, which cause a range of related neurodegenerative diseases, including Huntington's disease, can be alleviated in cell and animal models by enhancing autophagy using small molecules (*Nat Chem Biol* 2008). **Read** uncovered a new mechanism for the modulation of blood pressure, in which the redox state of the serpin angiotensinogen affects its activity as a substrate for renin (*Nature* 2010). **Marciniak** and Lomas (who moved to UCL in 2012) showed that Z $\alpha_1$-antitrypsin is retained within hepatocyte endoplasmic reticulum following the formation of ordered loop-sheet polymers and identified mechanisms through which alteration of endoplasmic reticulum function affects cell growth and survival (*NEJM* 2010).

**Future Strategy.** Over the next five years the CIMR will develop further as a centre for cellular medicine, enhancing its inter-disciplinary environment. There will be a scientific focus on using cell biology to understand pathogenic mechanisms and pathways of disease in order to contribute to diagnosis and therapy as well as creating 'bi-directional' translation by using recent advances in the pathogenesis and genetics of disease to inform research on fundamental cell biology. This will complement research in the Dept of Pathology where fostering translational opportunities that lead to effective diagnostic and treatment regimes will continue to be a strong focus. Novel human disease gene discovery by large-scale exome and genome resequencing studies will continue apace, complemented by increasing numbers of studies into the role of genomics in clinical practice and the role of epigenetic modification/non-coding regulatory sequences in disease pathogenesis and expression.

**7. Stem Cell Biology and Medicine**

**Progress since 2008.** Over the past 5 years the basic biology and biomedical potential of stem cells has developed into a major research field in Cambridge, identified as a University Strategic Research Initiative. Targeted recruitment at both senior and junior levels has led to international recognition and formation of the Cambridge Stem Cell Institute (SCI) with joint core support from The Wellcome Trust and MRC. The SCI brings together 25 laboratories comprising over 150 post-

doctoral researchers and PhD students (http://www.stemcells.cam.ac.uk/). 9 principal investigators are returned in UoA1 (all presently located in existing accommodation on the Cambridge Biomedical Campus including space refurbished since 2008) with the remainder in UoA5 (located in central Cambridge). Equal attention is paid to embryonic and tissue stem cells. Fundamental research is focussed at the molecular level on mechanisms governing self-renewal, commitment, differentiation and reprogramming. These studies extend naturally into interrogation of stem cell functions in development, physiology, pathology and tissue repair. Patient-specific induced pluripotent stem cells are used to model degenerative processes and dissect mechanisms of molecular pathogenesis. Pre-clinical and clinical studies evaluate recruitment of endogenous stem cells for regeneration and transplantation approaches to cell replacement. The concept that leukaemias and some solid tumours originate through dysregulation of normal stem cells and may be maintained by distinct 'cancer stem cells' is a focus of investigation. Myeloid malignancies, transcriptional regulation of blood stem and progenitor cells, developmental haematopoiesis and megakaryopoeisis are particular research strengths. The haematopoiesis community has strong collaborative links with the Babraham Institute and especially the Sanger Institute – two clinically trained haematologists (**Campbell, Vassiliou,** Cat C) are on the faculty of the latter. Cambridge has also been designated as a Specialised Centre of Research by the US based Leukemia and Lymphoma Society (LLS), with a centre grant of $6M over five years. Cambridge is currently the only such LLS centre outside the USA. The recent appointment of **McCaskie** to a new Chair of Orthopaedic Surgery (from Sept 2013) has strengthened translational stem cell medicine. He is Director of the Arthritis Research UK Tissue Engineering Centre that seeks to understand how autologous stem cells can be harnessed to repair early bone and cartilage defects, with an emphasis on early clinical trials in patients with osteoarthritis. Transplantation and Regenerative Medicine is one of eight research themes in the NIHR BRC. In conjunction with the SCI, the BRC has established both a core facility to generate induced pluripotent stem (iPS) cells from patient groups for disease modelling and drug-development research, and a Stem Cell GMP facility. Building on these developments, Cambridge is partnering with the Universities of Sheffield and Loughborough in the new UK RMP 'Pluripotent Stem Cell Platform' hub. The SCI also profits from multiple collaborations with groups at neighbouring research institutes Core technology platforms and resources in the SCI include stem cell culture, advanced flow cytometry, *in vitro* and *in vivo* cell tracking, bioinformatics, and, most importantly, mouse and rat transgenesis. The SCI hosts the only Wellcome Trust PhD Programme in the UK dedicated to stem cell biology and medicine.

**Selected Research Highlights. Vallier** and **Marciniak** provided the first proof of principle for the potential of combining human induced pluripotent stem cells with genetic correction to generate clinically relevant cells for autologous cell-based therapies, specifically taking us closer to a cell based therapy for 1-antitrypsin deficiency and the serpinopathies (*Nature* 2011). **Dawson**, **Gottgens**, **Green** and **Kouzarides** identified a novel function for Janus kinase 2 (JAK2) in the nucleus of haematopoietic cells that has provided new insights into haematological malignancies (*Nature* 2009), and **Dawson**, **Huntly** and **Kouzarides** showed activity in acute myeloid leukaemia of a new class of small molecule inhibitors targeting protein interactions between transcriptional regulators (*Nature* 2011). Ferguson-Smith (UoA5) and **Green** identified a new pathogenetic mechanism associated with acquired chromosome deletions (*JCI* 2013), and Alexander (Babraham Inst) and **Pedersen** reported novel insights into the mechanisms and consequences of TGF-beta family-induced stem cell differentiation (*Cell Stem Cell* 2011). **Huntly** and **Green** showed that oncogenic tyrosine kinases inhibit the normal response to DNA damage by primary cells from patients with myeloid malignancies (*NEJM* 2008).

**Future Strategy.** We aim to maximise interaction and synergy between basic researchers and clinician scientists in the area of stem cell medicine and to develop a critical mass of internationally leading researchers applying stem cell biology to questions of disease pathogenesis and therapy

In order to facilitate this we will build a purpose-designed 16000m$^2$ research building (estimated cost £70M) on the Cambridge Biomedical Campus, 8000m$^2$ of which will house the SCI, bringing together SCI scientists presently located in central Cambridge and on Cambridge Biomedical Campus. It will be the main location for both fundamental and translational stem cell research.

**c. People, including:**

**i. Staffing strategy and staff development**

Our overall staffing strategy is to develop and strengthen critical mass in our key thematic areas identified above, to exploit the potential for inter-disciplinary research within the University, and to

make appointments that strengthen our links with nearby research institutes, teaching hospitals and major industrial R&D facilities. Honorary clinical appointments for medically-qualified academics, joint cross-school appointments and joint appointments with industry (e.g. Bullmore, UoA4) are used to maximize these links. Whilst we are mindful of the need to appoint research leaders we also pay attention to appointing and developing early career researchers and other research and support staff who underpin our research excellence. The University operates an employer-justified retirement age of 67, which ensures that vacancies arise in established posts to allow renewal of our cohort of research leaders. All staff returned under UoA1 are members of University Depts and Institutes that follow the codes of practice published on the University website, and all staff undergo initial induction, mentoring and regular appraisal to assist career development.

For senior academics, the University offers an annual four day leadership training course that includes strategy development. Development of established academic staff is also supported through entitlement to sabbatical leave for University Lecturers and above, at the rate of one term for every six terms of service (part-time workers accrue sabbatical leave entitlement on an equivalent basis). We provide support for staff at key career transition points, including promotion to personal professorships, readerships and senior lectureships based on significant international research reputation and strong external support that is run through an annual competitive exercise with final decisions made by a committee chaired by the Vice-Chancellor. Since 2008, 6 Category A staff eligible for return in UoA1 were promoted to Senior Lecturer, 10 to Reader, 16 to Professor and 3 (**Farooqi, Gribble** and **Wilkinson**) to Reader then Professor. A related promotion scheme operates for research staff.

The University is committed to the seven principles of the Concordat to support the career development of researchers and, in recognition of its work in this area, has received the European Commission's 'HR Excellence in Research' award. The University launched its Employment and Career Management Scheme in April 2011, which sets out a clear framework for the induction, probation and appraisal of contract research staff. In addition to these policies the University also meets the Concordat principles in other ways including University-wide induction events (in the SCM there are quarterly induction events at which the Head of School meets and greets all new staff), an accommodation service that gives priority to new arrivals, transparent pay scales clearly aligned to grade profiles, extensive specialist and transferable skills training, and HR teams based in each School that support all staff. Depts/institutes are encouraged to involve research staff in decision-making processes such as committees and working groups. The SCM has a monthly staff newsletter and the larger departments/institutes also have regular newsletters to inform and involve all staff.

**Early career researchers.** The Depts and institutes covered by UoA1 all use the University's schemes supporting early career researchers. For newly appointed Lecturers, Pathways in Higher Education Practice offers personal, flexible orientation and professional development during the probationary period with full information on line at http://www.admin.cam.ac.uk/offices/hr/ppd/information/academic/phep/. The University Careers Service offers specialist careers advice for contract research staff and post-docs with a bespoke Life Science advice programme. In 2012, postdoctoral research workers became the largest staff group in the University (now over 37%). In response to this growth the University has embarked on a major property development in North West Cambridge (NWC). In the first, £300M, phase, due to open in 2015–16, high-quality and sustainable housing will be provided for over 600 postdocs and their families, together with retail and social facilities, and homes for graduate students and the private sector. In addition, the University has created the new role of Director of Postdoctoral Affairs (Prof. Chris Abell) who will coordinate and develop strategy for the entire postdoctoral community, spearhead fund-raising for further NWC facilities, and act as an advocate for postdocs in the governance machinery of the University. Already in existence is 'Postdocs Of Cambridge' (PdOC), chaired by Maya Ghoussaini (Oncology), which offers guidance and represents post-doctoral fellows on career development and employment conditions (http://groups.ds.cam.ac.uk/pdoc/cpd.shtml). PdOC links with the Graduate Students and Post-docs group at the SCM, which reports to the Graduate Education Committee and receives School funds for activities including specific skills seminars. Complementing this, a Clinical Academic Training Office (CATO) was established in 2009 by the SCM overseeing our externally funded research training programmes for clinicians, in particular the Academic Foundation, NIHR-Integrated Academic Training (ACFs

and ACLs) and NIHR BRC Training programmes as well as PhD and MPhil programmes (see below). CATO now reports on over £20M in funding, looks after over 380 trainees/students and, perhaps most notably, has been instrumental in expanding these programmes using local funding (e.g. a 50% increase in AFY posts, 35 additional non-NIHR funded local ACFs, and a doubling of ACL numbers, currently 64 within the School). CATO provides comprehensive administrative support for all its programmes, including handling the complex interface between the University, hospitals and HEEoE-Postgraduate office. CATO has influenced national policy through its Director (**Chilvers**) who sits on the Health Education England Medical Programme Board and Academy of Medical Sciences Council. Additional metrics include a 100% appointment rate for ACFs/ACLs for 2011-13, the award of 45 externally funded RTFs to ACFs and 25 Wellcome Trust/AMS Starter grants to our ACFs.

**Equality and Diversity.** In September 2013 the SCM won an Athena Swan Silver award covering all its depts and Institutes, in recognition of achievements in implementing working practices and activities that contribute towards a more positive working environment for all. This followed a thorough review of current equality and diversity policies and practices at the SCM that included a comprehensive action plan to address the priorities identified, along with a timeline for completion. The Silver Award for the SCM builds on the Bronze Award for the University as a whole. The University of Cambridge is committed to supporting Equality and Diversity and there are a number of infrastructures and policies in place at a University level. Led by a specialist Equality and Diversity team, the University of Cambridge abides by its Equal Opportunities, Disability and Dignity@Work policies, and a Combined Equality Scheme that sets out how it meets its commitment to equal opportunities. In 2009 it appointed Equality Champions within each dept who lead and support equality and diversity initiatives, including the Black and Minority Ethnic Staff Network, the Disabled Staff Network, the LGB&T Staff Network and the Women's Staff Network. Cambridge Occupational Health provides a support service that promotes and preserves both the physical and mental well-being of all staff, and the Disability Resource Centre advises staff on issues relating to disability in the University context and coordinates the University's network of Departmental Disability Liaison Officers. Since 2008, the University has maintained an advisory group on equal pay (currently the Gender Equality Group) and offers a range of equality and diversity training opportunities. The University's Women in Science, Engineering and Technology Initiative (WiSETI) promotes and supports women at all levels and organises activities including an annual WiSETI lecture, a CV mentoring scheme for women and career development seminars. Staff are entitled to paid maternity, paternity or adoption leave with graduated return from such leave and the opportunity for career breaks for exceptional/unforeseen family/domestic responsibilities. In this REF period, 212 staff in UoA1 depts/institutes took maternity leave, 62 paternity leave, 0 additional paternity leave, 10 parental leave and 2 adoption leave. University staff may request flexible working hours to fit in with care arrangements and a model flexi-time scheme is available applicable to all staff. The University has two workplace nurseries offering up to 100 places and it participates in the Cambridge Universities' Holiday Playscheme and the local Childcare Information Service. In 2010, the SCM established an Academic Clinical Women's Forum (ACWF), creating a network that now includes over 100 women researchers/academics with regular events. In 2012, an SCM Returning Carers Fund was established, with 19 researchers supported to date, receiving awards ranging from hundreds to thousands of pounds to enable them to return to their experimental work efficiently.

### ii. Research students

In the UoA1 depts and institutes there are currently over 100 PhD students starting each year, including MB/PhD students and students funded through theme-specific 4-year programmes (see below). For all students there is a rigorous recruitment procedure, including interview and a review after the end of the first PhD year before formal registration. Those on 4-year programmes are examined for a Master of Research degree at the end of the first (pre-PhD) year. Monitoring student progress includes a termly supervisor's report and oversight by a department/institute Local Graduate Education Committee. All students are also supported by a second supervisor and/or mentors and all are members of Cambridge Colleges that provide a further layer of tutorial/pastoral support. All students linked to UoA1 are members of the Graduate School of Life Sciences (GSLS), which is run jointly between the SCM and SBS. Through its website, the GSLS provides a comprehensive list of training offered across the University that may be of interest to

doctoral students in its departments and includes training in business skills through the Judge Business School and statistical training through the University Statistics Clinic. In addition to support provided to post-graduate students by the GSLS and Departmental/Institute Graduate Administrators, the SCM's CATO supports students on several graduate programmes including the Wellcome Trust Translational Medicine and Therapeutics, NIHR TRC Rare Disease Training, Wellcome Trust Mathematics, Genomics and Medicine (MGM), NIH OxCam Graduate and Howard Hughes Medical Institute (HHMI) Graduate Programmes (see below) as well the MPhil in Clinical Sciences. With the exception of HHMI, the Directors of each of these programmes are based in UoA1. CATO provides comprehensive administrative support these programmes, including support for the Directors. UoA1 students can also draw on the specific provision made by the University for all graduate students, including skills courses through the Cambridge University Skills Portal, the Graduate Development Programme, the University's Personal and Professional Development team, entrepreneurial skills courses offered by the Centre for Entrepreneurial Learning, language courses provided by the University Language Centre, bibliographic software and other courses run by The Cambridge University Library, public communications training by the Office of External Affairs and Communications and comprehensive careers advice from the Cambridge Careers Service. In the 2011 Postgraduate Research Experience Survey, 86% of respondents from Cambridge stated that their experience of their research programme either met or exceeded expectations, up from 81% in 2009.

Most of our research themes are associated with a 4-year PhD programme (several renewed in 2013), the majority of which are hosted in UoA1 depts or institutes. These include the CRUK CI PhD programme (10 students p.a); the Wellcome Trust programmes in Infection and Immunity (6 students p.a), Mathematical Genomics and Medicine (5 students p.a), for Clinicians (7 students p.a); Metabolic and Cardiovascular Disease (5 students p.a); Wellcome Trust and MRC programme in Stem Cell Biology (5 students p.a); the CIMR PhD programme (Wellcome Trust and MRC funded; 4 students p.a); BHF programme in Cardiovascular Research (4 students p.a); and NIHR BRC studentships (2 students p.a). Additional PhD programmes that encompass all research themes include the NIH-OxCam Graduate Partnership (11 students p.a.), students funded through the MRC DTA (up to 16 students p.a), the Howard Hughes Medical Institute Janelia Farm Graduate Programme (3 students p.a.) and the BBSRC Doctoral Training Programme across the SCM and SBS, including the Department of Pathology and partner institutes (up to 20 students p.a.). Two of our research themes have additional PhD studentship schemes/programmes: In cancer research, there is targeted entry through studentships held as part of the core provision to the Hutchison/MRC Institute, and the Gurdon Institute, competitive studentships within Integrated Academic Training Path ("Walport") programmes in Oncology and Clinical Imaging, the CRUK CI Molecular Pathology PhD programme (shared between Cambridge and Barts); in Infection and Immunity, there are MRC Capacity Building studentships. In addition to PhD students the £2.75M Translational Medicine and Therapeutics MPhil programme (funded jointly by the Wellcome Trust and industry through GlaxoSmithKline, with up to 14 students p.a.) 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. As well as the above programmes, UoA1 includes the MB/PhD programme that each year enables 8 students to undertake a 3-year full time PhD integrated within the standard undergraduate clinical course. This programme, led by **Cox**, is open to students from all medical schools in the UK subject to acceptance on the Cambridge clinical course and has been running since 1989. A recently review of outcomes (Cox et al., 2012. *Clin. Med.* 12: 530) showed 80% of its graduates remain in academic medicine. The success of the Wellcome Trust Research Capacity Building in Africa Programme led by Dunne, with strong links to Makarere University and the London School of Hygiene and Tropical Medicine was crucial to the success of Cambridge in being designated as a Wellcome Centre for Global Health Research.

**d. Income, infrastructure and facilities**

**(i) Income** In UoA1 research income has grown from £61m in 2008/9 to £83m in 2012/13. In most research themes there have been major strategic awards, many personal support awards (also in section b) and many programme grants, including: in Cancer, from CRUK to **Ponder, Kouzarides, Caldas, Murphy, Neal, Pharaoh, Coleman** and **Tavaré**, from MRC to **Venkitaraman, Watson**, from LLR to **Du, Green, Gottgens**; in Infection and Immunity, from MRC to **Hughes, Sinclair** and **K. Smith**, from WT to **Koronakis** (now Senior Investigator), **Cooke, Kaufmann, Trowsdale,**

**Moffet**, **Rudd** (PRF), **Smith GL** (PRF), **Goodfellow** (SRF) from EPSRC to **Ajioka**; in Systems Medicine Metabolic, MRC Programme Grants to **Vidal-Puig** and **O'Rahilly** (both rolled into new MRC Unit funding), **Cox**, major WT funding to **Ron** (PRF), **O'Rahilly, Chatterjee, Maxwell** (Senior Investigators), **Farooqi, Gribble, Savage, Reddy** and **Semple** (all SCRF/SRF), BHF Senior fellowship (**Ozanne**), BHF Programme Grant **Vidal-Puig**; in Cardio-Respiratory, from BHF to **Bennett** (x2), **Morrell, Ouwehand, Mallat, Brown** and **Wilkinson**, from MRC to **Morrell** (Experimental Challenge Award); in Reproductive Medicine, MRC to **Smith GC**, Wellcome Trust to **Moffitt** and **Charnock-Jones;** in Genomics, Structural and Cell Biology, from MRC to **Seaman** and **Siniossoglou** (both SRF), **Marciniak** (SCRF) and programmes to **Luzio, Rubinsztein** and **Huntington,** from WT to **Griffiths, Owen, Read, Robinson, Rubinsztein** (all PRF) and **Reid** (SCRF) and programme to **Karet**; in Stem Cells MRC programmes to **Gottgens, Pedersen** and **Vallier** (SRF). Trust Fund Income over the REF period in UoA1 includes Genzyme Fund for Experimental Medicine (£0.5M), PHSA Engage Mutual Health Fund (£2M), Isabelle Bouhon Fund (£0.3M), and Strangeways Research Laboratory Trust £1.2M. The Dept of Pathology also received a donation of £1.6M to **Affara** from BlueGnome Cambridge to endow research in molecular genetics.

**(ii) Infrastructure/ Buildings** The Cambridge Biomedical Campus is in the middle of a phase of unprecedented physical development that will allow delivery of the SCM's mission to maintain its position as a leading international centre of clinical excellence.
Buildings/major refurbishments, housing UoA1 staff, completed during the 2008-13 REF period include:

- West Forvie Building £11.1M University £8.6M, MRC £2M, BHF £0.5M
- University Space in new LMB £8.5M University £7.5M, Wolfson Foundation £1M
- EASIH Sequencing Hub Laboratory Refurbishment £0.7M University £0.7M
- Deakin Centre £0.6M University £0.6M
- Category 3 facilities £0.5M University £0.5M

Planned buildings/major refurbishments to be completed during the next 5 years, with financial commitment and housing UoA1 staff plus recruits, include:

- Translational Medicine Technologies Hub £100M University £100M
- 16,000m$^2$ Building £70M University £35M, Other £35M
- Cambridge Heart and Lung Research Institute £23M University £5M, Other £18M
- Extension to Addenbrooke's Clinical Research Centre (ACRC) £17M University £11.5M, Other £5.5M
- Fit-Out of 3$^{rd}$ Floor in CRUK-CI £7M University £1M, CRUK £6M
- Refurbishment of Dept Medicine £2M University £2M

**(iii) Facilities** Research infrastructure important to UoA1 includes some that is provided across the whole University (eg library facilities and basic IT) and some that is provided across the SCS and SBS, taking into account the Schools have major research activities on two sites about 1.5 miles apart. Increasingly, provision of key resources and large-scale equipment is predicated on 'institute' and 'hub-and-spoke' models. Core facilities in SBS/SCM are overseen by joint strategy groups with wide user representation. Since 2008 University funds contributing to major equipment have exceeded £6m. All UoA1 staff benefit from the **University Library**, a legal deposit (copyright) library housing over two million volumes on open shelves that attracts researchers from across the world. It offers a digital library open 24 hours a day to all Cambridge members, providing access to over 21,000 full-text electronic journals, ~400 databases and a growing collection of electronic books. The library also offers a range of supporting courses for academics in the use of their IT system, as well as information management. Open Access publishing is encouraged by the University with a single advice and reference point for all research staff submitting publications at https://www.openaccess.cam.ac.uk.
'Text removed for publication'. **Computing and Bioinformatics** provision and support include plans for the relocation of a University data storage facility at West Cambridge, for 'off-site' back-up

and excellent high-quality bioinformatics training co-ordinated with local non-university research institutes including the Sanger and Babraham Institutes and EBI. **Genomics** A central facility for high throughput sequencing, the Eastern Sequence and Informatics Hub (EASIH), was established with funding from the MRC (with additional funds from the NIHR BRC and University, in collaboration with the EBI). In 2013 EASIH was subsumed into the Genomics Core facility at the CRUK CI and the NIHR BRC Cambridge Translational Genomics Laboratory. In addition, the Dept of Pathology has established a large genomics facility offering array analysis (Affymetrix and Illumina platforms) for high-throughput genotyping, gene expression and methylation analysis, and is also expanding its next generation sequencing capacity. **Proteomics** Coordinated facilities in the IMS, CIMR and CRUK CI between them provide access for all UoA1 staff. **Structural Biology** facilities include in-house rotating anode X-ray generators with image plate area detectors in the Dept of Biochemistry and in the CIMR with high-field NMR facilities also available in the Dept of Biochemistry and in the LMB (that can be accessed by collaborators amongst UoA1 staff).
**Imaging/Microscopy** Core facilities at specific hubs include the Cambridge Advanced Imaging Centre (based in Dept of Physiology, Development & Neuroscience), CIMR, IMS and CRUK CI, which house confocal and electron microscopes, and the Gurdon Institute, which houses super-resolution microscopy. **Flow Cytometry** cell-sorting and analysis facilities are housed in hubs in both SBS and SCM. **Clinical Imaging** facilities include instruments in the Dept of Radiology and two 3T MRI instruments in the Wolfson Brain Imaging Centre, one of which is dedicated to MR spectroscopy. **Clinical Research Facilities** are provided by the SCM and CUHFT in the Addenbrooke's Clinical Research Centre, which hosts one of five Wellcome Trust-funded Clinical Research Facilities in the UK (Director **Chatterjee**). Specialised clinical research facilities include an endoscopy suite (GSK-funded) for upper and lower GI work with two days weekly of protected research time on a 3T MRI and a PET-CT scanner. There is a long-established human tissue bank, managed within the CUHFT governance by a high-level Committee (Chair **Neal**) to ensure appropriate handling procedures, audit, ethical approval, and access for researchers. The Cambridge Clinical Trials Unit brings together the administration, data management and research nurse support needed to run both phase III and experimental medicine clinical trials.

**e. Collaboration or contribution to the discipline or research base**

**i) Evidence of excellence in contribution to the discipline from election to National and International Academies of Science.** Election to reputable national and international academies of science is an imperfect, but useful, shorthand for assessing whether a researcher has been viewed by the broader community as having contributed to the discipline and research base. In our cohort of UoA1 Category A staff we have 9 fellows of the Royal Society (five since 2008; **Griffiths G, Kouzarides, Robinson, Tavaré** and **Todd**); forty Fellows of the Academy of Medical Sciences (ten since 2008, **Chilvers, Farooqi, Fitzgerald, Jayne, Morrell, Patel**, **Peacock, Ron, Smith GC.** and **Woods**) and nine EMBO members (four since 2008: **O'Rahilly, Owen, Ron, Rubinsztein**); **Ponder** was a founding fellow of the European Academy of Cancer Sciences in 2009 and subsequently **Caldas** and **Neal** have also been elected. Other honours include **Lever** (Fellow of the Royal Society of Chemistry), **O'Rahilly** (2011 Foreign Associate of the National Academy of Sciences of the USA 2011), **Smith GL** (2011 Member of the German National Academy of Sciences (Leopoldina), **Lever** and **Hughes** (Fellows of the Learned Society of Wales) and **Ponder**, Sissons and **O'Rahilly** (Knights Bachelor for services to medical science).

ii) **Evidence of excellence in contribution to the discipline from the award of scientific prizes.** Many of our scientists have been awarded major national and international research prizes: Calne (2012 Lasker-deBakey prize); **Ponder** (2008 Alfred Knudson award; US National Cancer Institute; 2013 CRUK Lifetime Achievement in Cancer Research Prize); **Griffiths J** (2010 Gold Medal of the International Society for Magnetic Resonance in Medicine; 2010 European Magnetic Resonance Award); **Warren** (2013 Honorary Professorship from the University of Zurich); **Venkitaraman** (2012 Jubilee Professorship, Indian Academy of Sciences); **Todd** (2011 Rumbough Award of the Juvenile Diabetes Research Foundation); **Smith GL** (2011 Member of the German National Academy of Sciences (Leopoldina); 2012 GSK International Member of the Year Award, American Society for Microbiology); **Gaston** (2010 Heberden Medal British Society of Rheumatology); **Kaser** (2009 Paracelsus Award, Austrian Society of Internal Medicine); **Cooke** (2010 Hon. Doctorate, University of Copenhagen); **Smith K** (2013 Distinguished Innovator Award, Lupus Research Inst); **O'Rahilly** (2013 TOPS award of the Obesity Society of North America; 2013 Ulysses Medal UC Dublin; 2010 Inbev Baillet Latour International Prize for Health; 2010 Dale

Medal Society for Endocrinology; Hon. Doctorates Warwick, Dundee, Dublin and Buckingham); **Farooqi** (2012 Graham Bull Prize of RCP (London); 2011 European Society for Endocrinology Prize; 2010 Society for Endocrinology Medal); **Compston** (2009 Haddad Award of the International Bone and Mineral Society; 2009 Bartter Award American Society of Bone and Mineral Research); **Hovorka** (2013 Dorothy Hodgkin Lecturer, Diabetes UK); **Murphy** (2011 Joseph Hoet award, EASD Diabetes and Pregnancy Study Group, 2012; Janet Kitson Award of Diabetes UK); **Dunger** (2012 Prader Award, European Society for Paediatric Endocrinology); **Ron** (2012 Edwin Astwood Award, Endocrine Society of North America); **Wilkinson** (2010 GSK Prize for Research, British Pharmacological Society; 2009 Award for Research Excellence, European Association of Clinical Pharmacology); **Mallat** (2010 Roy Vacouloux Prize for Research in Cardiology of the French Academy of Sciences); **Floto** (2010 BUPA Foundation, Investigator Award); **Smith GC** (2010 Distinguished Researcher Award of International Stillbirth Alliance); **Rubinsztein** (2009 Spinoza Visiting Professor of the University of Amsterdam); and **Vallier** (2009 NC3R prize). Prizes for scientists at earlier stages of their career include **Odom** (2009 EMBO Young Investigator award; 2013 Royal Society Crick Lecturer); **Gallagher** (2009 Young Investigator Award, MRS/Academy of Medical Sciences); **Fitzgerald** (2008 Lister Institute Prize); CRUK Future Leaders Prize to **Carroll** (2009) and **Rosenfeld** (2013); **Reddy** (2011 Colworth Medal; Biochemical Society (first clinician-scientist to be thus honoured); 2011 EMBO Young Investigator Award; 2012 Lister Prize; 2013 Foulkes Medal of the Academy of Medical Sciences); **Gribble** (2010 Minkowski Prize, European Association for the Study of Diabetes); **Gottgens** (2010 McCulloch and Till Award, International Society for Experimental Haematology).

**iii) Contribution to the discipline and research base through activities in peer review and provision of scientific advice to research councils, research charities and major academic institutions.** Our Category A UoA 1 returned staff have provided a total of ~170 editorships, associate editorships or memberships of editorial boards of national and international scientific journals. Some examples include: **Griffiths J** (Editor of NMR in Biomedicine from 2013); **Morrell** (Editor-in-chief Pulmonary Circulation from 2010); **Davenport** (Editor of British Journal of Pharmacology from 2010); **Lever** (Co-editor in Chief, Retrovirology from 2013); and **Sinclai**r (Editor J Gen Virol from 2013). **Cox** is one of three editors of the distinguished Oxford Textbook of Medicine. Our staff have also provided extensive support to Learned Academies, Research Councils, Research Charities and Academic Institutions through peer review and the provision of advice regarding scientific strategy. At the Royal Society **Smith GL** has Chaired Section Committee 7 since 2012 and **O'Rahilly** is serving a second term on Section Committee 10 from 2013. In the Academy of Medical Sciences, **Maxwell** served as registrar from 2006-2012 and four members of UoA1 (**O'Rahilly, Karet, Chilvers** and **Tavaré**) have served on the Council. At the MRC, **Luzio** chaired the Molecular and Cellular Medicine Board from 2007-2012, **O'Rahilly** chaired the MRC Translational Research Group from 2009-2011 and **Brown** was Deputy Chair of the Fellowship panel 2007-2010. Both **O'Rahilly** 2009-present and **Luzio** 2007-2012 served on MRC Strategy Board. Several of our researchers (including **Peacock, Smith GL, Smith K, Chilvers** and **Morrell)** have served as MRC Board members or members of Fellowship and Career Development panels. At the Wellcome Trust, **Maxwell** has served as Chair, and **O'Rahilly** and **Morrell** as members of the Physiological Sciences panel. **Barroso** and **Robinson** have been members, and **Lehner** and **Rubinsztein** have chaired Investigator Awards Expert Review Groups. Many of our investigators have also served disease-focused charities in a leadership and/or scientific advisory capacity.

**iv) Contribution to UK health and wealth through service to Government and Industry.** Our researchers have made substantial contributions to UK society and international health through their service on a variety of government bodies which use scientific information to inform public policy. **Smith GL** has chaired the WHO Advisory Committee on Smallpox since 2004 and is a Member if the WHO committee on Viral Infections. **Neal** is the Chair of the Prostate Cancer Advisory Group, Dept of Health and a member of NICE Prostate Cancer Guideline Development Group. **Collins** chairs the Pathology Committee of the National Cancer Intelligence Network. **Rintoul** (Cat C) has been a member of NICE Lung Cancer Quality Standards and Guidelines Development groups. **Compston** has chaired the National Osteoporosis Guidelines Group and been a member of several NICE committees evaluating the treatment and prevention of osteoporosis. Our investigators are fully engaged with the UK wealth agenda and have extensive

interactions with the UK pharmaceutical and biotechnology industry through relationships that are advisory and/or collaborative, rather than providing contract research services. Details of the entrepreneurial activities of our investigators are provided in Ref3a.

**v) Collaboration.** The University's Research Strategy Office proactively seeks out opportunities to collaborate, both internally and externally and is in constant communication with University academics highlighting opportunities to respond to national and international calls for collaborative research. ***Local*** The local environment is very rich scientifically, with the University being only one element of a powerful network that includes major research institutes e.g. Sanger Institute (Wellcome Trust), EBI (EMBL), Babraham Institute (BBSRC), LMB and other MRC units, world-leading hospitals (Addenbrooke's, Papworth) and a vibrant network of locally based SMEs. The University has recently established mechanisms for supporting and encouraging cross-disciplinary working. Three of the six recently established University of Cambridge Strategic Initiatives (Cancer, Infectious Diseases and Stem Cells) directly relate to this UoA1 submission, as do two of the seven recently established Strategic Networks (Immunology and Metabolism). ***National*** Through our partnership with CUHFT in the NIHR BRC we have participated and/or led several national NIHR-led initiatives, including leading the development of the NIHR BioResource in collaboration with five other NIHR BRCs and taken leadership of the NIHR Rare Diseases Initiative. Many of our investigators (e.g. **Neal, Brown, Wilkinson** and others) lead large national collaborations in stratified medicine, in response to MRC, TSB and NIHR initiatives and/or investigator-led clinical trials in their disease areas. ***International*** Cambridge PIs based at the SCM have participated in eighty-one and led three (Eurochip, INTERACT, EPIC-CVD) Health–related EU FP7 Networks since 2008. Examples of other partnerships with international academic organisations include the Cambridge-Yale Cardiovascular Disease Partnership, a German-funded formal Alliance with the Helmholtz Institute for Diabetes and Obesity in Munich, European leadership of a Leducq Transatlantic Network (**Morrell**) and formal collaborations with several Universities in Africa (**Lee H, Dunne, Moffett).** ***Collaborations with Industry*** There are extensive collaborations with industry, with the main partners being GSK, who have their only remaining phase 1/Experimental Medicine Unit on the Cambridge Biomedical campus and with AstraZeneca as they plan the move of their world headquarters and major research facilities onto the campus.