Institution: University College London (UCL)

Unit of assessment: UoA 01 Clinical Medicine

A. OVERVIEW

A1 UCL's submission to UoA 1 includes 449.8 whole time equivalent (WTE) Category A staff in the School of Life and Medical Sciences (SLMS). It represents an integrated grouping of basic and clinical research, in **partnership** with multiple NHS Trusts (consolidated by three Biomedical Research Centre awards (BRC)), industry (consolidated by mutual recognition of biomedical expertise) and other Higher Education Institutions (HEIs; consolidated by strategic alliances).

A2 Eight Institutes/Divisions in UCL SLMS are being returned (in part or entirely) to UoA1. These are:

1. Faculty of Medical Sciences
   a. Cancer Institute
   b. Division of Infection and Immunity
   c. Division of Medicine
   d. Division of Surgery and Interventional Sciences

2. Faculty of Population Health Sciences
   a. Institute of Cardiovascular Science
   b. Institute of Child Health
   c. Institute for Women's Health

3. Faculty of Brain Sciences
   a. Institute of Ophthalmology

A3 Research in UoA1 is critically dependent on strategic alignment with the NHS, exploiting the co-location and commonality of purpose that exists between UCL academics and the following companion NHS Trusts:

1. MEH Moorfield's Eye Hospital NHS Foundation Trust
2. UCLH University College London Hospitals NHS Foundation Trust
3. RFL Royal Free London NHS Foundation Trust
4. RNOH Royal National Orthopaedic Hospital NHS Trust
5. GOSH Great Ormond Street Hospital for Children NHS Foundation Trust
6. WH Whittington Hospital NHS Trust

A4 The success of the UCL/NHS partnerships is exemplified by the three BRC awards amounting to the most substantial investment in the UK by the National Institute for Health Research (NIHR) in the REF period:

1. BRC, UCL/UCLH (£100M)
2. BRC in Child Health, ICH/GOSH (£35M)
3. BRC in Ophthalmology, IO/MEH (£26.5M)

A5 We have established strategic alliances with industry, at the transition between discovery and invention, which exploit the complementary skillset of our UoA and its industrial partners, particularly GSK and Pfizer. We have also sought partnership with other major UK Universities, including those in London, Manchester, Newcastle, Oxford and Cambridge, with the ultimate aim of developing in the UK, a research base to challenge that of North America.

A6 Research Themes that we have prioritised in this UoA are:

1. Cancer
2. Infection, Immunity & Inflammation
3. Experimental Medicine
4. Ophthalmology
5. Child Health

A7 The vitality of our research is demonstrated by substantial investment in infrastructure, major scientific discoveries, innate interdisciplinarity, our training initiatives and impact of our research in addressing important health issues. For example:

1. Outstanding facilities and infrastructure, including major institutional investment in buildings (£33.6M) and major investment in equipment (£25M; including the first UK clinical PET-MR for research) in the REF period. Our total estate holdings are 37,300m^2, and there are 241 technical posts across the UoA that support research.
2. The newly built UCLH Macmillan Cancer Centre aligned with the Cancer Institute (£110M).
3. External validation of research excellence: e.g. renewal of the three BRCs in 2012, which are almost entirely based on the excellence of our research in Child Health, Ophthalmology, Infection, Immunity and Inflammation, Cancer and Experimental Medicine.
4. Creation of a UCL Institute for Immunity and Transplantation at RFL (£47M, opened June 2013).
5. 19% of published papers are in Science, Nature, Cell, Lancet, NEJM, JAMA, Immunity, JCI, J Exp Med and PNAS.
6. External research expenditure has risen from an average of £60M per annum for RAE2008 to £119M per annum in the current REF period, amounting to £1.3M per WTE researcher during the REF period.
7. Research activity sustained by eight vibrant doctoral training programmes which includes PhD programmes funded by CRUK, British Heart Foundation (BHF), EPSRC and Wellcome Trust (WT). We host one of only two MBPhD programmes in the UK and one of only five WT PhD programmes for Clinicians (2013-).
8. Substantial engagement with industry, with £47M of new funding awarded to UCL in the REF period, leading to major and diverse impacts as described in our impact statement and our impact case studies.
9. 72 newly promoted Chairs and 57 new recruits at professorial level, with three MRC Strategic appointment awards (£1.3M).
10. Senior Research Fellowships (eight WT, one BHF, one MRC), three WT Senior Investigator Awards, six Clinician Scientist Awards, one NIHR Clinical Professorship and 13 HEFCE Clinical Senior Lecturers. In total there were 87 Fellowships active during the REF period of which 71 were awarded after 2008.
11. Prioritising the needs of UCL researchers emerging into independence with the promotion within UoA1 of 45 UCL post-doctoral researchers to new investigator status. In addition, there has been the recruitment of 42 early career researchers, and a total of 42 Intermediate/Career Development Fellowships.
12. 161 programme grants or equivalent active during REF (£227M), with 95 awarded after 2008 (£123M), including, three WT Strategic Awards (2.4M) and the largest portfolio of MRC DPFS awards in the UK (12; £7.2M), six MRC DCS awards (£11.6M), three Wellcome Trust Translational Awards (£5.6M) and four EME awards from MRC/NIHR (£4.3M).
13. 46 impact case studies demonstrating improvements in the diagnosis of 14 and in the monitoring of 13 diseases, 17 new drug treatments (or drug combinations), two new devices, 10 examples where we have introduced novel non-drug treatments, three examples of commercialisation of our discovery science and 20 disease areas where

our advances have reduced health care costs.
14. An increase the number of WTEs being returned; there were 349 WTEs in UoA2, UoA3 and UoA4 in RAE2008 compared with 449.8 in REF2014.
15. Our interdisciplinarity is evidenced by 72 academics from UoA1 Divisions/Institutes being returned to other UoAs (2,4,5,8,11,15); 52% of our academics have interdisciplinary collaborations.

B. RESEARCH STRATEGY

Our aim is to achieve clinical impact through **partnership with the NHS, Industry and other HEIs.**

B1 Evolution of our research environment since RAE2008

Cancer research has seen major growth, both in the number of principal investigators (PIs) from 40 in 2008 to 78 in 2013, and also by the opening of the UCLH Macmillan Cancer Centre adjacent to the Cancer Institute in 2012. The Institute of Cardiovascular Science, with 27 PIs, was founded at UCL in 2011, bringing together cardiovascular investigators from all parts of UoA1 into a single unit spanning the entire life-course of cardiovascular disease. The Division of Infection and Immunity relocated to new laboratories in a central site on the Bloomsbury Campus in 2011, to further exploit the benefits of co-location with other inflammation groups. In partnership with the RFL, an Institute of Immunity and Transplantation was opened in 2013 at the RFL, funded by a £47M investment. The Institute for Liver and Digestive Health was founded in 2012 and brought together research activity in gastro-hepatology on the RFL Campus. Each of these developments has accelerated the fusion of basic with clinical science, supported by an enriched clinical research infrastructure. We continue to apply integrative molecular, cellular and imaging techniques, to use experimental medicine in early phase investigation and scale up to late phase clinical trials and epidemiological population-based approaches. Together with investment in the new technologies (-omics, imaging, informatics) we have made advances in disease phenotyping, illuminated mechanisms of pathogenesis, and discovered diagnostic and therapeutic interventions in children, adolescents and adults.

B1.2 Key mechanisms for achieving our strategic goals

1. Major research centres in Cancer, Ophthalmology, Child Health, Infection, Immunology, Inflammation, Rheumatology, Hepatology, Cardiovascular, Respiratory Medicine, and Nephrology. Maintaining an effective research environment and infrastructure, based around strong research groups led by outstanding individuals and funded by regular and longer-term research grants.
2. Interdisciplinarity: supported by the SLMS Domain structure that facilitates and resources collaborative work incorporating a broad range of related disciplines.
3. Career development: operating a well-structured career-development programme for both junior and senior academics and research staff through the Academic Careers Office http://www.ucl.ac.uk/slms/aco/homepage. This includes mentoring and future leaders programmes and continual interaction within and across research groups.
4. International co-operation: interacting globally through visiting professorships (25) numerous international collaborations, a high intensity of international conference participation, training networks, major involvement in editorial work for leading international journals, plus staff (i.e. 15% of new recruits being returned) and student (i.e. 20% of current postgraduate students) recruitment from overseas (section E2).
5. Enterprise and knowledge transfer in relation to significant issues in health and wellbeing. We support and encourage this key aspect of the research of many staff members and of the research centres to which they are attached (see impact statement REF3a).
6. Well-resourced state-of-the-art doctoral programmes: running training programmes with a significant teaching component, including PhD-specific courses in theory, methods, and core skills, opportunities for international exchange, major involvement with research

centres, and extensive interaction with experts.
7. Extensive engagement with our partner NHS hospitals, with 232 of our academics actively contributing to clinical service as medical practitioners or as clinical leaders.
8. Partnership with industry in areas of mutual benefit, representing 419 funded projects active during REF, with 133 currently active.
9. Partnership with other Universities, with many strategic initiatives outlined in section E1.

Below in sections B2-B6 we describe activity and achievements in our research themes, since 2008.
Note: superscripts prefixed 'O' relate to the numbered REF2 publications by specific lead (first or senior) authors. Underlining of staff names indicates Early Career Researcher.

B2 Cancer
Since 2008, we have seen a major transformation of cancer research at UCL. There are 73.4 Cat A staff leading cancer research across each component of UoA1. UCL's total grant income for cancer-related research is £161M (increased from £112M in 2008). The UCLH Macmillan Cancer Centre is the UK's most advanced ambulatory cancer care facility (£110M; 15,000m^2). UCL hosts a CRUK Centre, an Experimental Cancer Medicine Centre and a CRUK Clinical Trials Centre (CTC, the second largest CTC in the UK). The CRUK Lung Cancer Centre of Excellence was awarded to UCL and Manchester in 2013. The CRUK UCL Centre had its funding renewed in 2013 with an award of £8.3M.

B2.1 Major research groups
Our cancer programmes focus on developing translational research in cancers in which UCL has an international reputation, and include: gastrointestinal, neuroendocrine, gynaecological, lung, and urological cancers, leukaemia, lymphoma, sarcoma and tumours of the nervous system. Research is organised into cross-disciplinary centres that span the entirety of UoA1. These are:
- **Cancer biology and genomics**: Model organisms (yeast, drosophila, xenopus, zebrafish and mouse) are employed to study fundamental aspects of cell biology, as well as state-of-the-art genomics technologies to study chromatin modification, tumour-initiating cells, non-coding RNAs and epigenetic signatures associated with specific cancers.
- **Gene therapy, immunotherapy and stem cell transplantation**: The breadth of expertise in tumour immunology, immune-regulation, cancer vaccines, adoptive immunotherapy, T-cell engineering, chimeric antigen receptor (CAR)-engineered lymphocytes and vector design has been exploited to deliver gene, cellular and immune-based cancer therapies, for treatment resistant CD19+ lymphoma, and TCR-mediated gene therapies (WT1-TCR), and adoptive cellular therapies for viral infection (IMPACT, ASPECT, CMV-TCR).
- **Cell death, inflammation and immunity**: This Centre collaborates with the lung, gastrointestinal, gynaecological and brain cancer programmes as well as more broadly with investigators in Infection, Immunity and Inflammation.
- **KCL/UCL Comprehensive Cancer Imaging Centre**: Has recently been renewed and will develop imaging that elucidates the molecular and physiological processes of cancer. The work is interdisciplinary, is pan-UoA1 and includes engineering, chemistry and physics.

B2.2 Key recruits
The recruitment of **Walczak** and **Quezada** as leads for the Centre for Cell Death has significantly enhanced our competitiveness in this area. Since 2012, we have recruited **Swanton** between UCL and the **Francis Crick Institute** to develop personalised medicine and lead lung cancer research. This is exemplified by the award of TracerX (£14M) and the establishment of a Joint CRUK Lung Cancer Centre with Manchester (£2M). **Enver** was recruited to lead cancer stem cell research. **Calvert** was appointed to increase our expertise

in early phase drug development, and, in this, has been supported by the recruitment of **Arkenau** who also directs drug development at the Sarah Canon Research Institute (SCRI) http://sarahcannonresearch.co.uk. Partnership with SCRI increases access for our patients to the latest novel anti-cancer agents though a joint portfolio and establishes a research partnership focused on personalising cancer therapy.

B2.3 Key funding awards

Cancer Imaging Centre funding was renewed (CRUK and the EPSRC) with £7.5M in 2013, following an award of £8M in 2008. **Widschwendter** was awarded a €6M FP7 grant in 2012. There were 23 programme grants or equivalent awarded during the REF period, with a total award value of £29.6M, including seven from CRUK, six from the European Commission, one from the MRC, one from Marie Curie Cancer Care, two from the WT, one from Children with Cancer UK, one from Brain Tumour Charity, one from NHS Blood and Transplant and three from Leukaemia & Lymphoma Research. Senior Fellowships were awarded to **Janes** (WT) and **Swanton** (MRC), Clinician Scientist Fellowships to **Thirlwell** (CRUK) and **Ahmed** (MRC), and Intermediate/Career Development Fellowships to **Ooi**, (BBSRC) **Quezada** (CRUK), **Tomita** (CRUK), **Jenner** (EU), **Jennings** (MRC), **Hadjur** (MRC), **Kruse** (NHMRC), **Strauss** (SARC), **Hergovich** (WT), **Payne** (WT). **Rodriguez-Viciana** won an MRC Investigator award.

B2.4 Research highlights

Clinical Trials: **Peggs**[O2] (J Exp Med) developed new protocols to boost the immune system using an antibody targeting anti-CTLA4 (CTL-associated antigen 4) to enhance anti-tumour T cell function and to inhibit immune dampening T-regulatory cells. **Bridgewater**[O1] (NEJM) identified the current best chemotherapy combination for advanced gall bladder and bile duct cancer. **Vaidya**[O4] (Lancet) demonstrated that a single dose of intraoperative radiation therapy was as effective as a prolonged course of external beam radiotherapy in breast cancer. **Mackinnon**[O1,O3] and **Peggs**[O1] (J Clin Oncol X3) demonstrated that T-cell-depleted reduced-intensity transplantation followed by donor leukocyte infusions result in the best ever reported long-term survival in patients with multiply relapsed Hodgkin and non-Hodgkin lymphoma. **Ledermann**[O1] (NEJM) demonstrated the effect of PARP inhibition with olaparib in relapsed serous ovarian cancer. **Hackshaw**[O2] (NEJM) published the new gold standard treatment for thyroid cancer. **Emberton**[O4] (Lancet Oncology) led a first-in-human study of a novel tissue-preserving therapy for men with early prostate cancer.

Cancer genetics: **Flanagan**[O2] (Nat Gen) discovered the genetic abnormality driving Ollier disease/Maffucci syndrome (which are characterised by multiple bone tumours). **Gale**[O1,O4] (J Clin Oncol; Blood) discovered the prognostic implications of mutations in CEBPA FLT3, IDH1/2 and NPM1 in acute myeloid leukaemia, work which has major implications for treatment stratification. **Swanton**[O1] (NEJM) conducted the first genome-wide analysis of genetic variation within tumours and demonstrated marked temporal and spatial variation in genetic mutations within the same tumour, with implications for the likely success of personalised cancer therapies.

Cancer pathogenesis: **Boshoff**[O1] (Nat Cell Biol) discovered that oncogenic viruses exploit microRNAs to evade host immune responses. **Enver**[O2] (Nat Cell Biol) discovered a mechanism whereby cells leave the stem cell state and enter lineage specialisation and commitment. **Swanton**[O1] (Nature) implicated a central role for replication stress in the generation of structural and numerical cancer chromosomal instability, which could inform new therapeutic approaches to limit intra-tumour heterogeneity. **Walczak**[O1] (Nature) discovered the relevance of linear ubiquitination *in vivo* in preventing inflammation and TNF-regulating immune signalling, with implications for cancer-related immunity and cell death.

Experimental therapy: **Quezada**[O1] (J Exp Med) discovered the role of CD4+ T cells during anti-CTLA4 treatment, to increase antitumour activity against advanced melanoma in an experimental model. **Chakraverty**[O1] (J Clin Invest) showed that nonhematopoietic antigen blocks memory programming of alloreactive CD8+ T cells and drives their eventual exhaustion in mouse models of bone marrow transplantation.

Validation of screening tests: **Menon**[O1,O3] (Lancet Oncology x2) established the sensitivity and specificity of prevalence screening for ovarian and endometrial cancer.

B3 Infection, immunity and inflammation

This return includes 64.5 WTE Category A investigators in the Division of Medicine and the Division of Infection and Immunity. There is a MRC/UCL Centre for Medical Molecular Virology that has joint appointments with the Wellcome Trust Sanger Institute (**Kellam**) and the Crick Institute (**Stockinger**) to facilitate interactions. **The Institute of Immunity and Transplantation** has been developed in partnership with the RFL and was opened in June 2013 occupying 1800m^2 of newly refurbished space. Recently, £11M of funding from HEFCE and £22M of charity funds has been secured to build a new state-of-the-art research building over the next three years. **The Bloomsbury Research Institute** is a joint initiative between UCL and the London School of Hygiene and Tropical Medicine, bringing together Europe's largest groupings of infection-related researchers in a purpose built facility on the Bloomsbury campus. 1300m^2 of lab space was refurbished at the RFL campus in 2011 for the Amyloidosis and Rheumatology groups and included the establishment of the **Wolfson Drug Discovery Unit** at a cost of £2M. In 2012, the first ARUK Adolescent Rheumatology Centre was established, jointly between ICH and the Division of Medicine (£2.2M). The **Oliver Bird PhD Programme** in Rheumatology funded by the Nuffield Foundation, supported 10, four-year PhD studentships in the REF period, and was renewed in 2009 following a national competition. **Mauri** was awarded EU IMI funding (ABRISK) for studying biomarkers in rheumatic diseases (€20M).

B3.1 Major research groups

Our programmes bring together research expertise in pathogen biology, innate and adaptive immunity and chronic inflammation, to better understand the aetiology of disease, improve diagnostics and disease prevention and develop new therapies. Pathogen and host genomics are combined with deep cellular and molecular phenotyping in humans and functional testing in experimental animal models to gain new insights in the following areas:

- **Epidemiology of infection:** Next generation sequencing has been established as powerful tool to reveal the mechanisms of drug resistance (**Pillay)** and to track the origin and epidemiology of virus outbreaks (**Zumla**).
- **Host-pathogen interactions:** Mechanistic cell biology and genetic approaches have been used to uncover new molecular targets to prevent HIV entry and infection (**Towers**, **Weiss**).
- **Immunobiology:** Includes research on T cell function, novel T cell subsets, and mechanism of T cell senescence in humans (**Stockinger, Walker**, **Sansom**, **Akbar**).
- **Immunodeficiency:** Genetic screening of families using single nucleotide polymorphisms has revealed susceptibility genes for fungal infection, hyper IgE syndrome, early onset inflammatory bowel disease and certain autoimmune conditions (**Grimbacher**, **Burns**).
- **Immunotherapy:** Research includes the CMV kinetics in patients, and studies of the response to CMV-vaccination **(Griffiths**), and preclinical T cell engineering research for gene therapy trials **(Morris, Stauss**).
- **Rheumatology**: We host the largest Rheumatology groups in the UK, with particular expertise in SLE, Rheumatoid Arthritis, Anti-Phospholipid Antibody Syndrome and Scleroderma (**Isenberg**, **Ehrenstein**, **Rahman, Denton**). Rheumatology has established a worldwide reputation for the introduction of B cell depletion to treat patients with rheumatoid arthritis, systemic lupus erythematosis (including childhood onset SLE), myositis and vasculitis.
- **Innate immunity**: Research in this domain spans the innate responses to infection and tissue injury, and is a cornerstone of adaptive responses; activity focuses on biology of monocytes, macrophages and neutrophils (**Yona**, **Gilroy, Segal**), particularly the origins of these cell types, and the consequences of defects in their function.

- **Systemic inflammatory conditions:** The Centre for Amyloidosis & Acute Phase Proteins (incorporating the UCL Wolfson Drug Discovery Unit and NHS National Amyloidosis Centre) is world leading in translational amyloidosis research. A novel therapy concept has been chosen by GSK as a flagship project for potential adaptive licensing by the FDA and EMA, and is the subject of discussions aimed at reducing the time between demonstration of clinical efficacy and availability of the medicine for patients (**Pepys**, **Hawkins**).

B3.2 Key recruits

Includes internationally known professors: **Breuer** (to strengthen expertise in the biology and epidemiology of herpes virus), **Goldstein** (to bring expertise in computational biology), **Sansom** (to provide expertise in immune activation/inhibition), **Stockinger** (0.2 WTE; to provide expertise in immune regulation and a strategic link into the Crick Institute), **Walker** (to bring expertise in immune aspects of type I diabetes). **Bellotti** (to provide biochemistry expertise) and **Wood** (to provide protein crystallography expertise) were recruited to the Centre for Amyloidosis & Acute Phase Proteins.

B3.3 Key funding awards

There were 16 programme grants or equivalent awarded, with a total award value of £24.8M, including three from Arthritis Research UK, two from Leukaemia and Lymphoma Research, three from the European Commission, six from the MRC, one from the NIHR and one from the WT. **Maini** won a WT Senior Investigator award, Senior Fellowships were awarded to **Gilroy** (WT), **Towers** (WT), and Intermediate/Career Development Fellowships to **Marks** (WT), **Antoniou**, **Derrett-Smith**, **Jury** x2, **Holmes**, **Poulet** (all ARUK), **Ponticos** (BHF), **Jolly** (MRC), **Noursadeghi** (WT), **Gupta** (WT) and **Nistala** (WT). A HEFCE Clinical Senior Lectureship was awarded to **Burns.** The MRC Medical Molecular Virology Centre was renewed (£2.3M) and **Brocklehurst** was awarded £1.1M WT Strategic Award to investigate infection and immunity in the Life Study (new birth cohort).

B3.4 Research highlights

Epidemiology of infection: **Zumla**[O1,O2,O3] (Lancet x2, NEJM) played a key role in studies showing the benefit of early treatment of HIV/TB co-infection in Africa, validating rapid microarray-based diagnosis of bacterial sepsis, and employing viral sequencing technologies to track the spread of the fatal Middle East respiratory syndrome coronavirus (MERS- CoV) infection in the hospital setting. **Pillay**[O2] (Lancet ID) was a leader in a large study providing clear evidence for the importance of resistance testing in HIV infected, treatment naïve patients. **Gupta**[O1] (Lancet) showed the impact of the rollout of antiretroviral treatment on the incidence of drug resistance in treatment of naïve patients. **Kinloch**[O3] (NEJM) was the trial investigator in this study that established the benefit of early anti-retroviral therapy in patients with primary HIV infection. **Brocklehurst**[O4] (Lancet) in a clinical trial demonstrated the equivalence of established techniques for caesarean section on outcomes of post-partum infection.

Host-pathogen interactions: In collaboration with structural biologists **Towers**[O3] (Nat Struct Mol Biol) showed how sequence changes in HIV capsid and TRIM molecules affect binding properties and restriction of HIV infection. This has informed the development of new gene therapy approaches to prevent HIV infection. **Towers** and **Noursadeghi**[O4] (Nature) have recently discovered novel molecular interactions that allow HIV to escape innate immune recognition. The study by **Gupta**[O4] (PNAS) revealed how HIV Vpu and SIV env restrict infection by binding to distinct epitopes of cellular tetherin, demonstrating the importance of tetherin in protecting mammals against viral infection. **Maini**[O1] (J Exp Med) revealed how chronic hepatitis B virus (HBV) infection alters the molecular profile of HBV-specific T cells and provided insight into how immune deviation might contribute to chronic viral infection. **Goldstein**[O4] (PNAS) described the concept of amino acid co-evolution, which provides a new framework to analyse mutational changes in pathogen and host proteins. The work of **Jolly**[O4] (Nat Cell Biol) revealed that nanotubes connecting T cells over long distances could

facilitate HIV transmission, raising the possibility that nanotube disruption may impair virus spread in vivo. **McKendry**[O2] (Nature Nanotechnology) used a novel nanomechanical system for detection of vancomycin resistance in bacteria, offering the possibility of near-patient testing in low resource countries.

Immunobiology: **Sansom**[O2] (Science) has uncovered a novel mechanism by which CTLA-4 down-regulates immune responses. **Walker**[O1] (J Exp Med) found that CD30 and OX40 signaling contributes to autoimmunity in mice lacking regulatory T cells. **Vukmanovic-Stejic**[O2] (J Clin Invest) demonstrated the accumulation of regulatory T cells in human skin during antigen challenge. **Stauss**[O1] (PNAS) developed T cell receptor gene transfer to produce antigen-specific regulatory T cells. Studies by **Seddon**[O1] (PNAS) demonstrated the role of asymmetric cell death in setting the ratio of CD4 and CD8 T cells. **Stockinger**[O1,O4] (Nature, Nat Immunol) showed that the aryl hydrocarbon receptor plays an important role in regulating Th17 cells, and that the plasticity of the Th17 cells is required for IgA production. **Maini**[O2] (J Clin Invest) and **Nebbia**[O1] (J Exp Med) found that Bim and NK-mediated deletion impairs the function of HBV-specific T cells in humans.

Immunodeficiency: **Grimbacher**[O1O2] (NEJM, Lancet) identified that mutations in CARD9 cause susceptibility to fungal infection in humans, and that mutations in IL10/IL10R cause early onset inflammatory bowel disease that responds well to treatment by bone marrow transplantation.

Immunotherapy: **Griffiths**[O1] (Lancet) showed in a clinical trial that a CMV vaccine given before renal or liver transplantation decreased CMV complications and the need for anti-viral therapy post transplantation. **Weiss**[O1] (J Exp Med) has used immunisation of llamas to develop therapeutic antibodies for broad neutralisation of HIV. **Brocklehurst**[O1] (NEJM) demonstrated conclusively that adjuvant immunoglobulin did not alter the outcomes of neonatal sepsis.

Inflammation: **Belotti**[O1] (NEJM) established that hereditary systemic amyloidosis was caused by mutation in the β2-microglobulin gene. **Hawkins**[O1,O4] (NEJM, J Exp Med) described the effect of interleukin antagonism in cryopyrin-associated periodic syndromes, which led to the licensing of canukinumab for these conditions. **Pepys**[O3] demonstrated that antibodies to serum amyloid P could reduce visceral deposits of amyloid, now in phase 2 testing. **Simons**[O1] (PNAS) identified loss of phosphatidylinositol 4-kinase 2 alpha activity as causal in late onset degeneration of spinal cord axons. **Yona**[O1] (Immunity) used fate mapping to identify that tissue macrophages originated during embryogenesis and represent an autonomous cell population independent of bone marrow derived cells; these findings and the transgenic mice that were developed have enabled macrophage biology to be explored in novel ways. **Segal**[O3] (J Exp Med) determined that disordered macrophage cytokine secretion underlies impaired acute inflammation and bacterial clearance in Crohn's disease.

Rheumatology: **Mauri**[O1] (Immunity) showed defective B-regulatory cells in patients with systemic lupus erythematosis, and suggests this cellular compartment might be a new target for therapies and that abnormalities in iNKT cells could be corrected by B cell depletion.

Jury[O1] (Immunity) determined that lipid signalling by B cells was critical to Natural Killer cell function and that rituximab might work in part by restoring the ability of B cells to perform this function.

B4 Experimental Medicine

Experimental Medicine returns 151 WTE from the Divisions of Medicine and Surgery and Interventional Sciences, the Institute of Cardiovascular Science and the Institute for Women's Health. Research is largely organ-based, incorporates biomedical imaging, novel surgical approaches to the treatment of pre-malignancy and larger scale clinical trial activity. There were three Efficacy and Mechanism Evaluation (EME) awards during REF (£3.2M), reflecting the success of Experimental Medicine in progressing its basic discoveries through to phase 3 clinical trials.

B4.1 Major research groups

- **Institute for Liver and Digestive Health** (**Pinzani**) encompasses basic and clinical research on all aspects of liver disease, but particularly viral hepatitis, liver fibrosis, portal hypertension, liver failure and liver transplantation.
- **Renal Medicine** (**Unwin**) is the largest academic centre for research on kidney disease in the UK, with particular strengths renal tubular function and genetics.
- **UCL Respiratory** (**Chambers**) spans basic and clinical science in lung fibrosis, lung cancer and chronic obstructive pulmonary disease, and hosts two major collaborations with GSK in drug discovery.
- **Cardiovascular Science** (**Hingorani**) includes cardiac development, morphology and structural heart disease, inherited heart disease (encompassing myocardial disorders and arrhythmias), atherosclerosis and vascular disease with major strength in cardiovascular phenotyping, cardiovascular genomics and cardiovascular prevention and outcomes research.
- **Biomedical Imaging** (**Lythgoe, Taylor** and **Groves**) provides comprehensive modalities for small animal and clinical imaging (section D2.2.2) delivered by 10 Cat A academics in UoA1 and three being returned in UoA15.
- **Tissue and Energy** (**Lovat)** embraces the full range of novel energy sources that are used to induce irreversible necrosis (usually to treat cancer) in a range of organs (halo radiofrequency; high intensity focused ultrasound; electroporation; thermo-magnetism) and builds on the expertise developed within the former UCL National Medical Laser Centre.
- **Women's Health (Peebles, Raivich and Robertson)** explore the impact of hypoxia and inflammation on brain development in utero and in the early neonatal period, leading to a pipe-line of neuroprotective agents for early phase trials; (**David**) develops and uses gene therapy for a variety of pregnancy conditions, including the potential for in utero cure of a range of congenital disorders.

B4.2 Key recruits

Tooke was recruited as Vice Provost for Health and **Lomas** as Dean of the Faculty of Medical Sciences**. Pinzani** was recruited to head the newly formed Institute of Liver and Digestive Health, aided by the recruitment of **Burroughs**. Cardiovascular Science was strengthened by the recruitments of **Williams,** and **Hughes** and Nuclear Medicine by **Miles.**

B4.3 Key funding awards

There were 19 programme grants or equivalent awarded during REF period including three from the British Heart Foundation, three from the European Commission FP7 (including €6M to **David** in 2011 for a gene therapy trial in pregnancy), five from the MRC, four from the NIHR, three from the NIHR/MRC, and one from the WT. A £1.5M award to **Halligan** (HTA in 2008) funded the Siggar trials. Senior Fellowships were awarded to **Walker-Samuel** (WT) and **Hausenloy** (BHF). Clinician Scientist Fellowships were awarded to **Ackland** (Academy of Medical Sciences) and **Thayyil** (NIHR), and Intermediate/Career Development Fellowships were awarded to **Sen-Chowdhry** (BHF) **Smith A** (BHF), **Marina-Gonzalez** (BHF), **Giangreco** (ERC), **Motamedi-Shad** (Marie Curie), **Schievano** (Royal Academy of Engineering), **Dhar** (Jason Boas) and **Gale D** (MRC). HEFCE Clinical Senior Lectureships were awarded to **Khoo**, **Lipman**, **Porter (Joanna), David and Tsui**. MRC New Investigator Awards were made to **Pineda-Torra** and **Porter**. There were two Wellcome Trust/DoH HICF awards in 2012 (£4.4million), and London Olympic legacy funding (£10M). A new facility to support imaging for structural heart disease and device development at the ICH/GOSH campus was funded by the BRC. **MacAllister** (£0.9M) was awarded an NIHR/MRC EME grant to establish the mechanism and treatment effect of remote preconditioning in kidney transplantation. Other EME awards have been to **Hausenloy (**£1.5M) to refine the effect of remote preconditioning in cardiac surgery and **Williams** (£0.7M) to determine the utility of central blood pressure measurements.

B4.4 Research highlights

Renal medicine: **Gale**[O1] described a complement mutation causing a rare variant of glomerulonephritis; work that led to reclassification of this variant and suggests anti-complement antibodies might be therapeutically useful. **Kleta**[O1] (NEJM) described mutations in NT5E causing tissue calcification. **Kleta**[O3] (Nat Gen) described mutations in TRPV4 causing Charcot-Marie-Tooth disease. **Kleta**[O4] (NEJM) also described mutations in KCNJ10 resulting in a complex renal/neurological phenotype and **Klootwijk**[O3] (NEJM) identified a causal role for peroxisomal protein mistargetting in inherited Fanconi syndrome. **Salama**[O1] (J Clin Invest) identified a pathogenic role for the mannose receptor in crescentic glomerulonephritis. **Stanescu**[O1] (NEJM) identified genetic variations with a pathogenic role in membranous nephropathy and **Walsh**[O1] (Nat Med) identified the mechanism of hypertension induced by calcineurin inhibitors with implications for more targeted antihypertensive treatment.

Respiratory medicine*:* **Chambers**[O1] (J Clin Invest) refined the causal role of factor X in lung fibrosis in humans, findings that explained the null effects of clinical trials using warfarin. **Lomas**[O1] (Nature) used gene therapy to correct alpha-1-antitrypsin deficiency in human stem cells. **Lomas**[O2] (PNAS) refined the mechanism of serpin polymerisation. **Hurst**[O3] (NEJM) identified a frequent exacerbator phenotype in COPD, work that has informed the design of COPD clinical trials. **Martin**[O4] (NEJM) shed light on alveolar function in conditions of high altitude (summiting Everest), work that has implications for the pathophysiology of clinical hypoxia, with the consequent media attention increasing public awareness of critical illness. **Ashcroft**[O1] (J Clin Invest) identified human CHCHD4 mitochondrial proteins that regulate cellular metabolism and hypoxia signalling.

Cardiovascular science: **Mikhailidis**[O1] (Lancet) highlighted long term harms associated with statin use. **Charakida**[O1] (JAMA) identified vascular dysfunction in women with antiphospholipid syndrome; a likely surrogate outcome measure to be used in future clinical trials. **Kakkar**[O4] (NEJM) demonstrated that adding low molecular weight heparin to compression hosiery did not reduce mortality in acutely ill medical patients. **Nathwani**[O1] (NEJM) used gene therapy to correct the defect in haemophilia B. **Hingorani**[O2] (Lancet) identified IL6 as a risk factor and drug target for coronary disease. **Hingorani**[O3] (JAMA) also determined that the bioactivation of clopidogrel was not a determinant of its efficacy in patients with cardiovascular disease, which has simplified the use of this drug in acute coronary syndromes. **Humphries**[O4] (Lancet) described that the majority of patients with a clinical diagnosis of familial hypercholesterolaemia have polygenic hypercholesterolaemia. **Batterham**[O2] (J CIin Invest) showed how the obesity-risk gene FTO, influences plasma ghrelin concentration and activity to account for its action to cause weight gain, validating this hormone as a drug target.

Imaging science: **Nicolaides**[O1] (NEJM) identified that cervical length at mid-pregnancy is an independent predictor of the risk of caesarean delivery at term in primiparous women. **Walker-Samuel**[O1] (Nat Med) invented an MRI-based technique to measure glucose metabolism in tumours. **Halligan**[O3,O4] (Lancet x2) demonstrated the superiority of CT colonography compared to other imaging modalities in the diagnosis of bowel cancer.

B5 Ophthalmology

The Institute of Ophthalmology (IO) is the pre-eminent centre for research in eyes and vision in Europe. There are 6,800 m^2 of research space on a site adjacent to MEH. A tightly integrated programme of discovery science, translational programmes and clinical research from the 52 Category A staff being returned, provides the strategic framework for success. There is close working relationship with industry (£14.5M commercial funding out of a total of £88.6M in REF period). A Web of Science search disclosed 1309 publications from IO from 2008–2013. IO generates more publications on vision and eye disease than other equivalent partnerships in the world (Boston Consulting Group 2012) and in 2011 it received a Queen's Anniversary Award for Higher Education for 'research excellence'.

B5.1 Major research groups

- **Gene therapy:** A pioneering gene therapy programme that delivered the first clinical trial for gene therapy in retinal degeneration continues to innovate in ocular gene delivery technology. Proof-of-principle has been demonstrated in many models and a further round of trials is being embarked on.
- **Regenerative medicine for eye disease:** A major centre for cellular therapies, we have the advantage of a GMP facility that has been used for ocular surface disease and is about to deliver novel retinal therapies for age-related macular degeneration. The discovery science behind this includes pivotal research on photoreceptor transplantation.
- **Visual Neuroscience:** Groups address key questions of central visual processing in experimental models and in psychophysical studies of children and adults. Linking function to retinal structure and low vision are important themes.
- **Cellular basis of disease:** This embraces a wide range of discovery science including tight junctions, angiogenesis and endothelial cell biology, endosomal pathways and informatics.
- **Genetics:** Extensive genotype phenotype studies combined with increasing functional studies addressing retinal degeneration, cataract, glaucoma, eye development and corneal disease.

B5.2 Key recruits

We have 12 new internationally known Professors, and two new Readers, largely through internal promotion. New recruits include two HEFCE Clinical Senior Lectureships (**Sagoo**, **Michaelides**) and three Lectureships. **Marshall** has brought unique experience in translational use of lasers in ophthalmology.

B5.3 Key funding awards

There were 16 programme grants or equivalent awarded during REF, with a total award value of £21.5M, including five from the MRC, five from the WT, one from the EU FP7, one from Fight For Sight, one from the Lincy Foundation, one from the NIHR, one from the International Glaucoma Association and one from Retinitis Pigmentosa Fighting Blindness. There were two Wellcome Trust Investigator Awards (**Carandini, Ruhrberg**), and an NIHR Clinical Professorship (**Bainbridge**). Intermediate/Career Development Fellowships were awarded to **Pearson** (Royal Society) and **Cammack** (Leverhulme Trust). We opened a new enlarged GMP laboratory to meet escalating demand for cells for human use (Jules Thorn £750K). Other equipment includes a Wellcome Trust imaging award (£750K) and MRC FACS facility (£750K). The London Project (**Coffey**) was established in 2007 and has received funding of £6.7M since 2008: its goal is the treatment of late-stage age-related macular degeneration with hES–derived retinal pigment epithelial (RPE) cells, using the the GMP facility. Since 2010, we have invested £3.3M in the clinical research facility at MEH (NIHR, MEH Special Trustees) and £5.3M for experimental medicine infrastructure. Specific major projects include Wellcome Trust/DoH Health Innovation Challenge Fund for gene therapy for choroideremia (£1.2M: **Webster** with Robert E Maclaren, NIHR Oxford BRC) an NIHR EME award for light masks to prevent dark adaptation in the treatment of early diabetic macular oedema (£1.1M), an MRC/Wellcome Trust/NIHR Centre grant for “Health service and academic partnership in translational e-health research (£4.4M **Moore** et al) and a GSK discovery and reprofiling partnership (£6M).

B5.4 Research Highlights

Gene therapy: Having established proof of principle in animal models this world-leading programme, carried out the first clinical trial for gene therapy for a retinal disease (**Bainbridge**[O1] NEJM 2008). Since then other gene defects including achromatopsia (**Ali**[O1] Hum Mol Gen) and AIPL1-deficiency (**Ali**[O2] Hum Mol Gen) have been corrected experimentally. Since 2008 this programme has generated £6.7M grant income that is now

in part underpinning further trials.

Regenerative medicine for eye disease: We have a long history of translational research into cellular therapies for eye disease having established the basis for photoreceptor rescue by cell transplantation. We received £18.5M of funding for this in the review period. **Coffey** leads the London Project, which aims to restore retinal function by replacing retinal pigment epithelium. The pre-clinical investigations are complete and clinical studies will start in 2014 in partnership with Pfizer. Two pre-clinical programmes are exploring different strategies for rescuing/replacing retinal neurons. One (**Limb**, **Khaw**) is taking advantage of Muller stem cells to rescue retinal ganglion cells. The other has established the remarkable capacity of photoreceptor progenitor cells to integrate into an adult retina to restore vision (**Pearson**[O1,O2] (Nature, PNAS). Critically, photoreceptor progenitors grown in 3-D culture systems integrate and restore vision in adults (**Ali**[O3] Nat Biotech).
Visual Neuroscience: Carandini[O2O4] (Nature, Nat Neurosci) has shaped our understanding of the dynamics of processing in the visual cortex and **Cordeiro**[O3] (Patent) is translating novel imaging of retinal neurons for clinical use. **Dakin**[O2-O4] (PNAS, Curr Biolx2) has elucidated the process of visual crowding. **Nardini**[O1,O2] (PNAS, Curr Biol) has defined elements of the development of visual cue perception in children.
Cellular basis of disease: The critical mass of cell biology expertise focussed on eye disease at IO optimises delivery in this area. Publications since 2008 include three in Nature Genetics, one in Cell, nine in PNAS, one in Nature, two in Developmental Cell and two in Blood. **Greenwood**[O4] (Nature) has identified a novel Lrg1 pathway specifically involved in pathological angiogenesis. **Futter**[O2] (Nat Cell Biol) has proposed a generic mechanism for protein interaction between endosomes and ER, and **Matter**[O2] (Nat Cell Biol), has shown spatially restricted activation of RhoA regulates epithelial junction formation and epithelial morphogenesis. **Ruhrberg**[O1,O3,O4] (Neuron, Dev Cell) has shown how VEGF–neuropilin signalling is involved in vessel and axonal guidance as well as how a specific class of macrophage guides vessel loop formation (Blood).
Genetics: This group has generated 16 papers in Am J Hum Gen, 13 in Nat Gen and 23 in Human Mol Gen since 2008. These studies exploit the massive patient base at MEH and a now well-established global network of collaborators. **Bhattacharya**[O1] (Nat Gen) showed how EYS could cause retinal degeneration and many other publications from this group report novel mutations leading to retinal degeneration, cataract and corneal disease.

B6 Child Health
Led by **Copp** (to 2012) and **Smyth** (from 2012), the Institute of Child Health (ICH) is the largest children's research institute in Europe. On publication metrics, ICH has performed consistently within the top five in the world (the other four being in N America). ICH shares a site with GOSH, together forming a Biomedical Research Centre (£7M pa; 5-year funding renewed in 2012). Initiatives have included the **Newlife Birth Defects Research Centre** (2012; 1006m^2; GOSH Special Trustees, £7.5M; Newlife, £1.5M) to create the first centre of excellence for basic and applied research in congenital disease. The **Children's Translational Cancer Research Centre** (£3M, GOSH Children's Charity) links cell/molecular research with clinical trials at GOSH. The **Louis Dundas Centre for Palliative Care of Children and Young People** (2011; GOSH Special Trustees, £6.5M; True Colours Trust, £1.25M) provides the UK's first research centre dedicated to children with terminal conditions. ICH is returning 109 Cat A staff in UoA1, staff amongst whom are 15 early career researchers; 29 Cat A staff are being returned in UoA2.

B6.1 Major research groups
- **Cancer** (led by **Pritchard-Jones**, with **Anderson**, **Ham**, **Sebire**) combines basic cancer biology investigations with translational cancer research and clinical trials, particularly linking with the children's haematology-oncology clinical service in GOSH and the Cancer Institute.

- **Developmental Biology, Stem Cells & Regeneration** (led by **Copp**, with **De Coppi**, **Ferretti**, **Greene**, **Martinez-Barbera**, **Scambler,** **Sowden**) brings together developmental biologists determining the prenatal origin of birth defects, stem cell & tissue engineering laboratory studies, and clinical translation through stem cell and organ transplantation.
- **General & Adolescent Paediatrics** (led by **Stephenson**, with **Fewtrell**, **Lakhanpaul**, **Lucas**, **O'Callaghan**, **Singhal**, **Smyth**, **Stocks**, **Viner**) is developing academic excellence in research relating to topics of widespread importance in paediatric practice, complementing the tertiary/quaternary specialist research/clinical work at GOSH.
- **Genetics & Genomics** (led by **Beales**, with **Bitner-Glindzicz**, **Clayton**, **Dattani**, **Gissen**, **Heales**, **Hubank**, **Moore**, **Stanier**) is applying next generation genomics technologies to determining the genetic basis of rare childhood diseases.
- **Infection, Immunity & Inflammation** (led by **Thrasher**, with **Amrolia**, **Callard**, **Crompton**, **Gaspar**, **Goldblatt**, **Hart**, **Kinnon**, **Klein**, **Wedderburn**) combines basic research in immunology and infectious disease with translational work towards developing novel therapies, particularly gene therapy, for immune system disorders.
- **Neurosciences & Mental Health** (led by **Muntoni** with **Clark**, **Cross**, **Gadian**, **Kirkham**, **Morgan**, **Skuse**, **Vargha-Khadem**) brings together paediatric neurologists, psychiatrists and neuropsychologists to examine the developmental basis of childhood brain and neuromuscular disorders and the introduction of novel therapies.

B6.2 Recruitment

ICH recruited 18 new group leaders in the REF period, including 10 professors (seven clinical, three non-clinical) and eight early career investigators. **O'Callaghan** and **Smyth** strengthened paediatric respiratory research, **Pritchard-Jones** developed translational paediatric cancer research, **Stephenson** became Nuffield Professor of Child Health and head of the Children's Health Policy Unit (DoH, £3M), **Bluebond-Langner** (recruited from Rutgers University) developed the UK's first Children's Palliative Care Research Unit, **Lakhanpaul** became ICH's first Professor of Community Child Health, and **Gissen** and **Heales** strengthened basic and clinical research in children's metabolic disorders. **Muntoni** and **Morgan** were recruited to head neuromuscular disease research and a new clinical programme at GOSH, **Carmichael** and **Clayden** strengthened neuroimaging, **Shafran** and **Micali** enhanced critical mass in child psychology/psychiatry, together with GOSH appointment of **Heyman**. Early career appointments in basic paediatric science were: **Michod** (cancer biology), **Pauws** (craniofacial biology) and **Alexandre** (neurobiology).

B6.3 Key funding awards

ICH's total grant expenditure rose during the REF period: £22.4M in 2012-13 compared with £20.9M in 2008-09. There were 21 programme grants or equivalent awarded during the REF period, with a total award value of £22.3M including five from the MRC, five from the WT, four from the NIHR, four from the BHF, one from ARUK, one from the EU FP7, and one from Wellbeing Of Women. Fellowships include Wellcome Trust Senior Clinical Fellowship awards (**Gissen, Beales**) and renewals (**Achermann**, **Thrasher**), Wellcome Trust University Awards (**Martinez-Barbera**, **Morgan**), five new HEFCE Clinical Senior Lectureships (**Bockenhauer**, **Brogan**, **Hussain**, **Jacques**, **Peters**), Clinician Scientist awards from NIHR (**Micali**) and MRC **(Waters),** Wellcome Trust Intermediate Clinical Fellowship (**Kurian**), New Investigator Awards from MRC (**Long**) and BBSRC (**Howe**), Royal Society Dorothy Hodgkin Fellowship (**Alexandre**), BBSRC David Phillips Fellowship (**Ono**), and MRC Methodology Fellowships (**Barenco**, **Standing**). Intermediate/Career Development awards were made to **Loukogeorgakis** (WT) and **Chapgier** (BHF).

B6.4 Research highlights

Cancer: Anderson[O1] (Cancer Res) identified anti-tumour activity of cellular immune responses against PAX5; **Martinez-Barbera**[O2] (PNAS) showed predisposition to

craniopharyngioma after increased Wnt signalling in pituitary stem cells; **Jacques**[O2] (EMBO J) determined the combinations of genetic mutations in adult neural stem cells that determine brain tumour phenotype.
Developmental Biology, Stem Cells and Regeneration: De Coppi[O1] (Lancet) documented two-year progress following pioneering childhood tracheal transplantation; **Sowden**[O2] (Stem Cells) established cell selection methods for photoreceptor precursor transplantation into the retina; **Thapar**[O1] (Gastroenterology) achieved enteric neuronal stem cell harvest from endoscopies; **Copp**[O3] (PNAS) identified the role of apoptosis in CNS formation; **Scambler**[O1] (J Clin Invest) identified genetic influences on great vessel formation; **Alexandre**[O1] (Nat Neurosci) identified the mode of asymmetric stem cell division that generates brain neurons.
General & Adolescent Paediatrics: Viner[O1,O2] (Lancet x2) identified social determinants of health specifically associated with adolescent mortality trends; and described child and adolescent mortality rates in low and high-income countries; **Fewtrell**[O3] (BMJ) evaluated the evidence for benefits of six months exclusive breast feeding; **Viner**[O4] (Lancet Neurol) characterised outcomes of invasive meningococcal disease; **Scott**[O2] (Lancet Neurol) showed the extent of shortcomings in the treatment of status epilepticus in community health care; **Sebire**[O1] (Lancet) identified bacterial infection as a possible explanation for sudden infant death. **Brocklehurst**[O2] (NEJM) led a pivotal trial demonstrating the benefits of whole body cooling to reduce perinatal asphyxia encephalopathy.
Genetics & Genomics: Beales[O1] (PNAS) identified a contribution of neural crest migration to the Bardet-Biedel syndrome phenotype; **Beales**[O2] (Nat Genet) identified mutations causing 3MC syndrome; **Chapgier**[O2] (J Clin Invest) identified a STAT1 mutation causing childhood immunodeficiency; **Mitchison**[O1] (Nat Genet) identified the gene responsible for primary ciliary dyskinesia; **Hussain**[O1] (Science) determined the genetic basis for hypoglycaemia; **Rahman**[O1] (NEJM) determined the nature of the mitochondrial predisposition to antibiotic-induced deafness and **Gissen**[O2] (Nat Genet) identified the cause of ARC syndrome, a childhood metabolic disorder.
Infection, Immunity & Inflammation: Crompton[O1-O3] (Blood x3) identified the contribution of hedgehog genes to haematopoietic development; **Amrolia**[O1] (Lancet x2) demonstrated that reduced intensity immunosuppression facilitated transplantation in immunodeficiency; **Gaspar**[O2] (Science Transl Med) demonstrated the long-term success of clinical gene therapy for adenosine-deaminase deficiency; **Thrasher**[O1] (Science Transl Med) similarly demonstrated the success of clinical gene therapy for X-linked immunodeficiency; **Wedderburn**[O4] (Blood) defined a subset of T-lymphocytes producing pro-inflammatory cytokines in juvenile arthritis.
Neurosciences & Mental Health: Kurian[O1] (Lancet Neurol) identified the genetic basis for infantile Parkinsonism; **Cross**[O2] (Lancet Neurol) demonstrated by RCT that a ketogenic diet is as effective as drug therapy in childhood epilepsy; **Muntoni**[O1] (Lancet) showed that systemic antisense oligonucleotide therapy is feasible for the treatment of Duchenne muscular dystrophy; **Greene**[O1] (Brain) showed that nucleotides can substitute for folic acid in preventing spina bifida and **Walker**[O4] (Brain) identified the central neuroimmune mechanism determining adult pain responses after neonatal pain experience.

B7 Interdisciplinarity
In a survey of UoA1 academics in 2013, 52% were involved in interdisciplinary research during the REF period. In RAE2008 there were 17 WTE returned in other UoAs (Biosciences, Engineering and Chemistry), whereas in REF 2014 this figure has increased to 72. We host eight interdisciplinary PhD programmes (see section C2.3). In total, there were 91 funding awards shared between more than a single UoA1 Division/Institute, amounting to £17.9M of investment, and including the ARUK Adolescent Rheumatology Centre. A condition of Capital Investment Funding for equipment by SLMS was inter-faculty involvement to promote interdisciplinarity, and £8.9M has been disbursed to these initiatives, including funding for multi-user two-photon imaging, Biobank support, and pre-clinical PET-MR. Similarly, the UCLH BRC has invested in equipment including a clinical PET-MR (£1.1M), a research 3T MR system (£1.1M), a radiopharmaceutical GMP laboratory (£1.2M)

and £1M to fund support posts for imaging to support research across UoA1 and the wider SLMS. Our PIs in imaging have played a crucial role as drivers of interdisciplinary research and have been co-investigators on funding awards amounting to £20.8M since 2008. The recent BRC High Impact initiatives are also strongly interdisciplinary and included awards to develop informatics (£0.3M), exploit genome-based drug target prioritisation (£0.7M), establish Computational Imaging Infrastructure (£0.7M) and establish UCLH/UCL at the SBC (£1.3M; see impact statement).

B8 Alignment with the NHS

Increasingly this is achieved through current UCL Partners (UCLP) research programmes (where 10 Programme Directors are academics being returned in UoA1). In the renewal for the UCLP Academic Health Science Centre, focus will be on six programmes, five of which (Cancer, Cardiovascular, Child Health Infection, Eyes and Vision, and Immunity and Inflammation) map onto the research themes described here. These will feed directly into each of the 5 Integrated Programmes of the recently awarded UCLP Academic Health Science Network, to implement best clinical practice for the 6.3 million population of North London, and includes integrated Cancer, Cardiovascular Health, Comorbidities, Integrated Mental Health and Lifecourse for Women and Children. For UCLP a unified R&D approval process has been established across the network. Through UCLP there was agreement to focus specialist cancer services (prostate, bladder and brain cancer at UCLH, kidney cancer at RFL, haemato-oncology at UCLH/GOSH). UoA1 researchers and clinicians will make substantial contribution to achieving health and wealth impact over the next four-five years. These will include **specific health outcomes**, including improving one-year survival for all cancers and to identify and treat 25% more cardiovascular risk factors and so reduce cardiovascular events by 2017. A whole-systems approach will be used that will integrate best available evidence, education, recruitment to late phase clinical trials, informatics to capture routinely collected clinical data and organisational change that will facilitate primary and secondary integration. The major infrastructure projects in Cancer, Infection and Immunity, Surgery and Interventional Sciences, and the Institute of Ophthalmology (see section B12) are made possible by similar strategic aims of UCL and partner hospitals within UoA1.

B9 Alignment with Industry

The approach we promote is one of mutual collaboration, building on the strengths of either partner, with engagement at the early phase of drug or device development. Key examples are the collaborations with GSK in amyloidosis (**Pepys**), alpha-1-antitrypsin deficiency (**Lomas**) and a recent development in fibrosis. We have been working in close collaboration with GSK over the last three years to enable the development of novel anti-fibrotic agents through preclinical target validation (**Chambers**), and via the development of translational tools (imaging biomarkers) in humans (**Groves**). This partnership has delivered packages of work critical to support a Phase II study of a novel PI3 kinase inhibitor in IPF (http://clinicaltrials.gov/ct2/show/NCT01725139) and the selection of a candidate molecule targeted against the αvβ6 integrin for human testing. Importantly, two other compounds have not progressed to clinical testing based on reliable negative data generated by our collaborative work (IL-13, EP4). To date, all of this work has been focused on the lung, but now, through a significant expansion in the programme and the planned formation of an integrated UCL-GSK Fibrosis Translational Research Centre (FTRC), this work will be extended to other organs. Investment from GSK so far has been £2.4M over three years, with upwards of £5M to be awarded to UCL over the next five years (milestone driven). An ongoing partnership with GSK and the Institute of Ophthalmology (commenced 2009; £6M over six years) has focused on preclinical reprofiling of GSK compounds, taking advantage of our understanding of disease mechanism and access to a large repertoire of animal models of disease. The same programme has a discovery component seeking new targets in retinal degeneration. The London Project (**Coffey**) is a partnership between UCL and Pfizer. This major regenerative medicine project is about to move to first-in-human studies of

hES cells transplantation under the retina on a specially designed patch to treat the blinding complications of age-related macular degeneration. Collaboration with the Devices Industries is extensive, and includes developmental work in Phase 1/2 that progresses to late phase trials; e.g. for vascular-targeted phototherapy in prostate cancer, early phase studies (**Emberton**) in collaboration with Tookad SolubleTM led to a randomised phase 3 study (€100M investment) that has completed recruitment within the EU (CI **Emberton**). Similarly, Sonacare invested over $1M in a phase 2 study of high intensity focussed ultrasound for early prostate cancer (**Emberton**) and this was followed by monies from the Wellcome Trust/DoH Health Innovation Challenge Fund (two awards amounting to £3.5M) to perform phase 3 studies of this technology. Throughout UoA1 there is there is a commitment to achieving **specific targets for industry collaboration and wealth generation**. For example in 2010 in Cancer, we signed a partnership agreement with Sarah Cannon Research Institute (SCRI) to form a strategic relationship to develop early-phase clinical trials with associated translational projects. UCLH/UCL and SCRI have opened Phase 1 facilities in central London, with joint appointments and operating procedures. Since 2010, the number of patients treated in early phase cancer studies has increased from 35 to 120, and the number of open studies from 10 to 36.

B10 Responsiveness to national priorities

Government, and the major biomedical research funding agencies wish to see more rapid translation of scientific discovery into economic, social and health gain (impact). UoA1 has taken a strategic, cooperative approach to do this, and this is described in detail in REF3a. Our clinical academics (232 in UoA1) contribute to the delivery of research-based clinical care of patients locally and nationally, influencing the provision of healthcare within the NHS and driving the quality of care upwards. We have responded to the need for capacity building in life sciences by increasing the number of scientists in training, and progressing academics into scientific independence.

B11 Link to RAE2008

Much of what was planned has been delivered including the establishment of UCLP, the Clinical Research Facilities and acceleration of clinical research approvals. We have expanded our PhD programmes and increased our capacity to perform ATMP trials with expansion of the GMP facilities (section D2.2). We have made investment in our preclinical and clinical imaging infrastructure (section D2.2). The plan to expand Cancer research has been delivered with a substantial increase in investigators (i.e. from 40.40 WTEs in RAE 2008 to 72.40 WTEs presently) and research income (i.e. from an average expenditure of £10.3M per annum for RAE 2008 to £18.4M per annum for REF 2014). In Infection, Immunity and Inflammation we have made the expected progress in basic virology, focusing on HIV, Hepatitis B and viral spread. There has been progress in vaccine development including the use of lentiviral vaccines to trigger immune responses by infecting dendritic cells in vivo, and clinical studies of CMV vaccines. In autoimmunity, we have achieved good integration of adult rheumatology at the Bloomsbury campus (focus on lupus and rheumatoid arthritis), the Royal Free campus (focus on scleroderma and pulmonary hypertension) and Great Ormond Street (focus on juvenile arthritis) with the award of the Adolescent Rheumatology Centre.

B12 Research plans over next five years

We will further streamline approvals for clinical studies with a view to having the most rapid and safe arrangements in the UK. We will establish a clinical informatics framework (electronic health record system with research capability) for patient selection and stratification for trials and data-mining facilities linked to various UCL e-health initiatives. This is a collaboration is between UCLP (including the UCL Farr Institute), the Francis Crick Institute, the Wellcome Trust Sanger Centre and the European Bioinformatics Institute. The aim is to develop an eMedLab that provides integrated genomic, imaging and clinical data for population health research and to stratify individuals for clinical trials. We also plan a

Research Training Academy to co-ordinate training of bioinformaticians across UCLP.

In **Cancer** during the next five years we will develop **Cancer Biology and Genomics** as the fulcrum of our activities in fundamental cancer research and translational genomics, dovetailing with the UK Governments 100K genome project (**Lomas** was Chair of the Strategic Priorities Group). We will exploit our expertise in **Gene Therapy, Immunotherapy and Stem Cell Transplantation** using expertise in tumour immunology, immune-regulation, cancer vaccines, adoptive immunotherapy, T-cell engineering, T Cell Receptor (TCR) and chimeric antigen receptor (CAR)-engineered lymphocytes and vector design. Examples of future work for this Centre include development of TCR- and CAR-gene transfer technologies and initiation and delivery of trials in resistant lymphoma and CMV infection, a phase 1 gene therapy study for liver, oesophageal and gastric cancer and melanoma and the use of imaging and molecular makers to stratify leukaemia and lymphoma patients. Research into **cell death, inflammation and immunity** is crucial for understanding tumour genesis and development of resistance to therapy. With the recruitment of **Walczak** and **Quezada** we aim to develop biotherapeutics that target the TRAIL or CD95 death-receptor systems, specific ubiquitin ligase and de-ubiquitinase inhibitors, and immune-regulation as cancer treatments. The **KCL/UCL Comprehensive Cancer Imaging Centre**, funded by CRUK and the EPSRC, will develop imaging, in combination with clinicopathological assessment, genomics and in-house optical proteomics techniques, to elucidate the molecular and physiological processes of cancer. We plan to develop targeted multifunctional nanoparticles for tracking by two or more imaging modalities (PET, SPECT, optical, MR), which simultaneously deliver small molecule therapeutics to primary tumours and metastases, integrate imaging modalities with genomics and protein interaction analysis to understand cancer genome heterogeneity and predict individualised clinical outcome, and enhance understanding of spatial heterogeneity of the cancer genome using next generation sequencing on image-obtained surgical samples. We have plans to double the footprint of the UCL Cancer Institute by developing a new building, recruiting circa 300 researchers (2018; £80M; 9000m^2) and opening a high energy Proton Beam Therapy Centre (2018; £125M; 8000m^2).

Two exciting initiatives are being developed in **Infection and Immunity.** The Bloomsbury Research Institute (BRI) is a joint initiative with the London School of Hygiene and Tropical Medicine, bringing together a strong critical mass of infection-focused research. Together we will create a world-class centre of research excellence in infectious diseases with the aim of eradicating global killers such as HIV, TB and malaria and influencing global health policy. With UCL's and LSHTM's complementary strengths the BRI will have unique competitive advantage over world centres such as the Pasteur Institute due to the breadth and reach of our scientific approaches, and our critical mass of scientists. Next generation pathogen sequencing will reveal how organisms spread through communities, and uncover the interaction of pathogen biology with human behaviour, whether through migration, spatial proximity or sexual relations. Bringing together the understanding of pathogen, human biology and global populations creates the possibility of a step change in the control and eradication of infectious diseases. Phase 2 of the Institute of Immunity and Transplantation will apply UCL research expertise in the study of immune system functions in humans to explore immune aspects of cancer, chronic infection and autoimmunity. It will also develop immune interventions to prevent the rejection of transplanted organs, including bioengineered organs. The Institute brings together multi-disciplinary teams of scientists, academic clinicians, clinical trial specialists and nurses to develop immune-enhancing therapies for the treatment of cancer and chronic infection, and identify tolerance-inducing strategies to treat autoimmune conditions and prevent immune attack of conventional and bioengineered transplants. Partnership with the Francis Crick Institute will further enhance research strength, while joint working with the UCLP Trusts will provide access to our patient population of 6.3 million.

In **Experimental Medicine**, a GMP radiochemistry laboratory will be built at UCL in 2014-2015, funding having been secured from the BRC and UCL (£1.5M). This facility will support a range of industrial collaborations (e.g. the GSK-fibrogenesis hub; see below), and biodistribution and dosimetry studies of radiolabelled antibodies, which are currently being performed abroad. We will develop our collaboration with the Radio-Pharmaceutical Division of GE Healthcare and Siemens, to manufacture radiolabelled ligands for the clinical investigation of biological pathways relevant to the major cardiovascular, neurological, oncological and inflammatory diseases. Two major refurbishments are underway in Bloomsbury and Stanmore, amounting to a £35million investment, in order to further integrate cross-disciplinary working between surgeons, engineers and imaging science. Charles Bell House, a five storey building on the Bloomsbury campus, will be thoroughly refurbished by 2015. The new building will be an Institute for Image-Directed Healthcare. The Institute will be cross cutting and comprise elements from the Division of Medicine and the Cancer Institute, as well as the enabling disciplines of medical physics, bioengineering, image processing and nano-technology. At Stanmore, an academic centre will be developed by 2016, in a collaboration between UCL and the Royal National Orthopaedic Hospital (RNOH). This will be a new building, jointly funded, and will be part of the RNOH site redevelopment, which includes a new hospital. There will be enhanced research and teaching facilities, and the building will house Faculty of Engineering research teams alongside teams from the Division of Surgery. In Surgery, three themes will be prioritised which are inherently cross-disciplinarity; Energy and Tissue (UoA1) and two others in UoA15 (Materials and Tissue, and Nanotechnology). A fourth theme is being planned which will be peri-operative Medicine. The integration of surgical science with bioengineering, physics and imaging science is a key strategic objective shared between UoA1 and UCL Engineering. With regard to the NHS we will align surgery with the needs of patients with colorectal, upper-GI, and renal cancer. Our strategy is to exploit the concentration of clinical services and the opportunities for high calibre basic and clinical science.

In **Ophthalmology** plans are currently focused on moving the Institute of Ophthalmology and Moorfields Eye Hospital to a single purpose–built approximately 50,000m^2 joint facility closer to the main UCL campus at a projected cost of £350M. We intend to have much closer integration between clinical and lab–based research space with tight links to a new, enlarged Clinical Research Facility (part funded from Sir Jules Thorn Foundation, £5m). A major component of this will be a next generation imaging/experimental medicine facility where we will probe in real time retinal function at the cellular level as well as extending the utility of current anatomical methods. **Dainty** has been recruited to lead the imaging technology initiative to support this. We plan a significant expansion of clinical and translational research capability. The latter will be supported not only by our local discovery science, but also through the creation of close collaborative links with other UCL departments and the Crick Institute. We will expand translational neuroscience (particularly psychophysics) to enhance early detection and monitoring of visual function in community as well as clinical settings. This, combined with the imaging, will make it possible to intervene early in disease and prevent blinding complications. Many of our novel therapeutic interventions target the retina and retinal physiology is another priority. A major informatics initiative, that will include the creation of a new Department of Clinical Informatics, will draw on the large patient base at MEH, UCL e-health initiatives, our innovative open source electronic health record, OpenEyes and growing collaborative networks. An example of such a network is the UNITE collaboration (E1.2) between London, Bristol, USA and China and further, generally disease – specific networks will be created. We seek to become a global informatics hub for ophthalmology to enable further understanding of disease, stratify patients for clinical trials, data mining and post-licensing surveillance. The opportunities for commercial collaboration in ophthalmology are considerable and we intend to create a bio-incubator as well as a joint enterprise platform with MEH.

In **Child Health**, a new academic strategy with GOSH, led by Smyth, and informed by visits to other world-leading children's academic medical centres, will focus activities into five academic programmes: Genetics and Genomic Medicine (led by **Beales**), Developmental Biology and Cancer (led by **Copp**), Infection, Inflammation and Immunity (led by **Thrasher**), Developmental Neurosciences (led by **Muntoni**) and Population, Policy and Practice (led by **Law**, returned to UoA2). These new programmes will foster greater cross-disciplinary work. For example, Developmental Biology & Cancer will strengthen the integration of embryonic and tumour studies, capitalising on recent advances in the role of Wnt signalling in the origin of childhood craniopharyngioma (*Cell Stem Cell* 2013) and the parallels between cortical dysplasia and tuberous sclerosis (led by **Jacques**). Children's Rare Disease Research is relevant to all these programmes and a large capital project is the new **Centre for Children's Rare Disease Research** (CCRDR), due to open on a site adjacent to ICH/GOSH in 2017. HEFCE Capital funding (£10M) has been awarded and the rest of the funding has been committed by GOSH Children's Charity. Over 6,000 rare disease entities exist and the patient cohort at GOSH is unique in including children with a range of these conditions, in sufficient numbers for productive research. Gene discovery and bioinformatics analysis (led by **Beales**, **Hubank**) will enable UCL to define genetic causation for rare diseases with no known cause. Development of novel viral vectors and implementation via bone marrow transplantation (led by **Gaspar**, **Thrasher**, **Amrolia**) will capitalise on ICH's pioneering work in gene therapy for immunodeficiency disease. Stem cell therapy and tissue engineering for childhood surgical conditions (led by **De Coppi**), development of shRNA tools to ameliorate muscular dystrophies (led by **Muntoni**), and immunotherapy for childhood malignancy (led by **Anderson**) are also included amongst the research programmes within the CCRDR. The **ARUK Adolescent Rheumatology Centre** was established in 2012, and will provide an unparalleled resource for translational research into the poorly understood group of diseases affecting the joints of young people. The ARUK Centre will also pursue the establishment of a National Network for Adolescent and Young Adult Rheumatology, to bring together experts in the field throughout the UK and, importantly, to engage fully with adolescents and young adults in order to involve them in research planning. The **Birth Defects Research Centre**, founded in 2012, represents Europe's largest critical mass of developmental biologists, geneticists and stem cell biologists focusing on the origin and treatment of congenital diseases. Planned developments include a new focus on confocal-based live imaging of embryonic development as birth defects arise, enhanced by the 2013 recruitment of **Alexandre** (Royal Society Dorothy Hodgkin Fellow) with special expertise in zebrafish live imaging.

C. PEOPLE

C1 Staffing strategy and staff development

Each unit in UoA1 is committed to sustaining an active research culture as its highest priority. Attention to developing research excellence marks our policies at all levels, including annual staff appraisal in a UCL-wide formal procedure. The development of an international research profile is the expected norm for each academic member of staff, and is a key feature of mentoring and staff review. This policy is also implemented through research excellence as a major criterion for staff appointments and promotion.

C1.1 Recruitment and retention

Considerable resources have been committed to staff recruitment. These include 130 new recruits at Senior Research Associate/Lectureship level, 66 new recruits at Principal Research Associate/Reader level and 57 at professorial level. We have prioritised early career researchers, and include 78 in the return 45 of whom have emerged from post-doctoral positions at UCL. Generous start-up funds of £1.3M were awarded to 22 Early Career Investigators (avg. £60K each) to enable new early career staff to set up their research. Care is taken to limit teaching and tutorial loads during the three years of probation. HR Organisational Development runs a dedicated professional development programme for early career research staff

(http://www.ucl.ac.uk/hr/osd/research/programme/index.php). Information on UCL's implementation plan for the Concordat to Support the Development of Research staff is found at (http://www.ucl.ac.uk/hr/osd/research/Concordat_Implementation_Plan.pdf). Our Early Career Researchers have been successful in winning independent grant funding since being recruited, averaging 2.2 grants per researcher. In addition to recruitments of outstanding researchers to UoA1 to enhance the research environment, we also aim to promote job security for high achieving research staff. Since 2008, 28 individuals have moved from time-limited research contracts to tenured academic posts. £5.8M was spent on retention packages for 19 academics in the REF period, as salary uplifts (with £1.2M to be annual recurrent costs), or funds for equipment or infrastructure.

C1.2 Research Fellowships

Staff are encouraged to apply for prestigious and competitive personal research fellowships in open competition in order to enhance their personal development and the vitality of their research groups. Since 2008, successes include 10 Senior Research Fellowships (eight WT, one BHF, one MRC), three WT Senior Investigator Awards, six Clinician Scientist Awards and one NIHR Clinical Professorship and 13 HEFCE Clinical Senior Lecturers. In total there were 87 Fellowships active during the REF period of which 71 were awarded after 2008, with 42 Intermediate/Career Development Fellowships.

C1.3 Integration between clinical and basic scientists

Research groups are composed of clinicians and basic scientists throughout UoA1, and the overall relative proportions of basic/clinical Cat A staff is 47/53% respectively. Careful attention is paid in employment contracts and annual monitoring schemes to ensure that clinically active staff have sufficient time for scholarly work, and that there is an appropriate balance of duties.

C1.4 Appraisal and promotion

All staff are appraised within the UCL Appraisal, Review and Development scheme which is an annual appraisal with the Head of Department or manager, for the setting of research and training goals, incorporating planning towards progression and promotion. Academic and research staff are recognised and rewarded via a School-wide set of robust processes for promotion, with clear criteria that are addressed through annual appraisal. Promotions are not solely contingent on the availability of grant funds but are based on ability and achievements. Since 2008, 72 staff have been promoted to Professorships, 65 to Readerships, and 17 to Senior Lectureships.

C1.5 Training

UCL provides a large variety of short courses ranging from presentation skills for junior personnel to leadership development for senior staff. Staff have access to UCLP multi-professional and on-site taught modules and the UCL Professional Development Programme for Researchers. Staff are encouraged to use the Researcher Development Framework professional development tool to enhance the knowledge, attributes and skills required for success as professional researchers. Funds are available through UCL Graduate School for conferences, and exchanges with other academic institutions are actively encouraged. Each Division/Institute ensures that training is delivered to its 114 externally funded Research Assistants and 379 post-doctoral research assistants. UCL has a formal Career Structure policy for research staff, which adopts the guidelines of the CVCP/Research Council Concordat. Staff are required to complete 10 days per year of skills training.

C1.6 Equality and diversity

Key equality objectives at UCL are given in the 2011-2014 Equalities & Diversity Strategy and Divisions/Institutes in UoA1 are committed to monitoring and delivering improvements in the equalities profiles at all levels. To this end the Division of Medicine, Institute of

Ophthalmology, and the Institute for Women's Health each won a Silver Athena Swan award in September 2013. The introduction of a more inclusive and considered promotions process, the award of contributions points, representation on committees, and annual professorial pay evaluations support this process. Objectives are being agreed to deliver improved ethnic balance at the higher levels in the longer term, with training and panel reviews to ensure that bias and discrimination are eliminated. UoA1 compares favourably across UCL and nationally with regard to gender balance and reward, but further work is needed.

C1.7 Sabbatical leave

Sabbatical leave may be granted at the discretion of the relevant Head of Department, Dean, Vice-Provost or Provost for a period of one term after three years qualifying service with UCL. In addition to the qualification period, research active academics returning from maternity, adoption, extended carers', or long term sickness leave are entitled to one term of sabbatical leave without teaching commitments. This leave will enable staff to more quickly re-establish their research activity. By the end of a period of sabbatical leave academic staff are expected to produce tangible outcomes in furtherance of their research or teaching.

C1.8 Consultancy

Academics are permitted to undertake a maximum of 40 days consultancy work per year, which requires time away from UCL duties, on days when an individual would be expected to attend work at UCL. Permission to undertake such consultancy work will be subject to their HoD's approval. Additional details are described in our impact statement (REF3a).

C2 Research students

As of September 2013, 722 doctoral students were conducting research in UoA1 Institutes/Divisions, including those on professional training programmes. Postgraduate training is a key component of our research and scholarly activity. 688 doctorates have been awarded in the period 08/09 to 12/13 in the components of UoA1, compared to 603 for the previous 5 years relating to RAE2008. The completion rate within four years (award of degree for F/T PhD students) has risen from 58% (05/06 entry) to 80% (07/08 entry). Two MRes and 40 MSc programmes, with nearly 700 enrolled students currently, provide strong recruitment to further research degree programmes. Students on these courses spend at least four out of 12 months exclusively on a major research project, and graduate well prepared for PhD or research posts.

C2.1 Role of the Graduate School

Research degree expectations are detailed in the Code of Practice for Research Degrees given to all students on arrival and overseen by the Graduate School. The Graduate School runs three induction sessions for new research students to introduce UCL's research environment and support services. Monitoring of student progress is undertaken through UCL's on-line Research Student Log. Students submit six-monthly reports (plus an extra one at month three) for discussion and approval by the supervisory team. This documents academic progression and skills development training, and reflects a dialogue between students and principal and secondary supervisors. This also records review meetings (including important milestones such as the MPhil to PhD upgrade) and discussions on academic (subject discipline), generic and transferable skills training. These are also used by the Graduate Tutors to view progress of the cohort using a traffic light system. The statistics for upgrade from MPhil to PhD (an assessment undertaken between nine and 18 months) and submission rates within four years (six for part time students) are reported annually to the Research Degrees Committee and reviewed by Departments for action where appropriate. The Graduate School's Skills Development Programme is open to all graduate research students at UCL. The Graduate School's Skills Development Programme provides courses that cover all four domains of VITAE's Researcher Development Framework. Currently there are over 220 different courses in 675 sessions across the full

range of skill domains defined by the Researcher Development Framework and in 2011/12 there were over 12,000 course registrations. Each training event is allocated points (one point for each half day of training and each student is recommended to achieve 20 points per year). The training record and point count is recorded in each student's record in the Research Student Log for review by the supervisory team and Graduate Tutors. Indicative data on graduate student training by department in the period Jan 2008-Jul 2013 is available from https://researchlog.grad.ucl.ac.uk/reports/course_report.php. The Graduate School runs an annual Research Poster Competition which gives students an opportunity to communicate their work, to obtain experience preparing and presenting posters, and promotes cross fertilisation of research.

C2.2 Recruitment

Recruitment to PhD training in UoA1 has been strong, thanks to the excellent reputation of UCL coupled with the active engagement of staff with other HEIs, third sector organisations and industry. We have been successful in obtaining consistent funding of studentships through MRC (139), BBSRC (24), BHF (80), WT (49), CRUK (23) and ARUK (7). UCL has also introduced two PhD studentship programmes to enhance capacity. Impact studentships involve collaborations with industry or third sector organisations, with UCL providing 50% of the funding from internal resources. The UCL School of Life and Medical Sciences Grand Challenge studentships are co-funded by UCL and the NIHR Biomedical Research Centres and 94 PhD students have been funded through these schemes. We have been successful in obtaining CASE awards in collaboration with industry (23). In total, there were 575 PhD studentships in the REF period, an increase from 401 in RAE2008.

C2.3 PhD Programmes

The **UCL MBPhD Programme** has been run from the Division of Medicine since 1994 and has enrolled 110 students in this time. The aim has been to bring on future clinical academics, adept at both clinical medicine and biomedical research. Modelled on the US 'MDPhD' programmes, the students intercalate a PhD within a clinical course. The PhD can be undertaken at UCL, or at the London Research Institutes of CRUK, or the National Institute for Medical Research at Mill Hill (these will merge into the Crick Institute within the next few years). Clinical tutoring continues during the PhD phase. The PhD is typically funded through the Programme itself (although PhDs undertaken at CRUK and NIMR are funded via the respective institutions). The Programme receives a scholarship via the MRC DTA scheme, UCL/UCLH CRBRC, the Rosetrees Trust, The Astor Foundation and the International Journal for Experimental Pathology. In the present REF period, we have enrolled 41 students, all of whom are still within the Programme at UCL. One of our first graduates (**Swanton)** has now supervised three MBPhD students, and one has published two Nature papers in 2013. The completion rate is 98% with 80% completing in fewer than four years; 30% of the graduates have progressed to clinical academic appointments. The **UCL Doctoral Training Programme in Medical and Biomedical Imaging** (EPSRC; £5.6M) hosted by the Centre for Biomedical Imaging provides a comprehensive and integrative doctoral training in imaging science and methods. It was created by **Lythgoe** in 2009 and co-directed by him since 2010. The programme has a strong focus on new image acquisition technologies, novel data analysis methods and integration with computational modelling. This is a four-year PhD programme designed to prepare students for successful careers in academia, industry and healthcare. The trained scientists will be experts in imaging science, technology, computation, mathematics and/or their application and translation to clinical solutions and market impact. In 2012, it received over 250 applications, highlighting the competitive nature of the programme and the high demand for this training. Now in its fifth intake, it has already received over 200 applications (as of 1st June 2013), and there are 48 students currently enrolled. In 2013 it was renewed (EPSRC award of £6M) as a Centre for Doctoral Training in Medical Imaging to train 72 students over the next five years. The **WT four-year PhD in Stem Cell and Developmental Biology** (co-led by **Copp**) is now in its fifth year, with the first year's students all graduated. The **Oliver Bird four-year**

PhD Programme has funded 10 PhD students in two cohorts and nine have graduated, six of whom are in post-doctoral positions (including a winner of the prestigious 2013 Garrod Prize from the British Society For Rheumatology) one is in industry and one works for the European Medicines Agency. **CRUK UCL Centre** training funds have been used to establish a new four-year PhD 'rotation' style programme for four PhD students per year (two clinical). The **BHF four-year PhD programme** has had 573 applicants for 20 places in the five years that it has been running within UoA1. Of the 2009 intake, all are on course to submit this year, and 13 have published in journals including J Clin Invest, BMJ, Blood, PLoS Genetics and Nature Protocols. The **Bench to Bedside PhD Programme in Infection**, a four-year MRC-funded PhD programme, has been developed to combine research training in cutting edge biomedical science with an opportunity to experience the clinical context of the research. From 2013, UoA1 will host a **Wellcome Trust PhD Programme for Clinicians,** (Director **Lomas**), representing a £6.5M award over the next five years.

C.2.4 Sustainable doctoral training

A number of processes are in place to ensure that our doctoral training is effective and sustainable, and that students are supported throughout their training. Each of the Divisions/Institutes in UoA1 has a team of Graduate Tutors who have responsibility for ensuring fair and equitable student recruitment, appropriate supervision and progress from MPhil to PhD registration and thesis submission. The Graduate Tutors also advise students about how to access additional resources that may be necessary to their work, and provide support when they are in difficulties. All students are allocated to an experienced principal supervisor with a named secondary supervisor. Academic and research staff are required to attend a course on PhD supervision before being permitted to supervise, and must act as a subsidiary supervisor right through to submission before being allowed to become a primary supervisor. We have made active efforts to increase the proportion of academic staff involved in PhD supervision. Special systems have been established to support part-time PhD students, many of whom are either clinicians or research assistants. Work plans are scrutinised by graduate tutors to ensure that candidates are given adequate time and facilities for their doctoral studies so that they are not disadvantaged by competing responsibilities.

C2.5 Integration into research culture

Doctoral students are an integral element of our research activity. The majority of students are involved in collaborative, often interdisciplinary, projects rather than stand-alone studies, and all are affiliated with specific research groups within the research departments and sections contributing to UoA1. They therefore participate actively in the research programmes of these groups, attending research planning meetings, contributing to research articles, giving presentations of their work and attending conferences in the same way as other junior research staff. In addition, specific mechanisms are in place to ensure effective integration of students into the research culture and to prepare them for scholarly careers. All the Divisions/Institutes in UoA1 run regular research seminar programmes at which students present their work as well as attend. Annual PhD presentation days are opportunities to showcase the best research for presentation orally or using posters, keynote speakers are invited, and prizes awarded for the best presentations by the students. PhD students are encouraged to give presentations at national and international research conferences. Typically, students present at one or two national and one overseas conference during their training, supported by funds from the Graduate School and individual research groups.

C2.6 Employability of research staff and students

Of the 42 Cat A staff returned in RAE2008 who have left UCL, 37 have secured career advancement in other academic centres, including 15 in posts abroad. For other research staff, we have a careers service offering specialised services. As well as providing employer-led programmes, the Careers Service also organises employers' forums with PhD recruiters,

an internship scheme for research students, and one-on-one advice sessions particularly for early career researchers by dedicated staff with research experience. Secondments of research students and early careers researchers to external organisations are facilitated.

D. INCOME, INFRASTRUCTURE AND FACILITIES

D1 Income

Research income has increased by 11% over the REF period and new grants totalling £579M have been won. In comparison to RAE 2008 (i.e. UoAs 2, 3 and 4) the average annual grant expenditure per WTE researcher per year has increased by 67%, from £158K to £264K. We have continued to secure funding from Research Councils and UK charities relevant to our research and have achieved strong growth in awards from the NIHR (240%), the EU (58%), and industry (120%) over the period.

D2 Infrastructure

D2.1 Core infrastructure and facilities within the constituent parts of UoA1:

The SLMS Capital Equipment fund provides resources (£2M pa) for the acquisition of equipment. UCL is also a recipient of Wellcome Trust Institutional Strategic Support funding, and during the REF period these funds (£8.9M to UoA1) have been used almost exclusively for equipment that is cross-faculty and multidisciplinary (see B.7).

D2.1.1 GMP facilities for gene and cellular therapy: UCL researchers conduct more gene and cellular therapy human studies than any other centre in the UK. There are four dedicated GMP Facilities for gene and cellular therapies in UoA1. The Laboratory of Cellular Therapeutics (LCT) at RFL is being re-built and expanded (£2M) to create a 220m^2 facility providing level three GMP manufacturing capacity for ATMPs as investigational medicines and "specials" under MHRA and Human Tissue Act (HTA) licensing. It will include five grade B laboratories, one of which will be suitable for genetically modified products, one large grade C laboratory for long term cell culture, and three grade D laboratories for closed system processing and process validation towards downstream product commercialisation. The facility has six permanent staff members and an annual budget of £400K, and clinical trial production is supported by grant-funded UCL research staff. The facility currently manufactures ATMP IMPs for seven trials at UCLP hospitals (RFL, UCLH, GOSH, Moorfields and Stanmore) and three UK national phase 2 trials in conjunction with the UK biopharma company Cell Medica. There are two GMP facilities for cell manipulation and gene transfer at Great Ormond Street Hospital that have underpinned success in gene therapy for immune deficiency. There is core staff of five (QA manager, Production manager, three technicians), specialist staff according to manufacture in progress and a clinical trials officer. The GMP facility at the Institute of Ophthalmology (two Grade B rooms) produces cultured cell therapies for transplantation in accordance with HTA guidelines (with whom we have a licence) and the EU Tissues and Cells Directive. The Wolfson Cell and Gene Therapy Laboratories at Chenies Mews allows viral vector production and cell processing for gene therapy, funded by the Wellcome Trust (until 2011) and the Wolfson Foundation, and now funded by the UCLH/UCL BRC (£0.5M). Its current contracts and grants for GMP vectors are worth over £5M. In total, our facilities manufactured over 330 ATMPs plus 200 transplant products in 2012 making them by far the most active non-industrial GMP facility for ATMPs in Europe.

D2.1.2 Imaging: Our imaging infrastructure spans a range of innovative basic and clinical facilities. The Centre for Advanced Biomedical Imaging (**CABI**) is a multidisciplinary research centre for preclinical imaging and it brings together in-vivo imaging technologies across UCL with specific applications in the biomedical sciences. The main aims are to create an integrated strategy for preclinical imaging with open access for researchers to test their hypotheses in vivo, and provide an experimental medicine platform for clinical translational of novel in vivo imaging methods and therapeutics. There are 10 state-of-the-art small animal imaging modalities in CABI: magnetic resonance imaging, photoacoustic imaging,

ultrasound, bioluminescence and fluorescence imaging, optical projection tomography, light-sheet imaging as well as SPECT/CT, PET/CT and confocal endoscopy. It interacts with all other imaging domains at UCL, such as CMIC and Medical Physics. CABI is a founding member of ImagingSciences@UCL an initiative to bring together those working in methodological research applied to medical and biomedical imaging across UCL. The **Centre for Medical Imaging** has expertise in development and validation of clinical imaging with focus on microstructural and functional MRI. Based within University College London Hospital, the centre has access to two 3T Philips MRI and four 1.5T Siemens MRI systems, in addition to three Siemens 64 slice CT and six ultrasound machines. The 3T MRI scanners funded by NIHR and Wolfson Foundation grants each provide 50% scan time for research studies focused on translation of novel MRI methods for imaging neurological, inflammatory and oncological diseases. In addition, the centre provides the infrastructure for clinical investigator access to conventional scanning technology for over one hundred commercial and non-commercial clinical drug trials. The **Institute of Nuclear Medicine** is the largest single UK department committed to radioactive tracer methodology and has introduced to the UK several technologies and techniques (e.g. PET/CT, use of Rubidium-82 and gallium-68 generators, solid state cardiac-specific SPECT (first in Europe)). It has taken delivery of the first PET/MRI scanner in the UK (sixth in the world), which allows, for the first time, simultaneous acquisition of data from two imaging modalities. This complements our existing two PET/CT and five SPECT scanners.

D2.1.3 Clinical Trials Units (CTU): UCL has established an Institute of Clinical Trials and Methodology that incorporates four CTUs (MRC CTU, the UCL CTU, PRIMENT and the UCL CRUK and UCL Cancer Trials Centre). The Institute allows academic staff to design, conduct and analyse clinical trials using innovative methodologies. We have strong connections with several international groups and a growing international portfolio. Future objectives include small-scale early phase studies weighted towards translational endpoints and trials with ATMPs and whole exome sequencing of tumour samples from patients entering phase 1-3 studies, providing an opportunity to link genomics analysis to trial data, and to stratify patients to specific studies.

D2.1.4 Clinical Research Facilities: UCL Clinical Research Facilities at UCLH, GOSH and MEH provide dedicated clinical space, research nurses, data managers and research administrators. Their specific remit is experimental medicine, and much of their activity is early phase clinical trials, and a range of other interventional and non-interventional studies to better understand the origins of human disease. For a detailed description see our impact statement (REF3a).

D2.2.5 Biobanking resources: The UCL-UCLH Biobank for Health and Disease (**Flanagan**), has archived paraffin-embedded histopathological material. Biobanked material includes common and rare cancers, including 3000 fresh frozen sarcomas and 500 metastatic tumours. The core service provides access to a selection of appropriate tissue from diagnostic archives and biobanks, cutting of paraffin embedded/frozen tissue, extraction of nucleic acid and protein, analysis of tumours for genetic alterations (miSeq, Ion Torrent), immunohistochemistry, FISH, and tissue microarrays. The Centre is rolling out a consent process for all hospitals in UCLP and will expand core services to allow banking of tissue from patients in early phase trials, rare tumours and core collections of more common malignancies (gastric, ovarian cancers). The UCL-RFH BioBank (**Lowdell**) is both a physical repository, with capacity for up to one million cryogenically stored samples and a virtual repository for all tissue, cell, plasma, serum, DNA and RNA samples stored throughout UCLP. In particular, samples considered 'relevant material', such as tissues and cells that are licensed by the HYA, can be stored long term. The Baby Biobank (**Moore**) is a repository of samples from complications of pregnancies (intra-uterine growth restriction (IUGR), pre-eclampsia, prematurity and recurrent miscarriages) and normal pregnancies, funded by the Wellbeing of Women Charity, and is a collaboration with Imperial College London. The

Human Developmental Biology Resource (**Copp**), is a national human fetal biobank providing samples for research into congenital disease and genomics. The HTA-licensed Moorfields Biobank, though principally used to curate corneas for transplantation surgery, also provides for the needs of researchers.

D2.2.6 Specialist laboratory services: **GOSgene lab service** was established to accelerate gene discovery in families with rare inherited disease. In 2013, a cancer molecular pathology service will rollout next generation sequencing (NGS) from a new clinically accredited laboratory. This laboratory will introduce whole exome sequencing amongst other technologies, to make available a comprehensive molecular profiling menu in support of clinical trials and translational research. During the REF period we have formalised a relationship with the **Northwick Park Research Institute** in order to benefit from the unique infrastructure that exists in relation to undertaking pre-clinical work in large animals. The Institute is now an affiliate of UCL and both are working towards closer integration. The Institute has been granted a Home Office licence (the first in the UK) to undertake surgical training on this site. To date, surgical trainees wishing to gain expertise with a new technology have had to travel to France or Denmark to achieve this. The **transgenic facility** at RFL occupies an area of approximately 320 m^2, including laboratory, surgery and procedure rooms and holding capacity for up to 4500 mice. Excluding staff costs, turnover of the unit is £~350K per annum. The Unit operates on a collaborative basis, providing support throughout the lifetime of projects, from idea development and grant writing through experimental work, including phenotypic analysis, to publication of results. As appropriate, new transgenics are designed and generated, or existing suitable animals are procured from elsewhere. At present, approximately 30 different lines of mice are under investigation in the Unit; the majority of which were generated in-house. Over the assessment period, the Unit has provided support for grants to seven UCL PIs (£11.8M), and 11 additional UK, US and European laboratories, including several collaborations with GSK.

E. COLLABORATION AND CONTRIBUTION TO THE DISCIPLINE OR RESEARCH BASE

E1 Collaboration

E1.1 Collaboration nationally: Throughout UoA1, researchers play leading roles in UCL's major collaborative initiatives in Biomedicine. The **Francis Crick Institute** (formerly the UK Centre for Medical Research and Innovation) will open in 2015 under Director Prof Sir Paul Nurse. UCL was chosen as the founding academic partner for the Institute because of its research excellence in Life and Medical Sciences, and it is located close to the UCL campus, near St. Pancras station, with funding of £750M from MRC, Cancer Research UK, Wellcome, Imperial, and King's, in addition to UCL. It will employ 1,250 scientists and have an operating budget of >£100M pa. The Crick brings together two existing premier research institutes, Cancer Research UK's London Research Institute (LRI) and the MRC National Institute of Medical Research (NIMR). The UCL-Crick partnership (academic lead **Lomas**) is underpinned by joint appointments (**Swanton** and **Stockinger**).

UCL remains an active partner in the **Global Medical Excellence Cluster (GMEC**; academic lead **Tooke**) also involving KCL, ICL, Oxford and Cambridge. Collaboration, as in the formation of 'clusters' of expertise, is seen as a crucial attractor for the Pharma and Biotech sectors internationally, as evidenced by the growth of such conglomerations in Boston, Singapore, Shanghai etc. **Centre for Advanced Sustainable Medical Innovation (CASMI)** is a joint venture between Oxford University and UCL (academic lead **Tooke**), founded in 2013, and hosts experts from industry and government agencies. Its focus is the decline in R&D productivity, and CASMI will drive the development and piloting of new innovation models in medicine and health technologies. **IMANOVA** is a collaboration between MRC, UCL, Imperial, and King's, IMANOVA has received £47M of investment in equipment and infrastructure since opening in 2007. It provides state-of-the-art facilities for imaging sciences, radiochemistry, and their application to drug and diagnostic development.

The **UCL CRUK Clinical Trials Centre** leads phase 1-2 studies across the UK, with active recruitment from 17 ECMCs. The KCL/UCL Comprehensive Cancer Imaging Centre has joint appointments (**Ng**) and functions as an integrated Centre across two Universities. This is one of three CRUK/EPSRC Imaging Centres, and was renewed in 2013. The Manchester/UCL Lung Cancer Centre of Excellence is developing a 'joined-up' Centre strategy, with networking collaborations across the UK. This was the only Lung Cancer Centre award by CRUK (£2.5M, 2013). A joint bid between UCLH and the Christie Hospital Manchester has been accepted by the Department of Health for the creation of a UK National Proton Beam Therapy Service, at a cost of £125M for the centre at UCLH. A collaborative program of research on the immuno-biology of malignant melanoma is ongoing with the Royal Marsden Hospital/ICR (**Quezada** and **Peggs** at UCL and Martin Gore at RMH). We are working with KCL on gene therapy vector production with (**Collins** and **Pule** at UCL, and Farzanah at KCL). To facilitate this interaction Michael Linden, previously appointed solely at KCL, has now been given a joint contract between KCL and UCL and is in charge of the viral Vector Production Unit at UCLH/UCL. A longstanding collaboration between UCL (**Linch** and **Gale**) and Cardiff University (Burnett and Hills) on the genetics of acute myeloid leukaemia, with studies in patients entered onto the national trials programme (MRC, LLR and NIHR). The **Bloomsbury Research Institute (BRI)** is described in section B12.2. The UCL Fibrosis Hub is an alliance between GSK, UCL and Newcastle University. Other recent funding awards include £4.4M from the MRC to establish a UK Regenerative Medicine Programme Safety Hub (Liverpool University in collaboration with Edinburgh, Manchester and UCL) and £2M MRC DPFS grant with Cambridge for the investigation of NMDA expression using PET/MRI in patients with epilepsy.

E1.2 Collaboration internationally: The UCL-Yale Collaborative is a multi-disciplinary, transatlantic research, education, training and clinical collaboration between UCL/UCLP and Yale University/Yale-New Haven Hospitals. A Framework Agreement between Yale University, University College London, Yale Hospitals and UCL Hospitals Partners was signed between the Presidents of the two Universities and the CEOs of their hospitals in Yale in 2009 and presented to the UK science minister in Parliament in 2011. The objectives of the Collaborative are to increase the quality of creative ideas, to share resources, to gain access to funding that would not have been accessed alone and to strengthen weaknesses in the other. In Biomedicine there are 20 joint projects, including joint funding and exchange of PhD students. Examples include the Cardiac Devices Initiative (Alexandra Lansky, Mike Simons, Yale; **Andrew Taylor**, **John Martin** UCL), which takes US invented cardiac devices, and these are used in patients for the first time in UCLH. A Yale/UCL Devices International meeting involving industry, regulators, funders and clinicians is organised yearly. Joint grants include a €6M grant from the European Commission to develop a novel device invented in UCL (Al Sinusas, Tarek, Famy, Yale; **Zachary**, **Martin** UCL) and an NIH grant to investigate the genetics of congenital heart disease (Lifton, Yale; **Deanfield,** UCL). The genetics of HELPP syndrome is under joint investigation (Lifton, Yale; **Hingorani,** UCL), A joint project on dengue fever involves biologists, chemists and structural biologists on both sides (Gorgo Modis,Yale; **Jacobs** UCL). A number of collaborative cancer programs are planned, the first being in immunotherapy (Lynch, Herbst and Chen, Yale; **Quezada**, **Peggs**, **Swanton** and **Stauss**, UCL), which has resulted in a joint application for a strategic award in lung cancer immunotherapy (Herbst; Yale and **Swanton**, UCL). Yale have exome-sequenced >100 sarcoma samples from our tissue biobank. Links in nephrology have enabled an acute kidney injury biomarker project to be initiated, enabling one of our clinical fellows to be seconded to Yale; the advantage here has been allowing UCL scientists access to the rich technical –omics resources at Yale, and in return granting access to UCL rich sample depository**.**

The IO has recently formed the UNITE Partnership with the University of Bristol, the National Eye Institute (US) and Zhongshan Ophthalmic Centre, Guangzhou in China so that it will, in the future, be able to extend its current focus on classical inflammatory eye disease (uveitis)

as well as inflammatory processes in age-related macular degeneration and diabetic retinopathy. IO has also developed a collaboration with Singapore Eye Research Institute, to on meet the needs of the pharmaceutical industry in a way that neither Institute could achieve on its own. Through the Beckman Institute (USA) IO is also part of a large international consortium addressing the challenge of age-related macular degeneration, in particular the transition from early to late disease. In surgery, there are strong collaborations with many groups overseas. For example, the Phase 1-3 innovation programme (over 3,000 patients randomised) in breast cancer treatment led by **Vaidya** has created an international network/collaboration that began at UCL and has now reached all five continents.

E2. CONTRIBUTION TO THE DISCIPLINE

Data in this section were obtained from a comprehensive survey completed by submitted UoA1 staff in August 2013. Regarding our Cat A academics, in the REF period:

- 50% have served on national (Research Council or similar) or international grants committees, 28% on learned societies and 32% on professional bodies
- 49% served on journal editorial boards
- 65% have participated in conference organisation, with 54% serving as conference programme chairs and 55% have given invited keynote lectures
- 37% have served on university research advisory panels (e.g., ethics, research governance)
- 95% have refereed manuscripts for journals and 86% have refereed research funding proposals
- 76% have examined doctorates
- 62% have engaged with industry through research or in advisory capacities and 38% have taken steps to commercialise their research
- 71% have directly engaged with non-academic users of research, including 65% who have participated in organised public engagement activities

Specific examples are described below that illustrate the range of activities our academics have undertaken.

Charities, research councils and other funding bodies

Linch is the Director of the Lymphoma Trials Office for CRUK. **Lomas** chairs the MRC Population and Systems Medicine Board, Chair of the Grants Committee of the British Lung Foundation and is a member of the MRC Strategy Board. **Williams** is a member of the NIHR Strategy Board, and a member of the NIHR/MRC EME grant board. **Rosenberg** is the Scientific Adviser to NOCRI. **Cheetham** served on the WT Neurosciences and Mental Health Board. **Brocklehurst** Chairs the DoH Policy Research Programme Commissioning Panel, Wellbeing of Women Research Advisory Committee, and is a member of the NIHR Health Technology Assessment Programme. **Hughes** was Deputy Chair of the NIHR Medicines for Children Clinical Research Group. **Halligan** is a member of the NIHR HTA Commissioning Board and the NIHR HTA Strategy Group. **Isenberg** is a member of The Executive Board of Arthritis Research UK (ARUK). **Tooke** chairs the British Heart Foundation Chairs and Programme Grants Committee and is a member of the NIHR Advisory Board. **Fielding** is a member of National Cancer Research Institute (UK NCRI) Haematological Oncology Clinical Studies Group, Chairs the UK NCRI Adult ALL subgroup, is a member of the UK NCRI Industry Adoption Panel, and a member of the NIHR Health Technology Assessment Interventional Panel. UoA1 academics serve on the following panels: WT (**Cheetham**, **Griffiths, Weiss, Singer and Goldblatt**) Fight for Sight (**Cheetham**, **Greenwood**, **Rubin**) BHF (**Greenwood**, **Hingorani**, **Zachary**), MRC (**Martin**, **Enver**, **Pillay** X2**, Collins**, **Hingorani**, **Ali**) and CRUK (**Khwaja**, **Bridgewater**). **Pepys** is on

the Science and Medicine Panel of the Wolfson Foundation.

Learned societies

Gaspar has been Chair of the Gene Therapy Working Party of the European Society for Immunodeficiencies (ESID), and Chair of the Inborn Errors Working Party of the European Blood and Marrow Transplantation Society (EBMT). **Thrasher** was president of the British Society for Gene and Cell Therapy (BSGCT). **Tooke** is the President of the Academy of Medical Sciences. **Peggs** recently chaired the expert panel on behalf of British Committee for Standards in Haematology for the development of guidelines in relapsed and resistant lymphoma and the British Society for Blood and Marrow Transplantation 'indications' panel for lymphomas. **Wedzicha** is Guidelines Director and member of Executive Committee, European Respiratory Society (ERS), Chair of ERS Publications Committee and Chair of ERS Steering Group for development of guidelines on COPD Exacerbations. **Martin** has been President of the European Critical Care Foundation, Vice President of the European Society of Cardiology, and Chair of the task force on Stem Cells and the Heart of the European Society of Cardiology. **Wheeler** was President of the Renal Association.

NHS

Humphries was the lead clinical advisor on the NICE guideline committee for the identification and management of FH patients in 2008. **Cross** is the clinical advisor for the Children's Epilepsy Surgery Service. **Halligan** is the clinical advisor for the UK National Bowel Screening programme. **Williams** is Chair of the NICE hypertension Guideline Development Group. **Wedzicha** was a member of the Programme Board for the COPD NSF and of the NICE Guideline Development Group for COPD and the DoH Advisory Committee on Home Oxygen Services. **Shafran** is on the NICE Guideline Committee for the Development of Care Pathways for Common Mental Health Problems and also the NICE Evidence Update for OCD. **Hochhauser** is a member of the NICE Technology Appraisal Committee.

Regulators

Thrasher has advised the US Recombinant DNA Advisory Committee (RAC), the US Federal Drugs Administration (FDA), the UK Gene Therapy Advisory Committee (GTAC), the Medicines Control Agency (MCA) and the European Medicines Evaluation Agency (EMEA). **MacAllister** is a member of the MHRA Person Appointed Panel.

Industry

Lomas was Board member GlaxoSmithKline Respiratory Centre of Excellence in Drug Discovery and is currently Chairman, Respiratory Therapy Area Board, GlaxoSmithKline. In total fifteen of our academics sit on the Scientific Advisory Boards of major Pharmaceutical companies (**Bellingan, Cheetham, Foster, Greenwood, Lightman, Lomas, Luthert, Muntoni, Ng, Peggs, Shima, Singhal, Stauss, Unwin, Wedzicha**).