Institution: University of Bristol

Unit of Assessment: 1 – Clinical Medicine

a. Overview

The aim of this Unit of Assessment is to conduct research in the core medical science and clinical research disciplines, to advance science and benefit patients, health care professionals and health care delivery. This is achieved by enhanced fundamental understanding of disease, improving disease management and developing novel therapeutic remedies. We combine basic, translational and clinical research, focussing on areas of established strength and critical mass, emphasising interdisciplinarity within and beyond this Unit of Assessment. There are 84.45 FTE staff included, responsible for £63.3m of research income spend and over 161 completed doctoral degrees.

Research in this Unit of Assessment is conducted across six Research Groups: Infection and Immunity; Cardiovascular Science; Regenerative Medicine; Musculoskeletal Research; Metabolism and Renal Medicine; Cancer Biology. They are presented here in an order reflecting a combination of size, links with formal University Research Themes and where their research activity overlaps. Examples of key translational achievements by these Groups since 2008 are:

- Identification of novel immune-modulatory pathways and therapeutic targets (Wraith-2), which have been translated to improved patient care by successful phase I clinical trials and close links with industry including the spin-out company Apitope.
- Changing cardiac surgery practice through off-pump coronary artery bypass (Angelini-1).
- Advances in stem cell biology leading to the first tissue-engineered human airway to be used in clinical practice (Hollander-1).
- Identified very high failure rates for both stemmed and resurfacing metal-on-metal hip replacements, leading to a policy change in the UK and the Netherlands (Blom-1; Blom-2).

Research in this Unit of Assessment is key to seven University Research Themes (Bristol Vision, Cancer, Cardiovascular Science, Dynamic Cell Biology, Infection and Immunity, Population Health, Predictive Life Sciences), all of which link our researchers with those in other Units of Assessment in priority areas recognised by the University. Moreover, the governance, strategic development and delivery of many of these themes are formal partnerships with Bristol NHS Trusts, such as for Cancer and Cardiovascular Science. This aligns our research strategy with excellence in the delivery of specialist care so as to capitalise on the potential for clinical translation of our research, and likewise there are strong partnerships with industry including spin-out companies.

This submission comprises research from three Schools in two of the University's six Faculties: the School of Clinical Sciences in the Faculty of Medicine and Dentistry; the School of Cellular and Molecular Medicine and the School of Physiology and Pharmacology in the Faculty of Medical and Veterinary Sciences. This Unit of Assessment accounts for about two-thirds of submitted staff in these Schools, with the remainder being in Unit of Assessment 4. The six Research Groups are:

Infection and Immunity research spans basic science through to clinical trials and successful translation into commercial enterprise. Staff are based in the School of Cellular and Molecular Medicine and the School of Clinical Sciences, including three staff holding formal joint appointments across these two Schools.

Cardiovascular Science research involves staff in the School of Clinical Sciences and the School of Physiology and Pharmacology. At its core is the Bristol Heart Institute (BHI), a leading centre of clinical and basic science research, bringing together about 300 scientists and clinicians. The BHI Steering Committee comprises representatives from all constituents, including the local NHS.

Regenerative Medicine research spans the School of Cellular and Molecular Medicine and the School of Clinical Sciences, overlapping several of the other Research Groups and Unit of Assessment 4 – namely, cardiovascular, musculoskeletal and neural regeneration.

Musculoskeletal research is conducted by the Musculoskeletal Research Unit in the School of Clinical Sciences, formed in 2010 by merging the Rheumatology and Orthopaedic research groups to foster a comprehensive environment for basic science, clinical and health services research.

Metabolism and Renal Medicine researchers in the School of Clinical Sciences are in purpose-built laboratories at Southmead Hospital, and there is overlap with vascular research in the Cardiovascular Research Group in this School and the School of Physiology and Pharmacology.

Cancer Biology is one of the three major elements of the University of Bristol Research Theme in Cancer, with this Research Group comprising staff in the School of Cellular and Molecular Medicine and the School of Clinical Sciences, all fully integrated with Bristol-wide cancer research.

b. Research strategy

Our research strategy aims to deliver groundbreaking discoveries in basic science and pioneering treatments for patients across the specialties and conditions where we have established critical mass – these include major areas such as cardiovascular, renal and musculoskeletal health, regenerative medicine, autoimmune diseases and ophthalmology. We contribute to the University's Research and Enterprise Strategy in developing a portfolio of high-impact interdisciplinary research to answer important societal questions and hence improve the population's social, political and economic well-being. This is achieved by conducting fundamental, translational and clinical research, focussing on our areas of strength in collaboration with colleagues in the NHS and other Units of Assessment, and on fully exploiting our close links with industry including spin-out companies. The strategy covers the translational gaps relating to driving fundamental scientific discovery through to clinical testing in first-in-human studies, and from taking evidence of efficacy derived from such early studies through to large-scale phase III trials.

Translation of our research is aided by University structures such as Research Themes and the Elizabeth Blackwell Institute for Health Research (EBI), supported by a Wellcome Trust Institutional Strategic Award and matched University funds. We also play a key role in Bristol Health Partners, a formally constituted link between the Bristol universities and local health and social care services. Set up in 2012, this is an academic health sciences partnership for research and innovation, and has created Health Integration Teams (HITs) as inter-organisational groups of commissioners, academics, health and social care practitioners set up to harness research, innovation, education, patient care and prevention pathways. As evidence of the connectivity of our research strategy with excellence in local health care delivery, we lead the HITs on retinal and musculoskeletal diseases.

In terms of key strategic developments, our staff lead an NIHR Biomedical Research Unit (BRU) in Cardiovascular Disease and are partners in a BRU in Nutrition, Diet and Lifestyle, both of which strengthen integration between research and service delivery in these areas and attract industrial interest. Other partnerships in which we play leading roles include: a Biomedical Research Centre (BRC) in Ophthalmology at Moorfields Eye Hospital/UCL, with leadership from Bristol in terms of inflammation and immunotherapeutics; a research and training agreement on ocular immunology between the NHS (BRC) and the United States NIH; the Royal College of Surgeons-funded Bristol Surgical Trials Centre; the £12m EPSRC-funded SPHERE collaboration led by the University of Bristol investigating an innovative sensor platform for remote healthcare monitoring in residential environments for those with chronic conditions or following discharge from complex surgery; a £3.8m MRC- and University-funded preclinical in-vivo imaging platform for translational medicine.

Our overall strategic aim for research from 2008 to 2013 has been to focus investment in areas of existing excellence to ensure their sustainability while expanding selectively to capitalise on emerging strengths or opportunities, as detailed below for the six Research Groups in turn.

Infection and Immunity

Particular strengths in this group include autoimmunity, emerging and chronic viral diseases, microbial pathogenesis, antimicrobial resistance, mucosal immunology and vaccine immunology.

The group had £12.2m of research income spend since 2008, with major achievements including:

- Research on autoimmune diseases (multiple sclerosis and uveitis) and allergic diseases leading to industry-sponsored clinical trials and novel immunotherapies under development by three University spin-out companies (Apitope, with a $194m partnership deal with Merck; KWS BioTest, now turning over £2.4m per year after an initial investment of £200k from the Sulis Challenge Fund; Trident, funded by $20m of venture capital).
- Lead for the inflammation and immunotherapeutics theme (£1.8m) in the Ophthalmology BRC, and with the NHS to inform cost-benefit analyses of novel vaccine strategies.
- Lead role in an NHS (BRC)/NIH partnership for research and training in ocular immunology.
- Structural studies of microbial virulence factors and mechanistic studies of microbe-host cell interactions essential for the development of next generation antimicrobial products, supported by awards of £0.7m from the MRC and over £1m from the Wellcome Trust.
- Mechanisms of naturally-acquired and vaccine-induced immunity to pneumococcus and meningococcus of importance to current and future immunisation programmes.
- Advances in the epidemiology of: vaccine-preventable infections; the impact that vaccination and screening has on their prevalence; and the application of modern antiviral therapies to hepatitis and HIV infections in injecting drug users.
- Combining deep sequencing of mRNA and high throughput quantitative proteomics to show how adenoviruses take over a host cell, and to study human SARS-coronavirus, dengue virus, and feline infectious peritonitis virus.
- Novel imaging and mathematical modelling techniques, developed with the Wolfson Imaging facility and the NIH, to study spatiotemporal patterning of T cell signalling.

Cardiovascular Science

Specific research strengths are: adult and paediatric cardiac surgery; cardiorespiratory neural control; mechanisms of hypertension; vascular cell biology; cardiovascular pathobiology; atherothrombosis; platelet biology and cardiac physiology including the mitochondrial function; overlap between and active collaborations with those in the Regenerative Medicine and the Infection and Immunity Research Groups through, for instance, applications in ophthalmology and musculoskeletal medicine. Research income spend was £27.4m and highlights include:

- Two British Heart Foundation Chairs in Cardiac Surgery and Vascular Cell Biology.
- Department of Health's £60m investment in the Bristol Heart Institute Medical Centre opened in 2009 as a major facility for research and patient care including clinical trials.
- Award of an NIHR BRU in Cardiovascular Disease for 2008-12 and 2012-17 (total £13.3m).
- In the top seven UK universities for BHF and MRC funding by number and value of grants.
- The UKCRC fully-registered Clinical Trials and Evaluation Unit (CTEU) enabling over 90% of cardiac surgery patients being offered inclusion in a trial and over half being recruited.
- CTEU's involvement in the IVAN trial, showing that an unlicensed treatment for age-related macular degeneration was as effective and safe as a more expensive established drug – this trial was considered to be a model of such studies in an independent review of the NIHR HTA programme, with the potential to save the NHS over £85m per year (Raftery and Powell, Lancet 2013;382:1278-85).
- With colleagues in Unit of Assessment 2 and the Musculoskeletal Research Group, formed the Bristol Surgical Trials Centre with £0.5m from the Royal College of Surgeons (RCS).
- Long-term health outcomes with off-pump coronary artery bypass are similar to those with coronary artery bypass grafting with cardiopulmonary bypass.
- MicroRNAs as novel therapeutic targets and predictive biomarkers in ischaemic disease and cardiac/vascular surgery, with potential for clinical exploitation.
- Identification of nerve growth factor as capable of heart protection and regeneration, now being translated to a large animal study in preparation for a first-in-human clinical trial.
- A central chemosensor role for astrocytes in the control of breathing.
- Vein graft intimal thickening (a cause of graft failure) can be suppressed by gene therapy.
- Identification of a VEGF splicing factor influencing angiogenesis and Wilms' tumour growth.

Regenerative Medicine

Major cell biology and molecular medicine strengths applied to neurodegenerative, cardiovascular and musculoskeletal diseases drive discoveries in stem cells and tissue engineering through to first-in-human studies. Research income spend was £7.8m and major achievements include:

- Pericyte progenitor cells able to promote vascular regeneration and protect ischaemic heart adverse remodelling identified in the saphenous vein leftover from cardiac surgery, allowing expansion in culture for autologous transplantation and the potential for first-in-human trials.
- Human embryonic stem cells differentiation in vascular progenitor cells to treat critical limb ischaemia in a nude mouse model have been developed for a first-in-human clinical trial.
- Advances in stem cell biology leading to the first tissue-engineered human airway, created using a successfully implanted decellularised human donor trachea.
- First clinical trial of stem cells for torn meniscal cartilage by spin-out company Azellon Cell Therapeutics, with £1.6m from the Wellcome Trust, Technology Strategy Board and others.
- Epidermal growth factor is a mediator of dopamine-induced precursor cell proliferation in the subventricular zone, with potential implications for the treatment of Parkinson's disease.

Musculoskeletal Research

Strengths in toxicology, joint replacement and bone strength in research from onset to outcome of osteoarthritis, osteoporosis, fragility fractures and rheumatoid arthritis. This multidisciplinary group includes a Patient Experience Partnership for Research, ensuring activities are patient-centred and fully integrated into service delivery. Research income spend was £3.8m and highlights include:

- Two £2m NIHR Programme Grants on arthroplasty – one on patient perspectives, including peri-operative and long-term pain, one on treatment and causes of post-operative infection.
- In conjunction with others, £0.5m award for the RCS-funded Bristol Surgical Trials Centre.
- A £0.6m contract to analyse the National Joint Registry of England and Wales, by which outcomes are assessed to inform the practice of arthroplasty worldwide – including basic research into metal-on-metal prostheses failure and the causes of post-operative mortality.
- Novel understandings of how nanoparticles signal across barriers such as the placenta.
- Under the auspices of the EBI and with colleagues in the Cardiovascular Research Group, lead on patient-oriented aspects of a £12m EPSRC-funded in-home monitoring initiative.

Metabolism and Renal Medicine

Particular strengths are in genetic, clinical and experimental research into diabetes, obesity, membranous nephropathy, glomerular biology, insulin and insulin-like growth factor (IGF) signalling to the podocyte, with £8.5m of research income spend and the following major achievements:

- Lead for one of the four themes within the £4.5m NIHR BRU in Nutrition, Diet and Lifestyle.
- A £0.7m Diabetes UK(DUK)/NIHR-funded trial showed an intensive diet intervention improves glycaemic control in newly-diagnosed type 2 diabetics, but an activity intervention gave no further benefit (paper awarded RCGP/Novartis Diabetes Paper of the Year 2011).
- Retraining eating behaviour with a feedback device is a useful adjunct to standard lifestyle modification in treating obesity among adolescents.
- Prediction of type 1 diabetes using novel, validated islet autoantibody assays, with total awards of £1.4m from NIH, DUK and the Juvenile Diabetes Research Foundation (JDRF).
- Studies of the aetiopathogenesis and prevention of type 1 diabetes, including using our unique patient cohorts, with total awards of approximately £2m from JDRF, DUK and EU.
- A £0.6m MRC Programme Grant to develop unique human glomerular cell lines.
- Total of £2m from MRC and Kidney Research UK for glomerular transgenic mouse models revealing the key role of insulin and IGF signalling in the podocyte of the glomerulus.
- Leading several national and international clinical study groups examining membranous nephropathy and focal segmental glomerulosclerosis.

Cancer Biology

Our major strengths range from molecular and population-based studies through to clinical research, with particular strengths in: tumour cell biology; cancer epigenetics and the regulation of gene expression; and the identification and assessment of the prognostic value of biomarkers. The principal therapeutic focus is on cancers of the gastrointestinal tract (including colon), prostate and paediatric tumours. Research income spend was £3.6m and major achievements include:

- Internationally prominent colorectal tumour cell biology research including chemoprevention studies such as international clinical trials of aspirin, with two Cancer Research UK (CRUK) five-year programme grants of £1m and £1.2m commencing in 2006 and 2012 respectively.
- Advances in understanding Wilms' tumour and its transcriptional regulation, including that chemotherapeutic drugs can induce its proteolysis, with major implications treating diverse paediatric and adult tumours, with funding to Bristol of over £1m from BBSRC, MRC and CRUK, as well as nearly £0.8m of NIH funding to a US laboratory with the PI now in Bristol.
- Demonstration that IGF-1 levels are strongly related to prostate cancer disease progression and mortality, along with the identification of key nutritional determinants of systemic IGF-1 levels as potentially modifiable risk factors (CRUK funding of £0.4m from 2006-2010).

Research in Clinical Medicine at the University of Bristol for the five years from 2014

The context of our research will continue to be the University's research strategy, based on the mission to support individual scholarship and interdisciplinary research of the highest quality, especially that linked to the University Research Themes, so as to pursue and share knowledge and understanding to help society and for individuals to fulfil their potential. These themes are subject to regular formal University review, and emerging areas can receive this status once there is sufficient critical mass and research portfolio. This mission is delivered through a seven-year strategy plan, reflected in further plans within the relevant constituent Faculties and Schools.

A further development is the recent £9m award from the NIHR (with matched funding from the Universities and NHS organisations in Bristol) for an NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC*west*) as the focus for connecting high quality health research with service organisation and delivery, primarily through the established and further HITs. Within the University, health research is one of two major interdisciplinary areas of strength, and the focus of our research strategy for the next five years will therefore be Bristol Health Partners, CLAHRC*west* and the newly-formed Elizabeth Blackwell Institute (EBI).

The EBI was established in 2013 as one of two University Research Institutes, recognising health research as a key area of interdisciplinary research strength. Its mission is to address issues ranging from the basic sciences underpinning the understanding of health and disease to the clinical, social and population health sciences, with particular focus on the translation of this knowledge into effective health outcomes. Combining the Wellcome Trust Institutional Strategic Support Fund with matched University funding, the EBI provides £1.5m per year to support schemes including: providing salary and research costs funding for early and mid-career researchers to develop applications for nationally-competitive personal fellowships; continuing the University's long-standing scheme to provide financial support for women returning to research activities after a career break; an innovative Clinical Primer Scheme to enable active clinicians to gain between 3 and 9 months' experience in an academic environment to see if research could be part of their future career; flexible support and encouragement for hitherto separate groups to have the opportunity to develop novel interdisciplinary collaborations. Since the launch of these schemes in October 2011 we have secured £185,000 across these schemes, with highlights being SPHERE and a Wellcome Trust Training Fellowship awarded to a recipient of a clinical primer. The strategy also encompasses industry links, including that the University of Bristol's contribution to the joint initiative with Cardiff University (the Severnside Alliance for Translational Research, SARTRE), developed initially by £3.7m of MRC funding, is now under the aegis of the EBI.

In addition, the Research Groups have the following key future objectives:

Infection and Immunity

A strength of this University Research Theme is its clear ability to foster international, national and cross-Faculty collaboration; indeed, for experimental medicine in ophthalmology it is already agreed that our links will expand via the NIH and into China. The integration of clinical and basic science enables consolidation of the University of Bristol's position as a leading centre for this research, and through the EBI's infrastructure including that for industrial relationships we will:

- With colleagues in Unit of Assessment 2, apply to co-lead a Health Protection Research Unit to evaluate interventions concerned with infectious disease and immunisation.
- Increase the uptake of the EBI Clinical Primer Scheme by early career stage clinicians and hence to build on our success in securing Wellcome Trust and MRC Training Fellowships.
- Incorporate training in entrepreneurship into Infection and Immunity MSc and PhD research programmes to strengthen our connections with industry including spinout companies.
- Use the Infection and Immunity Research Tissue Bank as a template for the management of a Bristol-wide biobank supporting next generation clinical studies.
- Develop partnerships with the Faculties of Engineering and Science (especially the Schools of Physics and Chemistry) to support interdisciplinary symposia and develop applications to the Wellcome Trust for research on Sustaining Health – in particular on climate and health.

Cardiovascular Science

We plan to build on our critical mass and research excellence by taking opportunities to expand the numbers of key senior staff, in areas such as cardiac surgery and cardiology, so as to:

- Submit applications for 4-year BHF PhD studentships and a BHF Centre of Excellence.
- Success with senior awards such as BHF Chairs, Wellcome Trust Investigator Awards and European Research Council Grants.
- Recruit a Consultant Senior Lecturer in Cardiac Surgery.
- Continue to develop the activities within the existing NIHR BRU in Cardiovascular Disease.
- Develop a risk-profiled cardiovascular biobank within the Bristol-wide facility noted above.
- Together with colleagues in the Regenerative Medicine Research Group, continue to co-lead the MRC and University-funded initiative to provide new animal imaging facilities.
- Secure protected research time for leading clinical scientists through the EBI and relevant national funding schemes such as through the NIHR, RCUK and BHF.
- Disseminate the findings from the TransACT trials of autologous bone marrow-derived progenitor cells in cardiac surgery patients with acute or chronic myocardial infarction.

Regenerative Medicine

We will continue to develop our strong contributions to this expanding research area, in particular in relation to our established basic and clinical strengths in the cardiovascular, musculoskeletal and neural regeneration fields. We will forge closer links between fundamental and clinical researchers to increase the number of first-in-human trials. Central to the achievement of these aims are:

- To foster translational research, the Cardiovascular Regeneration Laboratories will be developed in close proximity to the adult and paediatric cardiac surgery, catheterization laboratory, vascular surgery and the Clinical Research and Imaging Centre (CRIC-Bristol).
- From 2013, the co-location of the researchers in stem cells and neural degeneration to newly refurbished laboratories adjacent to those researching into musculoskeletal disease; this initiative is on behalf of the two Schools and Faculties involved and reflects our general philosophy and practice that such structural issues are not an obstacle for collaboration.
- Take full advantage of infrastructure funding of £2.8m secured from the MRC and £1m from the University to establish new (MRI, PET) imaging facilities for small and large animals as well as large animal theatres for regenerative medicine research, linked to a potential £5m Translational Biomedical Centre.

- Develop our national and international reputation in cardiovascular regenerative medicine through the Vascular Regenerative Centre, with collaborations between staff in this and the Cardiovascular Research Group and funding from the BHF and NIHR including the BRU.

Musculoskeletal Research

In mid-2014 these researchers will move to purpose-built laboratory and clinical research facilities at Southmead. As well as enhancing existing close working relationships between orthopaedic surgery and rheumatology within the Musculoskeletal Research Unit, such researchers will then be co-located with basic and clinical scientists from other Research Groups, enabling the use of shared facilities and collaborations with researchers in metabolism and dementia. The second NIHR Programme Grant will facilitate a multicentre trials collaboration with five other UK centres and the University of Melbourne, aided by the Bristol Surgical Trials Centre. Specifically, we will:

- Recruit at least one Consultant Senior Lecturer in Orthopaedic Surgery.
- Support early career and established researchers, including clinicians, in applying for personal fellowships from RCUK, NIHR and relevant charity funders.
- Work towards an NIHR BRU in Musculoskeletal Research.

Metabolism and Renal Medicine

Through a combination of continuing the internationally influential activities of existing established researchers in this Research Group and the development of early career researchers, we will continue to expand our groups in these areas by:

- Increasing interdisciplinary research collaborations between renal researchers and cognate groups in Bristol such as cardiovascular and endocrinology, including through co-location.
- Continue to lead international collaborations for renal medicine and diabetes research, including the NIH TrialNet and The Environmental Determinants of Diabetes in the Young.
- Build on our excellent track record of supporting early career and established researchers in applying for personal junior and senior fellowships from RCUK, NIHR and charity funders including the Wellcome Trust, Diabetes UK and Kidney Research UK.

Cancer Biology

We will continue to develop our profile and capacity for this research, including identifying and translating biomarkers for the early detection and treatment of cancer, through for example:

- Develop a unique centre of excellence in Wilms' tumour and genome regulation research with the recent appointments of two non-clinical lecturers included in this submission.
- Building on the CRUK-funded research programme on colorectal tumour cell biology, work towards a CRUK Centre for Chemoprevention Research.
- Development of a cancer tissue bank as part of the planned centralised Biobank for Bristol, to for example enhance gene expression and epigenetics research.
- Consolidate the recent formation of a Bristol-wide Cancer Group in partnership with NHS Trusts and the University of the West of England, including consideration of a cancer HIT.

The University has a rich history of public engagement and involvement through its Centre for Public Engagement. Such activities include press and broadcast media, interactive exhibitions and public lectures as well as the production of literature and web-based information specifically geared to study participants and lay audiences. Many of our research staff give frequent media interviews, public talks and lectures. In addition, large groups such as the Bristol Heart Institute (BHI), the NIHR BRUs and BRC and the various University Research Themes have well-honed engagement strategies including a range of participant advisory panels, and University press releases result in coverage across the world. Through Bristol Health Partners, People and Research South West is a collaborative initiative that provides advice on involving people in health research and maintains

databases of local people interested in getting involved. To encourage students to embrace a career in medicine and biomedical research and to establish robust connections with our community, we have a tradition of hosting post-16 students from local schools for summer placements (sponsored by the Nuffield Foundation). Across the University we are also pursuing other contemporary modes of information delivery in efforts to widen outreach. Examples include the integration of social media (Twitter, Facebook, blogs) to publicise scientific events that involve the public and participants, and involvement in Science Festivals. In April 2013 Bristol Health Partners hosted one of the first medical versions of the Technology Entertainment Design (TED) event in the UK (TEDMED), at which five staff connected with this Unit of Assessment gave presentations. We will continue our active engagement with this enterprise in future.

c. People, including:

i. Staffing strategy and staff development

Line management in the University, including responsibility for career development, is organised though Schools and, where relevant sub-School structures. For example, within the School of Clinical Sciences there are six Sections with formally appointed Heads responsible for all aspects of career development including the annual Staff Review and Development process, four of which are encompassed by this Unit of Assessment (Cardiovascular Surgery and Vascular Biology, Regenerative Medicine and Immunity, Metabolism and Renal Cell Biology, Clinical Outcomes and Methodology). Within the School of Physiology and Pharmacology there are three overarching research groups/themes, one of which (Cardiovascular Science) is wholly in this Unit of Assessment and another (Cell Signalling and Biology) partly so. The remaining staff in these two Schools align with the Bristol Neuroscience University Research Theme and contribute to Unit of Assessment 4. Staff in the School of Cellular and Molecular Medicine specialise in three broad areas (Cancer Biology, Infection and Immunity, Regenerative Medicine/Stem Cell Biology), all of which are covered under this Unit of Assessment.

Each School is committed to a staffing policy to attract, develop and retain researchers of the highest calibre, both in their own fields and in an increasingly interdisciplinary environment. The research achievements highlighted above provide numerous examples of the successful integration of clinical and non-clinical academics at all levels of seniority. Formal mechanisms and general cultures are both crucial to the realisation of our staffing strategy, supported by University- and School-level policies and practices, including:

- For all staff, there are coherent research groups with sufficient critical mass and multidisciplinarity to provide a strong research environment for advice and collaboration.
- Frequent research group meetings to discuss developments in the field and present new data, supplemented by regular external and internal School research seminars.
- The annual Staff Review and Development process enables all staff to assess their career progression and training needs with their line manager, and thence to their Head of School.
- New members of staff have reduced teaching and administrative loads initially to allow them to establish their research, supported by a senior academic research mentor.
- Many of the University Research Themes (for instance, Cardiovascular Science, Infection and Immunity) with which our staff are aligned run events for and involving early career researchers, as well as seminar programmes of prestigious external and internal speakers.
- Practical and financial support for prestigious visiting scholars to spend time in Bristol, such as the Benjamin Meaker Awards run by the University's Institute for Advanced Studies.
- Career development is sustained though mentorship, training and support for writing grants and personal Fellowship applications, including organising mock interviews.
- Annual Fellows' Days are run in all Schools, where prospective internal/external candidates are invited to present proposals, meet potential sponsors/mentors and discuss support.
- Clinical Academic Fellows/Lecturers are supervised by senior clinical academics for their academic projects, with mentorship throughout their academic career.
- Availability of sabbaticals and flexible working arrangements to allow established staff to spend time on research activities including time abroad or at prestigious UK Universities.

- The University has a strong programme of research support and training that includes external training by the research councils and industry.
- In recognition of commitment to advancing the careers of women in science, the University of Bristol generally and the School of Clinical Sciences individually hold Athena Swan Bronze Awards and the School of Physiology and Pharmacology has a Silver Award.

To build capacity and ensure sustainability we have invested in new junior and senior posts since RAE2008, in line with the research strategy of one or more Research Groups. Almost all of the following senior posts were appointed or have been promoted to a Readership or Personal Chair: neuro-ophthalmology (*Atan*); cardiac imaging (*Buccarelli-Ducci*, *Cannell*); rheumatology (*Clark*, *Gregson*); paediatric nephrology (*Coward*); urology (*Drake*); ophthalmology (*Lee*); respiratory medicine (*Maskell*); cancer biology (*Roberts*); adult nephrology (*Satchell*); immunology (*Wuelfing*).

In the context of career development generally, the University's Code of Conduct for the REF and its full implementation of the Concordat to support the career development of researchers, we have been particularly supportive of Early Career Researchers in engaging with the REF. Indeed, about 1 in 8 of staff in our submission are formally in this category, including those currently with highly competitive early career fellowships such as *Foster* (BHF, 2010), *Maringer* (Wellcome Trust, 2012) and *Perriman* (EPSRC, 2013). We have also had considerable success in securing prestigious personal Fellowships – for example: a renewal of a Wellcome Trust Senior Research Fellowship in cancer biology (*Roberts*); three clinician scientists in renal medicine receiving prestigious MRC or Wellcome Trust intermediate awards (*Coward*, *Salmon*, *Satchell*); four HEFCE Consultant Senior Lecturer awards (including *Blom*, *Drake*, *Maskell*; the fourth progressed to a Chair at another HEI); an MRC Senior Clinical Fellowship (*Coward*); an Arthritis Research UK Clinician Scientist Fellowship (*Gregson*) and two BHF Senior Basic Science Research Fellowships (*Emanueli*, *Mundell*). We will utilise all the relevant EBI schemes to enhance these successes in future.

ii. Research students

Research students, including pre-doctoral training fellows, are an integral part of the delivery of the research strategy overall and in contributions to the Research Groups. Examples of outstanding achievements of past PhD students include subsequent awards such as an MRC Clinician Scientist Award followed by an MRC Senior Clinical Fellowship; a Wellcome Trust Intermediate Clinical Fellowship; a BHF Intermediate Fellowship for a colleague who is now a University of Edinburgh Chancellor Fellow; a prestigious Fulbright award along with a Diabetes UK Moffat Travelling Fellowship. There has been major success in gaining external funding for doctoral students including novel schemes to attract clinical researchers such as a new University Hospitals Bristol NHS Foundation Trust scheme currently supporting three of our clinical research training fellows. In general, funding has been from numerous AMRC sources, BBSRC, BBSRC-Industrial Case, BHF, four-year schemes from the Wellcome Trust and MRC, and a BBSRC Doctoral Training Grant. Over the REF period, we have supervised to completion over 161 doctorates – an average of over 32 students per year with a steady increase to recent levels of about 37 per year.

Evidence of a strong and integrated research student culture

Research and training at the University of Bristol are collaborative, multidisciplinary and widely recognised as very high quality, including in the thematic areas covered by the six Research Groups in this Unit of Assessment. This is illustrated by our ability to win doctoral training centres and related four-year PhD programmes, giving us experience in recruiting and working with cohorts of graduate students. The formation of the Bristol Doctoral College in September 2013 has built on the best practice developed through these initiatives and the key benefits to the students will be to provide an enhanced and coordinated approach to doctoral training in terms of skills training and support. Doctoral students benefit from our multidisciplinary culture, for instance in connecting supervisors from different parts of the organisation.

Student feedback on their doctoral experience is a highly valued component of our programme review mechanisms, including through Graduate Representatives nominated by the students. In addition, the University participates in the national Postgraduate Research Experience Survey, with 40-50% of doctoral students aligned to this Unit of Assessment taking part in 2013.

Effective and sustainable doctoral research training

As well as each student having at least two supervisors and two advisors external to the project, our postgraduate management structure includes a Faculty Education Director (Postgraduate) for each Faculty, a Director of Graduate Studies in each School, academic Graduate Tutors to oversee the pastoral care and general support each student requires, and dedicated School-level administrative staff. The academic supervisors are experts in the field, providing day-to-day guidance together with longer term oversight of the research project and the student's future career development. Independently of this, the School-based Graduate team provides pastoral support and advice so that any difficulties are dealt with quickly and effectively. To ensure successful completion of their doctoral studies within the times specified by grant awarding bodies and the University, all students undergo mandatory annual progress monitoring. This takes the form of a written report, oral presentation and mini-viva/interview assessed by the two advisors – a process supported and overseen by the relevant School and Faculty team, and staff and students in the School of Clinical Sciences have pioneered the implementation of a flexible on-line system of monitoring, objective-setting and general communications between students and their supervisors.

In addition, doctoral students engage in a wide range of skills training offered across the University, including in generic research skills and experimental techniques. A recent development is the eBiolabs Research Hub, the on-line home for postgraduate researchers in biomedical sciences. Initially populated with videos and animations from the highly successful undergraduate-level Dynamic Laboratory Manual, this enables students and researchers to share methods and techniques, find local experts and direct their own learning.

Attendance at training programmes is reviewed as part of the annual progress monitoring. In addition to the standard programmes summarised above, a wide range of other training opportunities are offered across the University to students, such as: commercialising your research/intellectual property; enterprise skills; language centre; personal development; teaching and learning. Finally, advice and support for determining future career opportunities are provided through careers workshops run by the University's Careers Service.

d. Income, infrastructure and facilities

Income

The total spend of our competitively awarded research income over the period of the REF was approximately £63.3m (£750k per FTE), averaging at £12.7m per year with a rising profile since 2009/10 and a most recent figure of over £13.2m. There have been increasing amounts from RCUK and NIHR, to £2.1m and £2.3m respectively in 2012/13. The upward trajectory was particularly marked for NIHR, with a more than five-fold increase in the annual figure through the REF period. Of the total spend, the six Research Groups account for the following percentages: Infection and Immunity (19%); Cardiovascular Science (43%); Regenerative Medicine (12%); Musculoskeletal Research (6%); Metabolism and Renal Medicine (14%); Cancer Biology (6%). These funds have been from a variety of commercial, RCUK, AMRC and Government sources including NIH and NIHR; highlights are a number of Programme Grants from Research Councils, NIH, NIHR, British Heart Foundation and CRUK, and nearly £3.7m of research income spend from industry sources. We have received over £8.3m NIHR income-in-kind, £610k RCUK income-in-kind and over £1.7m Department of Health Awarded Capital to the BRU in Cardiovascular Disease.

Infrastructure and Facilities

Our research is supported by a number of infrastructural developments and facilities, notably:

Wolfson Bioimaging Facility and Flow Cytometry Facility. The microscopy and flow cytometry facilities support staff across this Unit of Assessment. The total capital investment during the REF period is £3.1m. The Wolfson facility is unique in the UK in fully integrating two modalities, with new FEI electron microscopes housed alongside the latest Leica and Perkin Elmer confocal and TIRF microscopes. It enables high-resolution live cell imaging and correlative light and electron

microscopy, and provides the latest state-of-the-art as well as more routine facilities for both light and electron microscopy users. Flow cytometry offers three-laser four-way cell sorting (BD Influx) and up to 16-parameter automated acquisition and analysis (BD Fortessa). The facilities are run by three dedicated managers and team of technicians.

Clinical Research and Imaging Centre (CRIC-Bristol). This is a key development since the last RAE and provides research-dedicated human imaging facilities. This £6.4m collaborative strategic investment between the University and the University Hospitals Bristol NHS Foundation Trust includes a 3 Tesla Seimens Magnetron Skyra MRI scanner (funded by the Wolfson Foundation), recovery and anaesthesia suites, a two-bed sleep laboratory and four clinical research rooms. All rooms have full clinical support for infants, children and adults including medical gases. The University has supplemented this investment with new posts including a Professor of Imaging, a Senior Research Fellow and four support posts. Specialist infrastructure was installed in CRICBristol to take full advantage of the University's Advanced Computing Research Centre.

Advanced Computing Research Centre. BlueCrystal is the University's high performance computing machine (total investment in the review period £10m, with a further £3m in progress), providing access to serial and parallel computing for all researchers, along with full training and support. Ten researchers in this Unit of Assessment are High Performance Computing users, using for example more than 225,000 cpu hours in the first half of 2013. The Research Data Storage Facility provides integrated resilient petascale storage to all researches and, as at June 2013, 19 researchers in this Unit of Assessment were using 14TB of storage (5TB of disk storage is available to all researchers, with additional storage provided on a chargeable basis).

Purpose-built Laboratories and Clinical Research Facilities at Southmead Hospital. The Musculoskeletal Research Unit (MRU) has extensive laboratories and equipment including bone biology, cell culture and cytogenetics facilities, plus clinical research facilities including a DEXA unit. Other researchers at Southmead already have shared state-of-the-art cell biology and culture facilities, and an extension to the existing academic building at this site will from May 2014 house clinical and translational science dementia researchers, the MRU and Bristol Urological Institute.

University Animal Services Unit (ASU). In vivo facilities include barriered breeding for rodents of around 1000m^2. Within the main research area, there are facilities totalling approximately 2000m^2. The ASU currently houses around 120 lines of genetically modified mice, with many of our researchers being major users. Facilities include animal holding space, surgical procedure rooms and behaviour rooms. Capability exists to use viral vectors in animals up to Category II. Large animal facilities also exist, enabling translational and preclinical research. Total direct spend for the ASU is £2m per year with staff levels in 2013 of 28 full time equivalent; attributed costs amount to a further £3.2m annually. Investment in refurbishments is ongoing: around 600m^2 of space across the in vivo facilities are undergoing major refurbishment at an estimated cost of £3m, together with a further minor refurbishment of large animal facilities being carried out; a further £3.8m MRC and University-funded project to establish new MRI and PET imaging for small and large animals.

Proteomics Facility. Researchers in this Unit of Assessment mainly use the Orbitrap Velos mass spectrometer in this facility, which is also used by over 40 research groups across the University as well as external users including the Universities of Bath, Birmingham, Cambridge, Cardiff, Leeds, Sussex and Imperial College. Data generated from this facility have led to many high profile publications including papers in Nature Methods and Nature Cell Biology. A key objective of the facility is an upgrade to the new Orbitrap Fusion, ensuring that the facility stays at the forefront of high throughput biological mass spectrometry.

University of Bristol Research Tissue Banks. For example, the Infection and Immunity Research Theme tissue bank has full ethics approval operating within Human Tissue Act governance. It has a fully constituted multidisciplinary management committee including lay members, information sheets and consent forms. It receives, processes and (where appropriate) releases samples from a range of clinical studies and trials both within Bristol and externally. There is also a biobank resource for (healthy and diseased) human cardiovascular tissue within the BHI.

Equipment Sharing. We have forged strategic partnerships with other institutions for this purpose. Equipsouthwest.org.uk is a regional initiative between the Universities of Bristol, Bath, Cardiff and Exeter to make equipment and facilities more visible and easier to share. For example, the Musculoskeletal Research Unit has relocated its mechanical engineering facilities to the Department of Mechanical Engineering at the University of Bath to consolidate these ongoing collaborative links, and a pipetting robot for research use has been purchased by the Infection and Immunity Research Group to be located in the local Public Health England virology laboratory.

Research and Enterprise Development (RED). This central division within the University is a group of more than 80 staff with specialist skills and training, who work with academics to help sustain and grow research activity. This includes identifying funding opportunities, advising on the development of research proposals, coordinating large, collaborative or complex bids, negotiating research and consultancy contracts, strategic project management, improving the impact and commercialisation of research by working with business, and supporting research ethics and governance activity. Within RED, the Research Governance Team ensures that there are robust research governance policies available to all staff and students online, including: infrastructure; data storage and management; use of animals and human tissue in research; grant management and regulatory issues. These policies are augmented by on-site training in research ethics.

e. Collaboration or contribution to the discipline or research base

In addition to the numerous internal and external collaborations on individual projects, programmes and initiatives covered in the research highlights above, we have already detailed many of our strategic partnerships with NHS and other universities – in particular, through Bristol Health Partners, the HITs and our NIHR BRU and BRC awards. We also take full advantage of and contribute both strategically and organisationally to the highly effective clinical research structure embedded in the facilities of our NHS partners, such as the NIHR Medicines for Children Research Network South West (directed by *Finn*). A number of our Research Groups also have long-standing collaborations with the local NHS Blood and Transplant Authority, where for example bone marrow is processed to extract CD133-positive stem cells (or control) under GMP conditions for two ongoing clinical trials, and pericyte progenitor cells are prepared for autologous therapy in cardiac ischaemia patients. Moreover, the recently launched Great Western 4 (GW4) partnership between the Universities of Bath, Bristol, Cardiff and Exeter will facilitate the development of existing and new research collaborations across these institutions.

An example of a major academic collaboration is our partnerships in regenerative medicine (a theme in the NIHR BRU in Cardiovascular Disease) with groups such as the Universities of Glasgow, Edinburgh, Oxford, Cambridge and King's College London. We are key partners in two BHF-MRC Centres for Excellence in Regenerative Medicine and one of the UK Regenerative Medicine Platforms. Additional recent awards include considerable MRC and University of Bristol infrastructure funding for pre-clinical functional small and large animal imaging and surgical facilities. MicroRNA research in vascular regeneration is also being developed in a highly competitive Leducq Transatlantic Foundation grant with Yale, Frankfurt and Hannover Universities.

Another example is our national and international collaborations in renal medicine research, such as with the Lunenfeld-Tanenbaum Research Institute in Toronto in developing transgenic mouse models and a lead role in national and European collaborations in membranous nephropathy. The Metabolism and Renal Medicine Research Group also play a prominent role in international and national collaborations in type 1 diabetes, including two US NIH consortia (TrialNet and The Environmental Determinants of Diabetes in the Young study) and an EU FP7-funded consortium.

The Musculoskeletal Research Group leads a number of five-year NIHR Programme Grants for Applied Research, including one commencing in 2013 to investigate infection after joint replacements in collaboration with Universities of Melbourne, Cardiff, Exeter and Sheffield.

We also have major industrial links, including: with Apitope, successful phase I trials of immunotherapies for multiple sclerosis; an NIHR i4i grant with Orthox to develop a new meniscal replacement; collaboration with Azellon Cell Therapeutics to develop a stem cell therapy for meniscal repair (a first-in-human study is underway); a clinical trial with Stryker to assess a new type of knee replacement.

We make many contributions to our various disciplines, and below is a selection of key examples.

Chairing of regional, national or international panels and funding bodies

Academy of Medical Sciences (AMS) Wellcome Trust-funded INSPIRE programme (*Mathieson*); AMS Academic Careers Committee (*Mathieson*); Kidney Research UK Grants Committee (*Mathieson*); NIHR Comprehensive Clinical Research Network Urogenital Specialty Group (*Drake*); International Continence Society Standardisation Steering Committee (*Drake*); Research for Patient Benefit South West Committee (*Blom*); Scientific Affairs and Awards, European Society for Paediatric Infectious Diseases (*Finn*).

Membership of national or international funding bodies

MRC Regenerative Medicine Committee (*Hollander*, *Madeddu*); MRC Infection and Immunity Board (*Wraith*); MRC Molecular and Cellular Medicines Board (*Poole*); MRC Non-clinical Training and Career Development Panel (*Orchard*); Wellcome Trust Immunity in Health and Disease panel (*Wraith*); NIHR i4i Programme Board (*Bucciarelli-Ducci*); NIHR Health Technology Assessment Board (*Reeves*); BHF Chairs and programme Grants Committee (*Orchard*); BHF Project Grants Committee (*George*, *Hancox*, *Paton*, *Johnson*); National Osteoporosis Society Grants Committee (*Tobias*); World Cancer Research Fund International Grant Panel (*Paraskeva*); German Science Foundation Focussed Research Centres Programme (*Newby*); Biomolecular Medicine and Therapeutics Panel, Research Frontiers Programme of Science Foundation Ireland (*Virji*); Singapore National Medical Research Council Research Grants Committee (*Virji*); Netherlands Organisation for Scientific Research Grants Committee (*Virji*); Austrian Science Foundation (*Hancox*); Health Research Committee of New Zealand (*Cannell*, *Paton*); Italian Ministry of Health (*Ascione*); Danish Heart Foundation (*Ascione*); Helmholtz Geimenschcaft Germany (*Newby*); German Federal Ministry of Education and Research (*Reeves*).

Leading roles in national or international strategic panels or learned societies

Honorary President, 2013 International Union of Physiological Sciences (*Orchard*); President, Physiological Society (*Orchard*); President, International Cartilage Repair Society (*Hollander*); President, European Vascular Biology Organisation (*Newby*); President, British Renal Association (*Mathieson*); President, UK Bone Research Society (*Tobias*); Chair, Biochemical Society Genes Panel (*Roberts*); Chair-Elect and Secretary, British Atherosclerosis Society (*George*, *Johnson*); Secretary, European Vascular Biology Organisation (*George*); Council Member, The Royal Anthropological Institute (*Gooberman-Hill*); Board Member, European Orthopaedic Research Society (*Blom*); Chair, Working Group on Cardiac MRI, European Society of Cardiology (*Bucciarelli-Ducci*); European Director, International Society for Minimally Invasive Cardiothoracic Surgery (*Angelini*); Specialist Adviser/External Expert to NICE Interventional Procedure Programme/Medicines and Healthcare Products Regulatory Agency and Commission on Human Medicines (*Angelini*); AMS Sectional Committee 5 (*Angelini*).

Journal editorships

Journal of Medical Microbiology (*Avison*); British Journal of Urology International website (*Drake*); Urology, Map of Medicine (*Drake*); Pediatric Infectious Diseases Journal (*Finn*); Frontiers in Endocrinology (*Holly*); International Journal of Molecular Epidemiology and Genetics (*Holly*); Reviews in Endocrinology and Metabolism (*Holly*); British Journal of Cancer (*Paraskeva*); Carcinogenesis (*Paraskeva*, *Ann Williams*); Endocrinology (*Perks*); ISRN Endocrinology (*Perks*); Biochimica et Biophysica Acta – Gene Regulation Mechanisms (*Roberts*); Frontiers in Bone Research (*Tobias*); Immunotherapy (*Wraith*); Frontiers in Immunological Tolerance (*Wraith*); Open Immunology (*Wraith*). In addition, almost all staff have been or are on at least one Editorial Board.

Other contributions

These include organising roles for numerous national and international conferences as well as keynote and plenary presentations at such meetings including Gordon conferences. In addition, many of our staff have received national and international recognition for their achievements, including Fellowships of the Royal Society of New Zealand FRSNZ (*Cannell*) and Academy of Medical Sciences FMedSci (*Angelini, Dick, Mathieson*) and an NIHR Senior Investigator (*Angelini*).