Institution: University of Southampton

Unit of Assessment: 1 Clinical Medicine

a. Overview (Cat A appear in **Bold**; ECR are underlined and Cat C are *italicised*)

Following a major reorganisation of the University in 2010 into eight new Faculties, the Faculty of Medicine (FoM) was created from the former School of Medicine, placing the Dean of Medicine (**Cameron**) at the centre of the University leadership (University Executive Group).

The Faculty employs 184 academic staff comprising a professoriat of 77 plus 107 lecturers and readers who teach 1300 undergraduate medical students and supervise 214 postdocs and 287 research students. Annual research grant income through the University has grown by over 30% since 2008 and in 2012/13 was £26.1M. Faculty members have won an additional £28.49M of NIHR grants awarded to the NHS since 2008 for the University of Southampton (UoS)/University Hospital Southampton (UHS) partnership.

The Faculty has taken a leading role in delivering the University's multi-disciplinary research strategy, and our Associate Dean led the institution-wide interdisciplinary biosciences research vision known as the Institute for Life Sciences (**IfLS;** Director, Smith UoA5**,** Deputy Director**, Elliott).** We have also led a Research and Development partnership with University Hospital Southampton (UHS), which has the Southampton Centre for Biomedical Research (**SCBR**; Director **Djukanovic**) at its centre, a five-storey complex of clinical and laboratory space for translational research (£8M jointly funded by UHS, UoS and NIHR awards) opened in 2011 by the Secretary of State for Health.

The Faculty comprises four research-led Academic Units: Clinical and Experimental Sciences; Human Development and Health; Cancer Sciences; Primary Care and Population Sciences. All four Units are included in this submission, and in addition our primary care research within the Primary Care and Population Sciences Unit is returned to UoA2. The UoS/UHS Partnership lies at the heart of the new Wessex Academic Health Sciences Network (AHSN) linking Wessex Universities, NHS Commissioning Groups and Trusts and local life science businesses. The Faculty also leads on three out of six priority programmes within the new £9M NIHR Collaboration in Applied Health Research and Care (CLAHRC) Wessex: respiratory care, ageing and dementia and public health and primary care.

Four Research Centres are fully integrated with the Faculty: MRC Lifecourse Epidemiology University Unit (MRC LEU, Director **Cooper**); CR UK Cancer Centre and Experimental Cancer Medicine Centre (Director **Johnson**); NIHR Biomedical Research Centre for Nutrition (Director **Jackson**) and NIHR Biomedical Research Unit for Respiratory Medicine (Director **Djukanovic**).

Faculty strategy is established by the Faculty Leadership Team, comprising the Dean (**Cameron**), Associate Deans for Research (**Elliott**), Education (Stephens) and Enterprise/Internationalisation (**Oreffo, Holloway**), Heads of Academic Units (**Davies**, **Hanson**, **Glennie**, **Roderick**), and Heads of Faculty Finance, Operations and Human Resources. To assist delivery of strategy, the Research Management Committee (chaired by **Elliott**) brings together research stakeholders in the Faculty with the IfLS and UHS and controls a discretionary budget to support research innovation. The Faculty International and Enterprise Committee (chaired by **Oreffo, Holloway**) integrates University business development activity and the University international office with Faculty research strategy and controls a HEIF fund of £160K pa to stimulate research driving enterprise and internationalisation. In turn, Medicine's research strategy is aligned with the IfLS via the IfLS Steering Committee on which **Cameron** and **Elliott** sit; and UHS research strategy via the Joint Research Strategy Board, chaired by the Dean of Medicine (**Cameron**) and the Medical Director of UHS, with balanced representation from both organisations. In addition **Cameron** is a non-executive director on the UHS Trust Board. University representation on all NHS senior clinical appointments further aids an aligned UHS and University research strategy.

b. Research strategy

Introduction

Since 2008 we have pursued an ambitious strategy for growth, building on existing research strengths to develop new pillars within an overarching lifecourse approach to health and disease. Our guiding principles have been to enhance our capacity for translational research and to increase interdisciplinary research at the interface with the physical sciences, computing, engineering and mathematics – especially in areas where the University Is world-leading. To this

end, we have created 11 new chairs, 11 new clinical and 12 new nonclinical lectureships of which 4 are in partnership with other Faculties. We have made significant investment in infrastructure including an extensively modernised Biomedical Research Facility (BRF) for *in vivo* mammalian research models (£14M), with UHS a £3.5M extension to the Southampton Centre for Biomedical Research (SCBR), and guided a University investment of £55M in the IfLS building and associated appointments and research support. As part of the IfLS initiative we have invested over £2M in laboratory refurbishment to accommodate Biological Sciences staff with a strong biomedical research focus (returned to UoA5) to enhance collaborative opportunities.

Translational Medicine: *We have prosecuted a step-change in our translational medicine capability.*

Working with local, national and international collaborators, the partnership between UHS and UoS has a proven track record of producing high quality biomedical science that is translated through patient-based research and then progressed into later phase studies across the NIHR Clinical Research Networks. Our ethos is driven by the principle of "strategic localism" - that working together is more effective (by reducing duplication and creating economies of scale) and provides intellectual synergies for the benefit of patients. In 2011/12 UHS was the 3rd highest recruiting NHS Trust to NIHR portfolio studies (16,204 patients to 297 studies of which 37.4% were led by FoM investigators). We have renewed and substantially enhanced funding for our: Clinical Research Facility (CRF) (2012, £9.24M from NIHR: a 50% increase permitting expansion); NIHR Respiratory Biomedical Research Unit (2012, £7.31M: an uplift of 17.5%); NIHR Nutrition Biomedical Research Centre (2012, £9.68M: an enhancement from Unit to Centre status); NIHR/CR UK Experimental Cancer Medicine Centre (2012, £3.5M). Together with a new molecular sciences hub occupying one floor, these comprise the SCBR. We have received enhanced funding for the MRC LEU (2010, £14.4M and representing an enhancement of the Lifecourse Epidemiology Resource Centre to MRC Unit status) which became an integrated University Unit Partnership from 1st May 2013; NIHR/CR UK Clinical Trials Unit (2013, £2.29M with a portfolio of 29 trials valued at £7M and into which we have invested a senior trial statistician **Haviland** and senior statistician in applied biomarker evaluation Dimitrov (UoA2)); NIHR South Central Research Design Service (RDS), the hub of which is in Medicine (2009-18, £10.3M); and theNIHR National Evaluation Trials and Studies Coordinating Centre (NETSCC), which manages research programmes and activities for the NIHR (2013-2018, £66.3M). We have established "shadow" Biomedical Research Units for Bone and Joint Research, and Cardiovascular Research, with internal seedcorn funding of £200K each; built a 150m^2 category 3 containment facility to support translational microbiology and infectious disease; and a 300m^2 bespoke outreach facility for the LifeLab project (see section d), which reached the finals of the BBSRC social innovator of the year award in 2012.

Over the next 5 years, building on our excellent relationship with UHS we will:

- Further align Faculty and UHS research strategies, enlisting more NHS researchers into areas of strength and capitalising on the Trust's strong track record in clinical trials activity.
- Underpin the UHS/UoS Partnership with mutually enhancing infrastructure and defined research capacity, including a human pathogen challenge unit, and enhanced imaging facilities.
- Establish a knowledge management system and bioinformatics support for the integration of clinical, biometric, lifestyle and nutritional data to realise the full potential of our unique birth cohorts; and explore linkage of these to routine health care data in the Hampshire Health Record which integrates primary and secondary care data for over 70% of the population of Hampshire.
- Use the molecular sciences hub to support new areas of research between nutrition and immunology (including cancer, cohort vaccine studies, birth cohort longitudinal studies of immuneresponsiveness across generations); and lung cancer studies.
- Establish a Translational Vaccinology Centre, building on recent investment in infectious diseases, drawing on immunology and microbiology in Southampton and our regional neighbours, Public Heath England (PHE) Porton, where the Head of Research, Miles Carroll, holds an Honorary Chair in vaccinology.

Interdisciplinary Research: *We have delivered a step-change in interdisciplinary research by establishing and implementing the Institute for Life Sciences (IfLS).*

The IfLS has been supported by significant University investment in buildings and facilities including an award-winning Life Sciences Building (£55M, opened in 2010 by Professor Lord

Robert Winston), located centrally within the University Highfield campus and adjacent to other science and engineering departments.
This has boosted interdisciplinary research into biofilms (e.g. **Faust** with Webb and Barton in Biological Sciences and Stoodley in Engineering), hybrid biodevices (e.g. **Newman, West**, **Davies and JA Holloway** with Morgan Electronics and Computer Science), quantitative biology (e.g. **MacArthur with Oreffo**; **Elliott** with Werner in Biological Sciences and Microsoft Research; **Lewis** with Please in Mathematics and Sengers in Engineering), nanotoxicology (e.g. **Millar, Sanchez-Elsner, Newman, H Clark** with Kanaras in Physics) and biomechanics (**Oreffo** and **Evans** with Thurner, Hill and Sengers Engineering). Evidence that this strategy is successful lies in the fact that around 10% of outputs in REF2014 are from multidisciplinary teams involving physical sciences, electronics, engineering or mathematics. In addition, Biological Sciences staff with a strong biomedical research focus (Fleming, Perry, Smyth, Barton: UoA5) relocated to the Southampton General Hospital campus in 2010 into newly refurbished laboratories with access to an extensively modernised Animal Research Facility, which reopened in 2011, thereby enhancing our collaborative opportunities, particularly in developmental sciences (e.g. **Torrens, Cameron** with Fleming UoA5) neuroscience (e.g. **Boche, Nicoll, Holmes, Galea, Glennie** with Perry and Teeling UoA5)) and clinical biofilms. IfLS has made 5 new appointments to interdisciplinary areas relevant to medicine with particular emphasis on new enabling technologies: behavioural preclinical models for neurodegeneration; nanodrop technology; microfluidics and nanoelectronics (**West**); and optoelectronics for ion-conductance microscopy. In addition to funding 10 new cross-Faculty PhD studentships and 18 seedcorn grants which has leveraged £2.3M in new external funding since 2011, IfLS has held two of its annual conferences on medicine-related themes (Biofilms and, Biometrics in Infection and Vaccinology). We have also boosted interdisciplinary Population Health Sciences research with the appointment of **Newell** and **McGrath** thereby strengthening our links with Social Sciences, Health Sciences and Geography.
Over the next 5 years we will:

- Expedite the translation of devices into clinical trials / diagnostics / biomarker discovery programmes - for example microfluidic impedance devices and nanodrop technologies, using SCBR as a validation environment including the strategic development of the CTU to support device trials.
- In partnership with IfLS, build our bioinformatics capability with a value chain that links researchers with expertise in quantitative biology to the integration and analysis of complex clinical and biometric datasets.
- Build interdisciplinary neuroscience, linking neuroinflammation and behavioural models to pathologic mechanisms of cognitive decline and neurodegeneration in humans.
- Integrate Infectious Disease research with interdisciplinary biofilm research.
- Integrate “imaging in the nanodomain” into medicine research and expedite the flow of projects from medicine through the newly established crystallography “pipeline” to increase yield of structure-function data.

External Partnerships: *We have transformed the way we work with external partners.* The UHS/UoS partnership has an ambitious five year strategy to strengthen links with industry and increase commercial research in line with NIHR and Government policy. Having achieved full MHRA accreditation the SCBR is ideally placed to engage in research drawing on a relatively stable regional population of over 3 million, for whom the UHS provides tertiary services across all specialities. For example, as lead member of the NIHR Translational Research Partnership in inflammatory respiratory disease, we are providing the private sector with a direct route to research expertise and infrastructure. Similarly, membership of COPDMAP (http://copdmap.com/), a part of the MRC/Association of British Pharmaceutical Industries Inflammation and Immunology Initiative has strengthened our partnership with GlaxoSmithKline (GSK), Novartis, Astra Zeneca, Merck and Pfizer in the area of disease stratification. We are a founder member of the EU Innovative Medicines Initiative (IMI) public-private partnership for the discovery of biomarkers in asthma (UBIOPRED). With the Liggins Institute in Auckland, our researchers have founded EpiGen, an international consortium of academic and private partners working together to define epigenetic biomarkers linked to lifecourse outcomes relating to early life nutrition. In 2010, we signed a broad collaborative research and development agreement (£3.5M over 5yr) with GSK biologicals to develop a programme of joint discovery research, to complement large clinical trials, focussing on the microbial and immunological correlates of exacerbations in chronic obstructive

pulmonary disease (COPD). Since 2008, we have stepped up the level of interaction with other research partners for example with the MRC, resulting in the integration of the MRC LEU into the University in 2013; and with CRUK with whom UoS has launched a £20M campaign following a lead donation of £10M to create an international Centre for Cancer Immunology in Southampton to link with the Francis Crick Institute in London. Recently, the IfLS has led an initiative to co-ordinate immunology, microbiology and genetics research across UoS, UHS, Salisbury NHS Trust, PHE Porton and Dstl Porton. This Wessex Life Sciences Alliance has resulted in 12 joint research projects following two symposia and has attracted £400K of collaborative funding since 2011 and is fully incorporated into the Wessex AHSN.

Over the next 5 years we will:

- Develop our collaborative research deal with GSK to extend into other areas of mutual interest including cancer immunotherapy.
- Pursue similar deals with at least one other industrial partner. We believe that this will be catalysed by our track record in validated analytical immunology, microbiology and genetics and our investment in the molecular sciences hub within SCBR.
- Develop further collaborations with PHE and Dstl Porton, through a Translational Vaccinology Centre that brings together strengths in basic research, preclinical models, production and clinical trials in both locations, with particular focus on developing human challenge facilities in Southampton.
- Build a new international Centre for Cancer Immunology and make several key appointments including a Director as well as establish research collaborations with tumour immunologists at the Crick institute and underpin these with a joint postgraduate research training programme.

New Research Areas: *We have used our peaks of excellence to build new areas of research.* We have addressed feedback from RAE08 UoA4 sub-panel which noted that we have the capacity and infrastructure to develop new areas of research to a world leading level. Our existing strengths in immunology, respiratory disease, vaccine trials and microbiology have provided a foundation upon which to build infectious diseases research. We recruited **Read** to a newly created chair in 2011, in addition to early career researchers **Wilkinson** (influenza human challenge), **Tebruegge** (paediatric vaccines) and **Elkington** (TB). In parallel, we have developed bioinformatics and in 2012 appointed **Woelk**, who has expertise in correlates in infectious disease, along with Senior Lecturer **Ennis** (genomic informatics). These PIs are part of a University-wide group of 100 quantitative biologists, co-ordinated by IfLS, that includes other bioinformaticians (e.g. Gibson UoA5, medical statisticians (e.g. Bohning UoA10, Dimitrov UoA2) and modellers (e.g. **MacArthur**). Synergy between our research programmes in respiratory medicine and human development, and our integrated adult and paediatric disease perspective has opened up unique opportunities in critical care medicine and human integrative physiology where we have made significant new appointments to acute care medicine (**Grocott**) and integrative biology (**Feelisch**) to complement existing strengths in cardiovascular and respiratory physiology.

Over the next 5 years: we will build on new investments and:

- Develop a distinctive Experimental Infection Unit with associated clinical and laboratory containment facilities to enable intensive and safe translational research involving human volunteers undergoing experimental infection, and study of patients with severe community and hospital-acquired infections.
- Build an informatics pipeline and knowledge management platform to maximise the data yield from our unique cohorts, including birth cohorts which now span three generations.
- Develop integrative human physiology with increased focus on cardiovascular medicine.
- Capitalise on the synergy between nutrition and immunology research (especially applied to respiratory medicine and cancer).
- Use the new Centre for Cancer Immunology to integrate our pre-eminence in respiratory medicine and cancer research to develop a translational programme in lung cancer.

Research Support:

The Faculty has a dedicated research support team comprising a Senior Research Manager, three Research Support Officers and a Business Development Manager working on a daily basis with the Associate Deans for Research and Enterprise. All stages of the research project lifecycle are supported: including: horizon scanning and influencing calls (e.g. Respiratory IMI, ABPI); targeting calls to key PIs and assisting with industrial partnering; providing support for bid-preparation

(eligibility, generic statements, impact statements); organising internal peer review, setting up mock panels/interviews for fellowships and project-managing multi-Faculty bids (e.g. our successful 2011 application for an MRC multidisciplinary Doctoral Training Account, involving 6 Academic Units in 4 Faculties). Research support is fully informed by research intelligence by deploying tools such as Qlikview which integrates applications, awards, outputs and postgraduate supervision data at the level of individual PI. This allows us to target externally-run grant-writing workshops to specific individuals such as first-time applicants, or PIs with a lower-than-expected success rate. Pre-bid support for ECR Fellowships is linked to our mentorship programme. In addition, the Faculty hosts a monthly IfLS Life Sciences forum where PIs present ideas for new projects to a multidisciplinary audience in "chalk-and-talk" sessions. The Research Management Committee promotes and implements Faculty research strategy. It dispenses research awards of up to £15K (following peer-review) to support pump-priming of ECRs and inter-Faculty collaborations or as contributions to multi-user equipment. Since 2008 we have made 65 awards, totalling £690K. This has yielded preliminary data supporting 44 new applications to external funders, resulting in over £2.6M of new research grants: 15 to early career researchers; and has initiated 83 new collaborations, mostly with other Faculties. A second scheme, launched in March 2010, provides research-expenses for NHS-contracted Academic Clinical Fellows and has made 22 awards totalling £200K so far, and provides grant-writing practice at a very early stage of the clinical academic career.

Over the next 5 years we will:

- Increase the effectiveness of our research support by targeting it to where it is needed most, using up-to-date and comprehensive research intelligence at the resolution of individual PI.
- Professionalise our approach to initiating research partnerships with industry by working with our Business Development Manager to produce a toolbox of template agreement documents, capability briefing papers and directory of contacts.
- Continue to integrate our research support with UHS R&D where appropriate in order to ensure that our PIs with a mixed portfolio of NIHR/RC/charity/industry funding receive the best possible research support from the UHS/UoS partnership.

Internal and Cross-Institutional Dissemination of Research:

Weekly seminar series in each of the Academic Units and in the IfLS, comprising a mix of internal and external speakers, are timetabled not to clash and are well attended across Units thanks to strong cross cutting themes. These are re-enforced with specific events such as the bi-annual conferences of the Wessex Immunology Group and Wessex Life Sciences Alliance; and seminar series run by University Strategic Research Groups including Ageing and Lifelong Health, Population Health Sciences, Neuroscience and Nanoscience. The Faculty annual research conference in July offers postgraduate students, academic clinical fellows and postdoctoral research assistants and their collaborators in other Faculties to present their work and is concluded with a distinguished lecture (recent examples include Professor Steve Jones and Professor Sir Stephen O'Rahilly). This conference complements our Annual Translational Research Conference in November, organised in partnership with UHS showcasing research from the Faculty as well as NIHR-portfolio research sponsored by UHS and is concluded with the Wade Lecture (recent examples include Professor Dame Sally Davis and Professor Sir John Tooke). The conference runs contiguously with an enterprise half-day, comprising seminars from Faculty spinouts and their academic collaborators, with podium discussion with industry leaders (recent examples include Professor John Oxford, Scientific Director, Retroscreen Virology Ltd., and Dr Kenny Pollock, Head of Cell Development, ReNeuron). The first two annual IfLS conferences held in September have had UoA1 focussed themes (biofilms, vaccines).

Responsiveness to National and International Priorities and Initiatives:

Faculty research strategy is fully aligned with UK life science strategy as outlined in the two key Government publications in December 2011 (The "Strategy for UK Life Sciences" and "Innovation Health and Wealth") and with the 2006 Cooksey report which identified an unmet need to bridge the gap between discovery science and first-in-human clinical trials. We are working in close partnership with UHS to deliver these national priorities for health and wealth as evidenced by our joint investment in the SCBR. We have been successful in bidding for strategic funding, for example with the awards of the Nutrition BRC, Respiratory BRU, MRC University Unit, NIHR AHSN and CLAHRC and the Innovative Medicines Initiative partnership. In addition, we responded to the Plan for Growth (April 2011) by leading the UK-wide NIHR Translational Research

Partnership in Respiratory Disease (**Djukanovic**); and we were awarded one of 15 national CR UK Centres. We have also helped shape international health priorities, for example, by providing the largest evidence base for the WHO 2008-2013 Action Plan for the Global Strategy for the Prevention and Control Non-communicable Diseases (see impact case study 5).

Research Groupings:

We have achieved an integrated, multidisciplinary research profile with a strong translational focus. Primary research groupings occur within the administrative ***Academic Units*** of Clinical and Experimental Sciences; Human Development and Health; Cancer Sciences; and Primary Care and Population Sciences (of which the largest group – Primary Care Research – is returned to UoA2). By keeping administrative barriers between Academic Units low, we have fostered strong ***cross-cutting themes*** that reach beyond the Faculty thanks to support from the IfLS and other University Strategic Research Groups.

Academic Units

1) Clinical and Experimental Sciences (CES; Director: Professor Donna Davies)

The Clinical and Experimental Sciences Unit brings together researchers across several medical specialties with an emphasis on communicable disease: Infection and Immunology; Respiratory and Allergy; Clinical Neurosciences and Psychiatry; and Integrative Physiology and Critical Illness. The Unit comprises a community of over 152 researchers, including 63 academic (14ECRs) and 47 postdocs; with 111 postgraduate research students. The Unit has attracted 182 external awards totalling £24.6M and has an overall success rate of 47%. Since 2008 it has trained 64 PhD and 18 DM students. It has produced 911 peer-reviewed research papers (366 involving postgraduate research students) and 138 scholarly reviews, and has been granted 26 patents (with a further 18 filed). It is a strong supporter of enterprise and industry, working closely with pharma and supporting our spinout companies, especially Synairgen (see impact case study 18).

The Respiratory and Allergy Group (**Arshad, Barton, H Clark, Davies, Djukanovic, *Grainge*, Haitchi, Hinks, Holgate, JA Holloway, Howarth*, Kurukulaaratchy*, Lucas, Pike, Richeldi, G Roberts, Sanchez-Elsner, Swindle, Walls, Warner, Wilkinson, S Wilson**) operates at the clinical interface to dissect mechanisms of respiratory diseases, define biomarkers of disease severity and translate these findings into novel therapies. In asthma, recent achievements include the use of anti TNFα therapy in moderate-severe asthma; anti IL-5 (Mepolizumab) therapy to reduce the risk of exacerbations in patients with severe eosinophilic asthma; and the identification of novel therapeutic targets including CCR4 which we showed plays a key role in T cell recruitment in asthma. Furthermore, by capitalising on our expertise in the developmental origins of disease, and combining clinical expertise in both adult and paediatric asthma, we have shown that maternal allergy and IL-13 can lead to airway remodelling in early life via ADAM33 which we previously discovered to be an asthma susceptibility gene. We have developed a new focus on epigenetic mechanisms in asthma with a view to investigating transgenerational mechanisms of pathogenesis and have shown, for example that MicroRNA-155 targets IL13 pathways in macrophages and that the hypersensitivity site V has an important role in shaping chromatin structure in differentiating CD4+T cells. Monitoring the natural history of asthma and allergies through the Isle of Wight Birth Cohort, the Allergy Prevention Study and the Copenhagen Prospective Studies on Asthma in Childhood Cohort has led to the identification of other susceptibility genes for asthma in children, including ATPAF1 and CDHR3. The Group leads in the identification and validation of biomarkers of airways disease, having co-founded UBIOPRED (http://www.imi.europa.eu/content/u-biopred), a €22m programme in severe asthma funded by the EU and several pharmaceutical companies; and with Thomas and Dimitrov (UoA2) is looking at asthma biomarkers in primary care. It also plays a leading role in the NIHR Translational Research Partnership and COPDMAP. In adult asthma, we were the first to show that airway remodelling is a consequence of bronchoconstriction and not on-going inflammation, which has implications for asthma management (see impact case study 28). We have invested in new areas of respiratory disease research including interstitial lung disease with the appointment of **Richeldi** who also brings field-leading clinical trials expertise. The Respiratory group provided an important cornerstone for our strategic investment in infectious disease and in COPD; the group has made major contributions to understanding infection-induced exacerbations which has attracted a strategic collaboration with GSK to help develop new vaccines for COPD.

The Infection & Immunity Group (**Ardern-Jones, Christodoulides, T Clark, I Clarke, S Clarke, Elkington, Faust, Goss, Healy, Khakoo, Kirkham, Madsen, McCormick, McGrath, Newell,**

Read, Tezera) brings together expertise in microbial communities, molecular microbiology, epidemiology and immunology to understand host-pathogen interactions and facilitate vaccine development and evaluation (via our leadership of the UK Paediatric Vaccine Group). The Group's studies of bacterial populations have informed national vaccination policy, for example by demonstrating changes in serogroup and genotype prevalence among carried and disease-causing meningococci and pneumococci during vaccine implementation in the UK (with Moore, UoA2) and worldwide. This has led to a collaborative infectious diseases network in South East Asia, with high level strategic partnerships for research and training (A*STAR Singapore and the University of Malaya) and the recent secondment of **S Clarke** to the UoS South Malaysia campus to develop these research links further. We were the first to show that some meningococcal serotype C glycoconjugate vaccines rely on persistence of antibody levels rather than immunological memory for sustained protection, identifying a potential risk for long term protection after vaccination. Furthermore, in collaboration with GSK, the Group has developed vaccine strategies for effective functional antibody induction to meningococcus serotype-B pathogen-derived antigens for which no current candidates exist. Using molecular approaches, the Group has developed a transformation system for Chlamydia trachomatis, permitting genetic manipulation of the pathogen for the first time and, through an international collaboration involving The Wellcome Trust Sanger Institute, has undertaken whole genome analysis of diverse C. trachomatis strains to identify phylogenetic relationships masked by current clinical typing, with implications for monitoring and epidemiological tracking of infections. The Group is developing improved approaches for immunodiagnosis of human TB, and has provided the first evidence of how tuberculosis causes cavitation by showing that MMP-1 drives immunopathology in human tuberculosis and transgenic mice, suggesting that inhibition of MMP activity is a realistic goal as adjunctive therapy in TB. The Group has made key contributions to understanding innate immune mechanisms in humans including the first demonstration that surfactant protein D (SP-D) interacts with human rhinovirus and HIV-1. We have also pioneered the field of natural killer cells and the innate immune system in controlling hepatitis C virus infection, and as a result of this have discovered unexpected new mechanisms for activating and inhibiting natural killer cells, based on the peptide content of MHC Class I. We have demonstrated the importance of these peptides for both HIV and HCV infection. Recruitment of **Newell** and **McGrath** both from the Africa Centre for Health and Population Studies in South Africa, and bioinformatician **Woelk** expands our global expertise into the prevention and treatment of HIV infection.

The Clinical Neuroscience Group (**Baldwin, Boche, Carare, Gale, Galea, Hawkes, Holmes, Kennedy, Kingdon, Lotery, Newman, Nicoll, Ratnayaka, Sinclair, Vollmer, Willaime-Morawek** with Perry UoA5) is part of the University-wide Southampton Neurosciences Group (SoNG), established in 2001 to provide a focus for collaborative, interdisciplinary and applied neuroscience. SoNG is one of the University's Multidisciplinary Research Groups within the IfLS and integrates the region's major clinical services, including The Wessex Neurological Centre, the Dementia and Neurodegenerative Diseases Research Network (DeNDRoN) and the Memory Assessment and Research Centre (MARC). In Alzheimer's disease (AD), we have shown that systemic inflammation and raised peripheral pro-inflammatory cytokines accelerate long-term cognitive decline which, combined with collaborative genome wide association studies has revealed the importance of innate immune pathways in late onset AD. We have challenged the dominant pathogenetic hypothesis of AD by demonstrating variable effects of Aβ immunisation on plaque removal and, crucially, that plaque removal is not sufficient to halt cognitive decline (see impact case study 14). Furthermore our discovery that brain solutes are eliminated along basement membranes of microvasculature in the brain parenchyma may lead to new therapeutic strategies that facilitate this process, preventing vascular Aβ deposition. In collaboration with the Human Genetics group, ophthalmologists have helped define the aetiology of age-related macular degeneration in gene association studies. In hearing research, we have shown that comprehension and expression of language and reading are improved by exposure to universal newborn screening, work that led to the recommendation by the US Preventative Services Taskforce that screening be adopted across the USA (see impact case study 31).

The Integrative Physiology and Critical Illness Group (**Feelisch, Grocott, Postle**): The Group's stratified medicine approach to hypoxia tolerance through large-scale healthy volunteer field studies (**Grocott** leads the Xtreme Everest hypoxia research consortium comprising Southampton/UCL/Duke/Cambridge) combines high-resolution integrative physiological

phenotyping with advanced -omics approaches and has led to translational studies to test the concept of "permissive hypoxaemia" in critical illness and perioperative care in collaboration with the UCLH-UCL BRC. We have established an integrative physiology laboratory within the SCBR which has enabled the Fit-4-Surgery programme investigating the importance of physical fitness, exercise and perioperative care in cancer patients undergoing neoadjuvant chemotherapy.

2) Human Development and Health (HDH; Director, Professor Mark Hanson)

The Human Development and Health Academic Unit brings together epidemiology and physiology with genetics, epigenetics and biology for lifecourse studies that have facilitated translational research in non-communicable diseases. The Unit comprises 160 researchers, including 59 academic staff (6ECRs), 44 postdoctoral scientists and 100 postgraduate research students. During the assessment period the Unit has trained 63 PhD and 24 DM scientists. Since 2008 it has won 139 grants totalling £27.1M including £4.2M in programme grant funding (BHF, MRC, Wellcome Trust) and has a 46% success rate. Since 2008, the Unit has produced 1,570 peer reviewed research papers (572 with postgraduate students), 222 scholarly reviews, 5 public understanding of science books and text books, and has filed 6 patents. In addition, the MRC LEU, formally incorporated into the University in 2013 has received £14.4M in core funding.

The Epidemiology Group (**Aihie-Sayer, Baird, Coggon, Cooper, Dennison, Fall, Godfrey, Harvey, Inskip, Kumaran, Osmond, Palmer, S Robinson, Roderick, Walker-Bone**): The MRC LEU was established in 2010 following reconfiguration of the MRC Epidemiology Resource Centre based on the pioneering work of Prof David Barker OBE who died in 2013. It became an incorporated University Unit in 2013 under the directorship of **Cooper**. Its mission is to provide a centre of excellence using epidemiological methods to promote human health by: (a) delineating the environmental causes throughout the lifecourse of chronic musculoskeletal disorders; diabetes mellitus and cardiovascular disease, and thereby developing population-based and high risk preventive strategies against these disorders; (b) maintaining and developing long-term cohort studies assembled in Southampton as national and international resources to explore the developmental origins of health and disease (the Hertfordshire Cohort Study, the Southampton Women's Survey, the Southampton Initiative for Health, and the MAVIDOS trial: see impact case study 3); (c) informing health policy and practice through the provision of authoritative evidence and knowledge synthesis; and (d) promoting training, research capacity development, knowledge transfer and public engagement in the lifecourse epidemiology of chronic disease. The work of the MRC Unit is organised into five programmes comprising: lifecourse determinants of bone and joint disease (**Cooper, Dennison, Harvey**); sarcopenia, frailty and clinical practice (**Aihie-Sayer**); nutrition, development and lifelong health in European populations (**Inskip, Godfrey, S Robinson, Baird**); nutrition, development and lifelong health in developing populations (**Fall, Osmond**) and work and health (**Coggon, Palmer,** see impact case study 25).

Key scientific achievements include documentation that: (a) maternal vitamin D insufficiency during pregnancy is associated with reduced bone mass in offspring see impact case study number 3); (b) poor growth *in utero* is associated with sarcopenia in later life; (c) maternal micronutrient status is linked to body composition, insulin resistance and bone health in offspring; (d) women's perception of control over their lives is modifiable through a complex intervention entailing healthy conversation skills; and (e) in analyses exploring the cultural determinants of pain, striking differences are observed in rates of musculoskeletal symptoms and associated disability and sickness absence between workers doing similar jobs in different countries. In a linked programme of research into ageing, **Roderick** has identified the impact of chronic kidney disease in older people. The programmes have also contributed to international studies identifying genetic determinants of bone mass, fracture and other metabolic traits including the genetic determinants of vitamin D insufficiency. Novel observations on the epidemiology of osteoarthritis have confirmed an association between bisphosphonates and implant survival after primary total hip or knee arthroplasty.

The Nutrition & Metabolism Group (**Burdge, Byrne, Calder, Crozier, Elia, Green, Hanson, Holt, Jackson, Macklon, Margetts, Poore, Sheron, Torrens, Van Rijn**): takes a lifecourse approach to investigating nutritional components underlying non-communicable disease risk and the opportunities for specific interventions (see impact case study number 5). It has demonstrated the influence of unbalanced maternal diet on metabolic control, bone density, cardiovascular structure and function, lung development, asthma and atopy and cognitive development in offspring. The group integrates results from *in vitro* and *ex vivo* studies, small and large animal models,

population groups and translational research in patients. Particular phases in the lifecourse investigated include pre-conception, pregnancy, infancy, adolescence and old age. Our NIHR Nutrition BRC focuses on interventions to promote nutrition in development and the elderly, especially through behaviour change. We pioneered the use of epigenetic biomarkers to assess nutrition during prenatal development and future disease risk, and have obtained substantial industry funding through our EpiGen consortium. We developed a computational model of placental amino acid transport and related this to maternal body composition, behaviour and fetal development. Our nutritional algorithm for preterm infants, SPIN, is being widely adopted to support growth, optimal body composition and neurodevelopmental outcome. Our tool to measure nutritional status in various patient populations, MUST, is widely used (see impact case study 8). We have examined interventions with specific nutrients/nutraceuticals through RCTs, one leading to the discovery of a novel mechanism by which omega-3 fatty acids reduce atheromatous plaques and inflammatory profiles in cardiovascular disease patients. This is being translated into new strategies for reducing disease risk in vulnerable groups and intensive care patients (see impact case study 6). With primary care research (Moore UoA2, **Roderick, Parkes**) and through collaboration with the Institute of Psychiatry, the University of Oxford, the Alcohol Health Alliance UK and the European Union Alcohol Forum, our cross-Faculty research group (Wessex Alcohol Research Centre) has evaluated risk stratification of liver disease non-invasively to promote early identification of alcoholic liver disease in primary care with support from NIHR and the British Liver Trust. We have influenced health policy by leading the Government's Responsibility Deal Alcohol Network and advising DFID, WHO and UN agencies on nutrition and global health issues.

The Human Genetics and Medical Genomics group (**Collins A, Ennis, Jacobs, *Hammans*, Holloway JW, *Lachlan*, MacKay, O'Kelly, Riethmacher, *Ross,* Self, Temple, Vorechovsky, *Wellesley,* Wilson D, Wiskin**): maintains a strong link with the Regional Genetics Laboratory Service that co-locates with University laboratories on our Salisbury campus. Here, close links between clinicians and scientists has facilitated the development of new analytical tools (see impact case study 9) and rapid translation of basic science. For example our discovery that ZFP57 mutations cause neonatal diabetes via abnormal DNA methylation, has led to Southampton becoming the national referral centre for testing this and other rare imprinting disorders. There is strong collaboration with other Academic Units, including CES where we discovered SERPING1 as the genetic basis for age-related macular degeneration and identified multiple polymorphic loci that predispose to asthma and we are well disposed to integrate the disciplines needed to determine the mechanistic basis of these genetic associations as we have for previous discoveries including ADAM33 in asthma, ALMS1 in cardiovascular disease and ERAP1 in ankylosing spondylitis. A Cancer Genetics subgroup ensures that links with the Cancer Sciences Unit are especially close (see below).

The Bone and Joint Group (***N Clarke, Edwards*, Evans, Oreffo, Tare**): is developing strategies to regenerate bone and cartilage using stem cell technology. A central tenet has been translation through to the clinic and seminal findings include the first demonstration that nanotopography can modulate and induce retention of skeletal stem cell phenotype, and the first use of clay gels as unique regenerative environments which has helped us to take our novel polymer materials into the clinic for the first time (see impact case study 2). This work has been enhanced by the appointment, jointly with the Faculty of Engineering, of ECRs **Tare** and **Evans** and has allowed us to apply the same multidisciplinary principles to elucidate of mechanisms of wound healing and skin regeneration. We were appointed Arthritis Research UK Centre of Excellence for Sports Injury and Osteoarthritis in 2013.

The Clinical and Experimental Cardiovascular Sciences Group (**Clough, *Curzen*, Englyst, Shearman**): combines expertise in basic and clinical science with engineering to drive novel strategies in preventative and therapeutic cardiovascular medicine. Recent achievements include elucidating the early-life exposures that contribute to risk of CV disease, thereby opening opportunities for nutritional interventions in pregnant women. In close collaboration with Primary Care and Population Sciences (**Roderick**, Dimitrov UoA2) we have developed novel applications of early-adopted complex mapping technologies (CHIRON); remote patient management for heart failure (REM-HF); and a near-patient test of individualised responses of those undergoing coronary stent insertion (RIPCORD).

3) Cancer Sciences Academic Unit (CSU; Director Professor Martin Glennie)

The Cancer Science Academic Unit comprises over 161 research staff, including 36 academic

staff (8 ECRs), 67 postdocs and a further 60 postgraduate research students. During the assessment period it has trained 35 PhD and 8 DM postdoctoral scientists. The Academic Unit has won 151 grants totalling nearly £31.1M including: 5 programme grants from CRUK (£7.6M), LLR (£3M); 3 awards from the Wellcome Trust and MRC (£1.3M); with an overall success rate of 45%. Since 2008 it has produced 569 peer-reviewed articles (205 with postgraduate students), 63 reviews, 61 peer-reviewed commentaries, filed 20 patents and also had 12 patents granted. The Unit continues to collaborate with its successful 2006 spinout company Karus which now operates from the University Science Park.

Molecular Mechanisms Group (**Blaydes, Forconi, Garbis, Mirnezami, Oscier, Packham, Sahota, Sayan, Steele**): Since 2008, we have expanded research in the area of lymphoid malignancies, particularly Chronic Lymphocytic Leukaemia (CLL) with the appointment of two ECRs (**Strefford** and **Steele,** both subsequently promoted) and two senior academic haematologists (**Forconi** and **Oscier**). This work exploits strong collaboration with the Wessex Regional Genetics Laboratories, the Haematology Departments at Southampton General Hospital, the Royal Bournemouth Hospital, and the IfLS; and integrates with the UK national CLL strategy, via the UK CLL Trials Biobank. In 2010 Southampton was named an LLR Centre of Excellence for CLL research. Key discoveries include linking the IGHV mutational status to B-cell receptor signalling in lymphoid malignancies (see impact case study 21), the identification of somatic alterations driving CLL, and the identification of novel methods for inducing selective apoptosis in CLL cells.

We have expanded research on the molecular and cellular basis of major epithelial malignancies including the appointment of new non-clinical lecturer **Sayan.** Key findings in this area include a mechanism for p73-mediated control of apoptosis and a new CtBP regulatory mechanism linked to metabolic status in breast cancer which, via the IfLS has led to the synthesis of a novel class of inhibitors that target CtBP dimerization (**Blaydes** with Tavassoli, UoA8).

Tumour Immunological Environment Group (**Moutasim, Thomas**): A key strategic initiative since 2008 has been to develop research into the role of the tumour microenvironment in shaping tumour growth and anti-tumour immunity. In one of the largest clinical UK studies of its kind, we found that the strongest independent risk factor for early patient death in oral cancer patients was a myofibroblast-rich stroma, allowing early identification of aggressive cancers and the specific mechanism through which cancer cells generate a stromal response capable of supressing adaptive immunity. This work has allowed identification of a small group of HPV-positive patients with poor survival based on the presence of tumour-infiltrating CD8+ lymphocytes, and has led to a joint CRUK programme grant to **Thomas** and **Ottensmeier** focusing on improving immunotherapy in the context of stromal immunosuppression. The group has also identified novel signalling pathways regulating tumour cell epithelial mesenchymal transition thus enhancing links with the respiratory group investigating similar mechanisms in airway remodelling.

The Antibody and Vaccine Group (**Al-Shamkhani, Beers, Buchan, Cragg, Glennie, Gray, Lim, Ottensmeier, Savelyeva, Stevenson**): has made significant contributions to the development of new cancer treatments by building on a deep understanding of antibody effector functions, particularly mediated via Fc receptors, and the immunobiology of cytotoxic T cells. A recent important contribution has been to elucidate the effector mechanism of two fundamental types of anti-CD20 therapeutic mAb characterised by the FDA approved, ofatumumab and experimental therapeutic obinutuzumab (see impact case study 20) and the demonstration that FcgRIIb expression on tumour targets is a strong negative prognostic factor for anti-CD20 treatment. This has led to a new collaborative initiative with the Swedish Biotech company, BioInvent. Following the secondment of (then) ECR **Cragg** to the Walter and Eliza Hall Institute we also defined a new form of lysosomal-dependent cell death induced by a subset of cytolytic mAb. Prior to 2008, we were one of the first to identify immunostimulatory mAb and we have gone on to deliver a first-in-man anti-CD40 mAb, ChiLob-7-4, currently in phase I trials. In order to deploy a similar developmental pipeline to other potentially therapeutic mAb arising from our basic science programmes, we have established an 'Antibody Discovery' programme to generate immunostimulatory reagents which target the immune co-receptors of the TNFR superfamily. The first, an anti-CD27, has been developed in partnership with Celldex therapeutics, and is now in phase I trials. Further targets include 4-1BB and OX40, which we have shown to be key molecules in controlling the expansion and survival of T cell responses induced during vaccination.

The group continues to refine DNA fusion gene cancer vaccines for targeted therapy, and has

completed 5 PhaseI/II trials in lymphoma, MM and solid cancers since 2008. To improve vaccine intervention in MM during disease remission, the group was the first to investigate tumour-associated antigens retained at relapse, as rational targets for vaccination.

Molecular and Cellular Immunology Group (**Elliott, James, Mansour, Williams**). The development of new T cell based immunotherapies in cancer is supported by a deep understanding of the mechanisms of antigen processing and presentation. We were the first to define the immunological functions for the MHC I cofactors calreticulin and tapasin and the first to relate these to the generation of immunodominance to experimental vaccines. In a collaboration with biological sciences (Werner, UoA5) and Microsoft UK, and supported by Programme awards from CRUK (£1.7M) and BBSRC (£600K), we have developed a new, quantitative model for peptide selection by MHC I intended to help predict the immunological outcome of intracellular peptide selection events, and in collaboration with **Khakoo**, have shown for the first time how change in peptide selection is a rapid and potent mechanism for regulating NK cell activation. We were the first to demonstrate functional polymorphism in the antigen processing enzyme ERAP1 thus providing a mechanistic rationale for its association with diseases such as ankylosing spondylitis, psoriasis and cervical cancer and we have established collaborations with local rheumatologists and with **Thomas** to investigate this further. A strong, multidisciplinary interest in CD1 established in 2007 by Gadola (recruited to Novartis in 2012) led to the discovery that that β-D glucopyranoslyceramide is the major endogenous mammalian iNKT antigen that regulates function. Clinical Immunologist **Williams** is key to linking basic mechanisms to human tumour immunology and as director of the SCBR molecular sciences hub laboratory has helped increase the penetration of immunology into other areas of local research excellence including maternal nutrition, which has shown that dietary salmon intervention during pregnancy resulted in attenuation of the production of IL-10 in response to a range of stimulants, including TLR ligands and allergens.

Translational and Clinical Research Group (**Johnson, Primrose, Haviland**): The Central South Coast Cancer Research Network (CSCCRN) is one of the largest and most active in the country; 1200 patients enter cancer trials in Southampton annually. It is supported by the DH/CRUK Clinical Trials Unit and focuses on early phase and multi-centre clinical research in oncology and surgery, predominantly in immunotherapy and lymphoid biology (see impact case study 27) and has taken 12 reagents (DNA vaccines; monoclonal antibodies; radioimmunoconjugates) from our own laboratories into clinical trials in the current REF cycle. Surgical research provides leadership in liver resection for metastatic disease and the management of pancreatic disease.

Molecular Cancer- and Cyto-Genetics Group (**Copson, Cross, Eccles, Lucassen, Strefford, *White***): The Cancer Genetics Group links the Academic Unit of Cancer Sciences, the NHS Regional Clinical Genetics Service and the human genetics and medical genomics group in HDH. Over the last 5 years the group has identified clinical subgroups and recruited 2000 subjects to national and international collaborative studies facilitating the discovery of breast, colorectal and other cancer predisposition genes, and the characterisation of associated tumour phenotypes. We have been the first to identify specific, targetable genetic risk factors in myeloid disorders, and the identification of genetic prognosticators in multiple myeloma. **Lucassen** has developed a pan-University applied medical ethics research programme focussed on genomic analysis in collaboration with Montgomery (in Law), Neil (in Philosophy) and Parker (ETHOX, University of Oxford) whose translational outlet, Genethics Club is unique in the UK and aims to deliver research findings in areas such childhood genetic testing, consent and confidentiality and incidental finding into the clinic.

Cross-Cutting Themes

Immunology: which comprises 31 PIs, of whom 28 are returned in UoA1 is the driving force behind institutional initiatives including the molecular sciences hub laboratory in the SCBR, the Wessex Life Sciences Alliance vaccinology collaborative, and the new Cancer Immunology Centre. It brings together researchers with shared interests in mechanisms within the three broad areas of barrier immunity, innate immunity and adaptive immunity and immunotherapy and is supported by the British Society for Immunology. It is an IfLS priority theme with significant investment into the development of devices for next-generation immunometry (e.g.**West**) and the combination of functional immunometry and genomics.

Epidemiology, population genetics and bioinformatics*:* which brings together the MRC LEU with epidemiologists and medical statisticians in the Primary Care and Population Sciences

Academic Unit (**Coggon**, **Palmer**, **Roderick, Parkes,** Dimitrov (UoA2) and Boehning (in the Southampton Statistical Sciences Research Institute, S3RI)); and links to the Genetic Epidemiology and Informatics Group, established in 1988 by Newton Morton, and now headed by **A Collins** which contributes methodological development (see impact case study 9) and helps focus the wider University quantitative biology community of 50 PIs on the analysis of large "omics" datasets (eg **MacArthur**, and Brodzki in Mathematics). The recent strategic appointment of **Woelk** from UCSF significantly strengthens our bioinformatics capability by bringing specific expertise in machine learning approaches to integrative informatics, particularly in an infectious disease setting and supported by substantial NIH and EU awards. **Roderick** leads a group which aims to utilise the Hampshire Health Record, an individual patient linked primary and secondary care record for health research.

***Integrative Physiology*:** This brings together experimental physiology research on the impact of environmental factors during development (**Green, Poore, Clough, Englyst** based in the Human Development and Health Unit) with researchers in the Clinical Experimental Sciences Unit studying the health-impacts of external stressors in adults. We have made key strategic appointments to this theme including **Grocott** and **Feelisch** (hypoxia and physical exercise) and **Read** and **Wilkinson** (microbial challenge studies in humans). This theme also encompasses strong IfLS-supported collaborations with developmental biologists Fleming, Lillycrop and Smyth in Biological Sciences, and with engineers Chipperfield and Griffin who, with **Clough** and industry partner Moor Instruments, have developed innovative techniques for measuring microvascular function in patients with cardiometabolic disease.

Stem Cells and Regenerative Medicine: which brings together research on human embryonic and fetal tissues including cardiac (**Wilson D**, **O'Kelly**), mesenchymal stem cell (**Oreffo**), bone (**Oreffo**, **Tare**, **Evans**), lung (**Haitchi**, **Wilkinson**, **Sanchez-Elsner**), neuronal (**Willaime-Morawek**) and kidney (**Houghton, Collins J**) as well as cancer stem cells (**Sahota**). We have made strategic appointments to this theme including IfLS-sponsored joint appointments with Engineering (**Evans** and **Tare**) which has allowed us to develop novel explant models of organ and cell culture; unique cell sorting techniques for use in bio-devices; and distinctive approaches for the investigation of biomaterials and biomechanical structures. A third joint appointment, with Mathematics and IfLS (**MacArthur**), brings new computational modelling approaches to the experimental investigation of stem cell fate and strengthens our collaboration with mechanobiologist Sengers (in Engineering).

Southampton Health Technology Assessment Centre (**Clegg, Jones, Shepherd**): assesses the clinical and cost effectiveness of health technologies, provides the evidence that directly informs national policy for NHS from the Department of Health (e.g. National Institute for Health Care Excellence, National Clinical Directors, Advisory Group on National Specialist Services). Its research underlies guidance on the management of over 20 health conditions between 2008-2013, including cancers, obesity, malnutrition, hepatitis, heart disease, mental health conditions, and psoriasis.

c. People, including:

i. Staffing strategy and staff development

Staffing Strategy

We have pursued a three-pronged appointments strategy over the past five years, building upon our key themes of strong basic discovery and early clinical translation, collaboration at the life sciences interface and enterprise and innovation with deep links to industry. First we have fortified existing areas of strength in a sustainable way by appointing exceptional young researchers for example in Respiratory Medicine (**Haitchi**, **Wilkinson**, **Elkington**); Cancer (**Strefford**, **Steele**); bioengineering and regenerative medicine (**Evans**, **Tare**, **Harvey**). Second, we have built new areas by bridging peaks of excellence and appointing at more senior level. Examples include Infectious Diseases (**Read**, **Khakoo**, **Woelk)** ; Bioinformatics (Bohning, **Woelk**, **Ennis**) Innate Immunity (**Khakoo,** Gadola); Cancer Pathology and Cell Biology (**Thomas, Moutasim**); Acute/extreme Physiology (**Grocott**, **Feelisch**). Also new the appointment of Thomas (UoA2) brings expertise in primary and community aspects of asthma and COPD. Recruitment of **Newell** and **McGrath** expands our global health expertise into the prevention and treatment of HIV infection. Third, we have built substantial interdisciplinary programmes via joint appointments with other Faculties and/or the IfLS, for example Medical Statistics (Bohning with S3RI, returned to UoA10) and Quantitative Biology (**MacArthur**, with Mathematics); Microdevices for Immunometry –

(**West**, with IfLS); Biomechanics (**Evans**, with engineering); and biological Chemistry (Tavasoli with chemistry, returned to UoA8). In addition, **Cooper** and **Roderick** co-direct the cross University Strategic Research Group in Population Health, and **Elliott** is deputy director of the IfLS.

Staff Development

We have continued to support development during early, mid and late-career phases in a way that embraces diversity and inclusion and are working to Athena Swan Silver Award having successfully gained Bronze during the assessment period. For the past ten years our postdoctoral researchers have run their own professional society with representation on the Faculty Research Management Committee. All postdocs are enrolled on our mentorship programme and take part in the Faculty transferrable skills programme, covering the four domains of the Vitae Research Development Framework to provide a comprehensive skill base for our ECRs and postgraduate students (engagement, influence and impact; knowledge and intellectual abilities; research governance and organisation; personal effectiveness). The Faculty enables exceptional postdocs to develop independence while working under the umbrella of an established group by funding at least two Career-Track Fellows (CTF) per year: two years of salary funding with a consumables budget to provide a bridge between postdoctoral research and "first award". Applicants are shortlisted and interviewed by an internal panel of senior academics including the Associate Dean for Research, chaired by the Dean. In the past five years, we have supported 13 CTFs of whom 5 have gone on to become independent PIs as externally-funded research fellows or as lecturers. Mid-career investigators are eligible for our mentorship programme; and for grant-writing workshops, one of which is a "grant-writing refresher" and is task-focused to ensure that each participant generates a draft proposal. Via annual appraisal, the University promotions and rewards scheme is well utilised by Heads of Academic Unit and the UoA has attracted 19 Vice-Chancellor's awards for excellence (including **J Collins** for co-ordination of the first year of the 4yr PhD Programme; as well as awards for implementing the new animal research facility; and the new tissue bank). All senior academic staff are appraised annually (jointly with NHS for all clinical academics) focusing on achievements against clear objectives and linked directly to the University Rewards Scheme. The Faculty's Senior Leadership team is, in addition, coached regularly by an external consultant, individually and as a group, complementing the ongoing University Senior Leadership and Development Programme.

Clinical Academic Training

Currently we have 16 NIHR Academic Clinical Fellows (ACF) and 8 NIHR Clinical Lecturers (CL) in UoA1. Of the previous 31 ACFs: 6 have obtained clinical lecturer posts in Southampton; 15 are currently studying for a PhD (14 in Southampton) and of these 8 have obtained clinical training fellowships in open competition. All of our 6 previous CLs have obtained Senior Lecturer posts and 2 have obtained Clinician Scientist awards in open competition.

ii. Research students

Since 2008 we have trained 179 doctoral students: 138 PhD (75% non-clinical, 25% Clinical) and 41 DM. The majority of our postgraduate research students are full-time non-clinical researchers, over 85% of whom submit within four years.

Nonclinical integrated 4yr PhD Programme: Now in its 8th year, the programme was launched to address an emerging skills gap for researchers in experimental medicine equipped with interdisciplinary awareness highlighted by the UK biosciences sector (ABPI: Skills Needs for Biomedical Research, 2008). The programme incorporates a structured first year of three accredited taught and three laboratory rotations leading to an MRes, followed by a focused 3yr project with a supervisor of the student's choice. Students follow one of three pathways through the programme in either 1) cell biology or immunology of cancer, 2) infection and immunity or 3) stem cells, human development and regenerative medicine, thereby gaining structured access to our main research strengths. Rotations through "translational" laboratories and laboratories in biomedicine-affiliated physical science disciplines are encouraged. In a recent external examiners report, the quality of the programme was judged to be "of the same standard as a successful Wellcome Trust 4yr PhD Programme". Entry onto the programme is highly competitive with around 200 applications for up to 10 places annually. Over 70% of graduates from this programme go on to a first job in research. The programme is supported by the Faculty Doctoral Training Account, comprising a portfolio of funding including doctoral training grants from MRC and BBSRC, and studentships from local charities (Wessex Medical Research and the Gerald Kerkut Foundation) and private partners including GSK, Bioinvent, and Microsoft Research UK.

Nonclinical and Clinical 3yr programme: 80% of nonclinical PGR and all clinical PGR are trained via a more conventional route involving a 3 year research project which is enhanced by an integrated transferrable skills programme. 33% of PhD students and all DM students are enrolled in this programme part-time. Clinical trainees benefit from the Southampton Clinical Academic Training Scheme (SoCATS) run in collaboration with the Wessex Local Education and Training Board, covering the pipeline from Academic Foundation to Clinician Scientist/Honorary Consultant. The programme links with undergraduates through the intercalated Masters of Medical Science degree, and Academy of Medical Sciences INSPIRE activities, to encourage recruitment into academic medicine.
Overseas: The average annual breakdown of admissions to full-time PGR programmes is 65% UK, 15% EU and 20% overseas. Over the past 5 years we have developed strategic partnerships to diversify our PGR intake. For example, in 2007 UoS was one of 9 UK universities to form a strategic partnership with A* STAR, Singapore, through which the Faculty trains two students annually in aligned research areas (epigenetics, nutrition and infectious disease). In 2009 the Faculty created a partnership with the Academic Medical Centre in Groningen, around shared interests in respiratory medicine and cancer immunology, resulting in two jointly-funded students per annum. In 2011 UoS became a member of the Colombia- UK consortium of Universities supported by Colciencias which has led to two funded studentships per annum.
Over the next five years we will:

- Increase the number of funded international PhDs by building formal links with a small number of main international partners in South East Asia via our recently opened Malaysia campus where **S Clarke** is currently on a 2yr secondment to increase our research footprint in infectious disease there and to strengthen links with A*star; and in South America via the Colombia- UK consortium and "science without boundaries" (Brazil). We will expand our links with Groningen to encompass PhD training in other areas of shared interest such as cardiovascular genetics.
- Increase training fellowship opportunities aligned with industry.
- Integrate PhD studentships with the undergraduate MMedSci to provide BMPhD opportunities for selected students

d. Income, infrastructure and facilities

The UoS/UHS partnership benefits from its shared facilities on a single site. Thus, the SCBR, CTU, Sir Henry Wellcome Laboratories, Cancer Sciences Building, Institute of Developmental Sciences, MRC University Unit and Biomedical Research Facility are all located on the University Hospital campus with nowhere more than a 7minutes walk away.

Income

In the period August 2008 to July 2013, Researchers in UoA1 generated £104.7M of external grant income comprising £22.4M Research Councils, £49.9M Biomedical Charities, £15.2M DH, £4.1M Industry and £6.7M EU. A further £6.5M was generated from other sources such as UK local authorities and overseas sources. The UoA is fully integrated with the NIHR RBRU, NIHR NBRC, NIHR CRF, NIHR/CRUK ECMC and MRC LEU, which together add a further £48.5M of income; and the research environment of the partnership benefits from a further £0.6M of NIHR and industry funded research led by clinical colleagues who are not being returned.

Significant facilities and infrastructure

The Faculty's estate on the University Hospital campus has undergone substantial upgrading since 2008. In addition to major developments in translational medicine, and new animal research facility outlined on page 2, other facilities of note include: an HTA-licensed Tissue Bank with 4 dedicated quality assurance staff; new facilities for infectious disease research including a 7-hood category 3 suite, dedicated molecular microbiology labs and decontamination facilities; a Bioimaging Unit with three electron microscopes, two scanning confocal microscopes, live cell imaging and remote access fluorescence microscope; flow cytometry facility with eight instruments and a Laser Scanning Cytometer; a Histochemistry Unit ; a protein production facility hosted by the CRUK Centre and supported by two permanent staff who act as a conduit to the structural biology pipeline hosted by IfLS (see below).
New facilities in the SCBR include: 13 consulting rooms; an environmental laboratory with three containment level 2 environmental chambers; a physiology laboratory with state-of-the-art cardiorespiratory and body composition measurement; bronchoscopy/endoscopy suites and dual energy X-ray scanning. In addition, the Molecular Sciences Hub contains a GCLP core facility

where new immunomonitoring, genetic stratification, microbiological and micronutrient tests are developed for clinical trials to industry-regulated standards, in addition to a clinical mass spectrometry laboratory; Macro-Imaging equipment (with UHS) including CT, SPECT/CT, 3T MRI and PET/CT: Access to researchers is assured by a joint UoS-UHS research imaging group, supported by a dedicated Image analyst, research nurse and research radiographer; LifeLab an educational programme for school students, with 300m^2 of purpose-built laboratories including ultrasound equipment, wet lab, and equipment for assessments of body composition and respiratory function. Medicine is fully integrated with the IfLS where researchers have unrestricted access to: a state-of-the-art proteomics facility; structural biology facilities including a remote monitored crystallography pipeline for x-ray structure as well as NMR; a Biophysical Analysis suite including stopped-flow fluorimetry, analytical mass spectrometry and surface plasmon resonance; a 600m^2 purpose-built centre for the development of Biodevices, situated inside the IfLS building and which links directly to the £80M Mountbatten nanofabrication centre. Specific facilities include rapid prototyping, advanced microfluidic engineering, and nanodrop technology; in situ molecular imaging equipment "nanoscope" based in the Optoelectronics Institute; atomic force microscopy and ion-conductance microscopy for simultaneous structural and functional analysis at the single-molecule level.

e. Collaboration or contribution to the discipline or research base

Indicators of wider influence and contributions to the research base

Contributions include Chair of group for Global Alliance for Chronic Diseases (**Hanson**); Executive Board Member World Allergy Organisation (**Holgate**); Chief Clinician and Executive Board member, Cancer Research UK (**Johnson**); Chair of UK Medical Schools Council (**Cameron**); MRC Strategy Board and Academy of Medical Sciences Council (**Cooper, Holgate**); UK CRC Board (**Cameron, Johnson**); NIHR Advisory Board (**Cameron**); Scientific Chair of the European Respiratory Committee (**Holgate**); Comprehensive Local Research Network Director (**Primrose**) and lead for Pathology (**A Williams**)**;** Member, Nuffield Council on Bioethics and member of the 100,000 genomes Steering Group (**Lucassen**); RAE Panel member (**Cooper, Johnson**); REF2014 Main Panel chair (**Holgate**) and panel members (**Cameron, Cooper, Fall, Glennie**); Chair of the Council of Healthcare Professionals Diabetes UK (**Holt**), President of the British Microcirculation Society (**Clough**), President of the Lipids and Cardiovascular Risk section of the Royal Society of Medicine (**Byrne**); Chair of the Academic Training Committee, Royal College of Paediatrics and Child Health (**H Clark**), Executive Board Member European Academy of Allergy and Clinical Immunology (**Roberts**), Chair of the British Society for Immunology Wessex regional Group (**Beers**). 85 staff sit on steering committees including the National Cancer Research Institute Lymphoma studies group (**Johnson**), National Cancer Research Institute Clinical Studies Group (**Copson**); International extranodal lymphoma study group (**Johnson** board of Directors), Chair of the Malnutrition Action Group of BAPEN (**Elia**). 71 staff have organised international conferences either as chair or member of an organising committee including 8th World Congress on DoHAD (**Godfrey, Hanson**); 17th International Congress on Lung and Airways Fibrosis (**Richeldi**); Scientific Programme of the Infectious Disease Society of America (Chair, **Read**); Programmes Committee of the World Congress of Reproductive Biology 2014 (**Houghton**); WHO International Scientific Conference, Hyderabad, India (Chair, **Holgate**); 7th International Antigen Processing Workshop (Chair, **Elliott**); 2nd International Symposium on Brain Myeloid Cells (**Hawkes**); NanoBiotech Montreaux (**Vollmer**). 116 staff delivered named, plenary or keynote lectures.

Participation in the peer-review process

Chairmanship of grant-awarding bodies includes MRC Populations and Systems Medicine Board, Disease Cohorts Panel, Expert Group on CFS/ME, Stratified Medicine Initiative, Experimental Medicine Panel, Joint research councils Initiative on Environment and Human Health, ABPI/MRC Panel on Inflammation and Immunology, British Lung Foundation Grants Panel (**Holgate**); MRC Population Health Sciences Board, BHF Grants Committee (**Cooper**); Cancer Research UK Training and Development Board (**Johnson**); Wellcome Trust Expert Review Group for Infection and Immunology (Co-chair, **Elliott**) and Ethics and Society (**Lucassen**); MRC Population and systems Medicine Board and NIHR Clinician Scientist Panel (**Inskip**), NIHR Postdoctoral Research Fellowship Awards Panel (**Read**); National Eye Research Centre Grants Committee (**Lotery**); European Society for Clinical Microbiology and Infectious Diseases Grants Committee (**Read**). In addition memberships of grant awarding bodies include 10 on Research Council

Awards committees, 12 on NIHR Panels, 7 on MRCUK Panels and 6 on overseas grants panels including NIH (**Arshad, Stevenson**). 104 staff sit on the editorial board of at least one indexed journal, and 24 hold a significant editorial role including Editor in Chief: Br J Nutr (**Calder, Burdge**), J Nutr Sci (**Burdge**), Curr Op Inf Dis (**Read**), J Infect (**Read**), J Med Microbiol (**I Clarke**), Eye (**Lotery**),Occupational and Environmental Medicine (**Palmer**), Head and Neck Oncology (**Thomas**), Global J Surgery (**Mirnezami**); and Associate Editor: J Immunol (**Stevenson**), Clin Exp Allergy (**Arshad, JW Holloway**), Eur Resp J (**Djukanovic, Richeldi**), J Med Genet (**Eccles**), J Invest Dermatol (**Healy**), Clinical Science (**Holgate**), Diabetic Medicine (**Holt**).
External assessments of institutes by staff include Karolinska Institute and Canadian Institute for Health Research Ottawa, Chair of the advisory panel for the MRC Centre Cambridge, member of the assessment panel for CRUK centres (**Holgate**); Inserm Universite Paris Descartes Centre for Immunology, University of Groningen Postgraduate Medical Programme (**Elliott**); Human Reproductive Sciences Unit Edinburgh (**Cameron, Macklon);** MRC Asthma-UK Centre, Kings College London (**Davies**); School of Pharmacy and pharmacology, Trinity College Dublin and Department of Chemistry, Warwick (**Feelisch**); **.**

Fellowships, awards, and visiting professorships

CBE (**Jackson, Holgate**); OBE (**Jacobs**); Fellowships of the Royal Society (**Jacobs**), Fellowships of the Academy of Medical Sciences (**Cooper, Jacobs, Holgate, Newell, Stevenson, Coggon**), Fellowships of the Society of Biology (**Cameron, Elliott, Oreffo, Clough, Healy**); Fellow of the American Association of Physicians (**Holgate**); Fellow of the Institute of Biomedical Science (**Holgate**), Fellow of the National Academy of Science USA (**Jacobs**). NIHR Senior Investigators (**Cooper, Holgate, Lotery**); 45 Visiting Professorships including Harvard, University of Melbourne (**Holgate**); Universities of Tokyo, Budapest and Victoria NZ (**Cooper**); Scripps (**Glennie, Packham**); King Saud University, Riyadh (**Calder, Oreffo**); Southern Medical University, PR China (**Clough**); Universities of Melbourne and Sao Paulo (**A Collins**); Universities of Adelaide and Copenhagen (**Macklon**); National University of Singapore (**Hanson, Godfrey, S Clarke**); University of Groningen (**Lucassen**) and University of Malaya (**Newman**). Prestigious awards include March of Dimes Prize in Developmental Biology 2012 (**Jacobs**); American Thoracic Society Recognition Award for Scientific Accomplishments 2012 (**Holgate**); International Osteoporosis Foundation Medal of Achievement 2012, HRH Duchess of Cornwall Award for Research into Osteoporosis 2009 (**Cooper**); European Haematology Association Jean Bernard Life Time Achievement Award 2013 (**Stevenson**); International DoHAD Society David Barker Medal 2013 (**Fall**); Wilhelm Normann Medal of the German Society for Fat Research 2013 (**Calder**); . Distinguished awards to early Career Researchers include the BUPA Foundation Prize for Best Emerging Medical Researcher in the UK 2009 (**S Clarke**); European Respiratory Society Maurizio Vignola award - to leading respiratory researcher under age of 45 in Europe (**Wilkinson**); Cavenagh Prize 2013 of the British Neuropathological Society (**Hawkes**); 2009 Royal Society Presidents Prize (**Moutassim**) and the SPARKS/RCPCH Young Investigator of the Year Award 2013 (**Wiskin**). Career Development and Senior research fellowships include NIHR Senior Investigator Awards (**Cooper, Holgate**); MRC (**Blaydes, Boche, Evans, Lim**), Wellcome Trust (**McGrath**); CRUK (**Moutasim**), Parkinsons Disease Society, Alzheimers Research UK (**Hawkes**), GSK (**Vijayanand**), EU (**Vollmer, West**) and NIHR (**S Clarke**).

Effective academic collaboration and contribution

In the assessment period, the academic groups returned in UoA1 published 5,379 indexed publications including 3,009 peer-reviewed research articles, 416 scholarly reviews, and 344 commentaries or research correspondence, including **Holgate** (641), **Cooper** (630), **Calder** (172), **Hanson** (163), **Godfrey** (155) and **Dennison** (153). **Holgate** and **Cooper** are listed in the world's 100 most influential biomedical scientists (Eur.J.Clin.Invest. 2013). Publications include co-authors from 2,483 different collaborating organisations worldwide. Research articles alone have attracted 43,944 citations in the current assessment period (notably **Cooper** with 6,192 citations, **Hanson** 2,675, **Eccles** 2,169, **Calder** 2,191 ("top author in nutrition" globally according to Microsoft.com Ranklist). Reviews (eg. "Rethinking the pathogenesis of asthma" by **Holgate** and **Davies** (Immunity, 2009, 31:362-7) and books (eg "Mismatch: Why Our World No Longer Fits Our Bodies" by Gluckman and **Hanson** (OUP, 2006)) have been considered field changing. PhD students have published with 84% of submitted staff. 67% of our academic staff have major National, International or Industrial collaborations, which total 379 and include the EpiGen consortium, UBIOPRED, TRP and GSK.