Institution: University of Leicester

Unit of Assessment: 1 Clinical Medicine

a. Overview: This submission is from the **College of Medicine, Biological Sciences and Psychology** (CMBSP: Head, Prof David Wynford-Thomas), which was established as one of four Colleges through a major reorganisation of the University in 2009. The College comprises eleven Departments (four in Biological Sciences, six in Medicine and one in Psychology) which primarily reflect our teaching activities and provide administrative and management centres. Importantly, though, our research is organised, not through departments, but through **nine cross-disciplinary Themes.** These provide the key organisational units for the development and delivery of our research strategy, and form the basis of all our submissions to Main Panel A. **Four themes** in particular form the core of this submission **- Cardiovascular, Respiratory, Diabetes, and Cancer.** The Themes have produced a **step-change in translational research** by enabling cross-disciplinary collaboration combining expertise from laboratory, clinical and population-based sciences to address research questions held in common and by focussing on both T1 and T2 gaps. We have also facilitated translation by the colocation of basic and clinical researchers. The themes included here also benefit from collaboration and joint positions with the embedded **MRC Toxicology Unit,** located within the biomedical section of the University's central campus. Our clinical research is underpinned by an excellent and integrated relationship with the **University Hospitals of Leicester (UHL) NHS Trust** (Leicester Royal, Leicester General, and Glenfield Hospitals). The College is represented on the Trust Board and key sub-committees, while conversely, both the Medical Director and the Director of Research and Development for UHL are University employees (submitted with this UoA). The effectiveness of this partnership is best illustrated by our joint success during the REF period in winning and establishing **three NIHR Biomedical Research Units** (BRUs) - in Cardiovascular, Respiratory, & Lifestyle research - the largest number to be awarded outside the Oxbridge-London triangle and each representing the achievements of the cognate Themes. Moreover, our Cancer theme has renewed its **Experimental Cancer Medicine Centre (ECMC)** and, by capacity and partnership building has achieved **CR-UK Centre Status.** Finally, a wider University NHS collaboration has established first a local and now a regional **East Midlands Collaboration for Leadership in Applied Health Research and Care (CLAHRC)**.

b. Research strategy

SIGNIFICANT CHANGES 2008-2013: Following a review in 2008/9 we established a strategy based on the **four principles of FOCUS, INTEGRATION, INVESTMENT** and **PARTNERSHIP.** Our **FOCUS** has been on a relatively small number of **National and international Research Priority** areas where we have recognised strengths and capability and which are of high relevance to health. Thus, we have established our major research **Themes** and invested with demonstrable success in our **cardiovascular, respiratory and cancer** portfolios. We also encouraged groups to accumulate critical mass for support and investment, as exemplified in this period by **diabetes**, which has grown over the period to become a major theme.

INTEGRATION of basic and clinical research and promotion of **inter-disciplinary** research has been actively encouraged. Investigators whose work is predominantly clinical or lab-based work jointly within each of our Themes. We emphasise that our Themes should not be seen as "silos" and investigators often participate in more than one (e.g. Our strength in GWAS work reflects essential interactions with colleagues entered to UoA2 and clinical researchers; similarly, structural biologists and cell signalling specialists (UoA5) have also been essential to work reported here).

INVESTMENT, directed to theme priorities and **Building our Capacity and Sustainability** has been used to develop a high-quality **infrastructure** and provide excellent facilities and environments for our researchers. This has involved completion of four new construction projects (£35M) and development of key facilities (see section d). *In short, the landscape for biomedical research in Leicester has been absolutely transformed in the last 5 years.* Finally, we emphasise **PARTNERSHIP** with other organisations in the local and regional academic and health sectors has created a **seamless** structure which allows novel findings in the laboratory to be taken through translational research into patients then into clinical trials and implementation. This aspect of our strategy is aided by having a joint Research and Development Office with our main partner NHS Trust (UHL), and co-hosting three Biomedical Research Units, two clinical research networks (in Diabetes and Stroke) and the Leicestershire Northamptonshire and Rutland CLAHRC.

Wherever appropriate we promote **national and international collaborations** to ensure

excellence. Many areas of research require large-scale data or benefit from multi-level expertise and our researchers continue to play significant roles in major international consortia (see section e). The evidence of the success of this strategy is demonstrated below.

OVERARCHING RESEARCH PLANS

Our strategy will continue to follow the principles of focus, integration, investment and partnership. We first set out our overarching strategic objectives for the next five years then provide a theme (research grouping) specific commentary.

Main Objectives and Activities: We have established the capacity to acquire, store, analyse and translate into practice data from the phenotypes and genotypes of our patients in longitudinal and cross-sectional studies. Further involvement in regional, national and international studies will continue to enhance the strength of this work. *Our priorities will be:*

1. To achieve international recognition as a research centre for *Personalised/Stratified Medicine.* (>30% of our submitted outputs contribute to this area). Our development will be focussed on: i) Discovery and hypothesis generation by investing in our patient clinical infrastructure emphasising biobanking and informatics. ii) Mechanistic investigations pursuing these hypotheses by developing: (a) Use of *in vivo* models enabled by our new animal and transgenic facilities (CRF), (b) Use of tissue model systems based on primary explant cultures and induced pluripotential cells (iPCs) and (c) recall of patients based on genotype or phenotype. Our theme organisation and developments in our physical infrastructure have brought together clinical and lab workers to enable this. This work complements our established use of cellular and molecular model systems and provides an important drug development pipeline (see section d; CTT).
2. To maximise the research value of routinely collected clinical data through informatics investments focussed on our BRUs and Cancer theme. We highlight further development of our *Biomedical Research Informatics Centre* from its origin in the Cardiovascular BRU to serve the needs of the other BRUs and the Cancer group.
3. To further expand our portfolio of focussed research centres by hosting a *NIHR Biomedical Research Centre.*
4. To *redevelop and re-focus our main campus facilities* in the Medical Sciences Building following the opening of our new £30M Medical Teaching Building in 2015.

ACHIEVEMENTS AND PLANS OF OUR RESEARCH GROUPINGS: We identify below the category A FTE staff submitted under each heading but emphasise membership of the related Theme includes staff submitted to other UoAs and reflects cross-disciplinary collaboration. In each case total Theme membership including associated research staff ranges from ~60-120 FTE.

CARDIOVASCULAR SCIENCES (25.4FTE) The distinctive features of cardiovascular research in Leicester are its focus on common cardiovascular disorders and the strong translational emphasis, with close integration of basic and clinical researchers. We have three Sub-themes:

Genomic and Proteomic biomarkers: We are at the forefront of research that seeks to unravel the genetic basis of complex cardiovascular diseases and traits. This is exemplified by our leadership roles in major national and international genetics consortia (e.g. WTCCC, CARDIoGRAM+C4D, ICBP). Our principal focus has been on coronary artery disease (CAD) genetics (e.g. *Samani1,2; Tomaszewski1)* but extends to other cardiovascular diseases and traits including abdominal aortic aneurysms (*Bown1*), heart rate (*Samani3*), blood pressure (BP) (*Tomaszewski2*). Tobin and Wain (returned in UoA2) have co-led genome-wide meta-analysis of BP (ICBP, Nature, 2011;478103-9; Wain L et al Nat Genet 2011; 43:1005-11). In related work, a newly-appointed lecturer has generated critical evidence for a primary role of biological ageing in risk of CAD (*Codd1*). Altogether, researchers in Leicester have contributed to over 200 papers related to cardiovascular genetics since 2008. The findings have provided powerful new insights into the pathogenesis of these common disorders and identified several new therapeutic targets (e.g. see *Samani3*). Closely aligned to our genomics programme is our biomarker discovery and validation programme focused on heart failure and acute coronary syndromes. Building on previous work which contributed to the introduction of pre-pro BNP as a robust rule in/out marker for heart failure, we have identified several further novel biomarkers related to these diseases during this period (e.g. see *Ng LL1-4, Squire1,2*). Central to these programmes is the significant step change in biobanking of DNA, blood and tissue samples afforded by out BRU infrastructure.

Key achievements: 1) Identification of over 46 genetic loci that affect risk of CAD, providing novel insights into the pathophysiology of this disease (*Samani1*); 2) Demonstration of the role of variation in the Y chromosome with risk of CAD and link to innate immunity (*Tomaszewski1*); 3)

Identification of 7 loci associated with telomere length and use of these as genetic instruments to support a causal role for biological ageing in CAD (*Codd1*).

Cell biology and cell signalling: We work on platelets, leucocytes, endothelial cells, vascular smooth muscle cells and cardiomyocytes, focusing on signalling mechanisms through GCPRs, tyrosine kinase receptors and ion channels. The work benefits from a strong link with the genomics sub-theme through which we have identified novel proteins in human platelets that are shedding new light on the regulation of platelet function (*Goodall1,3,4; Mahaut Smith1,4*). We have further advanced understanding of the role of Tie receptors in vascular maintenance and protection (*Brindle*1-3) and developed a novel ligand-trap approach by directed evolution to create potential therapeutic agents (*Brindle* 4). Working with structural biologists, we have better defined the structure of the cardiomyocyte hERG K^+ channel and improved understanding of its drug interactions that may be relevant to drug-induced QT prolongation (*Mitcheson1-4*).

Key achievements: 4) Identification and characterisation of Kv1.3 as the sole voltage-gated K+ channel of human platelets and megakaryocytes, which has a regulatory role in platelet function and production (*Mahaut Smith1*); 5) First insight into the interaction of two intracellular structural domains regulating hERG-channel function and timing cardiac repolarisation (*Mitcheson4*)

Cardiovascular physiology and clinical trials: Key areas of physiological study which have directly led to clinical translation include (i) autoregulation of cerebral blood flow led by our Medical Physics group (*Panerai2,4*), which has contributed to the design and implementation of studies to examine the clinical consequences of blood pressure manipulation after stroke (*Robinson2,3*) (ii) the genesis of ventricular arrhythmias (in particular the role of the autonomic system) (*Brack1*) which has led to the development of a novel surface ECG based biomarker that predicts risk of sudden cardiac death in patients with ischemic cardiomyopathy (*Ng GA,2*); and (iii) the mechanisms that contribute to acute kidney injury during cardiac surgery (*Murphy1,2*), which have resulted in on-going clinical trials of sildenafil and blood transfusion to reduce kidney injury. At the same time major multi-centre clinical trials led by our researchers, some of them Category C, have informed or changed clinical practice (*Gershlick1; Robinson1, Coats1,2; Toff1; Peek1*).

Key achievements: 6) Evidence for a continuing role for thrombolytic therapy when primary percutaneous coronary intervention cannot be performed in an expeditious fashion (*Gershlick1& case study*); 7) randomised trial evidence for the benefits of extra corporeal membrane oxygenation in selected adult patients with severe cardio-respiratory distress (*Peek1*).

The headline outcomes of these activities have been the establishment in 2009 of our NIHR Cardiovascular BRU (with renewal in 2012), and the completion in 2012 of our new Cardiovascular Research Centre enabling colocation of CVS researchers at the Glenfield site. The award of a second BHF Chair in Cardiac Surgery to Murphy to complement the Chair in Cardiology held by Samani, and a £7 million endowment from the John and Lucille Van Geest Foundation to create a state-of-the-art proteomics facility and establish a Cardiovascular Research Fund further underline the recognition and momentum of our research.

Plans for the next 5 years:

1. To consolidate and further develop our work in cardiovascular genomics by (i) extending our discovery programme to other cardiovascular diseases (e.g. aortic valve disease); (ii) integrating a broader range of "-omics" data (e.g. through collaborating with the MRC-NIHR Phenome Centre to develop high quality metabolomics data in some of our key cohorts) (iii) expanding our functional genomics programme to understand the mechanisms by which the genetic variants we have identified affected cardiovascular risk and identify novel therapeutic targets. To this end we have made key new junior faculty appointments to lead our *in vitro* and *in vivo* studies, established a state-of-the-art biomarker and proteomics facility in the new BHF CRC to undertake functional genomic studies including approaches such as genomic editing of pluripotent stem cells and secured high-quality grants and international collaborations including with industry (e.g. the Leducq CADGenomics award and the EU FP7 programme CVgenes@target).
2. To harness the increasing potential of high throughput, unbiased proteomics that is made possible by our new Van Geest Biomarker facility to identify novel biomarkers related to cardiovascular diseases. Building on our success in systolic heart failure and acute coronary syndromes this resource will be applied to other diseases (e.g. diastolic heart failure) for which we already have significant cohorts and banked samples.
3. To strengthen and expand our basic science and translational research portfolio by making key strategic appointments, as illustrated by the recent appointments of Cao to lead work on

angiogenesis and the cross-talk between adipose function and atherogenesis and Condorelli (visiting chair) to help develop a programme of research on microRNAs in CVS disease.
4. To fully utilise the capabilities provided by our BRU to undertake early phase translational clinical studies Over 35 such studies are currently in progress covering a broad spectrum of cardiovascular conditions from ischemia-reperfusion injury, to detecting and reducing the risk of neurological damage during open heart surgery, to better predicting risk of sudden cardiac death. These examples originate from basic research conducted in house. We also plan to harness the opportunities provided by our strong genomics, proteomics and clinical trials capacities to develop studies in stratified medicine. We will also increase our already strong engagement with industry partners in early phase clinical research.
5. To continue to develop and lead major outcome clinical trials. Current multicentre trials include CULPRIT, which will inform whether coronary intervention for ST elevation MI should be restricted to the culprit vessel or include all vessels with stenoses and the UK TAVI assessing appropriate use of percutaneous aortic valve replacement (versus surgery) for severe aortic stenosis.
RESPIRATORY SCIENCES (15FTE): Our research falls into three main areas:
Airways Disease: Focussing on the pathogenesis and management of asthma and COPD, we have developed novel approaches to understanding disease heterogeneity including the use of bio-statistical techniques such as cluster analysis, the concept of endotypes of asthma and the deconstruction of airway disease into its component pathophysiological abnormalities. This has enabled recognition of distinctive roles for epithelial, mast, and smooth muscle cells (e.g.*Bradding4*), fungal sensitisation (*Wardlaw1*) and in particular, eosinophilic inflammation in airways disease (*Brightling1,4*) leading to the development of novel approaches to personalised medicine; notably, the testing of a therapeutic monoclonal antibody directed to eosinophilic inflammation in severe asthma. Our work is structured around the translational pathway embracing molecular discovery, phenotyping and biomarkers, clinical interventions and implementation. Molecular discovery is focused on mechanisms of lung inflammation and remodelling in asthma and COPD utilising our expertise in cell biology and using primary human tissue from patients and healthy controls. (particular interest being in ion channels as a target for therapeutic intervention (e.g. *Amrani3, Bradding3*)). These approaches are now being deployed to exploit the genetic information Tobin (UoA2) and Ian Hall have obtained to identify molecules that could be playing a role in lung remodelling. Brightling (supported by Siddiqui) is leading AirProm a large European funded programme using a systems biology approach with particular emphasis on novel imaging techniques. This followed a large MRC/AstraZeneca study in which deployed cluster analysis was deployed to recognise subtypes of COPD exacerbations. Such close partnerships with the pharmaceutical industry continue with the mepolizumab programme as our flagship example. Bradding and Amrani are using gene expression in bronchial tissue in asthma in collaboration with Genentech to identify molecules that control the different patterns of inflammation we have observed in asthma. We are members of the MRC-ABPI translational research partnership (TRP) into respiratory disease.
Key achievements: 1) Efficacy of anti-IL-5 monoclonal (mepolizumab) antibody in preventing severe exacerbations in asthma. (*Haldar2)*; **2)** Unbiased identification in a large biomarker study of three distinct biological clusters of COPD exacerbation (designated bacteria-, virus- or sputum eosinophilia- associated) opening up new opportunities for selective therapy. (*Bafadhel1)*;
3) Application of cluster analysis to demonstrate phenotypic subgroups in asthma with important implications for management. (*Haldar3)*
Lung Infection: This group encompasses microbiologists, immunologists and both respiratory and infectious diseases clinicians and benefits from collaboration with colleagues in UoA 5. In pneumococcal infection a long-standing programme has elucidated the importance of pneumolysin and neuraminidase in virulence. These studies have translated into vaccine, host susceptibility and, most recently a £3.6m WT (WT) seeding drug discovery programme leading to a recently established spin-out (Axendos Therapeutics). In tuberculosis our activity spans cost-benefit analyses of immigrant screening (*Pareek1)* to studies on bacterial physiology in vivo, particularly sputum, where our success in revealing long suspected multiple bacillary sub-populations has opened up new opportunities to study chemotherapy and transmission. The influenza group was closely involved in guiding the department of health during the “Swine” flu epidemic and delivered the first H1N1 vaccine trial. Our immunological studies are concentrated on the complement system and, while respiratory infection is a key focus together with sepsis, there are also strong

collaborations with cardiovascular and renal colleagues directed to reducing organ reperfusion injuries by counteracting complement-mediated pathology (*Schwaeble1*).
Key Achievements: 4) Recognition that a host molecule can determine the invasive outcome of a pneumococcal infection (*Andrew2)*; **5)** Discovery of persister-like phenotypes of *M. tuberculosis* in sputum with implications for the transmission and chemotherapy of TB. (*Barer1,2)*; **6)** Vaccine studies supporting the control effort of the H1N1 influenza outbreak. (*Nicholson1,2)*
Lung Cancer: This is addressed in the Cancer section.
The headline outcomes have been the securing in 2012 of NIHR-BRU status and the building of a new clinical respiratory research facility (see section d).
Plans for the next 5 years:
1. Our major priority is to secure renewal of our NIHR respiratory BRU in 2017. To help achieve this we aim to make new appointments over the next five years including: i) a non-clinical chair in respiratory immunology (appointed and due to start early 2014); ii) a clinical chair focussed on investigating novel therapeutic interventions; iii) a clinical chair in infectious diseases focussed on respiratory infection; iv) two non-clinical lecturers in inflammation biology related to airway disease; and v) a clinical senior lecturer in tuberculosis research.
2. To expand and enhance our respiratory laboratory sciences facility on the Glenfield site.
3. In partnership with the CTT, to establish a Centre for Respiratory Therapeutics to identify novel therapeutic targets in asthma, COPD and ILD.
DIABETES (5FTE): The group is based at the Leicester Diabetes Centre[d] at Leicester General Hospital. Our focus is in three areas: 1) **Screening and early detection,** 2) **Predictors of progression and prevention**, and 3) **Complex interventions and self-management programmes**. In area (1) Leicester is one of two UK and European centres leading in screening for both impaired glucose regulation and established type 2 diabetes. We have a particular emphasis on the young, black and minority ethnic populations and are also developing novel ways of accessing and engaging the wider population. In (2) we have established an inter-disciplinary platform combining expertise across the biomedical and sociological disciplines to develop and evaluate novel methods for preventing metabolic disease, particularly type 2 diabetes, and to improve the health of the nation. The work is particularly focussed on physical activity. Finally in (3) our group has led and hosted the diabetes education and self-management on-going and newly diagnosed collaborative (DESMOND) since 2002 and has also led the international and national research agendas in diabetes self-management. DESMOND is the only self-management intervention that has been rigorously assessed for effectiveness and cost-effectiveness and is now commissioned by more than half of all primary care organisations nationally as well as intly (Australia).
Key Achievements: 1) We have pioneered two new risk assessment scores. Our Self-Assessment Score is now available online at the Diabetes UK website and has attracted over 274,000 hits since its launch in July 2010 while our Practice Score is an automated tool ranking those at risk and applicable in General Practice. Incorporating the new diagnostic criteria for diabetes it has been used in the multicentre ADDITION Study. (*Davies2)*; **2)** We have significantly advanced the evidence-base for the importance of physical activity by leading an international collaborative which uniquely demonstrated that for every 2000 steps/day change over a year in pedometer assessed habitual walking activity there was an 8% difference in the subsequent risk of cardiovascular morbidity and mortality (*Yates 1)*; **3)** We have led the largest global randomised controlled trial of structured education in type 2 diabetes and have subsequently published cost effectiveness and long-term data. (*Davies1)*
The headline outcomes have been: 1) award of the Leicester / Loughborough Diet and Physical Activity BRU, 2) establishment of the Leicestershire, Northamptonshire and Rutland CLAHRC (recently renewed in partnership with Nottingham), 3) leadership of two NIHR programme grants and an HTA trial grant, and 4) leadership of the South East Midlands Diabetes Research Network.
Plans for the next 5 years: The group will consolidate and further develop the activities outlined above. We will establish new facilities for biomarker discovery and analysis, capability for insulin clamp techniques and vascular assessment and imaging. Our specialist focus will be on expanding the range of evidence-based lifestyle and self-management therapies available, applying the same rigor in development and evaluation as that traditionally afforded pharmaceutical products.
CANCER (22.2FTE): This theme represents our most significant achievement in convergence and cross-disciplinary integration in this UoA, involving staff from three College departments, the MRC

Toxicology Unit, the Respiratory BRU and the NHS. Cancer research activities comprise basic and clinical researchers leading and participating in international multicentre studies and trials. Research programmes benefit from extensive collaboration and interaction with colleagues in UoA5 and cover focussed topics in: **Cancer Cell Mechanisms, Tumour Biology, Cancer Chemoprevention and Stratified Medicine**. The conduit for translational and early phase clinical trials is the ECMC, underpinned by a dedicated early phase clinical trials unit, while our strategy to build our basic research portfolio so that we function across the full translational spectrum has led to the recent award of **CR-UK Centre status**. We also host leading UK research centres in thoracic oncology and B cell malignancies.

Cancer Cell Mechanisms: Understanding the core mechanisms by which cancer cells deregulate proliferation and evade cell death is a key aspect of our work and is integrated with drug development programmes. Mechanisms of control of mitotic progression, and how errors promote chromosomal instability, is a key area and uses a combination of X-ray crystallography, biochemistry, and cell biology (*Bayliss1-3*, *Fry1,2*). Cell death research has focussed on the BCL2 family as well as TRAIL, with recent determination of a new model for DISC formation (*MacFarlane1,2*) benefiting from a strong collaboration with structural biology (Schwabe and Fairall, UoA5). Gene expression control related to toxic injury is an additional strength, encompassing mechanistic studies of protein translation and miRNA regulation (*Willis1-4*).

Key Achievements: 1) Determination of the first atomic structure of mitotic kinase Nek7 showing that the kinase is autoinhibited, with Nek9 providing relief of autoinhibition, and thus identifying a target for selective kinase inhibitors *Bayliss1*; **2)** Reconstitution and structural modelling of the TRAIL DISC leading to a new model of a caspase-8 activating chain, and a novel therapeutic approach for targeting TRAIL *MacFarlane2.*

Tumour Biology: Research on primary human tumour tissue or mouse models genetically engineered to recapitulate the human disease is of increasing importance for understanding mechanisms of cancer progression *in vivo* and for preclinical evaluation of novel therapies or biomarkers. Through NHS links, we have excellent infrastructure for analysing and processing human tumour samples (particularly lung and colorectal cancers), coupled with an extensive mouse model portfolio.

Key Achievements: 3) Treatment of RAS mutant cancer cells with BRAF inhibitors paradoxically activates the ERK pathway inducing cell growth through CRAF with mouse model verification. This work highlighted the importance of patient stratification in the clinical use of vemurafenib *Pritchard1; **4)*** Expression of EMT-inducing transcription factors is reprogrammed during NRAS/BRAF-driven melanomagenesis leading to enhanced invasion and metastasis, pointing to the potential importance of EMT factors as targets for metastasis prevention *Tulchinsky2*.

Cancer Chemoprevention: The Leicester Cancer Chemoprevention group is the only major UK centre developing novel pharmacological approaches, many based on naturally-occurring compounds, to prevent cancer by targeting pre-cancerous cells in healthy individuals. We focus on mechanisms of action of chemopreventive agents. Natural diet-derived agents with promising cancer chemopreventive properties are being tested in rodents and early clinical evaluation with emphasis on GI malignancies and lung cancer. Curcumin and diindolylmethane (identified by us) have been advanced to human chemoprevention trials which we lead with CR-UK CTAAC funding.

Key Achievements: 5) Phase I study of resveratrol in colorectal cancer demonstrated significant reduction in cell proliferation thus incentivising further clinical evaluation *Brown3; **6)*** Sulfate metabolites were shown to be a stable form of resveratrol deliverable to target tissues and provide a reservoir for regeneration of the parent compound, thereby overcoming the barrier of rapid resveratrol metabolism in its clinical translation *Brown4*.

Stratified Medicine: In line with the overall strategy of this UoA, a key goal is development of personalised cancer treatment. Our activities focus on application of new genomic technologies for improved patient diagnosis, devising novel therapeutic approaches and, based on patient-specific tumour genetics, to predict adverse effects of radiation. Shaw leads a major programme centred on the genetic profiling of circulating free (cf) tumour DNA,. which has paved the way for a number of international collaborations including a position as the coordinating centre for cfDNA studies within TRACERx, a ~£13M multicentre CR-UK study on lung cancer. Our lead clinician scientists (Dyer, Fennell, LeQuesne, Wagner) use their clinical activities to inform laboratory studies on novel targets, biomarkers, combination therapies and resistance mechanisms while radiation research has identified novel biomarkers of radiotoxicity that are being validated in the clinical setting.

Key Achievements: 7) Demonstration that molecular portraits of cfDNA can distinguish patients with primary breast cancer, healthy controls and pre- and post-operative breast cancer patients, . highlighting cfDNA genetic profiling as an important technology for patient stratification *Shaw1;* ***8)***tFinding that the voltage-gated proton channel HVCN1 is expressed on the surface of B-lymphocytes and is critical for activation of the B-cell receptor, thus identifying HVCN1 as a potential new therapeutic target in B-cell malignancies *Dyer1*.

The headline outcomes have been: 1) enhanced grant funding, including five CR-UK Programme Grants; 2) Renewal of our ECMC status and 3) Successful application for a CR-UK Centre.

Plans for the next 5 years: We will concert our CR-UK Centre status reinforcing our membership of an elite group of cancer centres delivering top quality research and improved patient care. Our research objectives align closely with CR-UK's 2020 goals and focus on our unique strengths but complement and integrate with other CR-UK centres in the network. Specifically, we aim to:

1. Deliver on, and augment, our existing basic research programmes, capitalizing on our excellent research facilities, particularly in the areas of structural biology and *in vivo* tumour biology.
2. Utilise enhanced infrastructure provided by CR-UK and ECMC funding to translate new discoveries into the clinic, focusing on Cancer Chemoprevention and Stratified Medicine.
3. Consolidate a position as a national centre of excellence for research into Lung Cancers, Mesotheliomas and B cell malignancies and develop related practice changes.

MECHANISMS FOR RESEARCH DEVELOPMENT, PROMOTION AND DISSEMINATION

To support our new Theme structure, embed research-focussed management, enable timely responses to opportunities in line with our strategy and facilitate cross-disciplinary activity we have established a two tier structure. The College Research Committee (meetings x3 p.a.) reviews and develops strategy and policy; this is implemented by our Research Implementation Group (RIG) (meetings x2 per month). Both groups include all theme leads and enable us to maximise opportunities to integrate the activities of UoA1 with those of colleagues entered in UoAs 2, 4 and 5**.** Each Theme has its own development strategy which is delivered through a suite of centrally supported activities that underpin an **active and vital research culture**. These include: *guest and prize lectures, seminars, workshops, away-days, grant and paper development fora, and a well-developed internal peer-review system*.

Research Student Recruitment: We have a strong post-graduate community integrating clinical and non-clinical students which attracts high calibre applicants to MRC, BBSRC, Charity and College funded studentships. We aim to sustain our increased postgraduate numbers achieved during the previous assessment period by securing additional studentship programmes from sources such as the WT and other major charities (e.g. BHF) as well as encouraging recruitment of strong overseas students via institutional agreements and individual approaches.

Involvement of Service Users and Public engagement: In addition to direct patient involvement in the development and governance of our BRUs and extensive engagement with the Department of Health, NIHR and NICE (see section e), we have established an outreach strategy group through which these activities are coordinated and resourced. Our established programme of public engagement is most visible in our GENIE centre, which is focussed on public understanding of DNA and genetics and which delivers numerous events including the well-established "Dynamic DNA" day (600 yr 9 pupils in 2013). GENIE staff are working, initially with Cancer, to build public engagement events in other Thematic areas**.** The recent establishment of the University **Research Centre for Medical Humanities** enabled us to jointly plan lively public events and processes.

Inter-/ Multi-Disciplinary Activity with other Colleges. In addition to the Humanities interaction, multiple one to one collaborations, particularly with Mathematics and Engineering (e.g. *Dubrova4; NgGA2*) a more ambitious collaboration is exemplified by the commissioning in 2012 with ~£1M investment of our *Diagnostic Development Unit* (DDU) embedded in the UHL A&E department ("If we can attempt to detect life on Mars, why not in the local hospital…?"), which results from a collaboration between multiple CMBSP Themes, Space Physics, Chemistry and the HPA.

c. People, including:

i. Staffing strategy and staff development

Recruitment and Investment: We focus on our thematic priorities such that resources follow strategy. Bids for posts are jointly prepared by Departments and Themes and must describe their alignment to research strategy. They are reviewed by our Research Committee and submitted to the Management Board for decision ensuring strategic "fit" as well as traditional quality criteria.

Research Concordat: The University has implemented the principles of the Concordat to Support

the Career Development of Researchers, and in 2011 we were awarded the European Commission 'HR Excellence in Research' award in recognition of its commitment. Performance of the Action Plan is monitored and evaluated at regular intervals by a Concordat Steering Group.
Equality and diversity: We manage equal opportunities according to our published policy through the University's Equalities Unit (2 Equalities Advisors and an Athena SWAN coordinator). CMBSP has a professorial lead in this area who chairs our College Equal Opportunities Committee (x4 pa) which reports to the University Committee (senior PVC chair). We hold an Athena SWAN Bronze Award at University level, staff in this UoA all belong to departments holding Bronze awards and we are currently developing a joint Silver application for the Medical School. We support maternity leave with temporary appointments to sustain the academic's activity and take care that women speakers are represented in all research events.
Integration of Clinical academics and NHS researchers: Integration is seamless. University and NHS researchers develop studies, clinical trials and papers together; the majority of outputs submitted in this UoA include NHS colleagues as co-authors. Clinical research is supported by the jointly administered NHS R&D / University research office and the Clinical Trials Unit office.
Sustainable staff structure: Over the REF period there have been 11 professorial retirements/departures balanced by 10 internal and 3 external appointments to chairs in this UoA. Below this there have been 17 new academic recruits. Our flexible workload model enables individuals to shift their balance between research and teaching depending on career priorities.
Effective development and support of research work: The University Research Support Office (RSO) facilitates grant applications and research-related management. This includes: identification of funding opportunities, training in applying for grants; provision of information for planning and development**;** advice on costing and submission of applications; negotiation of funding and collaboration agreements; financial administration of externally funded research projects. RSO also provides regular opportunities (e.g. annual 'Research Fortnight') to hear directly from funders and attend grant-writing workshops. All grant applications are subject to monitored internal peer review.
Research career development: We have undertaken two College-wide reviews of academic staff activity profiles since 2009. The Academic Practice Unit provides professional development training for all members of staff engaged in conducting, supervising and managing research. This includes induction for research staff, the organization of mentoring, and an extensive programme of workshops in research leadership and management. These diverse workshops cover sourcing funding, research ethics and governance, pathways to impact, public engagement, PhD supervision and examination skills, and quantitative skills training. The 'Intrepid Researcher' series offers methodology taster sessions in which experts (from within and outside the University) provide overviews of particular research methods and their benefits and limitations.
Early career researchers (ECRs): Our strong clinical academic development programme recruited 53 ACFs and 35 ACLs over the assessment period. It is managed by a clinical academic in collaboration with the local PG Deanery. ACFs undertake an MRes training programme in research methods. Recruitment is focused on our strongest thematic areas and we apply this strategy to the specialties and projects offered in the annual ACF round through an internal call for proposals which are reviewed by the themes. NIHR-required mentorship and review systems are fully implemented and overseen by a Clinical Academic Development committee. In parallel, we have a robust support structure for our non-clinical academics with a College committee chaired by a senior academic; this works in concert with the University Staff Development Unit to enable junior faculty, post-doctoral and other research staff to realize their career potentials. Support includes workshops and networking on transferable skills, enterprise, impact, CV development and techniques for interviews as well as plentiful opportunities for post-docs to present their work.
ii Research students
Overview: Our current postgraduate research (PGR) population is 265 (CVS-73, RS-87, DM-9, Ca-66, Others 30) including 195 PhDs and 70 MDs. 76% of our studentship **funding** comes from: **Research Councils** (MRC and BBSRC) (27.5), **Medical Charities** (28), **MBSP College** (36.5), **NHS** (4) and **Commercial** (17) sources with the remainder made up from self-funded and overseas students. Allocation of studentships awarded to, or funded by, the College follows internal competition in which the Themes rank applications according to their strategy with final decisions made by the RIG. The College is committed to innovative and integrated PGR training complying with the Vitae Researcher Development Framework, aiming to empower researchers to make an impact in their careers and to strive for excellence. Training, supervision, monitoring and

assessment follow policies set out by the University Graduate Office, as agreed by Senate. The Training Development Working Group, chaired by the Graduate Dean, oversees training provision. Within CMBSP, Departmental PG Tutors report to the CMBSP Research Degrees Committee chaired by the Director of PGR.

Training: Subject-specific skills are taught within the supervisor's clinical practice or lab. First year training includes Governance and NHS/RCUK-required topics and thereafter offers a 28-wk (~100-hr) program, including skills in presentation, teaching, IT, career management, generic research (e.g. safety, experimental design & statistics, ethics, commercialisation), and specialist biomedical research (e.g. bioinformatics, structural biology, advanced microscopy), as well as transferable skills. Training is led by highly motivated research-active supervisors, includes specialist external courses, and is needs-based and reflective, being driven by feedback and monitored by active student involvement in committees. CMBSP pioneered the online PROSE progress management system. PGR students also participate in: tutorials and demonstrating to UG students; the annual University Festival of PGR in which 50 students are selected to present to academics, employers, and the public; residential Graduate School programmes and other training organised by Vitae; the Biotechnology YES, and similar competitions; outreach, e.g. demonstrating in public events. CMBSP runs an annual Postgraduate Careers Symposium, providing opportunities to hear about career pathways from past students, and to network with visitors and exhibitors. Students are fully integrated into the thematic programmes, attending seminars and presenting talks and posters.

Progression & recognition: PGR students are initially registered as Probationer PGs and at month 9 write a report and give a seminar, which form the basis for a viva with a Thesis Committee. Decisions on progression to PhD student status are approved by the Graduate Office. A second review before the end of year 2 checks potential complete their work by the end of year 3. Full-time students must submit before the end of year 4. After completion and examination, achievement is recognised by the Doctoral Inaugural Lecture series showcasing graduates who are outstanding academically and able to present their work to a wider audience; an annual prize is presented to the four best students graduating (2 clinical, 2 non-clinical). In the 2013 PGR experience survey (PRES) 82% of CMBSP students were satisfied with their experience, a figure in line with Russell Group universities. Almost 50% of our UoA1 submitted papers include at least one local MD or PhD student and 40 of our PG students won prizes or bursaries related to national meetings and a further 23 did so at international meetings.

d. Income, Infrastructure and Facilities:

INCOME: Total amounts awarded made to the groups in this UoA during the REF period together with major awards (>£1M) are summarized as follows: **Cardiovascular: £33M** including: NIHR-BRU 2012-17 £6.8M; BHF chairs £2.9M (Samani and Murphy), BHF Strategic Level award 2010-2013 £3M; John and Lucille Van Geest Foundation Cardiovascular Research Fund 2012-2017 £7.5M, EC Biostat-CHF 2010-2014 £1.95M, Leducq Foundation CADGenomics 2012-2017 $1M. **Respiratory: £20.5M** including NIHR BRU 2012-2017 4.5M, WT Seeding Drug Discovery Award (Pneumococcal Disease, P Andrew) 2009-2013 £3.5M. **Diabetes: £14.8M** NIHR BRU Nutrition, Diet and Lifestyle, 2012-2017 £2.3M. **Cancer: £11.5M** including five programme grants. We also attract an annual £0.5M **Wellcome Trust Institutional Strategic Support Fund** which is more than matched by access to a £2.5M pa University **Research Infrastructure Fund (RIF)** for which bids are considered tri-annually. Internal bids are managed by our RIG, which prioritises according to Theme-based advice. We use these funds to support major initiatives, career development, infrastructure, key outputs and outreach.

INFRASTRUCTURE AND FACILITIES: At University level we are supported by Research and Enterprise Offices and a Pro-Vice Chancellor (Prof Schürer). In addition we have a dedicated **College Research Office** led by an Assistant Registrar with 3.7FTE support which coordinates and manages applications for external and internal funding, operates our internal grant peer review system and organises our key research committees. It also provides 0.5FTE support to each of the themes and enables meeting, workshop and speaker organisation as well as website management. Altogether an annual budget of ~£2M is available for theme support, most of which is distributed on the basis of competitive bids assessed by a theme based process and governed by a transparent College-wide policy and ultimately delivered by RIG. Oversight is provided by the Head of College and the Director of Research (Prof Barer) and is integrated with the joint clinical R&D office (UHL R&D Director Prof Brunskill) and with our Governance procedures (see below). Substantial College investment (14 posts) and close liaison with UHL also underpins the **Leicester**

Clinical Trials Unit (CTU) which recently achieved full registration status and currently supports 14 active and 12 planned trials.
As indicated in section b, we have made major investments in our buildings and infrastructure to support our clinical and related laboratory research. We highlight our: **1) £17M Central Research Facility (CRF):** This building, opened in 2012, was part-funded by a £3.9M WT Capital Award. It centralises all our animal holding space and houses premium suites managed by CBS including Advanced Transgenics, Containment level 3 and pre-clinical *in vivo* imaging (see below).
2) £12.6M – BHF Cardiovascular Research Centre (CRC); 3) £3.2 M – Cardiovascular Clinical Research Facility including 3T MRI; 4) £3M – Respiratory Sciences Research Facility; 5) £2.2M – To refurbish and equip space for the Leicester Diabetes Centre; 6) £1M – To enhance the early phase Cancer Clinical Trials Unit.
We have also implemented 5 key developments that have improved infrastructure since RAE2008:
1) **Core Biotechnology Services (CBS):** Led by Fry this virtual department comprises 11 services and is supported by 30 FTE staff (~50:50 Grade 8/7 (Managers & Experimental Officers): Grade 5 technicians annual budget ~ £1M). Investment in new equipment since 2010 has been £2.5M. Services include: **Leicester Imaging Technologies** - light, fluorescence (with £78K URIF investment in high-sensitivity detectors) & electron microscopy (JEOL JEM-1400 and Hitachi S3000H), pre-clinical imaging (9.4T MRI, Quantum CT, bioluminescence & fluorescence, Vevo 2100 ultrasound), flow-cytometry, histology, and X-irradiation (£177K URIF investment); **Protein & DNA facility**, including Sanger sequencing, proteomics (LTQ-Orbitrap and high-sensitivity diagnostic validation via 4000Q-Trap mass spec) and the PROTEX protein expression laboratory; **Genomics** facility (including Roche GSFLX next-generation sequencing, SNP typing and transcriptomics including Illumina bead station and C-Scanner [£142K URIF investment], Q-PCR, robotics, DNA clean rooms); **GENETA** Transgenics offering a complete 'DNA to mouse' service; four containment level 3 laboratories; **Bio-informatics/-statistics**, a bioinformatician, biostatistician, and training officer to support experimental design and data analysis; **Biomedical Workshop** with 45 years' experience with specialist research equipment.
2) The **Centre for Translational Therapeutics (CTT)** provides a coordinated means to promote the design of novel therapeutics and diagnostics. It employs experienced scientific support staff, who can be allocated to work with investigators, and is well equipped, including a URIF -funded (£130K) mobility shift microfluidic enzyme assay platform.
3) The **Henry Wellcome Laboratories for Structural Biology** include, in addition to well-established NMR facilities, a new Rigaku microfocus 007HF X-ray generator, Varimax optics & CCD detector; new consoles for 600MHz spectrometers, plus upgrade of one with cryoprobe (URIF award of £475K); new CD machine, Caliper, Octet, Fluorescence plate reader, Mosquito crystallisation robot; WT-funded (£107K) anaerobic crystallisation facility. Supported by 3 University-funded Grade 8 positions, and 1.5 FTE technicians.
4) The University's **High Performance Computing cluster, ALICE** (2048 CPU cores)**,** was established in 2010 through a £2M Capital Infrastructure Fund award and is an essential tool for large scale statistical and bioinformatic analyses. The system is complemented by centralised secure research data storage.
Development of research infrastructure: We will continue to enhance our clinical research space, develop CBS and purchase state-of-the-art equipment via the URIF and external bids. Where possible we pursue a hub and spoke model with CBS (e.g. in our statistics, bioinformatics and microscopy support) where staff and resources are embedded in clinical facilities but supported by core communities led by senior academics on the central campus.
Cross-HEI use of facilities: Leicester is part of the **M5 group** of Midlands research-intensive universities, including Birmingham, Loughborough, Nottingham and Warwick, that is boosting research collaboration and use/sharing of specialist equipment. Its online equipment-sharing database (the UK's first) was launched in December 2012, and the group is now developing mechanisms for cross-institutional booking, and shared maintenance contracts across sites.
Research governance policy & practice: The University's Research Code of Conduct lays out the standards expected from its researchers. It covers publication & authorship, data storage & use, peer-review, supervision & management practice, and intellectual property. It also specifies how cases of research misconduct are dealt with. Published guidelines allow colleagues to make clear and consistent decisions regarding the acceptance or refusal of funding. The University is registered as a research sponsor with the Department of Health and we are fully compliant with the

requirements of the MRHA and the Human Tissue Act. The College has a Governance Manager and support team based within the Joint UL/UHL R and D Office, who co-ordinate and monitor this process. Outside the NHS process, projects involving human subjects undergo ethical review by a University committee. Use of genetically modified organisms is monitored by the Genetic Modification Sub-Committee of the University's Biological Safety Office. The University was among the first to sign the Concordat on openness in animal research following a national award-winning campaign. This included multiple media interviews and filming around the official opening of the CRF and a broadcast item on BBC Radio 4's Today programme.

e. Collaboration or Contribution to the discipline or research base

Participation in the peer-review process: All colleagues regularly review papers and grants and several serve or have served on national or international review panels. Examples include: **NATIONAL**: **Samani:** MRC Populations & Systems Medicine Board (PSMB) (11-14), WT Physiol Sci Ctte (08-11), Acad Med Sci Clin Lect Starter Grants Panel (08-12); **Panerai:** EPSRC College (03-12); **Brightling:** MRC PSMB (13-17); **Willis:** BBSRC: BCB Panel Deputy chair (04-08), Appointments ctte (2013-); Healthy organism strategy panel (10-11); **Bradding** NC3Rs Panel assessor (2011-); Biochem Soc Travel Grants panel (06-09) **Brindle:** Biochem Soc Signalling panel member; **Coats:** NIHR HTA "Emergency Care" call ctte (07-11); **Davies:** Novo Nordisk Res Foundn. Clin Fellowship Award panel (07 -11); Chair of the Novo Nordisk Res Foundn.; **Goodall:** NIHR Doctoral awards panel (05-10); **Lambert:** Nat Institute of Academic Anaesthesia Grants Ctte; **Mahaut-Smith:** BHF Chair competn (2012-); **Murphy:** NIHR Appl Prog Grants Ctte (11-12); **Robinson:** MRC Promoting Phys Activity panel (2013-); Res Awards Ctte, Stroke Assoc, (07 - 10); NIHR RFPB East Mid Funding Ctte (2012-). **Andrew:** Meningitis Trust Res Advisory Panel (-2013). **INTERNATIONAL**: **Fry:** Assoc for Int Cancer Res Grants Ctte (2011-); **Robinson:** NIH Nat & Regional Stroke Res Co-ordinating Centres Advisory Board Panel, USA, 2013; **Panerai:** Science Foundation of Irel& (Walton Fellowships panel) (07-10) **Steward:** Chair World Cancer Res Fund Grant Ctte (2009-); **Tomaszewski:** Int Soc Hypertension Awards Ctte (10-14); **Samani:** UGC Hong Kong Res Assess Exercise Panel (2014); Int jury, InBev-Baillet Latour Health Prize 2014

Wider contributions: Barer: Advisor to DEFRA & BBSRC on Bovine TB; Soc Gen Microbiol council member -2010; RCPath Res Ctte; Nominee 2013 John Maddox prize for st&ing up for science (animal res); **Brown:** Sec. UK Environ Mutagen Soc. (08-14); **Chung:** Brit Med Ultrasound Soc Council; **Coats:** UK Trauma Audit & Res Network – Chair (2003-); **Cooke:** Soc for Free Radical Res (Europe) Ctte (2010-); Founding Chair European Standards Ctte on Urinary (DNA) (2006-); UK Env Mutagen Soc Ctte (06-09); **Freestone:** Consultant for PBL - Innovation in Life Sciences; **Fry:** Faculty of 1000, Cell Biology (2010-); U. Leicester Ambassador Brit Soc Cell Biol (2004-); **Jones, D:** Brit Mass Spec Soc Ctte (07-12)**;** President, European Radiation Res Soc (13-15); Int Assoc for Radiation Res Council (07-15); NCRI Clin & Transl Radiother Res WG (2009-); Network Lead CTRad Biomarker Network (2010-); LH Gray Mem Trust Ctte & Trustee, (09-13); **Lambert:** Int NC-IUPHAR urotensin II receptor subctte; **Ng, L:** RCP Training Board – Specialist Advisor Ctte for Clin Pharm & Therap – Sec. (2008-); **Robinson:** UK Stroke Forum Chair Elect, then Chair (11-14); Europ Stroke Org, Membership Ctte (2012-); Scientific Ctte, Brit Assoc Stroke Physicians (2006-), then Chair (09-11); **Shaw:** Brit Assoc Cancer Res, Exec Ctte (2011-)

NICE & other bodies preparing Guidelines (7 colleagues): Brunskill: NICE MTAC Ctte (2013-); **Coats** NIHR Injuries & Emergencies Nat Specialist Group (09-13); **Davies:** NICE Guidance Ctte member & expert; **Murphy:** Int Soc for Minimally Invasive Cardiac Surgery Working Group for the Development of Evidence Based Guidelines on Blood Conservation in Cardiac Surgery (2011); NHS Blood & Transplant Systematic Review Initiative's Steering Group (2011); The Biomedical Excellence for Safer Transfusion (BEST) Collaborative - member (09-11); Int Initiative on Haemostasis Management in Cardiac Surgery (2008-); **Squire:** NICE Technology Appraisal Ctte A; **Symonds:** NCRN Gynaecological Cancer Ctte (96-201); **Gershlick:** DPFS panel.

SENIOR FELLOWSHIPS & other personal awards (14 colleagues): Bayliss, R: Royal Soc Res Fellowship (05-13); **Bown:** Hunterian Professorship (RCS England, 13-14); **Brightling:** WT Senior Res Fellowship (07-12); NIHR Senior investigator (2010); **Davies:** NIHR Senior Investigator (2009-); **Murphy:** BHF Chair (2012); Hans G Borst Award for Thoracic Aortic Surgery - European Assoc Cardiothoracic Surgeons (2011) **Ng, L:** Fellow Brit Pharm Soc; **Pritchard:** Royal Soc Res Merit Award; **Samani:** BHF Chair (2008-); NIHR Senior Investigator (2008-)Fellow UK Academy of Medical Sciences (2002-); Int Okamoto Award of the Japan Vascular Disease Res Foundn (2012); Deputy Lieutenant of Leicestershire (2010-) **Schwaeble:** Royal Soc Res Merit Award (12-17);

Vogler: UK Chronic Lymphocytic Leukaemia Forum - Young Investigator Prize: the Catovsky-Award (2008); **Wardlaw:** NIHR Senior investigator (2009); **Webb, D:** NovoNordisk UK Res Foundation Fellowship; **Willis:** BBSRC Professorial Fellowship (2009-); **Yates:** Health Foundation prize, best contribution improvement of science at Delivering Better Health Conference, 2011.
EDITORIAL involvement in scientific journals (22 colleagues) (Current Editorial board unless stated otherwise): **Barer:** J Med Microbiol (-2010)**; Barratt**: Kidney Int.; **Wardlaw:** (Editor) & **Bradding**: Clin.Exp.Allerg; **Brightling:** Clin.Sci; **Brindle**: Biotech.Appl.Biochem; Comput.&Math. Methods in Medicine (-10); **Brunskill**: Clin.Sci; (Editor) Kidney Int. [03-10]; **Chung**: Ultrasound; **Coats**: Sc&. J.Trauma; Resusc.&Emerg.Med; Emerg.Med.J.; **Cooke**: Biomarkers; **Freestone**: ISRN Bacteriol.; Recent Patents in Anti-infective Drug Discovery (09-12); **Fry**: Biochem.J.; PLoS ONE; (Editor) Biol.Cell [08-10]; **Goodall**: Platelets; **Herbert**: Cellular Senesc.&Therapy; **Lambert**: Anaesth.&Int.Care Med.; **Mahaut-Smith**: Thrombosis; Front.Memb.Physiol.&Biophys; Cell Memb. &Free Radical Resch; **Ng, L**: Clin.Sci; **Panerai**: J.Med.Eng. &Technol; Med.&Biol.Eng &Comput; Med.Eng.&Physics; Clin.Sci [09-12]; **Robinson**: Age&Ageing; **Samani:** Circulation Cardiovasc.Genet; J.Hypertens (08-10); Heart; JRSM Cardiovasc.Dis; **Shaw**: Kinome; **Squire**: J.Hypertens.; Clin.Sci.; **Steward**: J. Clin.Oncol.; Brit.J. Cancer; Eur.J.Cancer; Cancer Prevention Resch; **Stover**: PLOSOne; **Symonds**: Clin.Oncol; **Tomaszewski**: Gender Med. [11-12]*; Hypertens.; J.Hypertens; ClinSci [08-13]; **Webb, D**: BMJ; [Guest Editor] J.Exp.Diabetes Resch(2012); **Willis**: Cell Death Dis.; Front.Oncol.
Interdisciplinary activity at Leicester: Biological Sciences Brightling, Respiratory Medicine (Challiss – oxidative stress in asthma); Tomaszewski, Cardiovascular (Jobling – Y chromosome & heart disease); Dyer, Oncology (Royle – HHV6). Konje, Obstetrics & Gynaecology (Willets – Ectopic pregnancy); **Chemistry & Space Science:** Coats, Cardiovascular (Monks & Sims – DDU (section b)); **Engineering:** Brack, NgGA, Samani (Schlindwein - Signal processing of fibrillation)
EXTERNAL COLLABORATIONS: We have numerous strong national & international collaborations. Of our 273 submitted outputs 202 include external collaborators (122 with Leicester lead or corresponding authorship, (LL)); 56 with collaborators from North America (30 LL), 85 from Europe (46 LL) and 52 from other locations (33 LL). Overall, 73 of our collaborative outputs are co-authored with QS world top 20 universities.
Collaboration with external non-academic bodies, & patents: Andrew: patent – Novel Pyrrole Derivatives, PCT/GB2012/053022 (*&rew4*); **Bayliss, R:** MRC-T Strategic partnership (2012-) £375,000; **Bradding:** Award from ONO Pharmaceuticals Japan for assessment of novel BTK inhibitors; **Brindle**: Arius Res Inc, Toronto (Roche) consultant (07-10); **Coats:** Intelligent Fingerprinting (SME) - TSB funded collaboration (12-13); **Herbert:** Syngenta - case studentship (08-13); **Lambert:** Grunenthal Ltd UK - consultancy; **Mitcheson:** EPIX pharmaceuticals, Israel – consultancy/contract res (2008); AstraZeneca, UK – consultancy *(Mitcheson,1,2,3)*; **Murphy:** Ethicon Biosurgery (Johnson & Johnson), NovoNordisk, Abbott Pharmaceuticals, Invitrogen, Pfizer, Biocompatibles Ltd, Somanetics Ltd consutancies. **Ng, L:** BRAHMS AG (Thermo Fisher) – consultant; Squire: Novartis AG – investigator led study; **Schwaeble:** Omeros –case studentships; **Steward:** Roche, Sanofi, Merck, Bayer, Celgene – consultancies.
Conference Organising (CO) & Session Chairs (SC): Barratt: SC: Int Soc Nephrol, UK Renal Assoc, Asian Pacific Soc Nephrol; **Bradding**: SC American Soc for Haematology; **Brown:** CO Resveratrol 2012 (Dec 2012, Leicester); **Brunskill:** CO & Co-Chair, C-Peptide in Pathophysiol , An Update, EASD Meeting, Vienna; Invited Session Chair: C-peptide: an update. European Assoc for the Study of Diabetes. Prague September 2011; Invited SC World Congress of Nephrol, Hong Kong 2013; **Chung:** Scientific chair of the Brit Med Ultrasound Soc Annual Scientific Meeting 2012 & Young Investigator SC (BMUS ASM 2013); **Cohen:** CO Int conference on "Apoptosis & Cancer" Cambridge UK, 2012; **Cooke** Co-CO UKEMS 2008, Newcastle, UK; Int Organising Ctte, the 2nd Copenhagen Workshop on DNA Oxidation, 2009: **Fry:** SC EMBO Conference on Centrosomes & Spindle Pole Bodies October 2-6th 2012 Barcelona, Spain; **Murphy:** CO Symposia Anticoagulation & Bleeding in Cardiac Surgery: Optimal Management in Shifting Sands, The SCTS University, 2012; Current controversies in blood management; SCTS Annual Meeting Manchester 2012; Clin Strategies to Reduce Morbidity Associated with Coagulopathic Bleeding in Cardiac Surgery, The SCTS University, London 2011; Management of Severe Bleeding in Cardiac Surgery, SCTS annual meeting, Liverpool 2010; **Rufini:** CO 4th p64/p73 int workshop in Toronto, ON, Canada.