Institution: University of Oxford

Unit of Assessment: UoA1 Clinical Medicine

a. Overview

AIM

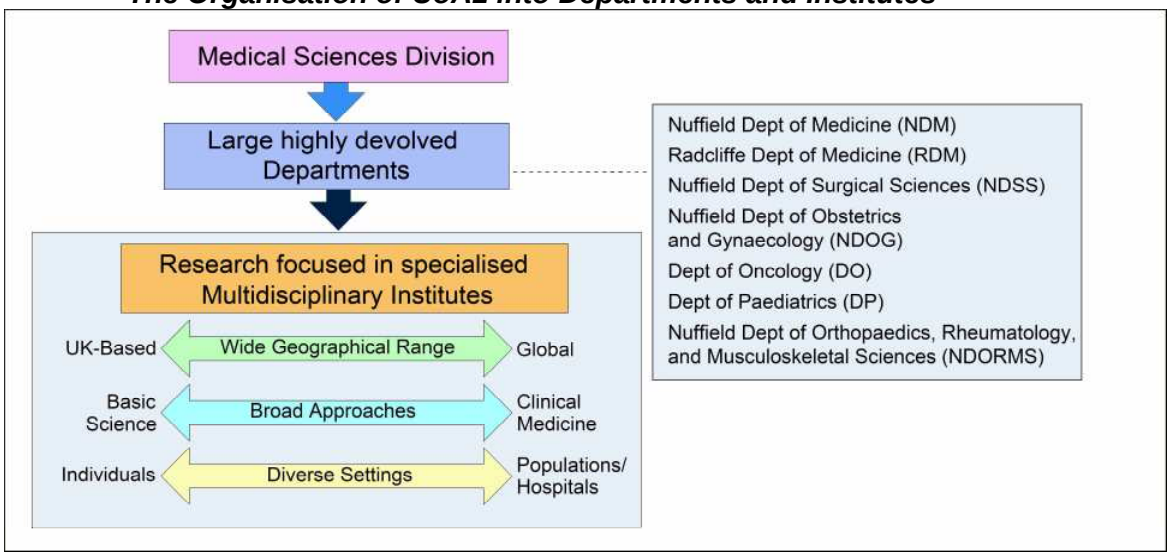
The aim of UoA1 is **to advance the scientific approach to medicine**.

STRUCTURE

The structure of UoA1 supports flexible and sustainable research. It creates groups of researchers with the critical mass to attract effective support, and promotes interactions across broad areas of expertise. This is achieved by:

- **Creation of a range of topic or technology-focused research institutes**, building on the paradigm of the Weatherall Institute of Molecular Medicine (WIMM).
- **Installation of the institutes within large departments**, which creates bridges between multiple institutes as well as with the hospitals and clinical training programmes.
- **Leadership of a single Medical Sciences Division**, which links the (classical) pre-clinical (UoA5) and clinical (UoA1, 2 and 4) departments, and manages high-level strategic interactions within the University.
- **Devolution of the financial and administrative management of the University structure to its departments**, fostering an ability to respond flexibly in support of individuals, research groups and strategic initiatives, innovation and collaboration.
- **Configuration of research groups** around ten key areas of clinically defined research and crosscutting technology, which often span institute and departmental boundaries.

The Organisation of UoA1 into Departments and Institutes



DISTINGUISHING COMMITMENTS

Embedded within the research strategy are a series of distinguishing commitments, which have been developed extensively during the REF2014 assessment period.

1. Commitment to create a world-class biomedical research environment on the hospital campus, including:

- **Major capital expenditure** on Oxford's Clinical School Campus of £98.2M in the REF2014 assessment period, creating >12,000m^2 of additional high quality laboratory space.
- **Substantial investment in technology platforms**, including the highest capacity for 'next generation' DNA sequencing outside the Sanger Institute; extensive groups linking biophysics-based structural biology, super-resolution microscopy and chemical probe development; a new technology centre dedicated to early-stage drug target validation with large biomedical mass spectrometry unit; novel 'high-content' screening and capacity for synthetic chemistry; and the largest clinical trials infrastructure in the UK, ranging from early phase trials to multicentre 'mega-trials'.

- **Educational focus on the scientific foundations of medicine**. This ranges from undergraduate training, where the Oxford Clinical School is consistently one of the top in the UK for student satisfaction (ranked 1st in 2013) and graduate prospects, to post-graduate education, where the Medical Sciences Division has created a Graduate School and hosts the largest set of Wellcome Trust-funded doctoral programmes in the UK. Between 2009 and 2013, UoA1 has increased its doctoral student cohort by 75%, and established new international training programmes with partners in China, Hong Kong, Brazil and Africa.
- **Close association between the University and the NHS**. UoA1 benefits from a major realignment of the University and NHS that led to the creation of the Oxford University Hospitals NHS Trust in 2011, the Oxford NIHR Comprehensive Biomedical Research Centre (renewed with a 50% funding uplift for 2012-2017), and the Oxford NIHR Biomedical Research Unit in Musculoskeletal Disease (renewed with a 100% funding uplift).

2. Commitment to develop novel multidisciplinary research groups, exemplified by:

- **Linking engineering science and medical innovation**, through the creation of a Wellcome/EPSRC Centre of Excellence in Medical Engineering (Personalised Healthcare, £8M) within the co-located Institute for Biomedical Engineering (UoA15), as well as a bioengineering theme in the successful NIHR Biomedical Research Centre renewal.
- **Bringing together strengths in chemistry and biomedicine**, through the creation of a £23.8M Target Discovery Institute (2013) that will focus on drug target discovery and early stage validation.
- **Co-location of staff from the departments of statistics and medicine** in the Wellcome Trust Centre for Human Genetics, to address the study of human populations, global genome-based pathogen surveillance, and the genetic basis of human disease susceptibility.
- **Clinical programmes linking physics and medicine**, including a £4.2M Acute Vascular Imaging Centre (AVIC, opened 2008) and the Gray Institute for Radiation Oncology and Biology, opened in the Old Road Campus Research Building (2008).

3. Commitment to multi-institutional partnerships (including industry), exemplified by:

- **Public-private consortia**. The Structural Genomics Consortium is an exemplar of the public-private partnership model; it involves eight pharmaceutical partners with a total budget >£32M (2011-2015), and is dedicated to development of novel probe compounds.
- **New working practices with industry**, for drug target selection and early stage validation, exemplified by the Target Discovery Institute and its industrial partners.
- **Inter-institutional collaborations through joint senior appointments** with major research institutions including the Wellcome Trust Sanger Institute, the Rutherford Appleton Laboratories and Diamond Light Source, and the UK Biobank.
- **Sharing facilities**. UoA1's Tropical Medicine Units host staff from the London School of Hygiene and Tropical Medicine, the Institute of Child Health, Imperial College London, and Cambridge, Warwick and Liverpool Universities.

4. Commitment to a global perspective in biomedical research

- **Its worldwide reach** in biomedical research has made UoA1 an international leader in tropical medicine. Its programmes link medical and social sciences to address major challenges in healthcare delivery, in settings ranging from rural Africa to areas of rapid urbanisation in India and South-East Asia.
- **Major development of the overseas programmes** to encompass over 20 countries worldwide with a grant income exceeding £20M/yr.
- **Expansion of primary tropical medicine units** in Thailand, Vietnam and Kenya, which have grown to employ more than 1,600 staff, and now manage directly funded research centres in 16 countries.
- **Opening of five major units in China**, addressing topics ranging from emerging infections and medical aspects of disaster response, to large-scale multicentre clinical trials and resources, including the Kadoorie Biobank.

b. Research strategy

THE UNIVERSITY STRATEGIC PLAN

The University of Oxford Strategic Plan 2008-2013 outlines its mission, objectives and values: "*…to achieve and sustain excellence in every area of its teaching and research, and… enrich international, national, and regional communities through the fruits of its research, the skills of its alumni, and the publishing of academic and educational materials*."

The plan has **four key research objectives**:

- Maintain research strength across the disciplinary range and encourage further interdisciplinary research initiatives.
- Support international research and collaboration.
- Ensure that the fruits of the University's research activities are exploited and disseminated for the benefit of society and the economy.
- Promote interactions between the University and industry.

STRATEGIC AIMS

UoA1 has nine strategic aims, which address both the research objectives of the University, and the mission of UoA1 *to advance the scientific approach to medicine*.

Aim 1. Create a dynamic administrative structure to support teaching and learning

The Medical Sciences Division has taken several steps to consolidate its administrative structure, to ensure there is a critical mass of support across the breadth of subjects, combined with flexibility and finances to address unmet needs and new opportunities. This is exemplified by:

- **The Department of Oncology** (2010), which has brought together the Gray Institute, the Department of Medical Oncology and the Department of Clinical Pharmacology.
- **The Radcliffe Department of Medicine** (2012), which has combined haematology, stem cell biology, cardiovascular medicine, molecular medicine, diabetes and endocrinology.
- **Expansion of the Major Overseas Programmes**, which provide UoA1 with its worldwide research capacity, and for which Oxford provides a central administrative structure.

Aim 2. Invest in world-class facilities and Infrastructure

As already articulated, UoA1 has continued to make major investment in infrastructure and technology as part of its plan to support multidisciplinary working and accelerate clinical translation.

- **New institutes**. Major new initiatives include: the *Old Road Campus Research Building* (2010), which brings together the Institute for Biomedical Engineering, the Ludwig Institute for Cancer Research, the Gray Institute and the Jenner Institute; the *Kennedy Institute of Rheumatology* (2013), which contains groups in tissue engineering, inflammation and imaging; the *Target Discovery Institute* (2013), and the *Big Data Institute* (to open 2015).
- **World-class technology**. UoA1 has invested widely in genomics, structural biology, mass spectrometry, bioinformatics, early phase trials, chemical biology, and high-end microscopy and imaging platforms, as already described. Additionally, £4.2M has been invested in imaging platforms within the Department of Oncology to create the most comprehensive small animal imaging facility in the UK.
- **Facilities to accelerate translation**. Significant investment has been made to support the pathway to translation by investing in a variety of shared resources, including the Oxford Biobanks (UoA1), UK Biobank (UoA2), Institute of Biomedical Engineering (UoA15), Clinical Biomanufacturing Facility (UoA1) and Clinical Trials Facilities (UoA1).

Aim 3. Build capacity by investing in people

The success and sustainability of UoA1's research is underpinned by its commitment to inspire, recruit, train and mentor the very best staff and students.

- **Inspiring the next generation**. As already described, through its Medical Sciences Graduate School (founded in 2011) and Clinical Academic Graduate School.
- **Recruiting and training the best graduates**. More than 70% of our graduate students go on to a biosciences-related position in academia or industry, and a quarter have become independent investigators since 1993.
- **Feeding the academic pipeline**. More than 40 junior research fellows currently in UoA1

have secured five-year fellowships that act as springboards for their independent careers. The majority obtain senior fellowships or tenure-track positions in Oxford or elsewhere.

- **Academic staff development**. Our commitment to the career development is evidenced by the return of 112 (44%) ECR or tenure-track staff in the REF2014 and a 75% increase in the number of women in senior posts (71 staff, 28%) since 2008. During REF2014, 34 staff have received professorial title in Oxford and 23 have been appointed to prestigious Chairs or equivalent elsewhere in the UK and internationally.
- **Recruiting leaders**. Since 2008, UoA1 has recruited 88 new Senior Investigators, building capacity in existing areas and launching new research themes.

Aim 4. Promote and strengthen interdisciplinary research across the breadth of medicine

As already articulated, UoA1's track record of novel discoveries and high-impact medical research builds upon its ability to bring together multidisciplinary groups in its institutes and cut across conventional scientific areas. This is exemplified by collaborations in the following fields:

- **Genetics, Diabetes, Metabolic** and **Cardiovascular Medicine**. Collaborations between mathematics and genetics (Donnelly, McVean), cardiovascular medicine (Watkins, Farrall), diabetes (McCarthy) and metabolism (Lindgren) have generated over 20 of the most highly cited genome wide association studies (GWAS) of the last 5 years.
- **Chemistry, Cellular Physiology** and **Cancer**. The discovery of the mechanism of hypoxic gene regulation by groups in medicine (Ratcliffe) and chemistry (Schofield), has led to advances in the field of cancer biology and investment in excess of £100M by the pharmaceutical industry in major drug discovery programmes.
- **Imaging** and **Vascular Biology**. Clinical scientists (Neubauer, Choudhury) and physicists (Robson, Schneider) have revolutionised applications of MR imaging and spectroscopy, clinical high field imaging, and hyperpolarised systems in cardiology.
- **Epidemiology, Tropical Medicine** and **Genetics**. Groups in Vietnam, Cambodia and Thailand (Farrar, Day, White) and Oxford (Kwiatkowski) have defined the extent of malaria resistance to artemisinin and are currently leading efforts to limit its spread.
- **Structural Biology**, **Oncology** and **Immunology and Infectious Disease**. Joint projects have led to new drugs to treat HIV and cancer, as well as the creation of stable genome-deficient viruses, which offer to transform vaccine delivery worldwide (Stuart, Jones).
- **New Fields of Research**. The strength of collaborations and crosscutting technology provides UoA1 with the platform to expand new areas of clinical research, notably in *Gastroenterology* (led by Powrie) and *Respiratory Medicine* (led by Pavord from late 2013).

Aim 5. Advance partnerships between the University and NHS

The step change in the relationship between University and the NHS is increasing opportunities for joint research and clinical trial facilities on the shared hospital campuses.

- **University involvement in management of the NHS**. The Strategic Partnership Board of the new *Oxford University Hospitals NHS Trust (OUHT)* links the local NHS and University to develop local healthcare. UoA1 staff direct two of the major divisions of the OUHT, *Surgery and Oncology* (Hamdy) and *Musculoskeletal and Rehabilitation Services* (Carr).
- **Oxford NIHR Biomedical Research Centre** (**NIHR BRC**). The University and NHS administer this £112M grant as a mechanism to accelerate clinical research (Chair, Channon). Groups have access to Clinical Research Centres; UoA1 Clinical Research Networks focus on disease including cancer, cardiovascular disease and diabetes.
- **New Clinical Research Centres**. Joint funding supported the £12M Acute Vascular Imaging Centre and the Cardiovascular Clinical Research Facility; and a joint initiative between HEFCE and charitable and industry partners will fund a £105M Targeted Cancer Research Centre (planned 2016).
- **Pathology Services**. Additional investment in pathology services across the spectrum of human disease has been made through the *Oxford NIHR BRC Translational Pathology Programme* including a major new programme in molecular diagnostics (Schuh).

Aim 6. Encourage innovative relationships with industry

UoA1 plans to accelerate commercial activity via innovative forms of partnership, which are

focused on the early and free dissemination of data at a pre-commercial stage, and the physical co-location of its industrial partners on the University and hospital campus.

- **Groundbreaking industrial partnerships**. The *Structural Genomics Consortium* (2003) provides the template for the UoA1 approach. It accelerates drug discovery through an open source model, sharing data, reagents, tools and expertise as widely as possible.
- **Knowledge and data sharing with industry**. A major challenge is how to use the wealth of genetic, molecular and physiological data to understand both common and rare diseases, and how to accelerate the identification and development of drug targets. The creation of the £45M *Big Data Institute* (2015) will create a commercial focus for health informatics in the UK; it has already attracted commercial partners, such as Illumina and Life Technologies, which require unique analytical skills capable of relating genetic variants to disease, as well as Microsoft and Oracle.
- **Adjacent commercial and academic activity**. To place its start-up companies adjacent to academic laboratories and clinical research centres, UoA1 is working together with the local government, business parks, NHS and Oxford Brookes University on plans to build a 5,500m^2 *BioEscalator Institute* on its Old Road Campus, subject to funding. This will attract growing firms and spinouts to the hospital site and link to local science parks.

Aim 7. Respond to new challenges

A high level of collaboration, scientific and financial independence ensures UoA1 can respond rapidly and effectively to new opportunities and challenges, including national emergencies.

- **H1N1 and H5N1 Influenza**. Access to clinical material through its overseas units, and a rapid commitment of core expertise in virology and genetics in Oxford, enabled UoA1 to be at the forefront of research and government and WHO planning for Avian and Swine Flu (Farrar, McMichael). During the H1N1 Swine Flu pandemic in 2009, the Oxford Vaccine Group (Pollard) carried out a clinical trial in only 5 weeks, which enabled the Department of Health to recommend immunisation of over 3 million children in the UK within 6 weeks of the study approval being obtained. The results informed global policy via the WHO.
- **The crisis in medical microbiology**. The UoA1-led UK Clinical Research Consortium 'Modernising Medical Microbiology' (Crook, Peto) is now applying the whole-genome sequencing of pathogens and new web-based tracking systems to improve national surveillance, and guide laboratory and clinical practice of microbiology across the UK.

Aim 8. Protect vulnerable subjects

UoA1 supports research in vulnerable subjects linked to national priorities, including:

- **Radiation Oncology**. In 2003, the NCRI Radiotherapy/Radiation Biology Progress Review Group concluded that radiation oncology research and treatment in the UK was lagging far behind other countries in both quantity and quality. The establishment of the *Gray Institute* (2008), now within the Department of Oncology, created the major UK centre for research and training into radiation oncology and biology; a nationwide network, the Clinical and Translational Radiotherapy Research Working Groups (CTRad), is led from UoA1 (Maughan).
- **Surgical Sciences**. In 2007, less than 2% of the UK biomedical research budget was spent on surgery, despite 30% of all NHS consultations and treatments being for surgical patients; over 50% of cancer patients are cured by surgery alone. UoA1 supports Surgical Sciences across the full spectrum of specialties, and hosts the first Royal College of Surgeons-designated *National Surgical Trials Unit*.

Aim 9. Disseminate knowledge widely

UoA1 projects impact on the global stage with its leadership of international consortia (Section E); the contributions of its staff to the development of health care policy, through the WHO and other national and international bodies; and its collaboration with industry.

- **Seminars**: over 500 UoA1-related seminars are held across the University each year, many by international speakers; 5-10 named lectures are held annually across UoA1.
- **Outreach**: researchers in UoA1 deliver over 50 public seminars and talks a year. UoA1 researchers published over 70 blogs, podcasts and lectures with over 500,000 downloads.

RESEARCH ACHIEVEMENTS

UoA1 is highly collaborative and interlinked, and many of the constituent units have researchers in more than one research grouping.

Group 1: Infection, Immunity and Inflammatory Disease

Achievements and Initiatives

- A new Director (Cerundolo) was named for the *MRC Human Immunology Unit*; this was followed by an indicative funding award of £20M at the Unit's successful five-year review.
- Incorporation of the *Jenner Institute for Vaccine Research* (Hill) (2008) and *Kennedy Institute for Rheumatology* (Feldmann) (2011).
- Foundation of the *Translational Gastroenterology Unit* (Powrie) (2009), *Developmental Immunology* (Hollander) (2009), and the *Wolfson Imaging Centre* (WIMM, Eggeling) (2013).
- The group continues to generate and share a wide range of tools and reagents with the wider community, including animal models, cell lines and human samples. It has broad collaborations in Oxford (notably in cell biology with the Dunn School, UoA5) and outside.

Forward Directions

- Maintain core research into the molecular and cellular basis of lymphocyte activation, lymphocyte and myeloid subsets, autoimmunity, allergy, and tumour immunity.
- Develop major programmes in pathogens and host genetics.
- Continue to invest in the development of vaccines against major human and animal pathogens (Hill, Pollard) and cancer immunotherapy in melanoma (Cerundolo).
- Extend its leadership in the field of mucosal immunity and the interplay of the intestinal flora, cytokines, lymphoid cells and genetic susceptibility in inflammatory disease (Powrie).
- Initiate a major programme in virology, including a £1.92M STOP-HCV vaccine programme led by the *Peter Medawar Institute for Pathogen Research* (Barnes).

Group 2: Tropical Medicine

Achievements and Initiatives

- The aim of the Tropical Medicine Group is to improve the health of the vast majority of the world's population living in tropical areas. Its three major overseas units in Thailand, Vietnam and Kenya now support several satellite units in Asia and Africa.
- The Thailand Unit (White, Day) is based at *Mahidol Oxford Tropical Medicine Research Unit* (MORU) in Bangkok, with clinical research units in Mae Sot on the NW border with Myanmar (Nosten), at Ubon Ratchathani and Udon Thani in NE Thailand, in Vientiane in the Lao PDR (Newton), in Siem Reap in Cambodia, and most recently in Kinshasa in the Democratic Republic of Congo and in Yangon, Myanmar.
- MORU coordinates multicentre clinical trials on the treatment of malaria (severe malaria, uncomplicated *P. falciparum* and *P. vivax* infections, and malaria in pregnancy), melioidosis and rickettsial infections. It coordinates TRAC (Tracking Resistance to Artemisinin Collaboration), which has 15 clinical study sites in 10 countries across Asia and Africa.
- The Vietnam Unit (Farrar; Thwaites from Oct 2013) is based in the *Hospital for Tropical Diseases* in Ho Chi Minh City, and at a dedicated *Institute for Clinical Research* (Hien). In 2006 an *Epidemiological and Public Health Research Unit* (Horby) was established in Hanoi. Groups in Thailand and Viet Nam have established units in Kathmandu, Nepal, the University of Indonesia, and the Eijkman Institute, Jakarta. Major collaborations in the region include Afghanistan, China, Indonesia, Nepal, Malaysia, Cambodia, Philippines, and Singapore.
- Vietnam researchers are part of the *DENCO Dengue Network* with groups in Cuba, Venezuela, Brazil, Nicaragua, and Ecuador; and the *Meningitis Network* in Malawi, Chile, Argentina, Netherlands, Finland, South Africa and UK. It hosts the regional and national offices of the *South East Asian Infectious Disease Clinical Research Network*.
- The Kenya Unit (Marsh) is located at Kilifi, which is a centre for clinical and population-based research, and in Nairobi, where it focuses on epidemiology, public health, health service and policy-based research. The unit supports work in Dar-es-Salaam in sickle cell disease, and national malaria control programmes in Uganda, Sudan, Somalia and Djibouti.
- The REF2014 period has seen new emphasis on emerging infections and chronic disease,

including diabetes, cardiovascular disease and malnutrition.
- Tropical Medicine researchers have established best-practice guidelines for treatment of severe and uncomplicated malaria, malaria in pregnancy, scrub and murine typhus, melioidosis, leptospirosis, enteric fever, bacterial and tuberculous meningitis, severe cryptococcal meningitis and viral encephalitis.

Forward Directions
- Major challenges include: development of more accurate diagnostics and clinical epidemiological information from rural areas; the conduct of pharmacokinetic and pharmacodynamic studies for antimalarial, anti-influenza and antituberculosis drugs; global mapping and understanding the molecular basis of antimicrobial drug resistance; and developing molecular/genomic epidemiological studies of major pathogens including malaria as an aid to public health policy and disease control.
- Increased focus on the challenge of emerging infections and chronic metabolic and cardiovascular disease in developing countries.
- Tropical Medicine is pursuing major new trials in treating *vivax* and *falciparum* malaria, leishmaniasis, neonatal sepsis, severe malaria, dengue, CNS infections, anaemia, respiratory diseases, severe malnutrition, HIV/AIDS, maternal and neonatal health, and enteric and zoonotic diseases caused by emerging pathogens.
- UoA1 researchers have revealed the problem of counterfeit and substandard anti-infective drugs; this has been investigated, brought to international attention, and tackled.

Group 3: Cancer

Achievements and Initiatives
- The *Department of Oncology* (McKenna) is co-located with the £126M purpose-built *Oxford Cancer and Haematology Centre* (OUH Trust, Hamdy) at the Churchill Hospital, which opened in April 2009.
- The *CRUK Oxford Cancer Research Centre*, which supports cancer research across UoA1, was renewed with major centre status in 2013 and graded outstanding.
- The Oxford branch of the *Ludwig Institute for Cancer Research* (Lu) opened in 2008, and has increased understanding of transcription factors in cell growth and death, stem cells and differentiation, angiogenesis, the cellular response to hypoxia and the epigenetic regulation of gene expression at the genome-wide level.
- The *Cancer Genomes Unit* (Tomlinson) has conducted pioneering studies into inherited predisposition to cancer, notably bowel cancer.
- The NIHR/BRC-funded *Oxford Experimental Cancer Medicine Centre* coordinates early phase medical and radiotherapy trials.
- The *Gray Institute for Radiation Oncology and Biology* (McKenna) (2008) addresses the treatment of cancer with radiation, focusing on DNA damage and its repair and the tumour microenvironment. It pioneers advanced radiotherapy technology including the application of functional imaging to radiotherapy planning and delivery.
- The *Oxford Cancer Imaging Centre (OCIC)* aimed at improving cancer diagnosis, therapy and prognosis is one of four national centres funded by CRUK and EPSRC (£9.8M/5yr).

Forward Directions
- The Ludwig Institute and Cancer Genomes Unit will address fundamental mechanisms of cancer biology and drug discovery, with the Structural Genomics Consortium.
- Further improvements to infrastructure will include the installation of a Cyclotron and GMP radiochemistry laboratories, as well as a comprehensive facility for Cancer Biobanking and Molecular Pathology, funded by NIHR/BRC Translational Pathology Programme.
- Plans are proceeding for construction of a joint University/NHS £105M *Oxford Targeted Cancer Research Centre*, also on the Churchill site, with inpatient facilities that will focus on treatment of early stage cancer, and all therapeutic modalities including proton therapy.
- The ongoing work in Medical Oncology (Harris and Middleton) aims to consolidate Oxford University's position as the leading UK centre for early phase 0 or phase I 'first in man' trials of new cancer drugs, including histone deacetylase (HDAC) inhibitors and antiangiogenic therapies (see later).

Group 4: Haematology and Stem Cell Biology

Achievements and Initiatives

- The *MRC Molecular Haematology Unit (MHU)* (Higgs, WIMM) aims to understand the differentiation of haematopoietic lineages and the maintenance of haematopoietic stem cells (HSCs).
- The REF2014 period has seen significant progress in integrating the MHU with the *Clinical Haematological Service* in the OUH Trust and a jointly run NIHR/BRC Haematology theme.
- Within the MHU, Patient has used zebrafish and *Xenopus* to define the earliest cellular origins of HSCs; Jacobsen was the first to define a new cell type referred to as the lymphoid-primed multipotent progenitor (LMPP), and has now shown that this cell type is responsible for seeding of the embryonic thymus.
- Vyas has advanced our understanding of leukaemia stem cells (LSCs) in acute myeloid leukaemia (AML) and children with Down's Syndrome and is bringing the first LSC-targeted therapeutic antibodies to phase I clinical trials with Weissman (Stanford USA).

Forward Directions

- Development of new drug treatments in haematological malignancy through participation in the *Structural Genomics Consortium* and *Target Discovery Institute*, using preclinical models of haematological tumours to validate targets (Rabbitts).
- The MHU will extend observations in populations of cells to single cells, and is developing capacity in single-cell level transcriptomics, the analysis of mutations in single cells and high resolution imaging (Wolfson Imaging Centre, Eggeling).
- Ongoing investigations into lineage differentiation of HSCs and the epigenetic and transcriptional regulation of this process in normal and disease states, including haematological cancer (Nerlov/Porcher/Milne).
- Continue groundbreaking work into understanding of ATRX and other chromatin associated proteins in thalassemia and other genetic diseases (Higgs and Gibbons).

Group 5: Genetics

Achievements and Initiatives

- UoA1 genetics programmes are focused around the *Wellcome Trust Centre for Human Genetics (WTCHG)* (Donnelly). This highly multidisciplinary unit involves the full range of groups in UoA1, including clinical and basic scientists, statistical geneticists and bioinformaticians. The Centre's objective is to gain insight into mechanisms underlying genetic susceptibility to human diseases.
- The WTCHG is a world leader in genetic susceptibility to common disease: its scientists have led many of the pioneering research studies, first via GWAS, then whole genome sequence data (WTCCC, GOT2D, WGS500) and large infrastructure projects (HapMap, 1,000 Genomes) (Donnelly, McCarthy, McVean and others).
- WTCHG and related groups contribute to pathogen genetics and pharmacogenomics, providing vital information to WHO on the emergence of malaria drug resistance (Kwiatowski), and have made contributions to multicentre case control trials.
- WTCHG scientists (Donnelly, McVean, Marchini, Lunter) are at the forefront of methods development for the statistical analysis of genomics data.
- Landmark studies in the use of model organisms and forward genetic studies, including the analysis of simple and complex traits (Mott, Lunter, Siggs, Cornall).

Forward Directions

- Maintain leadership in the development of tools to analyse phenotypic and genotypic information and establish causation in complex traits and conditions.
- The NIHR/BRC Genomic Medicine theme (Watkins) will translate genetic research into clinical practice, and will work closely with molecular diagnostics and the Big Data Institute.
- Further creation of a skills base in epigenetics on genome-wide and locus-specific levels, such as hypoxic gene regulation (Mole), the use of expression quantitative trait loci (Knight), and the development of animal models (Davies, Cornall, Lunter).
- Collaboration with the Jenner Institute and Structural Genomics Consortium to use genetic information in vaccine and drug discovery towards personalised and targeted medicine.

Group 6: Cardiovascular Medicine

Achievements and Initiatives

- Increased capacity for clinical research, through investment in a *Cardiovascular MR Research Unit* (Neubauer), dedicated *Cardiovascular Clinical Research Facility* (Leeson) and *Acute Vascular Imaging Centre (AVIC)* (Choudhury).
- The Cardiovascular Genetics group (Watkins) founded an NHS-commissioned national genetic testing service, completed the first WGS analysis in Mendelian heart muscle diseases and led the Coronary Artery Disease (C4D) Genetics Consortium, identifying multiple novel susceptibility loci.
- The *Clinical and Experimental Imaging* group (Neubauer/Robson) has pioneered clinical high field (7T) and hyperpolarised MRI systems, which are unique in Europe.
- Fundamental to the group's success has been a considerable track record in generating new tools for studying cardiac physiology: it is a world leader in the development of clinical applications of cardiac MRI.

Forward Directions

- Build on pioneering work in micro-CT high resolution imaging of mouse embryos, microscopy for high throughput cellular-based screening, and quantifiable fluorescent and bioluminescent imaging *in vivo*.
- Future challenges, in common with other themes, include how to use the wealth of genetic, molecular and physiological data generated to further understanding of common and rare diseases of the cardiovascular system, and how to identify and develop drug targets, linking to the *Target Discovery Institute* (Ratcliffe) and *Big Data Institute* (Bell).
- The group links cardiovascular epidemiology in the *Clinical Trial Service Unit* and the *George Institute* (UoA2) and the basic cardiac science in the *Department of Physiology, Anatomy, and Genetics* (UoA5), through the BHF Centre of Research Excellence.

Group 7: Metabolic, Endocrine and Reproductive Medicine

Achievements and Initiatives

- Research centres on both the *Oxford Centre for Diabetes, Endocrinology and Metabolism (OCDEM)*, a purpose-built multidisciplinary facility supported by the University, the OUH Trust and private industry funders; and the *Nuffield Department of Obstetrics and Gynaecology* (NDOG, Kennedy), where clinical and translational work on reproductive medicine are closely linked to inpatient services at the John Radcliffe Hospital.
- Recent advances in basic physiology include: understanding of endocrine tumours and renal, tubular, and hypercalciuric stone disorders (Thakker); description of the role of Wnt signaling in obesity-associated cardio-metabolic disease (Karpe); identification of new processes that control insulin secretion under physiological conditions and in clinical diabetes (Rorsman); and groundbreaking work defining the role of oxygen sensing enzymes in normal physiology and cancer biology (Ratcliffe).
- The *Diabetes Genetics Group* (McCarthy) has co-led the largest disease-based sequencing project for type 2 diabetes worldwide, and the *Genetic and Genomic Epidemiology Groups* (Lindgren and Morris) have contributed to our understanding of how DNA sequence variation controls metabolic traits, including waist-hip ratio.

Forward Directions

- The aim of the group is to understand and treat diseases of metabolism, endocrinology and reproductive medicine by bringing together expertise in molecular and cellular biology, electrophysiology, genetics, clinical medicine, epidemiology and drug trials.
- The group will continue to focus on human physiology, functional studies, drug screens and the validation of therapeutic targets, and link to the Target Discovery Institute.
- OCDEM will expand on its international links with collaborations in the USA, Europe, China, Sri Lanka, and Japan. NDOG is leading multinational programmes on development: INTERGROWTH-21st and INTERBIO-21st.
- The group will continue to build and expand its links to over 15 pharmaceutical companies through Innovative Medicines Initiative projects (SUMMIT, DIRECT and StemBANCC) and collaborations in the field of metabolism and diabetes with Takeda (Karpe) and Novo Nordisk (Gough).

Group 8: Musculoskeletal Medicine

Achievements and Initiatives

- The REF2014 period has seen several major initiatives to strengthen the research in the *Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences* (NDORMS, Carr), including the £11M *Botnar Research Centre Phase 2* (2013), which provides an additional 2000m^2 of research space.
- The *Kennedy Institute of Rheumatology* (Feldmann) was incorporated into NDORMS in 2011 and moved into a £28.1M facility in 2013; this has strengthened the research base in the fields of osteoarthritis and inflammatory disease and been a major vehicle for recruitment to Oxford (e.g. Dustin and others). It brings world-class experience in the development of biologics, building on its track record in anti-TNF therapy.
- Formation of a unified clinical service within the OUH Trust in 2011, centred on the *Nuffield Orthopaedic Centre*, creates both a shared vision and a capacity to address a wide range of musculoskeletal disorders and novel surgical and non-surgical treatments.

Forward Directions

- The *Botnar Centre* will continue its pioneering research into ultrasound and 7T-MRI to understand structural and functional changes in musculoskeletal disease. It leads (jointly with Nottingham) the *ARUK Centre of Excellence in Sports Injury and Arthritis Prevention* (Arden) and the *ARUK Experimental Medicine Centres in Rheumatology* (Taylor) and *Biomechanics* (Price).
- NDORMS houses the *Oxford Clinical Trials Research Unit* and the *Centre for Statistics in Medicine* (Altman, Lamb) and the Royal College of Surgeons-accredited *Orthopaedic Surgery and Interventional Research group (OSIRIS)* (Beard). These explore novel surgical technologies, including the development and worldwide application of Patient Reported Outcome Measures (PROMs, The Oxford Scores).
- The Kennedy Institute leads an *ARUK Centre of Excellence in the Pathogenesis of Osteoarthritis* (Vincent); its research into autoimmune disease is advancing our understanding of chronic inflammatory arthritis (Udalova and others) and antigen presentation in rheumatoid arthritis (Venables and Feldmann).

Group 9: Structural Biology

Achievements and Initiatives

- The *Division of Structural Biology* (STRUBI, Stuart and Jones) is one of the leading structural biology centres in Europe, strengthened by its close links to the Diamond Light Source at Harwell (Life Sciences Director Stuart). Its aim is to integrate analyses ranging from the atomic level of X-ray crystallography through cryo-electron microscopy (EM) and tomography, to the cellular level revealed by fluorescent light and X-ray microscopy.
- STRUBI studies dangerous CL3 pathogens in the purpose-built *Oxford Particle Imaging Centre (OPIC)*, which is unique in Europe. During the REF2014 period, the *Oxford Protein Production Facility (OPPF)* has become a national facility for crystallography (OPPF-UK).
- In evolution, the group's structural analysis has given major insights into links between Vaccinia and other dsDNA viruses across the domains of life (Grimes).
- In basic science with clinical applications, the group has identified RPTPσ as a bimodal switch responsible for neuronal growth and formation of excitatory synapses (Aricescu, Jones) and solved complex DNA-multiprotein structures giving insight into the action of tumour suppressors (Mancini)
- The *Structural Genomics Consortium (SGC)* has developed a nM inhibitor of the BET family of bromodomains, JQ1, which reduces proliferation and increase apoptosis in cells derived from an intractable human cancer, NUT midline carcinoma. It has also produced a further 9 novel inhibitors for epigenetic proteins, and makes them all freely available.
- The SGC is solving nearly 10% of all novel human soluble structures every year, and has now solved three novel human membrane protein structures (ABCB10, ZMPSTE24, TREK2).

Forward Directions

- The Virus and Vaccine Group (Grimes, Grunewald, Stuart) studies the structure of intact virus particles to understand disease pathogenesis and generate new therapeutics.

- The Cell Surface Receptors Group (Jones, Ariescu, Siebold) studies intracellular interactions and signal transduction, in the immune system, CNS and during development.
- The Membrane Protein Targeting group (Gilbert, Grunewald) studies intracellular targeting.
- The SGC covers themes in Chemical and Structural Biology (Knapp, von Delft), Genetics (Oppermann), Metabolism (Yue), Membrane Biology (Carpenter) and Growth Receptors (Bullock). It will consolidate its position as a world leader in human kinase structural biology, epigenetics, and chemical biology.
- STRUBI leads Instruct, the major European Infrastructure Project for structural biology; the SGC has assembled a collaborative network of more than 180 academic laboratories worldwide, and is a model of industry partnership and collaboration.

Group 10: Surgical Sciences

Achievements and Initiatives

- Surgical research and training was restructured and revitalised in Oxford in 2009. Alongside its partners in NDORMS, the *Nuffield Department of Surgical Sciences* (NDSS, Hamdy) has created a new pathway for surgical training and research, providing specialist support for its trainees in evidence-based surgery (with the UK Cochrane Centre, Burton) with a multidisciplinary approach based on strategic collaborations, joint projects and over 15 cross-departmental appointments and supervision.
- The Clinical Transplantation Research Unit (Friend, Ploeg) has collaborated with scientists in Biomedical Engineering (Coussios, UoA15) to create the first use of a machine for normothermic organ preservation. This will increase the number of viable organs and reduce the inflammatory response that occurs due to tissue damage.
- The Vascular Surgery Group (Halliday) includes the world's largest trial database (over 20,000 patients) of factors affecting stroke prevention after carotid endarterectomy.
- The NIHR/BRC Surgical Innovation and Evaluation Theme supports translational projects in ablative devices, device-targeted therapies and organ reconditioning, and is underpinned by the Surgical Intervention Trials Unit (run jointly with NDORMS).
- The NDSS has grown from 74 to 126 employees.

Forward Directions

- The Surgical Oncology group has joined with the Department of Oncology to establish multidisciplinary research in bladder and prostate cancer (Hamdy, Kiltie, Mushcel, Tomlinson), colorectal cancer (Shazad, Bodmer, Tomlinson) and intra-operative imaging (Hamdy, Vojnovic, Ahmed, Yeung); and the joint appointment of Edwards by the NDSS and NDORMS has established a new group in Cancer Induced Bone Disease.
- £35M funding from HEFCE and £70M from industrial partners was secured in October 2012, to establish the Oxford Targeted Cancer Research Centre jointly with Oncology.

c. People, including:

I STAFFING STRATEGY AND STAFF DEVELOPMENT

Aims: The staffing strategy for UoA1 is designed to focus the widest possible groupings and most effective scientific interactions on major biomedical problems. **Research excellence** is the overriding criterion for academic recruitment, and the University is committed to hiring only the very best academic staff, irrespective of gender, ethnicity, or nationality (subject to UK Border Agency controls). The Medical Sciences Division has a personnel committee with oversight and responsibility for policy, but the recruitment process and responsibility for staff development are devolved to departments. Each department identifies priority areas for appointments in the University's annual strategic planning round, with emphasis placed on those that address core teaching needs, actively support new initiatives, build upon existing research strengths, or open new areas of multidisciplinary and collaborative research. Joint appointments between departments are a priority over the next five years.

Great emphasis is placed on supporting young researchers and providing them with the intellectual and physical environment to develop their own careers. This capacity-building strategy brings a **vibrant youthful culture**, and provides a launchpad for future successes, in Oxford or elsewhere. Academics are appointed to either tenured/tenure-track posts or fixed term early career positions. Tenured and tenure-track staff are appointed to Statutory Chairs, Research Professorships (RSIV)

and University Lecturers (ULs). Statutory Professors and ULs are appointed both by the University and a College. There is no formal requirement for RSIV post-holders to be simultaneously appointed to a College; however, many choose to take advantage of a College affiliation. Statutory Chairs and RSIVs receive generous start-up packages to enable them to move their research programme to Oxford. Further integration into the University takes various routes depending on individual academic interests and synergies.

Senior Staff: Several features of our organisation and its staffing policies and infrastructure support the recruitment and development of senior staff.

Flexible structures that link disciplines and facilitate interactions among senior staff

- **Breadth of Expertise**. The research base encompasses a very broad range of expertise, from basic to clinical science.
- **Shared Space**. The structure, built on departments and shared institutes, brings senior scientists together. The organisation of staff in multidisciplinary groups within separate institutes creates a critical mass of expertise and effective sharing, without undermining the focus and innovation that comes from small, specialised units.
- **College Appointments**: bring senior staff together from across the University.
- **Sharing with other HEIs**: An important principle of the Tropical Medicine programme in UoA1 has been to include investigators from a number of other UK institutions. Moreover, the University encourages its staff to have affiliations with other institutions (see below).

Flexible appointment contracts encourage multidisciplinary working

- **Interdepartmental appointments**: for example, Donnelly, McVean (NDM and Statistics); Edwards, Altman (Surgery and NDORMS); and the new statutory chair in Musculoskeletal Science (Engineering and NDORMS).
- **Joint working with the NHS (OUHT and NIHR)**: UoA1 is highly integrated into the OUHT. Over 100 staff hold Honorary Consultant Contracts; more than 60 staff contribute to the on-call clinical service; and two of the current acute medical team are also FRS (White and Ratcliffe). Staff contribute to day-to-day management of the OUHT: Hamdy and Carr are OUHT Divisional Directors for Surgery and Musculoskeletal Medicine, respectively, as well as heads of University Departments (Surgery and NDORMS). 18 staff are supported by the NIHR and Oxford BRC.
- **Inter-institutional Appointments**: These include joint appointments between STRUBI and Diamond Light Source (Stuart), and WTCHG and the Wellcome Trust Sanger Institute (Kwiatkowski).
- **Interactions with Industry**: The University encourages its staff to interact with industry to accelerate the translation of its basic science. Academic staff are rewarded by consultancy arrangements.

Range of personal rewards and development opportunities for senior staff

- **Titular distinction**: The University conducts an assessment process to reward academic distinction; 95 UoA1 staff hold the title of University Professor.
- **Remuneration for merit**: The ability to reward excellence supports staff recruitment and retention.
- **Devolved funding model**: This provides discretionary funds to departments, which is essential for the development of research units and rapid innovation.
- **Focus on research as well as teaching effectiveness**: All academics are entitled to one term's sabbatical for every six terms of service; academics who are successful in securing funding for substantial research programmes can have a reduction in teaching commitments for the duration of the research project.
- **Training and development**: Academic Leadership courses are run by the Oxford Learning Institute, for Department Heads and others who wish to develop leadership skills.

The result of these initiatives has been the recruitment and retention of an exceptionally able cadre of research leaders: 36 of our staff are FMedSci and 13 are FRS. 33 staff hold Senior Investigator, Senior Fellowship or equivalent awards, and 30 staff are programme-holding members of MRC or similar units. **Notable appointments among the 88 new senior staff since RAE2008 include**: *Dustin*, *Hollander*, *Eggeling*, *Powrie*, and *Rehwinkel* (Infection, Immunity and

Inflammation); *Antioniades* and *Ashrafian* (Cardiovascular Disease); *D'Angiolella*, *Christianson*, *Goding*, *Gyrd-Hansen*, *Kriaucionis*, *Schuster-Bockler*, and *Tomlinson* (Cancer)*; Fulga*, *Milne*, *Nerlov*, *Rabbitts*, *Roberts*, and *Sauka-Spengler* (Haematology and Stem Cell Biology); *Barbosa-Morais*, *Christodoulides*, and *Pavord* (Metabolic, Endocrine and Respiratory Medicine); *Bowden*, *Donnelly*, *Lunter*, *McVean*, and *Spencer* (Genetics), *Udalova* (Musculoskeletal Diseases), *Baker*, *Thwaites*, *Wertheim*, and *Zurovac* (Tropical Medicine); *Bowden*, *Gruenewald*, *Filippakopoulos*, and *Padilla-Parra* (Structural Biology); and *Hamdy*, *Lilja*, and *Ploeg* (Surgical Sciences).

Early Career Staff

Oxford has one of the greatest concentrations of externally funded **early- and mid-career fellowships** in the UK. Our junior staff hold over 50 Wellcome Career Development, Royal Society University Fellowships, or similar intermediate awards. Former junior staff have gone on to hold senior positions in more than 80 universities since 1993, including heads of school in Cambridge, Imperial, and the National University of Singapore. The Medical Sciences Division offers regular career development opportunities for **postdoctoral research assistants**, and many of our current leaders have passed through local training on their way to running their own programmes.

Early career researchers (ECRs) are either appointed to fixed-term (5 year) Departmental Lecturer (DL) positions, or join the University having secured their own Independent Research Fellowship (IRF) from external funders. DLs and IRFs have the same status as tenured/tenure-track academic staff with regard to space allocation, access to facilities and input to policies. Post-doctoral research assistants (PDRAs) are recruited on externally funded grants awarded to academic staff.

The European Commission's HR Excellence in Research Award recognises the University's work in staff mentoring, career and professional development in line with the National Research Concordat. Notable features of support for junior staff include:

- **Formal mentorship scheme** run by senior staff under the University's Code of Practice for the Employment and Career Development of Research Staff, and annual appraisal.
- **Departmental research facilitators** who support fellowship applications.
- **Opportunities for teaching and training**. The Oxford Learning Institute (OLI) and MSD Skills Training Programme provided over 100 courses attended by UoA1 staff in 2012/13.
- **Specific leadership schemes** to support outstanding postdoctoral scientists: eight are in the NDM Leadership Scheme, and over 20 are in the BHF Centre of Excellence Scheme.
- **Cross-departmental postings to support and train junior investigators**, for example between NDS and Oncology (Edwards).
- **Industrial schemes**. UoA1 has developed a programme of postdoctoral fellowships jointly funded with industrial partners including UCB and NOVA.

The Oxford University **Clinical Academic Graduate School** (OUCAGS, Pugh) is a new venture to support the careers of clinical academics across the Medical Sciences Division, including seminars, an accredited programme of research training, overseas academic and clinical placements, and funding opportunities. UoA1 has staff with over 20 intermediate-level clinical fellowships. Notable achievements include:

- Expansion of the Academic Foundation doctors and Academic Clinical Fellowships to 40 and 57 per year, respectively.
- Expansion of Oxford's Wellcome Trust Clinical Doctoral Training Programme to 8 per year.
- Retention and expansion of the clinical lecturer grade to 46 posts, with 13 added in 2013.

Vibrant, Inclusive and Flexible Environment

Departments utilise central University support structures to coordinate and facilitate individual career development programmes. Support is provided by Personnel Services (HR matters), OLI (personal and professional development), Research Services (grant applications, ethical issues, and research integrity), the Equality and Diversity Unit, and the Careers Service. The University's work to support career development has been acknowledged by the European Commission's HR Excellence in Research Award.

Oxford University's commitment to hiring only the very best academic staff is achieved through a strategy of **worldwide recruitment**. The success of this policy is evidenced by the highly diverse nature of the staff returned in UoA1, and the close interactions between Oxford and its overseas programmes. Current principal investigators are from over 20 countries; the roster of research staff and postgraduate students similarly reflects this diversity. Each department in UoA1 has an **Athena SWAN** self-assessment team involved in implementing and monitoring the impact of strategies to provide equal opportunity to all staff, with a particular focus on women's careers. Five UoA1 departments or their constituents have been awarded Athena SWAN Bronze awards; several of the remaining departments and units will submit for awards in November 2013. This commitment to equality builds on the University's institutional Athena SWAN Bronze award.

Both formal and informal flexible working arrangements are common across UoA1. We aim to provide a family-friendly environment where everyone feels able to take the time they need for family, regardless of whether that time is spent with children, partners or aging parents. This ethos is as relevant to support staff as academic staff, and processes are in place to enable all staff to balance a successful professional career with a fulfilling personal life. For example, there are generous maternity, paternity, parental, and adoption leave terms and a comprehensive range of University childcare services. In most departments, women returning from maternity leave have reduced teaching loads so that they can focus on research. 13 staff returned in this submission had maternity leave during the assessment period.

II RESEARCH STUDENTS

UoA1's teaching mission is integral to its research. The excellence of the clinical school and graduate programmes enriches the full range of scientific work, and has led to major contributions from students to research activity. During the REF2014 period, UoA1 students have published first author papers in high profile journals such as *Nature*, and *Science*, and a quarter have received local or national awards. Since 1993, a fifth of our students have received personal fellowships on completion, and a quarter have progressed to become independent investigators in Oxford and elsewhere. This record is built on a careful programme of support and training.

Recruitment and Funding

The REF2014 period has seen several steps to radically improve access to its graduate programmes and increase the number and quality of its research students. This has been underpinned by strong collaboration between departments, as well as the formation of a **Medical Sciences Graduate School** (2011), which has created a single point of entry for applications and administrative support. As a result of these initiatives, the number of DPhil graduates in UoA1 has increased by 75% and the number of applicants per place has increased nearly threefold. Notable achievements have included:

- **Massive investment in new studentships**, introduced as access to central funding encourages departments to under-write the support for excellent applicants. In this way, the NDM alone has underwritten over £3M of funding to prize studentships from 2007-2012.
- **Establishment of a central Division-wide funding model (2009)**, which allocates unrestricted University and available RCUK funds (MRC/BBSRC) on the basis of academic merit to students worldwide.
- **More competitive stipends (>£18,000/yr) and four-year studentships as standard** (except for 3 year clinical trainees).
- **Access to the largest portfolio of Wellcome Trust funded doctoral programmes** in the UK, for clinicians and basic scientists in Genomic Medicine and Statistics, Structural Biology, Infection, Immunity, Radiation Biology and Translational Medicine, Chromosome and Developmental Biology, Neuroscience, and Ion Channels and Disease (total 35/year).
- **Ongoing support for major international graduate programmes** with the Scripps Institute and with the NIH (jointly with the University of Cambridge).
- **Launch of summer internship programmes (2009)**, to encourage overseas students from China, Japan and partner universities in Toronto, Singapore and Zurich.
- **Innovation in industrial partnerships**: including RCUK CASE awards (6/yr) and direct joint studentships, for example with Novartis Shanghai.

Support

Students are members of colleges; the University provides independent pastoral support through college advisors, who can act as student advocates, as well as specific support through the student counselling service. The Colleges provide libraries and computing facilities, access to travel funds and other bursaries, and a diverse intellectual environment. The University Careers Services provides advice.

Supervision

All research students have two supervisors who are responsible for their scientific training; they assess training needs, and identify appropriate courses that students should attend. The University has a "Code of Practice for Supervision of Research" under which supervisors must advise, guide and support research students in all aspects of their research project; have regular meetings; and encourage them to participate in the wider Oxford community. A termly reporting system facilitates close monitoring and support of students' progress, with input from students, supervisors and Directors of Graduate Studies. The academic milestones of Transfer of Status and Confirmation of Status, where student progress is evaluated by independent assessors, also ensure progression is adequately monitored.

During the REF2014 period, the Medical Sciences Division has taken steps to strengthen supervision, planning and feedback, as well as introducing dual supervision as standard:

- Supervisors and students write reports 3 times a year.
- At 1 year the student must pass a transfer to DPhil status, involving a report and *viva voce*.
- At 3 years the student must confirm this status, with a report, presentation and plan for completion within 4 years.

Training

Whether entering directly into a Department or into a Doctoral Training Centre, all students are trained in an environment in which there is an exceptionally strong critical mass of experts and resources. Induction programmes help integrate students into that environment as rapidly as possible, and events such as student symposia reinforce the cohort.

The Medical Sciences Graduate School provides thematic training and support for students within each of the groups of UoA1:

- Undergraduate lectures in the Medical Sciences Division are available to new graduates.
- Students have access to approximately 350 courses, including required courses in ethics, plagiarism and good laboratory practice.

d. Income, infrastructure and facilities

UoA1 is committed to the principle that the best way to support innovation and growth is for income to follow activity. Infrastructure projects are primarily funded through Departments, with support at the Divisional level. This strategy puts funding in the hands of researchers, and is flexible and responsive to new initiatives. Leadership at the Divisional level coupled with close collaboration between the Departments has supported our ability to create infrastructure in areas where research capacity faces the most potential limitation.

INCOME

UoA1's strategy is to maintain and build as diverse and sustainable a portfolio of funding as possible. Grant income in UoA1 grew by 30% over the period 2008-2012, and at 8-9.5% per annum, with the exception of the financially stringent period of 2009-10 (Table 1). Long-term (5 year) funding supports the majority of the research activity and UoA1 currently holds more than £400M total grants.

Table 1: UoA1 Income

Year	BIS/RCUK	UK Govt	EU	Charities	Industry	Overseas	Total
2008-09	£16.2M	£9.3M	£7.6M	£77.1M	£8.3M	£9.5M	£128.0M
2012-13	£31.8M	£17.2M	£9.5M	£89.4M	£15.3M	£2.9M	£166.1M

BUILDINGS

The Oxford Clinical Campus is principally located at two locations: the John Radcliffe Hospital (JR) and at the Churchill, Nuffield Orthopaedic and Warneford Hospital sites (Old Road Campus, ORC). The two campuses are only a mile apart, and have close links to departments in biological (UoA5) and physical sciences, which just over two miles away in central Oxford (South Parks Road Campus, SPR). Both the JR and ORC campuses have provided land for the expansion of the Medical School and the OUH NHS Trust; notably, in the case of the latter, the construction of the £109M Cancer and Haematology Centre at the Churchill Hospital in 2009, the £105M West Wing at the JR in 2004, and the £29M Oxford Heart Centre at the JR in 2010. As part of future planning, the University has recently increased its holding of land at the ORC by 78%.

During the REF2014 period the Medical Sciences Division has made a £98.2M capital investment in the physical construction of new buildings and institutes for UoA1 at its two campuses, including the £4.2M extension of the Weatherall Institute for Molecular Medicine in 2008, construction of a £1.5M Translational Gastroenterology Unit in 2009, and £4.2M Acute Vascular Imaging Centre in 2008 (JR); and the £3.5M Botnar Phase 2 Building, the £38.1M Kennedy Institute and the £23.8M Target Discovery Institute, all in 2013 (ORC). Further plans for development at ORC include the £45M Big Data Institute and £35M BioEscalator business incubator.

These developments add to existing laboratories at the two sites, including the Wellcome Trust Centre for Human Genetics (WTCHG, 1999), Richard Doll Building (2005), Oxford Particle Imaging Centre (OPIC, 2004), Henry Wellcome Centre for Cellular and Molecular Physiology (CCMP, 2004), Oxford Centre for Diabetes, Endocrinology and Metabolism (OCDEM, 2003), Old Road Campus Research Building (2008), and the Peter Medawar Building for Pathogen Research (SPR) (1999). The total laboratory and teaching space housing staff in UoA1 is slightly over 50,700m^2. The sustained investment in new buildings means that UoA1 staff work in high quality purpose-designed laboratories. Slightly further afield, UoA1 staff work closely with the nearby Diamond Light Source at Harwell, which is only 15 miles away in South Oxfordshire.

Research capacity in UoA1 has also benefited in the area of animal research from the University's commitment to the £30M Biomedical Sciences Building (SPR, 2008). Basic and translational research in medical sciences often requires the use of animal models, and the University provides the highest quality of support and care for animals in accordance with Home Office Regulations.

INFRASTRUCTURE AND FACILITIES – GOVERNANCE AND ADMINISTRATION

The University is rich in specialised infrastructure. A cross-Divisional committee chaired by the Pro-Vice Chancellor for Research manages the University's £4.5M Wellcome Trust Institutional Strategic Support Fund (£1.5M/year), and works to coordinate applications for infrastructure and equipment funding. The University and NHS Partnership Board (2011) governs research activity in the OUH Trust, with a joint Estates Committee to manage shared infrastructure.

Sharing Locally. In 2012, the University launched a new online searchable database of its research facilities and major equipment (1,200 items worth over £10,000, including over 500 items in UoA1), which was developed with funding from EPSRC. The database encourages collaboration and sharing between groups, and maintains our record of current assets. It is one of the facets of the University's response to the RCUK Task Group (chaired by Sir Bill Wakeham) urging higher intensity use of resources. The University participates in the South East England Science & Engineering Consortium (SEESEC), to facilitate sharing on a regional level.

Sharing on a National and International Scale. Researchers in the physical sciences have been sharing large items of equipment on national or international basis for a long time, but a similar requirement in medical sciences is relatively new. UoA1 sees this wider approach as an opportunity to build its own infrastructure base and collaborations. The European Instruct Project is a model for this sort of arrangement, initiated by the Structural Biology Division in UoA1 (Stuart and Jones). Instruct brings together groups with expertise in structural and cell biology and is the major strategic voice for integrative structural biology across Europe; its members share access to and training in state-of-the-art sample preparation and characterisation facilities. The project has grown out of a recognition that equipment at the cutting edge of structural biology is expensive to build and maintain, and will become more so in the future; no single European country possesses

the equipment and corresponding expertise across all structural biology technologies, making sharing critical to success.

STRATEGIC SUPPORT FOR BASIC SCIENCE INFRASTRUCTURE

As well as targeting new initiatives, UoA1 has aggressively tackled **areas of deficiency** in its support for basic research across all groups. One example is single cell imaging, which had an urgent need for intravital microscopy and ultra-high resolution imaging infrastructure. This was addressed through three major initiatives in 2012: (i) £3.4M was invested in the Wolfson Imaging Centre at the WIMM, including a Director (Eggeling) who is a world leader in single molecule imaging; (ii) confocal imaging in the WTCHG was refurbished and an expert in super high resolution microscopy appointed (Padilla-Parra); and (iii) a world leader in intravital imaging was recruited to lead the immunology programme at the Kennedy Institute (Dustin).

INFRASTRUCTURE TO ACCELERATE TRANSLATION

UoA1 has sought to develop and maintain infrastructure in areas that could limit pathways to translation, in the fields of engineering, drug and target discovery, imaging, manufacturing capacity, clinical trials, clinical facilities and data analysis. As well as the Institute of Biomedical Engineering, Structural Genomics Consortium, Target Discovery Institute, Big Data Institute and Acute Vascular Imaging Centre detailed above, other infrastructure includes:

The Oxford Biobanks: these incorporate national patient collections in UoA1, including the pregnancy Biobank, HCV, IBD, OxVASC, OxVasc Heart Disease, Oxford Cardiovascular Bioresource, and the Kennedy-Botnar Biobank. These are housed in a purpose-built facility at Cowley in Oxford, and interact closely with the Biobanks returned in UoA2.

The Clinical Biomanufacturing Facility: this is the University's Good Manufacturing Practice facility at ORC, and has over 16 years' experience in producing biological "investigational medicinal products" for early-phase clinical trials. This is one of only two GMP certified units at HEIs in the UK and is exceptionally important in enabling new vaccine trials.

Clinical Trials Centres: these are supported in Oxford and in each of our overseas units. As an example, MORU (Thailand) employs 444 staff working on its trials and conducts research into 15 diseases in 20 countries in Asia and Africa. In Oxford, £6M has been invested in infrastructure for an Oxford Clinical Trials Research Unit (Altman) to sit alongside the Diabetes Trial Unit (Holman). This is supported by collaboration with the Clinical Trial Services Unit (CTSU, Collins, UoA2), which consolidates Oxford's position as the largest clinical trials centre in the UK.

Clinical Research Centres. For example, the *Oxford Targeted Cancer Research Centre* (McKenna, Harris and Hamdy) will develop, test and implement personalised diagnosis, imaging and therapy in early stage cancer. This is a partnership including the University, the OUH NHS Trust, CRUK, Roche Diagnostics, GE Healthcare and others.

SUPPORT SERVICES

Research and Legal Services offices facilitate research across the institution and knowledge exchange between the University's researchers, government, community organisations and industry. In the academic year from 2011-2012, the Medical Sciences Division Research Services Office (Liwicki) handled 990 grant applications, 27 memoranda of understanding and 1,740 other inter-institutional agreements. The Clinical Trials and Research Governance Unit supports a huge number of clinical trials, including large numbers of overseas and first-in-human trials.

Libraries: UoA1 is supported by the Radcliffe Science Library, which houses more than 1 million volumes of printed materials, with over 120,000 books and 1400 print journals available on open shelves. In addition, the Radcliffe Science Library provides complete electronic access to conference proceedings and journals from all professional societies, including ACM, IEEE, SIAM, and AMS, and all major publishers. It is one of the Bodleian Libraries, which together contain over 11 million volumes of printed material.

Computing: In 2012 the University consolidated IT services by creating a Central ICT Department, directed by a Chief Scientific Information Officer (Trefethen) who has responsibility for ICT policy and strategy across Oxford. This infrastructure includes the **Oxford Supercomputing Centre** (OSC), which has a number of conventional clusters with a total of 2,500 cores, an extensive shared-memory system, and two GPU clusters. The University is a partner in the e-Infrastructure South (eIS) consortium with the Universities of Bristol, Southampton and UCL; eIS shares a £3.8M

12,000-core conventional Intel system (Iridis3) hosted at Southampton, and a novel 20,000-core 372-GPU system (Emerald) hosted at the Rutherford Appleton Laboratory in Harwell.
Technology Transfer: Extensive support is available to all staff to support technology transfer and promote the wider impact of their research. Isis Innovation Ltd, a wholly owned subsidiary of the University, is the main vehicle through which this support is provided (see below).

e. Collaboration and contribution to the discipline or research base

The majority of UoA1 research involves interaction on a national and international scale. Its work builds on a foundation of collaborative and multidisciplinary research; scientific leadership; shared knowledge; local, regional and global outreach; interfaces with NHS and industry; shared collections and physical infrastructure including buildings; commitment to training; participation in government and international advisory bodies; science funding; and communication. UoA1 actively promotes collaboration and major contributions to the discipline.

THE FOUNDATION OF MUTLIDISCIPLINARY RESEARCH IN OXFORD

The University has fostered multidisciplinary research in Oxford by establishing:

- **Inter-departmental appointments**, as described in Section C.
- **Multidisciplinary and inter-departmental Institutes**, as described in Section D.
- **The Oxford Martin School** (2005), which brings together more than 40 laboratories from 17 University Departments to address broad themes in multiple fields. In UoA1, this includes the Oxford Stem Cell Institute, Institute for Emerging Infections and Institute for Vaccine Design.

RESPONSIVENESS TO EMERGENCIES AND EMERGING RISKS

The flexible organisation of UoA1 enables it to respond rapidly and with a critical mass of expertise to address new challenges in the healthcare arena.

- During the **H1N1 and H5N1 flu pandemics**, rapid UoA1 research informed WHO guidelines and immunisation policy, as described in Section B.
- The **Institute for Emerging Infections** (**EMDIS**) is a multidisciplinary team of biologists, mathematicians and clinicians (from UoA1 and 5) who study recently emerged infections and use this to anticipate challenges posed by novel emerging infections in the 21st Century. EMDIS has provided scientific advice regarding the impact of a broad range of emerging infectious diseases, including SARS, influenza and Creutzfeldt-Jakob Disease.

LEADERSHIP OF NATIONAL AND INTERNATIONAL CONSORTIA

- **Infections and Immunology**: UoA1 staff have led major partnerships in the understanding and treatment of HIV, including the $186M Center for HIV/AIDS Vaccine Immunology (CHAVI, McMichael), with partners in the UK (Imperial College), South Africa and USA; SPARTAC (Phillips), which is the largest trial in early HIV, partnered with groups in the UK (Imperial College), Australia, Brazil, Kenya and South Africa; and the UKZN HIV Pathogenesis Programme (Goulder), based in KwaZulu-Natal with partners at MIT and Harvard University.
- **Tropical Medicine**: UoA1 promotes research networks and responses to challenges to world health, including CODFIN (Counterfeit Drug Forensic Investigation Network); the Melioidosis Clinical Trials Study Group; the Southeast Asia Infectious Disease Clinical Research Network (SEAICRN); the World-Wide Antimalarial Resistance Network (WWARN); the Tracking Resistance to Artemisinin Collaboration (TRAC); the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC); the WT-Institut Pasteur Collaboration; and the African Quinine versus Artesunate Severe Malaria Trial (AQUAMAT).
- **Cardiovascular Medicine**: major collaborations and consortia include PROCARDIS, the C4D and CARDIoGram+C4D genetics consortia; The FP7 Big Heart Project; a Leducq Transatlantic Network of Excellence; the STICS trial (Statin Therapy In Cardiac Surgery) in Atrial Fibrillation, in China. The Group also has collaborations with national and international organisations, including patient groups and the WHO.
- **Regenerative Medicine**: The Oxford Stem Cell Institute (OSCI) leads StemBANCC, a Europe-wide venture aimed at exploiting the benefits of induced pluripotent stem cells (iPS) for human disease modelling. The OSCI has contributed extensively to the development of government policy in the emerging field of regenerative medicine.
- **Genetics**: WTCHG scientists played a leading part in the HapMap and 1000 Genomes

projects, which involved researchers from over 10 countries, and in GWAS methods, leading over 20 major disease studies. A new focus is in whole-genome sequencing for Mendelian traits with NIHR partners and Bristol and Newcastle Universities.

- **Cancer**: The clinical trials capacity in UoA1 has been used nationally and internationally; Oxford oncologists are running over 70 trials and major collaborations, with over 40 HEI partners (11 outside the UK) and 15 pharmaceutical companies. This is exemplified by the ProtecT Study (Hamdy), the largest randomised controlled trial of treatment effectiveness in screen-detected prostate cancer worldwide, involving nine clinical centres in the UK and 110,000 tested subjects; it will report findings in 2015.
- **Growth, Nutrition and Reproductive Medicine**: INTERGROWTH-21st and INTERBIO-21st (Kennedy and Villar) are $24.1M population-based studies in Brazil, China, India, Italy, Kenya, Oman, the UK and USA, led from Oxford in collaboration with the WHO. They aim to produce fetal, newborn and pre-term postnatal international growth standards, and identify the causes of intrauterine growth retardation and pre-term birth syndromes.

CONTRIBUTIONS OF SPECIALISED KNOWLEDGE AND TRAINING

- **Genetics**: UoA1 has been a leader in developing tools for **High Throughput Sequencing**, including the read-mapper *Stampy*, the variant-caller *Platypus* (both Lunter) and the *de novo* assembly algorithm, *Cortex* (McVean). UoA1 supports these collaborations through access to its core facilities and capacity for the functional analysis of variants.
- **Radiation Biology**: The **Particle Therapy Cancer Research Institute** (**PTCRi**) formed in 2009 under the co-Directorship of Peach (Physics) and Jones (Oncology) promotes the adoption of charged particle therapy in the UK, through the EPSRC-funded PAMELA project to develop a new particle accelerator with improved performance over existing technologies, and three EU Framework 7 projects (ULICE, PARTNER and ENVISION) to develop instrumentation and informatics for this therapy.
- **Structural Biology**: UoA1 is one of the major structural biology centres in Europe. During the REF2014 period its **Oxford Protein Production Facility** (**OPPF**) has moved to become a national facility (**OPPF-UK**) at the Rutherford Appleton Laboratory.
- **Clinical Trials**: As described in Section D, UoA1 and UoA2 together have the largest capacity for clinical trials in the UK; the **Diabetes Trial Unit** in OCDEM (Holman) is the largest academic research organisation in the world specialising in large diabetes-related trials. UoA1 has conducted over 30 first-in-human trials in the REF period, of drugs and new vaccines.

SHARING PHYSICAL INFRASTRUCTURE

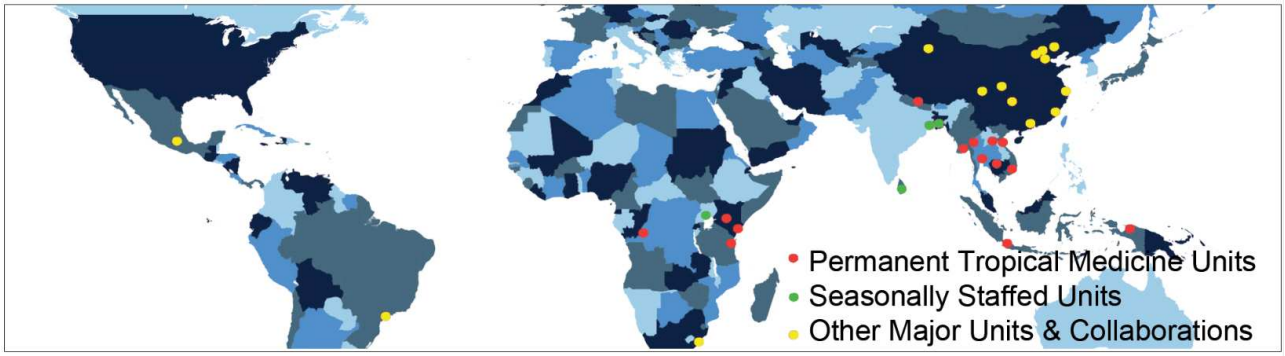
The UoA1 contributes to the wider research community by sharing physical resources, including clinical material, equipment and buildings, with multiple partner institutions. It will extend this concept in the period after the REF2014, through initiatives like the Big Data Institute.

- **Clinical Material**: National resources in UoA1 have been shared with over 105 institutions. As an example of field-specific leadership in musculoskeletal sciences, the Botnar-Kennedy Biobank has over 3,000 joint tissue samples from patients with inflammatory disease, osteoarthritis and sarcoma coupled to data from multiple imaging platforms.
- **Equipment and Resources**: As already articulated, UoA1 has a comprehensive strategy for sharing equipment nationally and internationally.
- **Oxford Buildings**: UoA1 shares physical space and infrastructure in Oxford and elsewhere through its formal partnerships, including partnerships with the Wellcome Trust Sanger Institute, involving investigators in immunology and infectious diseases, tropical medicine, and genetics; and with the Wellcome Trust Clinical Research Facility at Southampton University, involving musculoskeletal sciences.
- **Overseas Facilities**: Each UoA1 Tropical Medicine Unit strives to be as inclusive as possible, housing and working with PIs from a number of other UK institutions.

OUTREACH WORLDWIDE

Numerous examples have already been given of UoA1's outreach programmes and global collaborations (see figure below); new partnerships have been established with groups in Mexico and Brazil to study Chagas' and other diseases specific to the Americas.

Overseas Research Units in UoA1.



PARTNERSHIPS WITH THE NHS

UoA1 contributes to NHS research locally through the Oxford NIHR/Biomedical Research Centre, and nationally through ties to our partner Biomedical Research Centres at King's College, Imperial College, UCL, and University of Cambridge. This OUH Trust and its Clinical Research Centres underpin this activity, and will soon be joined by the Oxford Targeted Cancer Research Institute and Translational Gastroenterology Centre. Other examples include:

- The UK Clinical Research Consortium '**Modernising Medical Microbiology**' is funded by the Wellcome Trust, MRC and Oxford NIHR/BRC, and involves Oxford University and the OUH Trust as well as hospitals in Birmingham, Brighton, and Leeds, the Health Protection Agency, and the Sanger Institute.
- Addressing unmet need, UoA1 supports several **Trials in Orthopaedic Surgery**, including open versus arthroscopic rotator cuff repair (UKUFF); total versus unicompartmental knee replacement using the Oxford Knee (TOPKAT); the role of acromioplasty surgery in the treatment of shoulder pain (CSAW); and the effectiveness of autologous growth factors in association with acromioplasty surgery (PAROT).
- Research by the **Cardiovascular Genetics Group** (Watkins) has led to the foundation of an NHS commissioned national genetic testing service for inherited cardiomyopathies.
- The NIHR/BRC-funded **Oxford Experimental Cancer Medicine Centre Network** (Middleton) coordinates early phase medical and radiotherapy trials, for example in melanoma and sarcoma; in its involvement with the **Thames Valley Cancer Research Network**, it incorporates six further Hospital Trusts.

INNOVATION IN PARTNERSHIP WITH INDUSTRY

UoA1 collaborates with industry by encouraging the transfer of technology and knowledge; accelerating discovery through direct interactions in areas of basic and clinical research; improving the environment for the growth of new enterprises and supporting local biotechnology.

- **Transfer of technology and knowledge**: During the REF2014 period, the University's technology transfer company, Isis Innovation Ltd, has supported 4 new spinouts and secured nearly 200 patents in UoA1. UoA1 groups support significant knowledge transfer; for example, the Cardiovascular Medicine Group is an advisor to Siemens in the field of MRI development.
- **Accelerating discovery through direct interactions**: UoA1 has pioneered joint funding of institutes and multidisciplinary programmes, including OCDEM (Novo Nordisk, Takeda Ltd, and Servier UK); the Structural Genomics Consortium (Lilly, GSK, AbbVie, Boehringer Ingelheim, Janssen, Novartis, Pfizer and Takeda Ltd); the Target Discovery Institute (UCB Pharma, Takeda, Boehringer Ingelheim, Janssen, Abbott, and Life Technologies), the Big Data Institute (Illumina, Life Technologies, Microsoft and Oracle), and the Oxford Targeted Cancer Research Centre (Pronova, HIT, Roche Diagnostics and GE Healthcare).
- **Improving the environment for the growth of new enterprises**: The planned **BioEscalator** on the Old Road Campus will be an incubator, providing cost-effective space to grow new firms in life sciences close to the clinical and basic research hubs.
- **Supporting the Thames Valley High Technology Cluster**: Strategic initiatives between Oxford University and the local biotechnology sector (representing 170 small and medium sized enterprises) have been formalised in a joint partnership (Bell).
- **The Centre for the Advancement of Sustainable Medical Innovation** (**jointly with UCL**): contributes to partnerships by addressing legislative hurdles and other barriers to innovation.

OTHER NOTABLE CONTRIBUTIONS BY UOA1 2008-2013

Contributions to Governmental and International Advisory Bodies	
International Advisory Committees	WHO Malaria Treatment Guidelines (Chair White). WHO Dengue and Emerging Viral Diseases Disease Reference Group (Chair Farrar). WHO Antimalarial Drug Resistance and Containment (Chair, Dondorp). WHO Malaria Policy Advisory Committee (Chair, Marsh).
Leadership in UK Science	UK Government Office for Strategic Coordination of Health Research (OSCHR, Chair Bell); President of the Academy of Medical Sciences and author "Reaping the Rewards: A Vision for UK Medical Science" (2009 Bell). NIHR Clinical Evaluations and Trials Board (Chair, Lamb); Life Sciences Director, Diamond Light Source (Stuart).
Contributions to Science Funding	
National Funding Committees and Organisations	Director of the Wellcome Trust (Farrar, from October 2013). 89 staff on funding committee panels. Current chairs of major UK Panels: Wellcome Trust Physiology Review (Ratcliffe); KRUK Grant Committee (Cornall); BHF Project Grants (Cooper). Staff membership of major UK panels include: MRC 4; CRUK 3; ARUK 3; BHF 3; KRUK 1, Wellcome Trust 2. 66 staff serve on Charity Advisory Boards.
Contributions to Science Communication	
Journal Editorships	Served as journal editors: 29 staff. Membership of journal editorial boards: 104 staff.
Other Measures of Distinction	
Elections to Learned Societies	13 Fellow of the Royal Society, including new Powrie (2011), Wilkie (2013); 36 Fellows of the Academy of Medical Sciences, including new Snow (2008), Donnelly (2008), Day (2008), Brady (2008), Tomlinson (2009), Channon (2009), Carr (2009), Rorsman (2010), Altman (2011), Aziz (2012), Casadei (2013), English (2013), Lu (2013) Klenerman (2013), Scott (2013); 3 Members of US National Academy of Sciences.
Notable Invited Lectures	Francis Crick Lecture, Royal Society (Fisher 2008); Harveian Oration, Royal College of Physicians (Bell 2010); Francis Crick Lecture, Royal Society (McVean 2010), Goulstonian Lecture, Royal College Physicians (Knight 2011); Linacre Lecture, Royal College of Physicians (Chapman 2012); Fisher Lecture (Donnelly 2012).
Notable Prizes	Chalmers Medal, Royal Society of Tropical Medicine and Hygiene (English 2008); Weldon Prize (Donnelly 2008); Louis-Jeantet Prize for Medicine (Ratcliffe 2009); Graham Bull Prize, Royal College of Physicians (Klenerman 2009); Lasker Special Achievement Award (Weatherall 2010); Manson Medal, Royal Society of Tropical Medicine and Hygiene (White 2010); Gairdner Medical Prize (Ratcliffe 2010); Gairdner Global Health Award (White 2010); Mackay Medal, Royal Society of Tropical Medicine and Hygiene (Hien 2010); Pfizer Award, Royal Society (Makani 2011); Dorothy Hodgkin Prize, Diabetes UK (McCarthy 2010); Baly Medal, Royal College of Physicians (Ratcliffe 2011); MacDonald Medal, Royal Society of Tropical Medicine and Hygiene (Snow 2011); Graham Bull Prize, Royal College of Physicians (Knight 2011); Louis-Jeantet Prize for Medicine (Powrie 2012); Foundation Pfizer Award, Royal Society (Kariuki 2012); Lefoulon-Delalande Grand Prix Scientifique (Ratcliffe 2012); Weldon Prize (McVean 2012); Roentgen Medal (McKenna 2013); Royal Medal, Royal Society (Bodmer 2013); Buchanan Medal, Royal Society (Higgs 2013); Gold Medal, Royal College of Radiologists (McKenna 2013).