Environment template (REF5)

Institution: Queen Mary University of London

Unit of assessment: Clinical Medicine

A. OVERVIEW

Barts and the London School of Medicine and Dentistry (SMD) became part of Queen Mary in 1995; Queen Mary was admitted to the Russell Group in 2012. Research activities in UoA1 are based in 4 institutes, namely **Barts Cancer Institute (BCI), Blizard Institute, William Harvey Research Institute (WHRI)** and **Wolfson Institute for Preventive Medicine.** All offer **leading international** research programmes and report a 28% increase in research spend and a 43% increase in research income from 2008 to 2012 (2013 is excluded here and hereafter because of incomplete data). Each institute has key strategic themes supported by cross-cutting programmes (genomics, inflammation and immunology, experimental medicine and population sciences), spanning basic sciences through translation to clinical applications, and follow-through to implementation and impact. In the REF period we have extended the transformation of our research performance by building **key strategic partnerships**, for example:

- Barts Health is UK's largest NHS Trust. A £1.2 billion redevelopment has created the new Royal London Hospital (opened 2012) next to our iconic Blizard Institute (focusing on cognate basic and translational research). Barts hospital is being rebuilt as a major Cardiovascular and Cancer Centre. With £25m of philanthropic and Queen Mary funding, we have created the William Harvey Heart Centre. Collectively, the unified University/NHS partnership has had major impact on SMD's research performance and created new academic-NHS linkages in London's east end.
- In 2012, Queen Mary and Barts Health Trust became founding partners of the local Academic Health Sciences Network (UCL Partners) with UCL, LSHTM and UCLH. We have used this initiative to unify cardiovascular clinical and academic work, research and training at the Barts site. We recently won an MRC Electronic Health Informatics Research Centre (Farr Institute).
- Queen Mary is in the process of acquiring four acres of land in Whitechapel adjacent to the new Royal London Hospital to create a multi-disciplinary Life Sciences and Clinical Research Programme which will develop into a new Life Sciences Institute and translational research programme over the next REF period.

B RESEARCH STRATEGY

B1. STRATEGIC AIMS AND RESEARCH CULTURE

The over-arching strategy of the School of Medicine in 2008-13 has aimed to enhance our position as a top research-led institution, building on our success in RAE 2008 where we were placed 4th nationally in quality of outputs. Key to this is our staffing strategy (see C1). We have continued to recruit new staff at all levels, and are particularly proud of our success over this REF period of attracting a cohort of 33 outstanding early career researchers (ECRs), whom we are resourcing and supporting to make the transition from senior post-doc to independent researcher. For clarity, we list ambitions and achievements over the assessment period by institute, but in reality there is extensive cross-institute working, which we highlight with selected examples.

Across all four institutes we have adopted a number of strategies to achieve excellence:

- **Attract high-performing research leaders** in strategic priority themes. For example, **Trembath** (Nature Genetics x3) was appointed in 2011 as Vice Principal for Health. With **Van Heel** (Nature Genetics x4), he recently secured a £2.5M strategic award from Wellcome Trust for an ambitious community genome sequencing study (see Blizard – Genomic Medicine, page 4). Other leading research professors appointed since 2008 include **Tinker, Hobbs**, **Marelli-Berg** and **Deloukas** (WHRI), **Moss** (Wolfson), **Schmidt and Heeschen** (BCI) and **Dunkel**, a leading pediatric endocrinologist (review of delayed puberty in NEJM 2012) from Helsinki.
- **Recruit and develop the most able young researchers** (n=33) by mentoring and a strong start-up package (£30K pa consumables and a post-doc). **Branco** has been awarded a Wellcome Henry Dale fellowship, **Longhi** a BHF intermediate fellowship, **Charalambous** an MRC NIRG, and **Bianchi** a translational award from Barts and the London Charity. All ECRs are on course to achieve significant external funding to secure their careers.

- **Secure substantial research income**, predominantly from Research Councils but also diversify income streams (charities, EU, DH, industry). Over the REF period, income from the EU, for example, was £10M. Work closely with Barts and the London Charity to align their funding with our strategic aims and priorities. Total spend over the REF period was £248.7M which included £22M from Barts and the London Charity. Total research income was £277.7M
- **Build external collaborations and partnerships** to leverage income and resource. SMD is part of Guys and St Thomas' BRC with projects on mucosal inflammation, genomics and asthma. Queen Mary is a partner in UCLP and was recently awarded a £9.5M NIHR CLAHRC.
- **Engage extensively with end users of our research** including industry, the NHS, policymakers and the public. Examples are given below and in the Impact Template.

The **research culture** in the School of Medicine is designed to achieve and celebrate excellence by emphasising researcher development and clear performance targets (see C1). All grant applications are internally peer-reviewed and bespoke support is provided by experienced academics to ensure applications reach a competitive standard prior to submission. In the next section we describe the research achievements of the four individual institutes.

B2. BARTS CANCER INSTITUTE (BCI)

BCI was established at Charterhouse Square in 2004. Cancer at Queen Mary was ranked third on the proportion of 3*/4* outputs in RAE 2008. We have built on this platform to increase research achievements. BCI with the Wolfson's Centre for Cancer Prevention was accredited as a Cancer Research UK Centre of Excellence in 2009, supported by an annual core grant of £2M, one of the largest in the UK. A state of the art Cancer Centre with clinical trial facilities for early and late phase studies was opened in the new Barts Hospital in 2010. Medical school resources support basic, translational and population studies of tumour types where Barts Health NHS Trust is strong clinically and academically, with particular focus on five areas of cancer research that make Barts unique and internationally recognised: Haematological Malignancies; Pancreatic, Oesophageal and other Gastrointestinal Cancers; Women's Cancers (Breast, Cervix, Ovary); Male Genitourinary Cancers (Prostate, Testicular, Penile); and Lung Cancer. BCI has served as a magnet for ECRs; 13 of the 33 returned staff from BCI joined since 2008.

The research achievements of greatest significance in BCI since RAE 2008 are:

- **Recruitment into clinical trials** of 24% of all cancer patients (national figure is 18%: CRUK website), 85% of acute leukaemia patients and over 25,000 into prevention trials. **Seventy cancer clinical trials** have opened to recruitment and approximately 30 more are in set-up phase – an average of two major new studies every month;
- **Experimental Cancer Medicine Centre programme** was renewed by CRUK/NIHR (2012) in a newly configured Centre that doubled the previous patient throughput by installing a further recruitment centre at the Brighton and Sussex Cancer Centre;
- **Prolific publication of our research** in top peer-reviewed journals including Nature, Journal of the National Cancer Institute, NEJM, Cancer Research and EMBO;
- **Increased annual grant income** by 43% (2008 to 2012), with a research spend of £72.7M. Particularly notable is the 7-fold rise in EU grant income between 2008 and 2013;
- **Recruitment of two new professors** to lead strategic programmes in Experimental Cancer Medicine (Schmid) and Cancer & Stem Cell Biology (Heeschen).
- **Capacity building of young researchers:** 10 ECR Lecturers; expansion of new researcher training programme; 75 new research students and 24 Clinical Research Fellows;
- **Mid-career success:** Six Senior Fellowships / New Investigator Awards secured;
- **Successful spin-out company** (Activiomics) established with pharma for development of mass-spec technology for target analysis, and application to clinical samples;
- **Public engagement** with over 80,000 people in the community through our CRUK-funded research outreach programme, as well as innovative training and awareness raising course for improved early diagnosis among GPs across North and East London.

The main strategic research themes in BCI are described below.

<u>BCI – Molecular Oncology</u>

Led by **Lemoine** (Oncogene 2008, JCI 2009) whose own research focuses on genomics and

molecular pathology (CRUK programme grant with **Crnogorac-Jurcevic**) on viral immunotherapy for pancreatic cancer. Pancreatic cancer is also a focus for molecular research by **Heeschen** (Cell Stem Cell 2011), **Kocher** (Gastroenterology 2011, 2013), **Hagemann** (JCI 2011), **Wang** and **Hallden**; this centre is the UK's largest recipient of grants from Pancreatic Cancer Research Fund and Pancreatic Cancer UK. Therapeutic exploitation of the molecular oncology of lung cancer is led by **Sharp** (Nature Cell Biology 2011, PNAS 2010; CRUK and BBSRC project grants), **Martin** (MRC New Investigator Award) and for the future by the appointment of **Schmid** (joining from U of Sussex, November 2013); of prostate cancer by **Yu** (MRC-funded) and **Hallden** (Prostate Cancer UK-funded); and of haematological malignancies by **Fitzgibbon** (CRUK programme grant, Nature Genetics in press). DNA repair and maintenance of genome stability has been a focus for investment with recruitment of **Martin** (Cancer Cell 2010), **Godinho** (ECR-Nature 2009) and **MacClelland** (ECR-Nature 2013).

BCI – Tumour Biology

This theme is led by **Wright** (CRUK programme grant) and **Hodivala-Dilke** (CRUK programme grant) with a unifying interest in understanding the cellular and molecular events that drive tumour progression to the malignant phenotype, particularly the nature of cross talk between epithelial cancer cells and their stromal partners during cancer evolution. Analysis of the influences controlling clonal behaviour is the focus of work by **Wright** (Gastroenterology 2009, 2011), **Graham** (ECR-Gastroenterology 2012, PNAS 2013), **McDonald** (Gastroenterology 2008, 2011) and **Alison**. **Hodivala-Dilke** (Nature Medicine 2009, Nature 2010) is an international leader in angiogenesis and integrin biology, a field also investigated for development of novel therapeutics by **Marshall** (PNAS 2009, Oncogene 2011). A new area of investigation and investment is the role of ubiquitylation in the regulation of tissue growth as well as invasion and metastasis, with **Ribeiro** (ECR-Mol Cell 2010) dissecting the Hippo signalling in Drosophila.

BCI – Cancer, Inflammation and Immunomodulation

The overarching hypothesis driving this theme is that inflammatory mediators and cells found in cancer are more likely to enhance than inhibit tumour progression, so modulating these should be of therapeutic benefit. **Balkwill** (CRUK programme grant, ERC Senior Investigator Award) is a leader in the field of cytokine biology who has taken discoveries through phase I/II trials, and **Hagemann** (CRUK Senior Fellow, JCI 2009 and 2011, J Exp Med 2008) is investigating functional heterogeneity of the myeloid cell lineage in malignancy, particularly manipulation of macrophages in the treatment of pancreatic cancer. **Gribben** (NIH programme grant, JCI 2008, PNAS 2009) leads a translational programme on the molecular mechanisms whereby cancer cells induce changes in the host immune system and the use of allogeneic stem cell bone marrow transplant to induce a graft versus leukaemia effect. **Davies** (Science Translational Med 2013) is developing novel approaches to improve efficacy and reduce toxicity of allogeneic stem cell transplantation and adoptive immunotherapy. **Taussig** (Cell Stem Cell 2013, PNAS 2013) is examining how leukaemia out-competes normal haematopoietic stem cells to induce bone marrow failure, and characterising the unique phenotypic characteristics of leukaemia initiating cells that maintain a malignancy and lead to drug resistance and relapse. **Ivanov** (JECR-CI 2009) investigates mechanisms of tumour clearance in response to targeted therapy with monoclonal antibodies, notably non-apoptotic forms of cell death after ligation of surface antigens. **Jia** is developing approaches to enhance cell death in leukaemia and lymphoma. **Capasso** (LLR Bennett Fellow, Nature Immunol 2010) is characterising the basic functions of normal and malignant B cells.

Cell Signalling

Signalling remains a key component of BCI research; 3 ECR's have been recruited into this area. **Vanhaesebroeck** (CRUK & BBSRC programme grants, Nature 2008, PNAS 2008, 2010) has studied PI3-kinases as a commonly deregulated signalling pathway in cancer and demonstrated their role in inflammation, allergy and metabolism. **Cutillas** (Science Trans Med 2013, PNAS 2011) has developed innovative technology to interrogate signalling pathways in a global fashion using advanced mass spectrometry now licensed to Activiomics Ltd. **Kermogant** (Nature Cell Biol 2011) is examining Met kinase signalling in cancer cell biology. **Cameron** (ECR-Nat Struct Mol Biol 2009) is modelling PKN kinase involvement in tumour cell motility and invasion. **Bianchi** (ECR-Mol Cell 2011) studies the interplay between kinase and IAP signalling. **Castellano** (ECR-Cancer Cell 2013) demonstrated the interaction of PI 3-kinase p110a with RAS in lung cancer.

Experimental Cancer Medicine

Translation of discoveries into novel diagnostics and therapeutics is a fundamental principle for BCI researchers. The Experimental Cancer Medicine Centre has a substantial track record in early phase clinical trials of biological therapies for solid and haematological malignancies. Currently led by **Powles** (J Clin Oncol 2009, 2011) for solid tumour oncology, **Gribben** (JCI 2008, Blood 2008, 2009, J Clin Oncol 2012) for haematological malignancies, and **Lemoine** (Clin Cancer Res 2010, 2012) for translational oncology, the team is being strengthened further by the recruitment of Schmid (Lancet 2009, J Clin Oncol 2013).

B3. BLIZARD INSTITUTE

In RAE 2008, research in the Blizard Institute was returned in UoA4 (Hospital Based Medicine) and ranked 1st equal in the UK on percentage of 3*/4* publications. The juxtaposition of Centres from different clinical backgrounds with overlapping research themes within a single laboratory environment is designed to promote the development of interdisciplinary research. To facilitate this collaborative ethos, the research of the Institute is organised into four major themes – Genomic Medicine, Molecular and Cellular Medicine, Immune Systems, and Experimental Medicine, each based around common technologies and core facilities. In parallel, the clinical specialities of most relevance to our local population and partner NHS Trusts are represented by Centres; namely, Cutaneous Research; Digestive Diseases; Diabetes; Immunology and Infectious Disease, Paediatrics; Neuroscience and Trauma; and Primary Care and Public Health (returned in UoA 2).

The achievements of greatest significance in the Blizard since RAE 2008 are:

- **Annual research spend** increased from **£13.3M** in 2008 to **£20.4M** in 2012 (a 51% increase)**,** a total of **£92.3M** spend over the REF period; research income of **£105M,** with several significant awards including 42 grants in excess of £500K and 13 in the range £1M to £2.4M, including major awards from NIHR, Wellcome Trust, MRC and EU FP7 programmes.
- **Increased** capacity in surgical specialties such as **Trauma** and **Colorectal Disease (National Centre for Bowel Research and Surgical Innovation),** to meet an identified national need.
- **Outstanding record of publications** in top journals; Nature and Science family (n=35*);* PNAS (n=13), BMJ (n=44), Lancet family (n=25), NEJM (n=8), Cell (n=2);
- **Capacity building of young researchers:** ECRs (n=12) and Clinical Research Training Fellowships (n=16, from MRC, Wellcome Trust and other charities).

The main strategic research themes in the Blizard are listed below.

Genomic Medicine

This theme encompasses genetic variant discovery, gene function and diagnostics/prognostics in rare Mendelian and common diseases, and epigenetics. Based predominantly in the Blizard, it also incorporates genomic research groups in other institutes. **Van Heel** has led genome wide association studies (GWAS) in coeliac and autoimmune disease, discovering 40 new risk variants for coeliac disease (Nature Genetics 2008, 2010, 2011 x2), understanding the overlap between autoimmune diseases (NEJM 2008) and probing the role of rare variants (Nature 2013). **Van Heel** and **Trembath** have been awarded a £2.5M Wellcome Trust Strategic Award to sequence consanguineous East London populations to identify individuals carrying homozygous rare loss of function variants ("human knockouts") and recall them for deep phenotyping, a project that will play a key role in Queen Mary's proposed new **Life Sciences Institute. Kelsell** has identified the genetic and subsequent mechanistic basis of several monogenic skin disorders/syndromes (Am J Hum Genet 2012 – see impact case study), including the first highly penetrant gene for squamous oesophageal cancer (Am J Hum Gen 2012), and identified the first human knockout for ADAM17 (NEJM 2011). Kelsell has also been awarded a BHF Programme Grant (2013-2018 £1.1M).

Trembath has led GWAS for psoriasis as well as monogenic conditions including genito-patellar, Emberger, Hadju-Cheney and cutis aplasia syndromes (Nature Genetics 2010, 2011, 2012, Am J Hum Genet 2012). **Dokal** and **Vuillamy** have identified causes for the monogenic diseases dyskeratosis congenita and familial myelodysplasia (Am J Hum Genet 2012, 2013, PNAS 2008, Blood 2008). **Rakyan** has developed epigenetic methodology and used it to study ageing and fetal programing (Nature Biotechnology 2008, Genome Research 2008,20010,2012). **Leslie** on Type 1 diabetes (Plos Genetics 2011) and **Hitman** in fetal programing of Type 2

diabetes won two EU FP7 programme grants: BLUEPRINT (£500K) and GIFTS (£2.5M). Extending the basic science in this group, **Branco** (ECR) studies 5-hydroxymethylcytosine dynamics and epigenetics (Science 2012).

Molecular and Cellular Medicine (MCM)

This research theme has three overlapping sub-themes: Stem Cell Biology; Host/Pathogen Interactions; and Signalling and Epithelial Cell Biology. The goals are to understand the aetiology of disease at molecular and cellular level and to translate this knowledge into therapy.

In ***Stem Cell Biology***, a particular focus is stem/progenitor cell fate, with seminal publications describing the importance of the extracellular matrix (**Connelly**, Nat Cell Biol 2010, Nat Materials 2012), and identifying signalling pathways that regulate the cell cycle through p16INK4a by **Bishop** (ECR-Mol Cell 2010). The key role played by p16INK4a in neoplastic transformation has been demonstrated *in vivo* by development of a mouse model to measure p16INK4a expression under different pathophysiological conditions (**Beach**, Cell 2013). A new ECR **O'Loghlen** brings experience in chemokine and miRNA regulation of polycomb proteins known to regulate p16INK4a and complements our expertise in this field (Cell 2008 and Cell Stem Cell 2012). These four research leaders work synergistically to advance understanding of stem cell fate and the balance between senescence, regeneration and age-related disease. More translational stem cell research is represented by groups working on the pathophysiology of Downs syndrome (**Nizetic**, Am J Hum Genet 2008) and Muscular Dystrophy (ECR **Lin**, Nat Genet 2012). Both groups have induced pluripotency in adult cells derived from their respective patient groups and repaired genetic defects to generate unique isogenic models of disease. Re-differentiation of these IPSCs into distinct lineages should provide insights into the complex phenotypes of both diseases.

In ***Host/Pathogen Interactions***, **McKnight** (Retrovirology 2011) won the BioMed Central Research Prize in Microbiology, Immunology, Infection and Inflammation for research into HIV pathology and factors (identified using a global siRNA screen) that restrict infection of the host target cell. **Sloan** (ECR) brings expertise in interferon-induced transmembrane proteins (Retrovirology 2010, J Virol 2010, 2013) to exploit the advances made by **McKnight**.

In ***Signalling and Epithelial Cell Biology***, researchers made major advances in understanding signalling and regulatory mechanisms that control cellular homeostasis in the skin (**Bergamaschi** & **Harwood** EMBO 2011, J Exp Med 2013, **Philpott** Oncogene 2013). Pivotal use of tissue and organotypic cultures led to a £1M award from the Dr Hadwen Trust (**Philpott)** for the first chair of replacement science in the UK. In skin epithelial cells, **O'Toole** has identified the receptor tyrosine kinase Axl as a key regulator of epithelial-mesenchymal transition and also that cross-talk between the Axl- and Wnt-signalling pathways is a critical driver of metastasis (Oncogene 2013).

Immune Systems

The aim of this theme is to create critical mass for internationally competitive immunology and promote productive interaction and collaboration across SMD. Based in the Blizard but working with groups in other SMD institutes, we seek to understand the basic biology underpinning a healthy immune system and identify where and how these processes break down in disease. We build on considerable experience and expertise in the sub-themes of infectious disease, developmental immunology, and autoimmune pathologies. Key achievements are listed below.

In ***idiopathic inflammation*** highlights include **MacDonald's** Immunity article (2012) on the role of T-bet in intestinal inflammation; **Wang's** paper on the role of the Egr proteins in the prevention of inflammation (Immunity 2012); **Leslie** identified methylation signatures that precede disease in Type 1 Diabetes (PLoS Genetics). In this theme there is significant collaboration with Genomic Medicine, for example **van Heel's** GWAS on celiac disease (Nat Gen 2010), and the 2008 NEJM paper on the link between celiac disease and Type 1 Diabetes. **Kelsell and MacDonald** collaborated on the discovery of a child homozygous for an ADAM17 deletion-lethal in mice (NEJM 2011) and identified the cause of cryptogenic multifocal ulcerating stenosing enteritis as homozygous deletion mutations in cytosolic phospholipase A2-α (Gut 2014-on line).

In ***developmental immunology,*** highlights include **Pennington's** demonstration that the gamma/ delta T cell receptor's role in T cell development is ligand independent (Science Signalling 2011, Nat Immunology 2009, Nat Immunology 2013); and **Wang's** work on T cell tolerance (JEM 2008).

In ***infectious disease immunology,*** highlights include **Foster's** work on Hepatitis that resulted in

an NIHR award (£828K) to study screening for chronic viral hepatitis in ethnic minorities, and strong publications on new therapies for Hep C (NEJM). This was complemented by **Kennedy's** Barts and the London Charity award (£472K) to work on immune responses to Hepatitis B in the young. Other successes include **Martineau's** NIHR programme grant (£1.5M) to study vitamin D supplementation for a range of indicators including immune fitness to tuberculosis (PNAS x2, Lancet). **Prendergast** has been awarded funding to study immune fitness in African children (£0.9M Wellcome, £0.77M from MRC (see section E, international collaborations).

Blizard – Experimental Medicine

This theme includes clinically oriented research in Trauma (haemorrhage, coagulopathy, inflammation, brain & spinal cord injury); Neuroscience (multiple sclerosis, degenerative diseases); Gastrointestinal Disease (functional bowel disorders); Diabetes; and Paediatrics. These research groupings have attracted a total of over £20M in grant funding over the assessment period.

Brohi has an extensive research programme in acute trauma care, including work identifying mitochondria as Damage-Associated Molecular Patterns (Nature 2010) and analysing the effect of tranexamic acid on bleeding from major trauma (Lancet 2011), building on his internationally recognised work in major haemorrhage and coagulopathy. He won £3M infrastructure funding from Barts and the London Charity for a Trauma Research Centre linked to the outstanding trauma facilities at the Royal London. **Brohi and Thiermermann** (WHRI) recently won £760K from Wellcome Trust for a trial of Artesunate in trauma haemorrhage. **Giovannoni** (NEJM 2010, Lancet Neurol 2011) and **Schmierer** (Lancet 2008) have used immunomodulation to prevent relapse in multiple sclerosis. **Aziz's** research is aimed at understanding the neurophysiological basis of human brain-gut communication. Using fMRI, he identified that fatty acid-induced gut-brain signalling attenuates neural and behavioural effects of sad emotion in humans (J Clin Invest 2011).

Williams, currently President of the Royal College of Surgeons, co-directs ENTERIC, one of eight national Healthcare Technology Co-operatives (HTCs). Its aim is to be the premier centre for innovative technology in surgical gastrointestinal disorders for the NHS and beyond; it recently received NIHR infrastructure funding of £0.8M. ENTERIC, as a pilot HTC (2009-2012) leveraged £3M funding from TSB, NIHR and charities to progress several technology developments through to clinical trials over the REF period (see impact case study).

B4. WILLIAM HARVEY RESEARCH INSTITUTE (WHRI)

WHRI is the largest multidisciplinary pharmacological institute in terms of staff numbers in Europe. In RAE 2008 (Unit 15), WHRI was joint 3rd in UK in GPA. Whereas 28.6 FTE were returned in RAE 2008, 41.8 FTE are being returned in this REF. Research is divided into 3 main areas: Genomics and Stratified Medicine; Experimental Medicine and Pharmacology; and Translational Pharmacology and Therapeutic Innovation. They address three strategic themes: **Cardiovascular** (genomics, immunology, inflammation, regenerative medicine, translational pharmacology); **Inflammation** (gene therapy, inflammation pharmacology, regenerative medicine, musculoskeletal); and **Endocrinology** (genomics, molecular and paediatric endocrinology).

The achievements of greatest significance in WHRI since RAE 2008 are:

- **Substantial increase in research capacity:** Staff from WHRI have published 45 papers in Nature family or in the highest impact multidisciplinary journals over the REF period compared with 28 over the RAE period (a 63% increase). Research spend over the REF assessment period was £57.2M, with an increase of 43% from 2008 to 2012. Awards were £75.1M.
- **Major step change in new Programme Awards at WHRI:** In 2008, staff held 3 Programme grants. Over this REF period, staff in WHRI won one Wellcome Trust (WT) Senior Investigator Award (**Nourshargh**), 11 Programme grants (British Heart Foundation (BHF)/WT/MRC)-(**Caulfield** x 3, **Hobbs**, **Marelli-Berg, Munroe, Nourshargh, Perretti, Tinker** x 2, **Warner**) including two major European Union FP7 awards on stem cells (€11M), one Gates award (£1M, **Marelli-Berg**) and one EU Marie Curie Co-fund (€6.5M, **Korbonits**) award.
- **New major Initiatives and Centres.** Excellence in **Cardiovascular Research at WHRI** was recognised by the award of two National Institute for Health Research (NIHR) Biomedical Research Units (BRU) in CV Disease with our partners at Barts Health (£12M 2008-2017, **Caulfield**). These awards were key to securing an MRC Centre in Electronic Health Informatics Research Centre (£9M 2013-2018) with Academic Health Science System (AHSC) partners at

UCL and LSHTM. Our academics have leadership of major international CV Genomics Programmes in blood pressure (**Caulfield, Munroe**), coronary artery disease (**Ye**), arrhythmias (**Tinker**) and serum urate (**Caulfield, Munroe**). **Munroe** leads the MRC International Mouse Cardiovascular Traits Consortium (2011-2016).

- **Inflammation Research:** The Pathobiology of Early Arthritis Consortium (PEAC) exemplifies the strategy of using national initiatives to lever international partnerships. With MRC funding (£0.7M), **Pitzalis** led establishment of a unique national resource of ultrasound-directed synovial biopsy in rheumatoid arthritis from which he developed an international partnership with Genentech/Roche. This has attracted international industrial partners and led to the award of the MRC/AR-UK MATURA and an NIHR award for MRC and NIHR Stratified Medicine Programmes (**Pitzalis** £5.9M). Staff have won an Arthritis Research UK (AR-UK) Early Arthritis Treatment Centre (**Pitzalis, Perretti, Sasieni, Lemoine**) and partner Oxford in the AR-UK Centre of Excellence on the Pathogenesis of Osteoarthritis. Staff participate in the NIHR Translational Research Collaborative in Rheumatology to bring new therapies into the UK.
- **Endocrinology:** To sustain internationally quality research in paediatric endocrinology we recruited **Dunkel** in 2011 and invested in ECRs to investigate novel genes in adrenal/ pituitary development (**Gaston-Massuet, Charalambous-MRC NIRG**).
- **Internationally Successful Industry Partnerships:** The WHRI/Queen Mary strategic partnership with Quintiles Trans-national enabled the design and opening of the world's first Prime Site in 2008 that current**ly** runs 33 clinical trials across all therapeutic areas. Queen Mary has extended this across UCLP Academic Health Sciences Centre and in 2012-13 700 patients will be recruited into studies.

The main strategic research themes in WHRI are described below.

Genomics and Stratified Medicine

WHRI leads international collaborative programmes that have made major advances in the genetic architecture of Cardiovascular, Endocrine and Inflammatory diseases.

Cardiovascular genomics (NIHR BRU): Staff have have used the platform of Wellcome Trust Strategic Award funding via the Case Control Consortium to establish and lead international groupings, such as Global BP Gen and the International Consortium for Blood Pressure Genome-wide Studies (350 scientists from 234 centres worldwide), and Cardiogram which discovered 35 genes for blood pressure (**Caulfield, Munroe:** Nature 2011, Nat Genet 2009, 2013), 46 for Coronary Disease (**Deloukas** Nature Genetics 2011, 2012 x2, 2013, **Ye** Am J Hum Genet 2013).

Endocrinology genomics: Staff in this area have an extremely strong and sustained track record in rare inherited disease, with the discovery of six novel genes causing familial glucocorticoid deficiency, genes involved in the growth hormone axis, and gene mutations in familial pituitary adenoma (**Korbonits**, **Metherell, Chan**; PNAS 2009, NEJM 2011, JCI 2012, Nat Genet 2012).

Inflammation: From the platform of the MRC funded Pathogenesis of Early Arthritis (PEAC) Cohort and the AR-UK Early Arthritis Treatment Centre, **Pitzalis, Bombardieri, and Del Accio** exploited capability in ultrasound directed biopsy and identified synovial pathotypes, based on transciptomics, with Genentech and Roche that could lead to deeper phenotyping and patient stratification for better responses to biologics in rheumatoid arthritis.

Experimental Medicine and Pharmacology

Cardiovascular (NIHR BRU area): With BHF Programme Grant funding, **Marelli-Berg** discovered the role of the endothelium in T cell recruitment in heart transplantation (PNAS 2010, JCI 2008). **Mauro** (BHF Intermediate Fellow; Nat Cell Biol 2011) is studying the metabolic impact on T cell response whereas ECR **Longhi** (JEM 2009) focuses on dendritic cells in atherosclerosis and has just received a BHF intermediate fellowship. Mechanistic and therapeutic studies are carried out in vascular inflammation (**Solito,** PNAS 2013), acute & chronic renal disease (**Yaqoob,** NEJM 2009), and platelet biology (**Warner,** PNAS 2012,2013).

Inflammation: In inflammatory arthritis, **Bombardieri/Pitzalis** are studying breach of tolerance, T/B cell autoimmunity and auto-antigen retention (**El-Shikh,** J Exp Med 2010). This is being translated into the joint by in vivo models (**Perretti/Cooper**), using rheumatoid synovial samples to study mediator/receptor expression (**Perretti/Cooper/Pitzalis**) and to assess potential for stratification of response to biologics (**Pitzalis**). **Dell'Accio** is detailing signalling in chondrocytes

crelated to anabolism and cartilage formation (JCB 2011). A key focus is defining new molecular and cellular pathways focusing on GPCRs (which help resolve inflammation (**Perretti, Flower**; **Cooray,** WT Programme; Blood 2008, 2013, PNAS 2013). New ECRs **Haworth** (Nat Immunol 2008) and **Aksoy** (Nat Immunol 2012) are studying novel cellular mechanisms of inflammation resolution focusing on T cells and macrophage signalling, along with studies on omega-3 derivatives (**Norling,** Nature 2009). **Nourshargh** has a Wellcome Senior Investigator Award (£2.5M 2012-2019), building on a Wellcome Programme grant (2007-12) on leukocyte trafficking (also **Voisin,** JEM 2012; **Woodfin,** Nat Immunol 2011), involving evaluation of mechanisms that suppress cell migration (**Perretti, Cooper**).

Translational Pharmacology and Therapeutic Innovation

Cardiovascular (NIHR BRU): With BHF Project grant and Wellcome Programme grant funding, **Ahluwalia** (Hypertension) has shown that inorganic nitrate lowers BP, and has antiplatelet activity) **Hobbs** (Circulation) has shown that inorganic nitrate and may treat hypertension and pulmonary hypertension. **Inflammation:** With a Wellcome Trust Health Innovation Challenge Award (£1M) and NIHR funding, staff are repositioning therapeutics for ischaemia reperfusion injury (**Thiemermann**) after trauma, and in end-stage renal damage (**Yaqoob**).

B5. WOLFSON INSTITUTE FOR PREVENTIVE MEDICINE

The Wolfson is widely regarded as UK's leading research centre for the study and advancement of preventive medicine. In RAE 2008 staff were returned in Epidemiology and Public Health (Unit 6) and ranked 2nd in UK (80% of outputs 3*/4*). The research aims of the Wolfson are to advance knowledge in preventive medicine, epidemiology and public health through discovery, application of laboratory science and delivery and teaching of preventive medicine services. The priority is on scientific investigation into medical problems of public health importance, thereby influencing management and prevention of major diseases. Two of its three centres (Environmental and Preventive Medicine, Cancer) are returned in this UoA, while Psychiatry is returned in Unit 2.

We have made major advances in preventive medicine, notably development and evaluation of medicines to prevent cardiovascular disease and cancer; interventions to reduce smoking (active and passive); cancer screening and prevention; antenatal screening for birth defects; and improved risk and prognosis models for cancer. Our main achievements in 2008-13 are:

- **Significant awards:** Over the REF period, staff from the Wolfson returned in this UoA had £26.5M in spend with an increase of 51% (£4.1M in 2008 to £6.2M in 2012-13). This includes (£9.4M from CRUK. £4.7M from DoH and £0.9M from MRC). Research income was £27.9M
- **Excellent track record of publications:** Staff had 9 Lancet papers, 10 Lancet Oncology papers, 6 in BMJ, 8 in J Clin Oncol and 9 in NEJM.
- **Major influence on practice and policy with significant impact on health outcomes:** Staff in the Wolfson made major contributions on cancer screening adopted into policy, as evidenced by several of our impact case studies. **Cuzick's** work led to adoption of anastrozole for breast cancer in hormone receptor positive localised cancer in postmenopausal women, and that radiotherapy after surgery for ductal carcinoma in situ reduced invasive disease. **Duffy** showed improved quality of life in breast cancer patients managed with sentinel lymph node biopsy compared to those undergoing axillary lymph node dissection. **Sasieni** showed the efficacy of cervical screening to be age-dependent and that the optimal lower age of screening is 25.

Wolfson – Cancer Prevention and Treatment

Cuzick developed a prognostic index to identify risk of recurrence of oestrogen receptor positive breast cancer, currently being considered for routine use by NICE (J Clin Oncol 2011), and showed the value of radiotherapy in high-grade ductal carcinoma in situ (Lancet 2011); this has become standard care. **Cuzick** also led multi-centre trials showing the value of aromatase inhibitors in adjuvant treatment of breast cancer in postmenopausal women (Lancet Oncology 2010), and of tamoxifen in prevention of breast cancer in high-risk women (Lancet 2013). **Cuzick** evaluated the proposed change from cytology to HPV testing in cervical cancer screening (Lancet 2011), a policy now being piloted by the National Screening Committee. **Duffy** showed that double-reading mammograms in breast cancer screening could be replaced by single reading plus computer-aided detection (NEJM 2008; Radiology 2010). **Cuzick** and **Duffy** showed flexible sigmoidoscopy to be

effective in preventing bowel cancer. UK approval was given by the National Screening Committee in 2011, starting in England in 2012, to introduce flexible sigmoidoscopy to people aged 55-59 and fecal occult blood testing to those aged 60-74 (Lancet 2010). **Lorincz** showed the validity and economy of self-sampling in cervical cancer screening, particularly in low income countries (Lancet 2011). **Sasieni's** work on optimal age for starting cervical cancer screening (BMJ 2009) led to changing this cut-off (to age 25), increasing cost-effectiveness of screening.

Wolfson – Environmental and Preventive Medicine

N Wald developed the polypill for prevention of cardiovascular disease and demonstrated its effectiveness in a randomised trial (PLoS One 2012). **D Wald** showed a >60% reduction in heart attacks and sudden cardiac deaths from preventive angioplasty in a multicentre randomised trial (NEJM 2013). **N Wald** and **D Wald's** meta-analysis showed the benefit of a combination of blood pressure lowering drugs over monotherapy (**Wald N**, BMJ 2009 – prize for most important BMJ paper that year; **Wald D** Am J Med 2009). **N Wald** led a randomised trial of screening for hypothyroidism in pregnancy and cognitive development in the offspring and showed conclusively that such screening was not worthwhile (NEJM 2013).

Current activity

A broad-ranging portfolio of **ongoing cancer studies** include a 25-centre international trial of aromatase inhibitors in breast cancer prevention (**Cuzick**); value of aspirin in prevention of cancer, particularly large bowel (**Cuzick**); national research initiatives in cancer awareness screening in early diagnosis conducted through DoH with 7 partner institutions (**Duffy**); continuing work on efficacy and application of HPV screening for cervical cancer and flexible sigmoidoscopy in screening for colon cancer (**Cuzick, Duffy**); exploring the predictive value of collective risk factors in cancer prediction and extending application of the Tyrer-Cuzick model for breast cancer prediction (**Cuzick**). Environmental and preventive medicine studies include epidemiological research on teratogenicity of medicines in collaboration with EUROCAT, the European register of congenital malformations (**Morris**); feasibility of child-parent screening for familial hyper-cholesterolaemia in general practice (**D Wald**); two randomised trials of the polypill with a view to seeking MHRA market authorisation approval (**N Wald**); use of instant text messaging to enhance adherence to preventive medicines such as polypill or tamoxifen (**D Wald, Cuzick**); continuing a 19-year follow-up of very premature infants to determine factors associated with survival (**Morris**).

B6. FUTURE RESEARCH STRATEGY OF SMD AND QUEEN MARY

As part of an overall strategy to focus on major research themes characterised by significant infrastructure, substantial research capacity and external collaborations, SMD and Queen Mary plan a number of flagship initiatives:

1. Queen Mary expects to purchase land immediately north of the Blizard Institute to allow the development of a cross-disciplinary Life Sciences Institute directed at post-genomic population health (both physical and mental), with additional possibilities for student accommodation and expanded incubator facilities. The aim of this development is to establish Queen Mary at the forefront of academic activity in the 'post-genomic population health' elements of life sciences, an area in which we have considerable expertise.
2. SMD through the WHRI is establishing an integrated **Centre for Therapeutic Innovation** for validation and confidence building of medicines and device-based therapies in hypertension, arrhythmias and ischaemia reperfusion injury. This builds on multiple successful collaborations in genomics, vascular inflammation and pharmacology extending across the UCLP Academic Health Sciences System. This has been boosted by approval from NHS England to create the largest **unified UK Tertiary Cardiovascular Centre** at the new £300M Barts Hospital linked to the Crick Institute and partnering Yale University. The end result will be the premier European centre for cardiovascular therapeutic innovation.
3. SMD's contribution to the **MRC Centre in Electronic Health Informatics Research** will allow partnership, along with UCL and LSHTM, of the London node of the new MRC-funded Farr Institute (£9.5M, 2012-2017).
4. BCI, already the UK's premier centre for pancreatic cancer research, plans to build faculty in other priority areas eg lung and oesophageal cancer. A new **Centre for Cancer, Stem Cells & Ageing** led by **Heeschen** will stimulate research spanning molecular and patient biology to

address the twin issues of cancer and ageing in cells and individuals. This Centre will bring together staff from all institutes with expertise in DNA repair and genome stability, epigenetics and senescence, and ageing and immune function. There will be a focus on **metastasis,** the primary cause of cancer death but poorly understood. Understanding the survival circuitry that allows escape from one microenvironment and establishment in another is key to preventing and controlling metastatic disease. Enhancing links with **industry** will be a strategic imperative.

5. The Blizard Institute aims to place increased emphasis on Translational Medicine and in so doing be of direct benefit to its partner acute NHS Trusts and the local community, contributing particularly to the Life Sciences initiative (see above). Specific immediate priorities will be (i) to become the leading academic **acute trauma centre** in the UK, achieving Centre status from MRC or NIHR, (ii) to grow **preventative medicine in fetal, child and adult health**, (iii) to **study homozygous loss of function variants** in our local populations.
6. Wolfson Institute will extend its work in prevention of cardiovascular disease and cancer by developing a **Prevention of Chronic Diseases** group headed by the appointment of epidemiologist with experience at crossing organ boundaries. This new group will focus on neurological diseases (eg Alzheimer's, Parkinson's, multiple sclerosis), which, like cardiovascular disease and cancer, typically have a long natural history in which changes accumulate that gradually lead to clinical disease with chronic progression. The new group will work across the SMD institutes, especially with **Giovanonni** in the Blizard and colleagues beyond Queen Mary. It will build on existing expertise in laboratory research, fieldwork, and preventive intervention trials requiring pharmaceutical agents, and large randomised trials.

C. STAFFING STRATEGY AND STAFF DEVELOPMENT

C1. RECRUITING, DEVELOPING AND SUPPORTING RESEARCH STAFF

Our approach to staffing and staff development is shaped by **Queen Mary's strategic plan**, which focuses on investing in excellence, equal opportunities and supporting career development. Its *Concordat Implementation Plan* was developed after a review of policies and practices in 2011 on the Concordat to Support the Career Development of Researchers. In January 2012 Queen Mary won a *European Commission's 'HR excellence in research'* award for recognition that researchers' career development provision at Queen Mary is fully aligned with The European Charter for Researchers. Queen Mary was shortlisted for a *Times Higher Award* in 2011 for 'outstanding support to early career researchers'. College level support includes an Annual Fellowship Day, leadership training and events to support transition to independent researcher status.

In the RAE period (2001-07), SMD's approach to **capacity building** was to recruit established research groups. In the current period (2008-13), building on a much stronger base, we shifted to a strategy of **recruiting early career researchers** (ECRs). We attracted 33 ECRs (mostly non-clinical) across the medical school, identified for high academic potential and skills, and interests that match our in-house strengths. The new ECRs are immersed in an environment where they had access to high-quality resources, equipment and trained senior advisors. SMD's **career development activities** for these ECRs, detailed below, mirror the College's strategic plan, being strongly inter-disciplinary and focusing on bespoke individual support packages. They include:

- **Personal guidance/mentoring/promotion**. Young researchers are selected for their outstanding potential and appointed with generous resources and support from a named mentor to help develop independent research careers, including producing competitive publications and moving to principal investigator status. Researchers are encouraged to work towards promotion by building their CV and gaining leadership experience. Since 2008, 13 lecturers have been promoted to senior lecturer (SL), 25 from SL to reader, 9 SL to chair, and 12 reader to chair (12 of these 21 chairs were men, 9 women).
- **Clear performance targets**. New researchers are expected to achieve a trajectory where they will publish in their top specialty journals and have a research spend of £65K pa. Principal investigators are encouraged and supported to secure major awards, publish in top specialty journals, and have a research spend of > £150K pa. At annual appraisal, the staff member's achievements are formally reviewed using a structured 'researcher score-card' detailing progress in key areas, identifying unmet training and support needs, and setting future targets.
- **Special support for postdocs.** We have identified non-clinical post-docs as particularly in

need of career advice. Queen Mary's Concordat Implementation Plan takes a Faculty-specific approach to postdoctoral training and development, based on feedback from the 2011 Careers in Research Online Survey (CROS). The College's Centre for Academic and Professional Development (CAPD) have worked in partnership with SMD Institutes to establish postdoc networks to provide a bespoke and partnership approach to developmental activities. Postdocs from each research area participate in monthly forums to advise on master-classes to address the development needs of this cohort. See also C2, much of which is relevant to postdocs.

- **Lectures and seminars** A vibrant and varied programme of lectures and seminars is offered in all institutes, ranging from formal guest lectures by distinguished external speakers to presentation of in-progress research by staff. Examples of recent speakers include: Charles Serhan–Harvard, Bill Sessa- Yale, Alberto Mantovani- Rome, John Wallace–McGill, Nancy Hogg- CRUK, Tim Williams- Imperial, Mark Walport, Keith Channon-Oxford, John Collinge-UCL, Peter Rigby-ICR, Geoffrey Smith and Doug Higgs-Oxford, Phillip Cohen-Dundee, Godfrey Oakley Jr- Rollins School of Public Health at Emory, Peter Rothwell–Oxford.
- A highlight of the research year is the annual **William Harvey Day**, in which SMD staff, doctoral students and medical students come together for presentations, posters and prizes and a thanksgiving service for the founding of Barts Hospital. In 2013, 450 staff attended; there were 226 poster presentations, 10 talks by prizewinning young researchers, and keynote lectures, including Clare Matterson, Head of Public Engagement at Wellcome Trust.
- **Personal fellowships**. ECRs are strongly encouraged and supported to apply for fellowships, since this brings protected time and resources for personal development and predicts research career success. Queen Mary's Fellowship Day provides postdocs with information from Wellcome, MRC and BHF on how to gain a fellowship (50 attended in 2013). At Institute level, learning sets for key fellowship calls are organised. This strategic emphasis on personal fellowships has borne fruit, particularly in recent years. For example in 2013 Queen Mary was the top in the UK in winning BHF Intermediate Fellowships (n=6).
- **Masterclasses and workshops**. The annual SMD **Winning Grant Funding** master-class is a valuable opportunity to learn directly from senior SMD academics about grant writing and the application process and is attended by 50-75 post-docs. We also provide annual courses on **how to lead and manage research teams**, attended by 20-30 post-docs.
- **Career planning**. Queen Mary runs a 'Doctoral Transitions: Careers Beyond Academia' to inform about careers linked to research implementation and impact, especially the transition from academia into industry; 113 have attended in the last year. Data on the destinations of non-clinical post-docs in SMD 2008-13 showed that of 262 employed, 44% secured another post-doc, 16% went to industry, and 19% got faculty positions.
- **Senior leadership programme.** SMD nominates academic staff (both men and women) for a 'High Potential Leaders' programme run by the Centre for Academic and Professional Development. Fifteen SMD academic staff have participated in this programme since 2011. In addition, the college recently established a 'Women into Leadership programme' with Ashridge Business School to support promotion to senior positions.
- **Equality and diversity**. We follow Queen Mary's equality and diversity policies (eg all staff must undergo training and have regular updates on supporting staff with disabilities and sexual minorities). SMD holds an **Athena Swan bronze award** and is working towards silver, for which each institute has a named champion. We offer **flexible working** with no key meetings held outside core hours. An innovative **mentoring scheme for women academics** was established in 2012 by **Ahluwalia** (who had set up the UK's first learned society mentoring scheme at the British Pharmacology Society). Analysis of promotion data had identified a major bottleneck in the step from lecturer to senior lecturer. A register of mentors and mentees was created; structured training was provided for all participants; individuals from different institutes were matched to encourage interaction; and both mentors and mentees provided feedback on the mentoring experience to inform an iterative improvement cycle.
- **Measures to integrate clinical academics and NHS-employed active researchers**. The physical environment of SMD, and the applied focus of our research, supports integration of university and NHS researchers. On both campuses, a research Institute and an acute hospital are co-located with shared canteen, lecture theatres, and seminar rooms. This allows spontaneous and informal interaction as well as opportunities for cross-attendance at lectures, seminars and grand rounds. As detailed in 'Future Research Strategy' (B6, page 9), plans are

in place for extending university-NHS links through our Academic Health Sciences System. Where possible, NHS-employed researchers have honorary appointments at Queen Mary at all levels and joint annual appraisals with their academic line manager and clinical appraiser, prioritising fitness to practice and the revalidation criteria but seeking to align these with the person's research achievements and future objectives.

C2. SUPPORT FOR POSTGRADUATE RESEARCH (PGR) STUDENTS

Queen Mary, and SMD in particular, is one of the UK's most vibrant and stimulating settings for doctoral training. We offer an unparalleled environment for learning and personal development in interdisciplinary surroundings and with excellent NHS links. Of particular importance is the world-leading research community in London in general, which attracts the best students in Europe and gives them a vast range of post-doctoral options. The submitted groups for this Unit have presently a total of **347 registered doctoral students**.

In 2012 Queen Mary established a **Doctoral College** to support both PGR students and postdoctoral researchers. Strategically led by a Doctoral College Management Group, its activities are delivered and coordinated by two dedicated Researcher Development Officers (in the Centre for Academic and Professional Development) and a **Careers Adviser** for Researchers (QM Careers). These staff work in partnership with each Faculty to ensure that researcher development activities align to specific needs. Queen Mary operates a **points-based training system** to support delivery of our College-wide **training strategy** for PGR students, based on the RCUK endorsed **Vitae Researcher Development Framework**. This allows disciplinary flexibility, ensuring that all students receive career-appropriate transferable skills and research training. The Doctoral College also runs **PhD induction** for all PGR students, who are also encouraged to attend annual **Interdisciplinary Cohort Training** (courses include, for example, 'Maximising the Impact of Conferences and Networking'; and 'Understanding the Impact of your Research').

This combination of strong central governance, rigorous adherence to national training standards and a flexible and responsive approach Faculties enables all four Institutes returned in this UoA to provide a **personalised and discipline-specific programme** of PGR support, while making maximum use of various high-quality opportunities for PGR student development and interdisciplinary interaction provided by central services. Within SMD, all doctoral students have two **supervisors** (one of whom must have significant record of supervisory success) and all supervisors must undergo formal training, updated 3-yearly. Students have **formal milestones** with assessed submissions at 9 and 18 months and mock PhD vivas.

Our Institutes are **collegiate in ethos**, with formal and informal mentoring of early academics by more senior and experienced staff in close-knit subject families. All four institutes offer, in addition to numerous lecture and seminar programmes (see C1), opportunities to practice presentations and/or present work to fellow students and postdocs in a 'high challenge, low threat' intellectual environment. PGR students are strongly encouraged to present at conferences and participate in local and national competitions. Analysis of the destination of non-clinical PhDs from this unit over the REF period showed that of the 201 graduates, **60%** took up an academic post-doc.

Our institutes have an excellent record of attracting funding for discipline-specific doctoral training. BCI created **3 PhD studentships** from its **CRUK Centre grant**. WHRI hosted 4 prestigious PhD programmes: a **Nuffield Foundation Oliver Bird Studentship** scheme in rheumatology (16 students with KCL 2008-12); a new **British Heart Foundation** studentship scheme (16 students 2013-17); two successive **MRC *in-vivo* skills** MRes/PhD schemes; and an **MRC e-Health Centre** and **Translational Health Informatics Academy** (4 PhDs/year). We receive 3 MRC studentships and 2 students from **Barts Trustees** per year, and have attracted 16 **CASE studentships**.

D. INCOME, INFRASTRUCTURE AND FACILITIES

D1. INCOME

Total grant **expenditure** in this Unit from January 1 2008 to July 31 2013 was **£248M**, rising from **£40.3M** in 2008 to **£51.6M** in 2012 (a 28% increase). Grant **awards** totalled **£277.7** million over the REF period. With 144.4 FTEs, including 33 ECRs, the average income per REF returnable FTE in this unit in year 2012 is **£405K**. In 2008-13, our academics were involved in research collaborations with over **150** different companies. Research income from **industry partners** rose

from **£4.5M** in 2008-09 to **£6.1M** in 2012-13. Over the REF period staff in this unit received 25 EU awards (**£13.7M**). Total income from our local medical charity (Barts and the London Charity) was £**22**M. This included £3M to develop a Trauma Centre on the Whitechapel site and £0.5M for a Cytofluor Mass Spec cytometer to support the Immune Systems Theme. Institute-specific highlights in research income include:

- **Blizard:** Research spend increased from **£13.3M in 2008 to £20.4M in 2012** with several major awards including 42 grants of >£500K and 13 from £1M to £2.4M from NIHR, Wellcome Trust, MRC and EU FP7 programmes. Total research spend over the REF period was **£97M.**
- **BCI:** Increased annual grant income by 70% over the REF period with a total research spend of **£72.7**M. Particularly notable is the almost 7-fold rise in EU grant income 2008-13.
- **WHRI:** Research spend over the assessment period was **£57.2M** with an increase over the REF period of 43%. Staff in WHRI hold a Wellcome Senior Investigator Award, 11 Programme grants (BHF/WT/MRC), including 2 major European Union FP7 awards on stem cells (€11M), one Gates award (£1M) and one EU Marie Curie Co-fund (€6.5M) award.
- **Wolfson:** From Jan 1 2008 until July 31 2013, Wolfson staff returned in this unit had **£26.6**M in spend with an increase of 51% over the REF period. Research income was **£29.9M.** The **Wolfson Foundation** and **CRUK** have maintained their strong support for the Institute, together providing £1M infrastructure funding. The highlights were the establishment of the **Policy Research Unit in Cancer Awareness, Screening and Early Diagnosis** in 2010 and the awarding of **2 CRUK Programmes** In 2009**.**

D2. INFRASTRUCTURE AND FACILITIES

As described in Section A (Overview, page 1) and under individual institutes in Section B, Clinical Medicine research in this Unit has benefited from an unparalleled expansion and modernisation of adjacent NHS clinical facilities, with strategic juxtaposition of academic activity, with emphasis on attracting joint infrastructure funding to build academic-clinical collaborations. Headline developments on Charterhouse Square site include the **£300M Cancer Centre** at Barts Hospital linked to Barts Cancer Institute. The **Barts Clinical Trials Unit,** set up in 2006 (Sasieni, Wolfson), runs its own large-scale multi-centre trials and has grown to accommodate other trials in SMD, notably at BCI, which now has the highest levels of recruitment of NHS patients into cancer trials (see page 2), and its new partnership with the Facial Surgery Research Foundation to form the **National Facial, Oral and Oculoplastic Research Centre trials unit.** The £12M NIHR-funded **Biomedical Research Units** (BRU) in cardiovascular disease, which link research at the William Harvey Research Institute with clinical activity at Barts Health, are described on pages 6-7; they support career development of an expanding cohort of clinical scientists in this field. WHRI's clinical trials unit for pharmaceutical research maximises alignment of industry funding, NHS clinical care and the highest standards of clinical trial research (page 7); see also WHRI's arthritis Translational Research Centre. At Whitechapel, developments in infrastructure and laboratory facilities have allowed academics in the Blizard to align closely with clinical work in the new-build Royal London Hospital, driving experimental medicine findings directly into clinical practice, eg **Brohi's** £3M Trauma Research Centre, and **Williams's** Health Technology Collaborative in gastrointestinal surgery (page 5) in the £2.9M National Centre for Bowel and Cancer Research.

There has been continuing investment in **laboratory facilities** in all Institutes over the REF period, with refurbishment of the John Vane Science Centre (£8M), completion of the Heart Centre (£28M), and refurbishment and purchase of the ARC building (**new office and meeting room space** for 144 staff) in Whitechapel (£5M). Targeted investment in areas of strength have made a step-change in research capability. For example, the research activity of MCM in the Blizard (page 5) is underpinned by **s**tate of the art core facilities in Advanced Light Microscopy (capital investment of £2M) and a siRNA and miRNA genome–wide Screening Suite (£0.5M).

The Queen Mary Innovation Centre at Whitechapel (established 2010) was designed for start-ups but also provides 7000 ft^2 to house the **Joint Research Management Office** which offers a central service for ethics, grant applications, governance, costings, specialist support for EU applications, statistical support and data management, as well as post-award administration. See also Overview (page 1) and section B6 (page 9) for details of new facilities and projects.

E1. CONTRIBUTION TO THE DISCIPLINE OR RESEARCH BASE

Many staff are **international names in their field** and have gained the very highest recognition and accolades. For example, **N Wald (2008)** and **Wright (2005)** won **knighthoods**, **Costeloe** won a CBE for services to children (2008) and **Balkwill** OBE (2008) for science communication. **Balkwill** is a member of the Parliamentary Committee on Science and Technology (2010-15). **Flower, Wald** and **Beach** are **Fellows of the Royal Society**. The unit has **22 Fellows of the Academy of Medical Science**. **Cuzick** is **President of the International Society of Cancer Prevention** and **Williams** is **President of the Royal College of Surgeons**. **Caulfield** was recently made the **Chief Scientist of Genomics England**. **Wright** received honorary degrees from IC (2011), Durham (2009), St Andrews (2009), Bristol (2011) and Dundee (2012) and **Flower** from the University of Bath (2013), and in 2013 also received the Wellcome Gold Medal from the British Pharmacological Society. **Flower** was Chair of Royal Society's *Scientific Aspects of International Security* committee (2006-10), chair of Royal Society's *Brain Waves* panel (2010-present), and chair of Royal Society's *Industrial Fellowship Scheme* panel (2008-present). **MacDonald** received the Presidents Medal of the British Society for Gastroenterology 2008; **Van Heel** won BSG's Avery Jones Research Medal 2011; **Ahluwalia** won the GSK Clinical Pharmacology Prize 2012; **O'Toole** won Royal College of Physicians Parkes-Weber medal 2012; **Wald** won Jephcott Medal 2011 and Hamdan Award for Medical Research Excellence 2012; **Cuzick** won Honorary Fellowship, Royal College of Physicians 2012; **Duffy** the Alexander Margulis award for scientific excellence in radiology 2012; **Lorincz** won the Times Higher Research Project of Year 2012: **Korbonits** won the Society for Endocrinology Medal 2013; **McKnight won the** BMC Microbiology, Immunology, Infection and Inflammation Research Award 2012. Space restrictions mean that we are unable to list the **many international keynote lectures** given by staff.

E2. KEY COLLABORATIONS

We have taken a proactive and strategic approach to collaborations, which we illustrate with two examples. In **cardiovascular genomics**, we used a Wellcome Trust Strategic Award **(£15M**) from the WT Case Control Consortium to establish and lead international consortia such as **Global BP Gen** and **International Consortium for Blood Pressure Genome-wide Studies** (350 scientists from 234 centres worldwide: **Caulfield, Munroe**) and **Cardiogram** from which we have discovered 35 genes for blood pressure, 46 for coronary disease and 28 influencing urate and functional studies in arrhythmias. This leadership of major international genomics (**Munroe, Tinker, Caulfield**) enabled us to lead the **MRC International Mouse CV Traits Consortium** (2011-16) with multiple UK universities. In **inflammation research**, the **Pathobiology of Early Arthritis Consortium** (PEAC) is an MRC strategic funded (**£700K** 2008-13) multi-university partnership led by **Pitzalis**, which created national resource of ultrasound directed synovial biopsy in rheumatoid arthritis from which we developed a major international partnership with **Genentech-Roche**. Pitzalis attracted wide international industrial and national partnerships, leading to MRC/AR-UK MATURA **(£4.7M**) and NIHR (**£1.2M**) awards for Stratified Medicine Programmes of biologics in rheumatoid arthritis. Our reputation in Endocrinology has been used to create the **WHRI Translational Academy** with extensive university and Industrial partnerships for international postdoctoral exchange **(EU €6.5M**) award. Other major collaborations from SMD include:

INTERNATIONAL: Cuzick leads the **£7.7M** Astra Zeneca *International Breast Cancer Intervention Trial (IBIS-2),* 25 international centres (2004-12); **Dunkel**; **£492,585** Academy of Finland and Sigrid Juselius Foundation, *Modulation of Developmental Plasticity by Sex Steroids.* Co-Investigator Sankilampi, University of Eastern Finland (2008-2014); **Giovanonni: $3.5M** National MS Society, USA *A novel strategy to deliver growth factors to the sites of inflammation in multiple sclerosis* (2005- 2010); **Grigg**: **£2.3M** MRC *An advanced cookstove intervention to prevent pneumonia in children <5 in Malawi: cluster RCT,* with Liverpool (2013-17); **Hitman**; **£3.0m** Coordinator *EU FP7 program Genomic and lifestyle predictors of foetal outcome relevant to diabetes and obesity and their relevance to prevention strategies in South Asian peoples*, with 16 International partners across Europe and South Asia *(2012-15);* **Hobbs: £1.57M** Norwegian government, coinvestigator *SER100 for the Treatment of Resistant Hypertension in the Elderly*, with partners in Norway (2013-15); **MacDonald: £300K** GSK-USA lead, *Kinase inhibitors in IBD* (2011-13); **Martineau** (PI), MRC **£2.5M** *Trial of vitamin D supplementation for prevention of latent TB infection in Delhi primary schoolchildren (ViDiKids)* with partners in India (2014-19); NIHR £894K *Vitamin D & Longevity*

(VIDAL) trial, co-pi with Peto, LSHTM (2012-14); **Pennington** (PI)**,** with Silva-Santos, **Oporto** "Fundação para Ciência e Tecnologia" Portuguese government funding €400K to train Portuguese PhD students in UK labs (2009-present); **Perretti: $1.2M** UniGene Laboratories) Calcitonin-glucocorticoid cotherapy and novel annexin peptides, with industry partners in USA (2008-11; **Prendergast: $16.6M** (Gates Foundation 2010-16), **£3M** (DFID 2010-16) and **$866K** (Swiss Development Cooperation 2012-13) *Sanitation Hygiene Infant Nutrition Efficacy (SHINE) trial,* Zimbabwe, with Johns Hopkins USA; **$1.8M** (Gates) *Azithromycin to prevent growth faltering: understanding mechanisms for public health intervention*, with LSHTM (2008-13); **£834K** MRC *Role of enteropathy in pathogenesis of severe acute malnutrition in HIV-infected African children* (with partners in Zimbabwe/Zambia 2014-17); **£741K** MRC *Causes and consequences of residual immune activation in HIV-infected children on ART in resource-limited settings*, with UCL (2011-15); **Sifrim: £550K** Ono Pharmaceuticals Belgium (2012- 15); **Van Heel: £1.2M** Wellcome Trust, lead) *Extended genome wide association study in coeliac disease*, with Groningen (2008-11).

NATIONAL: Duffy: £4.7M lead, DoH *Policy Research Unit in Cancer Awareness, Screening and Early Diagnosis,* with 6 UK HEIs; **Foster: £4.9M** (MRC 2012-16, coapplicant) *StopHCV (Stratified Medicine Grant),* multicentre study led by Oxford; **£2M**, (Medical Research Foundation 2013-16, coapplicant) *Hep C Research UK*, multicentre study led by Glasgow; **Nizetic**: **£2.5M** (Wellcome Trust Strategic Award 2012-17), *The London Down Syndrome Consortium*; **Van Heel/Trembath: £2.5M** (Wellcome Trust Strategic Award 2013-17, joint leads) *British Autozygosity Population Gene Function Study*, with Sanger Institute, Broad Institute USA, U of Bradford, U of Cambridge; **Van Heel, MacDonald: £58.7M** (NIHR 2012-17, coapplicant) *Guy's and St Thomas' NHS Foundation Trust and King's College London Biomedical Research Centre*; **Van Heel, £**1.2M, MRC 2011-14, lead applicant) *Exome sequencing and mutation identification in familial coeliac disease*, with UCL.

Our academics are particularly well represented on **national panels that set research priorities and/or oversee training of young researchers**. Examples include:

- **MRC:** *Clinical Training and Career Development Panel* 2013-16, **Balkwill**; *Molecular & Cellular Medicine Board* 2008-12 **Gribben**; *Neuroinflammation steering group* 2013, **Giovanionni;** *Stratified Medicine Scientific Expert Panel* (2012-present); *TSB Biocatalyst Major Awards Panel* (2013-present), MRC Clinical Research & Career Development Panel *(2006-10, Chair); Stem Cell Fellowships Panel* (2005-9 Chair)-**Lemoine;** *Non-Clinical Training panel* (Chair), *Training and Careers panel* 2012-15**,** *PSMB* 2007-11, *Patient Cohort panel* 2009-11, *African Leaders of the Future* 2013-**MacDonald**; *PSMB* 2004-08-**Trembath**.
- **CRUK:** *Clinical Trials Advisory Committee*–**Gribben** (2008-11); *Scientific Advisory Board*-**Cuzick** 2013–current; *Drug Discovery Expert Review Panel, New Agents Committee* (2013-present)- **Hagemann**; *Research Bursaries Committee*, *Clinician Scientist Panel*-**Hodivala-Dilke** (2011-14); *Biomarker Expert Review Panel*-**Lemoine** (2012-present); *Population Research Committee* (2002-current); *New Investigator Awards* (2011-current)-**Sasieni**; *Biological Sciences Grant Committee*-**Van Haesebroeck** (2010-present).
- **NIHR:** *Clinician Scientist Board* (2012-present, Chair), *Invention for Innovation Challenge Panel* (2012-present, Chair)-**Lemoine**; *Programme Grant Panel* (2009)-**Martineau**; *Fellowships Committee* (2008-present)-**Thiemermann.**

Representation on other national and international grant panels (selected examples):
Ahluwalia, *BHF Project Grant panel* (2009-12); **Balkwill,** *Breakthrough Breast Cancer Scientific Advisory Panel (*2012-present); **Caulfield,** *NICE Quality Standards Group* (2012-13); **Chapple**, *BBSRC Panel D* (2014-17); **Cuzick,** *EUROGIN scientific advisory board* (2010 – current); **Dell'Accio,** *Arthritis Research UK project grants panel* (2013-15); **Flower,** *Chair, Diabetes UK Scientific Advisory Board (*2007-10); **Giovannoni,** *Institute of Medicine, USA Biomarker working group* (2009), *Wellcome Trust Seeding Drug Discovery Funding Committee* (2013), **Gribben,** *Leukaemia & Lymphoma Research Fund Advisory Panel* (2006-11), *MHRA Haematology Oncology Expert Panel* (2012-present); **Hitman**, *Diabetes UK Grants Panel* (2013-15); **Hodivala-Dilke**: *National Cancer Research Institute Science Committee* (2012-15), *Association for International Cancer Research Science Committee* (2012-15); **Lemoine**, *Irish Health Board / Medical Research Charities Advisory Panel* (2012-present, Chair), *Prostate Cancer UK Scientific Advisory Board* (2012-present Chair), *Diabetes UK Scientific Advisory Board* (2011-present Chair), *Pancreatic Cancer Research Fund Scientific Advisory Board* (2007-present Chair), *Pancreatic*

Cancer UK Scientific Advisory Board (2006-present Vice Chair), *Lister Institute of Preventive Medicine Scientific Advisory Committee* (2012-present), *Medical Research Foundation Trustee* (2008-present), *Portuguese Foundation for Science & Technology Advisory* Board (2004-present), *Hong Kong Research Grants Council Biology & Medicine Panel* (2007-13); **MacDonald,** *Action Medical Research (*2012-15), *NC3R's (*2013-15), *CrackIT -Virtual Infectious Disease Research (*2013 Chair), *Netherlands Genomic Initiative* (2005-12); **Marelli-Berg,** *Icelandic Research Fund Committee (*2010); *National Institute of Health/ National Institute of Arthritis and Musculoskeletal and Skin Diseases Centers of Research Translation Committee* (2010); *Deutsche Forschungsgemeinschaft (*2009-2011); **Marshall**, *Breast Cancer Campaign Scientific Advisory Board* (2011-present), *Dystrophic Epidermolysis Bullosa Research Association Advisory Board (* 2008-present), **Martineau,** *NICE Public Health Advisory Committee on Vitamin D,* (2013-14); **Moss,** *Breast Cancer Campaign Scientific Advisory Board* (2011-present; **Munroe,** *Swedish Research Council, Medicine and Health Panel* (2012- present); **Nourshargh,** *BHF Fellowship Committee (*2011-14), *Wellcome Trust's Peer Review College* (2012-present), *Chair of Academy of Medical Sciences Committee* (SC3) for election of new Fellows (2012-16), *Academy of Medical Sciences Clinical Fellowship panel* (2013); **Perretti,** *Wellcome Trust Physiology Panel* (2005-08); *Arthritis Research UK Fellowship Panel (*2013-present); **Sasieni,** *Ministerial Advisory Committee on Cervical Screening* (2002-present); **Tinker,** BHF Project Grant panel 2011-14, *CrackIt Panel Member for NC3Rs (*2013-14), *Wellcome Trust Physiology and Pharmacology panel* (2005-09); **Van Haesebroeck**, *CRUK Biological Sciences Grant Committee* (2010-present), *Association for International Cancer Research Science Committee* (2009-present), *Fonds de la Recherche Scientifique Belgique Life & Health Sciences Committee* (2010-present Chair); **Van Heel,** *Coeliac UK Health Advisory Committee* 2009- present, *CORE (British Society of Gastroenterology) Awards Panel (*2008-present); **Wright**, *British Skin Diseases Research Trust Scientific Committee* (2001-present Chair), *Kings Health Partners R&D Challenge Fund Scientific Committee* (2011-present Chair), *UEA Clinical Academic Initiative Advisory Board* (2010-present Chair).

EDITORIAL BOARD MEMBERSHIPS: Ahluwalia, Editor, *British Journal of Pharmacology* (2008-10), Senior Editor *British Journal of Pharmacology* (2010-present); **Blackshaw,** Editorial Boards, *Current Opinion in Pharmacology* (2001-present), *American Journal of Physiology: Gastrointestinal and Liver Physiology* (2009-present), Gut (2011-14); **Chernajovsky** Editor *Arthritis Research and Therapy* (1999-present); Gene Therapy (2001-present); **D'Acquisto** Editor, *Biochemical Pharmacology* (2008-present); *Mediators of Inflammation* (2007-present); *Frontiers in Immunology* (2010-present).**; Dokal,** Editorial boards, *Haematologica* (2007-present), *Bio-Med Central* (2002-present); **Dunkel** -Editor *Hormone Research* (2008-present); **Flower,** Editorial Boards: *British Journal of Pharmacology*. (1998-present), *Nature Reviews Drug Discovery* (2001-present), *Current Opinions in Pharmacology* (2001-present); **Foster** Editor-Elect, *Journal of Viral Hepatitis*; **Gribben,** Associate Editor, *Blood (2008-present);* **Grigg***,* Associate Editor, *Thorax* (2010-present); **Hitman** Editor-in-Chief, *Diabetic Medicine (2011-present)*; **Kelsell,** Section editor *Cell Tissue Research* (2011-), Associate editor *Journal of Investigative Dermatology* (2006-2011); **Lemoine**, Editor-in-Chief, *Gene Therapy (2008-present)*, Commissioning Editor, *British Medical Bulletin*; **Leslie,** *Diabetic Medicine* (2011-present), *Diabetes Care* (2009-12); **MacDonald** Section editor, *IBD Journal* (2010-present), Associate Editor, *Mucosal Immunology* (2009-present*);* **Marelli-Berg**, Editor, I*mmunology* (2010-present); *Frontiers in Pharmacology* (2011-present); *Journal of Immunology* (2011-present); *Frontiers in Immunology* (2012-present). **Munroe**, Editor *International Journal of Molecular Epidemiology and Genetics* (2010-present), *British J Pharmacology* (2008-12), *Cardiovascular Medicine* (2012-present); **Nourshargh** Editor, *European J Immunology* (2013-present); *British Journal of Pharmacology* (2010-12); *Microcirculation* (2009-11); **Perretti,** Editor *Inflammation* (2007-present), *Current Opinion in Pharmacology* (2010-present), *Frontiers in Pharmacology* (2010-present); **Pitzalis** Editorial board, *Arthritis Research & Therapy* (2010-present), *Inflammation* (2007-present); **Sifrim,** Editorial Board, *American Journal of Gastroenterology* (2009-present); **Thiemermann** Senior Editor (Europe), *Shock* (2003-present), Editor, *Critical Care Medicine* (2003-10), *Pharmacological Research* (2008-present); **Tinker,** Editor, *British J Pharmacology* (2005-09); **Ye –** Editor, *Heart* (2010-13), *BMC Medical Genetics (*2010-12), *Clinical Science* (2008-present).