Institution: University of Birmingham

Unit of Assessment: UoA1

a. OVERVIEW

Birmingham's research mission aims to deliver research across the spectrum from discovery to translation, with clinical need driving basic research and fundamental mechanistic discovery facilitating substantial clinical progress. Examples of such translational excellence include the development of antibodies to immunoglobulin free light chains resulting in a serum assay for rapid diagnosis of multiple myeloma, and research showing the link between triclosan usage and antibiotic resistance that prompted new EU wide regulation on the use of biocides.

This submission is drawn from the **College of Medical and Dental Sciences (MDS)**, one of the University's five Colleges, which comprises five **Schools;** namely, **Cancer Sciences (CS)**, **Immunity & Infection (I&I)** and **Clinical & Experimental Medicine (CEM)**, which all **contribute to UoA1**, as well as **Health & Population Sciences** (returned as UoA2) and **Dentistry** (returned in UoA3). The Schools provide organisational units for academic management, teaching delivery and financial oversight. Crucially, they also facilitate a flexible, cross-disciplinary and collaborative research Centre structure (Figure 1) that integrates clinical and non-clinical researchers and allows effective cross-School collaboration. The Centre structures also provide a vehicle for collaborative research with other Colleges in the University, with two prominent examples being: i) the newly established Institute of Microbiology and Infection, which was recently established as a joint venture between MDS and the College of Life and Environmental Sciences; and ii) the EPSRC-funded doctoral training programme Physical Sciences of Imaging in the Biomedical Sciences (PSIBS), which is based in the College of Engineering and Physical Sciences, but has strong links with MDS and serves to fuel multiple collaborative research projects.

Within UoA1 we return research in four major areas that consistently deliver excellence: **Cancer; Immunity, Inflammation & Infection; Hormones, Metabolism & Reproduction;** and **Cardiovascular Health**. Research is focussed on delivering effective translation of excellence in basic science into clinical application to improve human health. As recognised in the *MRC Translational Roadmap Peer Review*, "Birmingham is one of the very few centres internationally that can complete the full circle of Translational Medicine". Translational research is facilitated by the co-localisation of a highly research active University with major strengths in biomedical research and one of the UK's premier "super" hospitals, the Queen Elizabeth Hospital (QEH) at University Hospitals Birmingham (UHB) NHS Foundation Trust, with state-of-the-art patient focussed research facilities. Together with other affiliated NHS Trusts, this provides access to one of the largest patient catchment areas in Europe (5.5 million), with 800,000 patients being seen per year at the QEH alone.

b. RESEARCH STRATEGY

Our overarching research strategy focuses on identifying and nurturing existing strengths and developing new areas of strategic importance through horizon scanning. An important aim is to maximise synergistic activity within and between the areas of research excellence, e.g. cancer immunology, immune-endocrine interactions and cardiovascular inflammation. Furthermore, our strategy aims to enhance interdisciplinary collaboration across the University, as well as nationally and internationally.

Development, Promotion and Dissemination of Research

The Head of College, a Pro-Vice Chancellor and University Executive Board member, and the 5 Heads of School provide senior leadership for research. An over-arching College Director of Research & Knowledge Transfer (R&KT) has a crucial role in developing and delivering a dynamic research strategy and infrastructure including a core technology hub delivering major enabling techniques. The Dean of Medicine and the Vice-Dean for Applied Health Research provide a key link to ensure a seamless interface between basic and translational research and integrated working with the NHS. The establishment of Birmingham Health Partners (BHP), an Academic Health Sciences Centre (AHSC) under a strategic alliance model, chaired by the Dean provides a joint University-NHS research infrastructure promoting strategic planning and delivery in clinical research between the College and NHS members, UHB and the Birmingham Children's Hospital

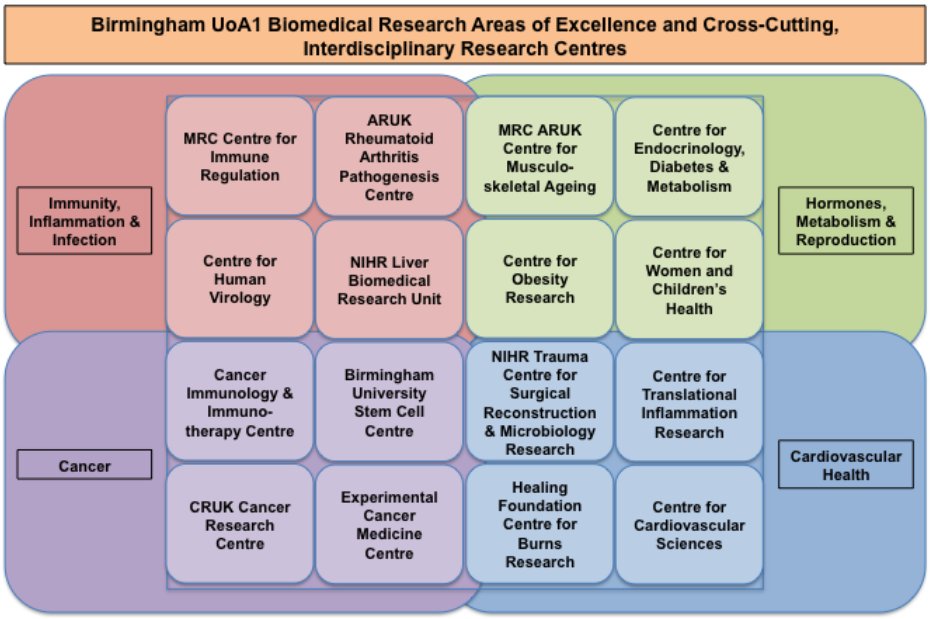
(BCH) NHS Foundation Trust. A core component of this translational partnership is our NIHR/Wellcome Trust Clinical Research Facility (CRF), one of the UK's original millennial CRFs, enhanced by further Wellcome funding for an extension including a dedicated metabolic assessment unit. In 2012 it was designated as an **NIHR CRF for Experimental Medicine** underpinned by a £12.8m grant, the largest awarded to any of the 19 successful NIHR CRF applications.

A Strategic Research Committee (SRC), chaired by the Director of R&KT and comprising both senior and early career research leads for the main research themes, drives cross-disciplinary interactions, horizon scans for new opportunities, plans for new strategic initiatives and oversees the activities of the designated research centres. The SRC reports to the College Board where research strategy and delivery are further integrated with teaching counterparts and enabling operations such as estates, administrative infrastructure and Human Resources to ensure adequate resourcing for effective delivery.

Traditional academic routes for dissemination through publications and presentations at conferences are supported by access to funding for young researchers presenting their work at international conferences and by a paper of the month competition to encourage publication in high impact journals. In addition, the College has an active marketing and communications team who promote College research output and impact in the local and national media. An active outreach programme also promotes science and medicine to local schools.

Mechanisms and Practices for Promoting Research, and Sustaining and Developing an Active and Vital Research Culture

Delivery across the four main thematic research areas and additional enhancement by inter-disciplinary exchange across the Schools and wider University is encouraged and supported by the creation of **research centres of excellence** as summarised in Figure 1 below.



The research centres represent functional cross-School and cross-College groupings that serve as vehicles for the strategic development of critical mass and expertise sufficient to compete for externally funded centres of excellence and to allow different disciplines to come together to focus on specific diseases or clinical targets.

The delivery and development of research is facilitated by the **R&KT Office,** which is organised into 5 teams: a) Research Development and Support, with a dedicated Senior Research Facilitator linked to each School, b) Strategic Projects, c) Business Engagement, d) Clinical Research and Compliance and e) Post-Graduate Training and Development. Research Facilitators ensure dissemination of research initiatives and funding information, linking directly to School and College strategic planning and support both the application and awards phases. Recent initiatives include a 'Research Handbook' given to all researchers covering key topics from grant writing and costing

to clinical governance and public engagement. A workshop series has also been developed on topics such as: 'Publishing in High-Impact Journals', 'Writing Your First Grant', 'Working with the NHS' and 'Interacting with Industry', with the aim of improving grant application success, publication and impact. To further improve the quality of applications, a system for pre- screening all applications has been implemented, which is followed, where required, by a **Grant Clinic Scheme** which provides review, advice and guidance from a **Panel of Experts.** Dedicated support is also provided by central Research & Innovation Services on European applications, industry collaboration and Technology Strategy Board calls.

We have coordinated several sources of internal and external funding to support researchers, especially those in the early stages of their career. Through internal funds, we established the College **Research Development Fund** in 2010 that provides up to £5k for: preliminary experiments specifically linked to external funding applications, more extensive experiments linked to publications under review, and for mobility awards to allow researchers to visit overseas collaborators. Birmingham was one of 23 universities to receive a **Wellcome Trust Institutional Strategic Support Fund** award, this has been targeted largely at UoA1 research via three main routes: awards of up to £25k for pilot data or interdisciplinary research; up to £50k for the early phases of more commercially-oriented translational work; and up to £20k for secondments to other laboratories, into industry, and funder or policy-related workplaces. Focused on more translational-oriented research, Birmingham was one of 14 universities to secure **MRC Confidence in Concept** funding (and in the top 50% of those funded, with a £600k allocation), which has allowed us to establish an approach that increases understanding of and adds value to early phase translational work. We have structured funding awards around milestone deliverables, allowing us to support projects that have a higher risk of failure but greater potential opportunities if successful, and linked each to a Project Translational Group, which consists of senior academics and external industry advisers, as well as our own Technology Transfer team. The **Enterprising Birmingham Fund** is a new University strategic fund of £200k per year intended to fund development of opportunities for commercialisation. Awards are made flexibly, although mostly below £40k. Funding is directed to activities to demonstrate proof of commercial viability, and awards are made following scrutiny by the University's technology transfer company, Alta Innovations. We have also created an **Enterprise Fellowship** scheme providing funding to give academics time to develop proof of commercial or translational viability of their research, or to spend a period in industry. Value has been proven by recent secondments to GSK and Novartis, the latter leading to licensing of a Salmonella vaccine technology.

Policy and Practice in Relation to Research Governance

The University's framework to support research governance is underpinned by the **Code of Practice for Research** that describes the expectations for researchers, including the need for all research projects to undergo an ethical self-assessment and, where further scrutiny is required, an ethical review by an appropriate University, or external ethical review committee. The Code of Practice also describes the requirement for staff to adhere to any required standards of work performance or conduct imposed by law or by the University in relation to particular categories of research. It specifically details the need for staff involved in research involving human participants falling within the remit of the Department of Health's Research Governance Framework or the Medicines for Human Use (Clinical Trials) Regulations to comply with all applicable requirements including Good Clinical Practice (GCP) principles.

The University's central **Research Governance & Ethics Team** manages the process for ethical review and Sponsorship. Within the MDS R&KT Office, the **Clinical Research and Compliance Team** is responsible for performing reviews and audits of research projects involving human tissue collection, clinical trials managed outside one of the University's Clinical Trials Units (CTUs), and University GCP laboratories. In addition, the team performs audits of the three University CTUs, develops processes and guidelines for researchers involved in clinical trials, and provides advice and training to the research staff. Clinical Trials of Investigational Medicinal Products are overseen by to the **Clinical Trials Oversight Committee**, which reports to the University Research Governance and Ethics Group chaired by the Pro Vice Chancellor for Research & Knowledge Transfer. BHP has a joint governance group that ensures sharing of best practice and resolves governance issues involving BHP members.

Research Groups and Achievement of Strategic Aims in the Assessment Period

• Cancer

A key strategic aim in this assessment period was to be awarded CRUK Centre status; this was achieved in 2009 (Director: Moss), with Birmingham the first University to gain this award. We also host an **Experimental Cancer Medicine Centre (ECMC)** (jointly supported by CRUK and the Department of Health; Director: Morton), which was renewed with increased funding in 2012. Cancer research at the University of Birmingham has been developed in recent years to encompass the breadth of the translational portfolio and as a consequence is now formed around six themes:

Translational Cancer Genetics seeks to exploit the advances in **cancer genetics and epigenetics** and to deliver patient stratification. Birmingham is one of three genetic testing centres within the **CRUK Stratified Medicine programme**, in partnership with the West Midlands Regional Genetics Service, the largest genetics laboratory in the UK. We are also one of eight clinical collection centres and the academic partner on two industry-led TSB stratified medicine programmes. Translational cancer genetics embraces our strength in research elucidating the mechanisms underlying the development of cancer, with a particular focus on epigenetics and DNA repair. Over the last five years we have invested in both areas with the recruitment of Bonifer, Morris, Petermann and Davies, and transition to newly refurbished laboratories. CRUK Centre support is used to translate this research to patient benefit, e.g. clinical trial of PARP inhibition in leukaemia, the national laboratory for ataxia telangiectasia and molecular assays for therapeutic decision-making in myeloid malignancies.

Viral Oncology is based around expertise in Epstein Barr Virus (EBV), Human Papillomavirus (HPV) and Hepatitis C. Teams led by Rickinson and Rowe study **EBV immunology and mechanisms of cell transformation**. To ensure sustainability, investment has been made in several junior investigators who study EBV entry mechanisms, CD4 processing and generation of the EBV-specific T cell repertoire. **HPV research** has grown strongly, underpinned by active recruitment, and is focused on HPV-associated tumours of the vulva, cervix and neck.

Cancer Immunology is one of our fastest developing areas receiving significant investment that integrates cancer teams with immunology and inflammation researchers. Willcox, the lead for the theme, secured a Wellcome New Investigator Award to continue his work on T cell recognition and its role in immune surveillance. Together with colleagues such as Moss, Cobbold, Adams and Lane, we have achieved a critical mass of expertise and established a **Cancer Immunology & Immunotherapy Centre (CIIC)**.

Haematology represents a shining example of the implementation of a translational pipeline. In the last decade Birmingham has established itself as a major international centre for investigation and treatment of blood cancers and is now the largest national recipient of Leukaemia & Lymphoma Research (LLR) funding. The theme includes programmes on the role of transcriptional and epigenetic regulation in blood stem cells and mechanisms of leukaemia initiation and maintenance (Frampton, Bonifer), the importance of DNA damage in lymphoid tumours (Stankovic), the biology of diffuse large cell lymphoma (Murray) and the alloreactive T cell response to leukaemia following stem cell transplantation (Moss, Malladi). Clinical research through the UHB Centre for Clinical Haematology and BCH focuses on rapid delivery of early phase clinical trials with embedded molecular stratification and immunophenotyping capability provided by the Clinical Immunology Service (Drayson). Our ability to integrate early phase trials with complementary research in stem cell, leukaemia and transplant biology has been recognised by the award of an **LLR Centre of Excellence**.

Surgical Oncology has a particular focus on **colorectal carcinoma** (CRC), the third most common cause of cancer death, and under the leadership of Morton, Birmingham has established an international research profile in this area. The FOxTROT trial assessed down staging chemotherapy for CRC and, in collaboration with Bristol and Imperial, the EFLEX study of local surgery will launch in 2014/15. Capability within **head and neck cancer** was transformed by the recruitment of Mehanna and Wiench, the latter studying DNA methylation and distal regulatory element function in oral cancer and response to epigenetic therapies. Mehanna developed PET NECK into the largest head and neck cancer surgical trial in the world, developing an integrated platform to evaluate new surgical interventions and devices. For **urological cancer** we run some of the strongest clinical trials in the world, including the ground breaking multi-arm STAMPEDE.

Laboratory research has focussed on epidemiology, immunology and gene therapy and adenovirus-delivered gene therapy is now being trialled in prostate cancer through local delivery of GMCSF-expressing virus and systemic delivery of pro-drug.

Cancers of Unmet Need is a research theme focussing on a number of cancers relatively neglected by research but which remain very challenging to treat; this includes cancers of the lung, brain, bladder and gynaecological cancer. We have made investment in order to drive research in this area, developing research activities alongside some of the largest clinical programmes within the UK, benefiting from leading statistical support for national trials (Billingham). Studies led by Birmingham have changed practice for muscle invasive bladder cancer. Our expertise in lung cancer was strategically strengthened by the recruitment of Middleton and Naidu as Chairs in Medical Oncology and Thoracic Surgery and we now hold a leading position in the CRUK TRACERx trial. Current research within brain tumours includes NMR spectroscopy (where Peet holds an NCRI Chair) and metabolomics. Gynaecological cancers have been targeted through our strong translational programmes in HPV-induced malignancy and clinical trials within ovarian cancer, further strengthened by the recruitment of Kehoe as Clinical Professor of Gynae-oncology.

• Immunity, Inflammation & Infection

Immunology research has been a longstanding strength in Birmingham, and since 1999 we have hosted the **MRC Centre for Immune Regulation**, comprising 40 investigators studying different facets of immune responses. Renewal of the Centre in 2010 allowed us to add new themes including chemokine biology, the latter being facilitated by recruitment of Antal Rot, an international leader in the field who discovered new mechanisms of chemokine regulation involving decoy receptors**.** This strategic appointment complements and strengthens our basic and translational research on leukocyte migration, which has led to clinical trials targeting chemokines in liver disease and graft-versus-host disease. The Centre and its facilities support the continued development of basic immunology research helping to secure 7 programme level grants since 2009 and drive research into new treatments for autoimmune and chronic inflammatory diseases. Recent key findings include identification of bipotent lymphoid progenitors important for lymph node formation; understanding signals involved in the development of germinal centres; uncovering novel links between innate and adaptive immunity for T-cell tolerance; the role of the thymic medulla in the selection of normal and regulatory T cell subsets, and the elucidation of the cellular mechanisms maintaining conventional and regulatory CD4 T cell memory.

Inflammation research has been developed in the last 5 years into the **Centre for Translational Inflammation Research (CTIR)**. The CTIR aims to identify shared biological mechanisms that define the functional features of chronic inflammatory disease by integrating disease specific expertise. CTIR has co-located basic and clinical scientists working on **inflammation in the joints, lung, eye and kidney** in a new facility in the QEH. This also allowed expansion including a new Chair in inflammation biology investigating anti-inflammatory mechanisms of glucocortiocids. The focus on common processes underlying chronic inflammatory disease has led to new insights into mucosal inflammation, rheumatoid arthritis and spondylarthropathies. This work links directly to studies on lymphoid tissue development carried out by Caamano, Anderson and Withers. The appointment of three new investigators in respiratory medicine (Turner, Sapey and Naidu) builds on strength in COPD research. The ability to carry out large clinical trials in acute lung injury and sepsis was expanded by the appointment of Gao-Smith. Key recent findings of renal inflammation research include the report of polymorphisms associated with increased graft loss and drug toxicity in renal transplant recipients and clinical trials in vasculitis therapy.

Inflammageing is a new research focus on age-related systemic inflammation and pathology, with Lord showing that inflammageing and autoimmunity are driven by immune senescence rather than by latent infections such as CMV. During the assessment period, RCUK designated understanding ageing and its influence on health as a strategic priority, leading the College to invest in ageing biology and to integrate groups already working in this area through the formation of the multi-disciplinary **Centre for Healthy Ageing Research**. Future sustainability and strength of this area was demonstrated by funding of an **MRC-ARUK Centre in Musculoskeletal Ageing Research**, a partnership with Nottingham University, spanning across CTIR and Endocrinology with links to the Schools of Sport, Exercise and Rehabilitation Sciences and Psychology.

The **Rheumatology** Research Group (RRG) focuses on the pathobiology and management of early Rheumatoid arthritis (RA). Buckley and Raza coordinate an **FP7 EU Consortium** exploring

very early prediction of RA, and the RRG hosts the **ARUK Centre of Excellence in the Pathogenesis of RA** and an **ARUK Experimental Arthritis Treatment Centre.** The recruitment of Clark and Fisher has strengthened basic expertise in mechanisms that drive the switch to persistence rather than resolution of disease and our translational reseach capacity as part of the MRC Stratified Medicine Initiatives in RA (MATURA and RA-MAP) and the **NIHR Translational Research Partnership** for joint and related inflammatory disease. A particular strength of our research is the exploration of the role of stromal cells and novel biomarkers, including metabolomics and imaging, in predicting and stratifying outcome in early disease.

Liver research is a major clinical theme and complementary to research within the MRC Centre for Immune Regulation and the CTIR. **Birmingham is one of the largest liver transplant centres in Europe for both adults and children**. The focus of our research is on the investigation of the immune-mediated mechanisms that drive hepatitis and fibrosis in response to metabolic syndrome, autoimmunity and viral infection. The recruitment of Hirschfield brought expertise in the genetics of inflammatory liver disease, now exploited as part of the MRC stratified medicine initiative in primary biliary cirrhosis. Aligned with the strategic aim to grow translational research from our areas of excellence, the basic science platform underpins first-in-man translational studies delivered through the **NIHR Biomedical Research Unit (BRU) in Liver Disease**. Key successes include the first application of HCV uptake inhibitors in liver transplantation patients, the first trial of anti-chemokine therapy in liver disease, and a clinical trial of dendritic cell therapy in liver cancer.

Virology research has a long history in Birmingham. Fulfilling our strategic aim to expand and integrate virology with our liver research excellence, McKeating leads work on the molecular mechanisms of Hepatitis C virus infection and has identified the importance of novel receptors, cell polarity and growth factors in HCV entry to the liver. The NIHR BRU in Liver Disease has facilitated the translation of her work by completing the first clinical trial of an SRB-1 entry inhibitor in patients after liver transplantation. The sustainability of this area has been enhanced with a cadre of younger researchers including Bailey, recruited through a Birmingham Fellowship for his work on the molecular determinants of virulence in RNA viruses, and Stamataki, a Royal Society Dorothy Hodgkin Fellows, who works on anti-viral immunity to Hepatitis C. Recent key findings include identifying new forms of EBV latent gene expression in Burkitt and Natural Killer / T-cell lymphoma, the first tetramer analysis of CD4+ T cell responses to viral infection and T-cell immunity to Kaposi's sarcoma-associated herpesvirus. The excellence and sustainability of our virology research is reflected in current funding, comprising 4 programme grants, an MRC EMC grant, a EU FP7 Consortium as well as the recent designation of the University **Centre for Human Virology**.

Microbiology research success is based on the combination of molecular studies on host-pathogen interactions and translation to the clinic through strong NHS collaborations. To integrate and expand this activity, and to forge links to other activity in UoB (returned under UoA5), an **Institute for Microbiology and Infection (IMI)** was established in 2011, co-locating 30 principal investigators including new strategic appointments. Recent key outputs include elucidation of the basis for disseminated Salmonella infections in HIV positive patients and the role of OmpD as an antigenic target in protective immunity against Salmonella. The appointment of Mitchell added expertise in immune cell-pathogen interactions in *Streptococcus pneumoniae*, an important infection in children and older adults. Elucidating the role of bacterial toxins in pathology of meningitis facilitates new treatments for and prevention of bacterial infections. Bacterial genomics has highlighted the effect of clinical intervention on evolution and variation of bacteria. Structural studies of bacterial transporters align with development of new antimicrobial agents (Piddock, chair of the Antibiotic Action group that advises Government).

• Hormones, Metabolism and Reproduction

Endocrine research at the University of Birmingham has a longstanding tradition. The **Centre for Endocrinology, Diabetes and Metabolism (CEDAM)** led by Arlt provides a vibrant, multi-disciplinary translational research environment and was awarded University Centre status in 2008. Co-location of all endocrine researchers to the Institute of Biomedical Research, in close proximity to developmental genetics and reproductive biology, has achieved further synergy, with delivery of our research strategy in this area driven by six thematic groupings:

Steroid Action and Human Disease is a major focus of CEDAM research. Over recent years we have combined unique capability for **steroid metabolome analysis,** using state-of-the-art mass

spectrometry technology, with *in vitro* and *in vivo* models, underpinned by major funding from MRC, Wellcome, BBSRC and EU. This integrated approach has been systematically applied to the understanding of mechanisms underlying both rare disorders and common disease such as obesity, diabetes, hypertension, polycystic ovary syndrome and chronic inflammation. This has yielded discoveries of major relevance to human disease, including the identification of novel monogenic disorders resulting in impaired glucocorticoid activation and altered sex steroid activation. Our work has uncovered that ageing enhances glucocorticoid activation in the skin and its reversal results in improved wound healing. Our ability to perform model-based in vivo research has been further enhanced by cutting edge zebrafish models, extended to study steroidogenesis.

Obesity, Insulin Resistance and Diabetes research addresses the obesity epidemic, the consequences of which have been identified as a top UK research priority, with obesity soon to become the major cause of liver failure and cancer. This research is drawn together through the multi-disciplinary **Centre for Obesity Research (COR)**, spearheaded by Tomlinson (MRC Senior Clinical Fellow). Defining the role of pre-receptor glucocorticoid metabolism in insulin resistance and obesity led us to identify mechanisms underpinning the adverse metabolic effects of glucocorticoids. We have demonstrated that idiopathic intracranial hypertension, a prevalent complication of obesity, is linked to glucocorticoid metabolism and can be ameliorated by weight loss. We are investigating diabetes complication including cardiac autonomic dysfunction and microvascular disease and their link to obstructive sleep apnoea syndrome. Our ethnically diverse, large population base has the highest incidence of obesity in the UK with up to 50% of children in some districts being obese, driving our research to target early onset obesity and type 2 diabetes in children (MRC Cohort study, Barrett). We have described a link between childhood weight and thyroid autoimmunity and maternal weight and obstetric outcomes.

Rare Endocrine and Metabolic Disease research is led by Barrett, who was recently made the national lead for the cross cutting paediatrics theme of the **NIHR NOCRI Translational Research Collaboration 'Rare Diseases'**. Our strategy focuses on rare endocrine and metabolic diseases such as disorders of adrenals, gonads, thyroid, bone and childhood diabetes syndromes. This work has resulted in the national commissioning of multi-disciplinary specialist clinics for rare forms of diabetes and obesity (Barrett/Tomlinson) and the leadership of Barrett in the EU-funded rare diseases registry for Wolfram, Alstrom and Bardet Biedl syndromes (**EUROWABB**). Successes also include the largest world wide study on long-term health outcomes in adults with congenital adrenal hyperplasia (CAH), **UK CaHASE,** led by Birmingham and Sheffield and the EU FP7 network **EuroDSD** (Arlt/Krone). This work is now supporting the development of the international registry for disorders of sex development **i-DSD** (MRC partnership grant led by Glasgow) and the newly created i-CAH registry. Research benefits from interaction with the West Midlands Regional Genetics Service (Macdonald, Oley), also feeding our **strengths in prenatal diagnosis** utilising novel steroid profiling (e.g. prenatal diagnosis of rare sterol and steroid disorders) and state-of-the-art genetic approaches (e.g. prenatal chromosomal microarray and cell-free foetal DNA in maternal circulation for prenatal disease prediction, recently underpinned by a £4M grant from the Health Innovation Challenge Fund).

Endocrine and Endocrine-Related Cancer research strength is recognised by a substantial role for Birmingham researchers in the NIHR **NOCRI Translational Research Collaboration 'Endocrine Neoplasia'**. Ongoing research has a particular focus on the pathogenesis of thyroid cancer, delineating the roles of Pituitary Tumour Transforming Gene (PTTG) and its binding factor PBF. The translational impact of our work on the management of thyroid tumours was also recognised by a recent major NIHR HTA grant on novel diagnostic approaches to thyroid nodules (Mehanna, Boelaert, Franklyn). PTTG also has a broader relevance in cancer biology, highlighted by recent publications on the role of PTTG in other solid organ tumours including breast cancer. The recruitment of Foster from industry has facilitated research on the role of steroid sulfatase inhibition in colon cancer. Supported by an MRC Biomarker Strategic Grant and drawing from our strength in steroid analysis we have pioneered a novel diagnostic approach to adrenal tumours, steroid metabolomics, combining mass spectrometry-based steroid profiling with machine learning-based computational data analysis; a prospective validation of this highly sensitive and specific test is currently led by Arlt, with pump-priming through the EU FP7 consortium **ENSAT-CANCER**.

Thyroid Disease and Health across the ages is an area of research strength across CEDAM that also contributes to the multidisciplinary ageing research community at Birmingham. Research has

improved knowledge of prevalence and phenotype of thyroid autoimmunity in older age, the UK-wide analysis of the prevalence of iodine deficiency in UK schoolgirls and the role of thyroid hormones and their transporters in human foetal development. Birmingham has taken a lead role in investigating the impact of thyroid status on early miscarriage and pregnancy outcome and is leading on the NIHR-funded TABLET trial investigating the impact of thyroid hormone supplementation on pregnancy outcome in women with positive TPO antibodies (lead Coomarasamy, with Chan, Boelaert, Franklyn, Kilby).

Our research into **Endocrine Determinants of Adverse Pregnancy Outcome** has yielded significant translational outputs. Coomarasamy investigates the impact of early pregnancy progesterone on miscarriage and leads an interventional trial assessing the effect of progesterone supplementation on pregnancy outcome (NIHR-funded PROMISE trial). The recently completed ECLIPSE trial has established the utility of a progesterone-containing intrauterine system for severe menorrhagia. Foetal Medicine research spans basic immune mechanisms underlying adverse pregnancy outcome and sperm motility to diagnostic test accuracy studies for prediction of pregnancy outcome and prenatal intervention studies. The PulseOx study has established the value of pulse oximetry in early postnatal screening for congenital heart defects in newborn infants, with near immediate impact through worldwide implementation into routine clinical practice.

• Cardiovascular Health

Strategy in this area is developed and coordinated by the **Centre for Cardiovascular Sciences** (led by Watson and Lip) that operates across Schools and Colleges, with close links with the MRC Centre for Immune Regulation and the CTIR. It is delivered through **three thematic research groupings** (one led by Health and Population Sciences and hence returned under UoA2) that have been systematically strengthened through recent external recruitment and internal promotion.

Vascular Inflammation, Thrombosis and Angogenesis (VITA) brings together research in platelet signalling and function, leukocyte trafficking and endothelial cell biology, aiming to alleviate a variety of pathologies including thrombo-inflammatory vascular pathology, platelet function disorders and cancer angiogenesis. Watson and Senis are international leaders in platelet signalling, supported by British Heart Foundation (BHF) Chair renewal (Watson), Programme grants from BHF and Wellcome Trust (Watson) and a BHF Senior Research Fellowship and promotion to Chair (Senis). They have uncovered novel pathways controlling thrombosis and platelet formation, including signalling through the unique 'hemITAM' receptor CLEC-2, the platelet phosphatome and specific tyrosine phosphatases. Nash and Rainger have developed unique *in vitro* models to study regulation of vascular endothelium, uncovering roles of stromal cells and flow in chronic inflammation and angiogenesis. Novel lipid mediators controlling neutrophil recruitment have been discovered and studies of reverse neutrophil migration extended to murine models, suggesting that these cells may contribute to lung pathology. Studies on endothelium have also revealed novel genes and pathways regulating angiogenesis. Bradbury has played a leading role in clinical trials changing clinical practice in peripheral vascular disease (BASIL trial).

Clinical Cardiovascular Science (CCS) centres on research in cardiac pathology, led by Lip and strengthened by the appointments of Kirchhof (Chair) and Fabritz. Our clinical research has defined the epidemiology of atrial fibrillation (AF), the value of screening for the condition in primary care and the efficacy of anticoagulant therapy. The Birmingham Atrial Fibrillation Treatment of the Aged (BAFTA) trial has also established the value of oral anticoagulation for stroke prevention in the elderly and new clinical risk assessment scores for AF-associated stroke and bleeding have been developed and internationally implemented. Kirchhof drives multi-centre randomised AF intervention trials such as Flec-SL and the ongoing EAST trial. Kirchhof and Fabritz have also brought new capability to study molecular mechanisms of heart disease. Pioneering studies in the mouse heart have been validated using tissue from carefully phenotyped patient cohorts, and used to identify mechanisms underlying sudden death, control of right ventricular function and heart rate regulation, which have provided the basis for devising a controlled clinical trial (PreVENT ARVC).

Future Strategic Aims and Goals for Research

Following the successes achieved, both in terms of inward investment, outputs and translational delivery, together with emerging imperatives from Government and the Health sector, the College forward look (through the R&KT Executive, SRC and College Board) has defined additional aims

and goals that it will build into the research strategy for UoA1 over the next 5-year period to support the four key research themes and at the same time expand our horizons, especially towards delivery of healthcare benefits.

The **CRUK Cancer Research Centre** at Birmingham has recently submitted a renewal application to sustain this research area of excellence. The success of academic ***Haematology*** has provided a model for the development of an **LLR-funded Trials Acceleration Programme (TAP)** by Craddock centred on a Birmingham regulatory hub that links research nurses in 13 national leukaemia centres. The TAP has created a novel early phase trial programme accessing 20 million population and was flagged as a significant achievement in the recent Government 'Strategy for UK Life Sciences: One Year On'. Following successful renewal it is currently being explored as a national level template for solid tumours and chronic diseases. The outputs from ***Surgical Oncology*** will be further strengthened by the National Surgical Trials Unit, which has been based in the Birmingham Clinical Trials Unit from 2013. ***Cancers of Unmet Need*** is undertaking advanced discussions regarding the status of a national **Brain Cancer Centre**. A Chair in Radiotherapy will be advertised for 2014, in order to take advantage of the outstanding local clinical infrastructure including the recent purchase of a 'Cyberknife' robotic radiotherapy system. Lung cancer research will be advanced through the MATRIX and TRACERx trials. The recent award of both the Chief Investigator (Middleton) and Trials Unit (Birmingham Cancer Clinical Trials Unit) to Birmingham for MATRIX, the flagship trial for Stratified Medicine 2, has also greatly strengthened ***Translational Cancer Genetics*** facilitating its crucial role delivering the **CRUK Stratified Medicine agenda**.

The *Cancer research* theme ***Cancer Immunology*** and the *Immunity, Inflammation & Infection research* themes ***Immunology*** and ***Liver*** will focus on the preparation of an application for a new MRC **Centre for Cellular Immunotherapy and Cancer Immunology.** To support this strategy, the relevant groups have been co-located in the IBR and strategic recruitment will be continued. This area will be supported through expansion of our capability in cell-based and immunological therapy, enabled by our investment in a Category 3 **Advanced Therapies Facility** (see section d) involving the NIHR Liver BRU and NHS Partners (UHB, BCH and NHS Blood & Transplant). New recruitment at Chair level and repositioning of some basic immunologists towards ***Inflammageing*** will also support the continued progress driven by the **MRC-ARUK Centre for Musculoskeletal Ageing Research** that will work towards ensuring its renewal in 2017.

The ***Virology*** and ***Viral Oncology*** research themes will continue their synergistic interaction that has already resulted in the creation of a University **Centre for Human Virology** that will be further strengthened by several strategic recruitments underpinning the preparations for an application for MRC/Charity Centre Status. Similarly, we will continue strategic work in the area of ***Microbiology*** research with the aim to have the activities of the **Institute of Microbiology & Infection** recognised by RCUK/Charity Centre status.

Within *Hormones, Metabolism and Reproduction research* a major strategic aim is the successful creation of a trans-regional, MRC-funded **Centre for Translational Steroid Endocrinology**, led by Birmingham in partnership with Manchester and Sheffield, aiming for rapid and integrated delivery of translational research of major importance to human health. To this end, we will maximise synergy between researchers within the groups focussing on ***steroid action and human disease***, ***obesity***, ***insulin resistance and diabetes***, ***rare endocrine disease*** and ***endocrine and endocrine-related cancer***, with interdisciplinary input from the research groupings ***Cancers of Unmet Need***, ***Immunology***, ***Inflammation*** and ***Inflammageing***. Secondly, the University **Centre for Obesity Research** will continue to work towards the creation of an integrated translational platform for obesity research, spanning across University and all relevant NHS trusts involved (e.g. largest bariatric surgery service in the UK at Heart of England NHS Foundation Trust), with the ultimate aim of creating an externally funded **Obesity Research Unit.** Strategic recruitment in support of both of these strategic aims is currently under way, further enhancing inter-disciplinary interaction and adding to the already significant mass of basic and clinical researchers.

Beyond ***endocrine determinants of adverse pregnancy outcome***, gynaecologists, foetal medicine specialists, neonatologists and paediatricians have reached a critical mass facilitating the recent creation of a University **Centre for Maternal and Child Health**. Birmingham is building a leading reputation in international maternal and child health research; we are a founder member and active partner of the annual international GLOW conference, aiming to bring better health care

through translational research closer to mothers and babies worldwide.

Thrombo-inflammatory processes and studies of their roles in vascular and cardiac pathologies are key targets of the **Centre for Cardiovascular Sciences**. Recent appointments (Fabritz, Kirchhoff, Brill) and BHF support at Senior Fellowship and Programme grant levels (Watson, Senis, Kirchhoff) will enable development of new animal models and translational studies leading to clinical trials through translational collaboration also exploiting international links such as the Atrial Fibrillation Competence Network.

Trauma and Regenerative Medicine Research has been identified as a strategic priority following the location of the Royal Centre for Defence Medicine (RCDM) at the QEH, which has been designated as a **Level 1 Major Trauma Centre**. UoB, UHB and RCDM worked together to create the **£15m NIHR Surgical Reconstruction and Microbiology Research Centre (SRMRC),** enhanced by the recent award of a £800k NIHR Healthcare Technology Co-operative in Trauma Management. Both NIHR SRMRC and the Healing Foundation Centre for Burns Research created in 2012 are enhanced by an emerging focus on the thrombo-inflammatory responses to acute injury led by Nash and Watson. The further development of this area will be facilitated appointment of a chair in Trauma Medicine and launching of a new MSc in Trauma Science.

Increased delivery of healthcare benefits is a core principle of our future strategy. This is exemplified by the **Institute of Translational Medicine** (ITM), which is described further in section d. The ITM is an example of strategic investment leveraging additional funds (in this case £12m from the government's City Deal for Birmingham) to support areas of scientific excellence in an integrated fashion, systematically enhancing synergistic interaction and new ways of working between University academics and research active NHS staff. The ITM will be a major component of our plans to expand our capacity and activity in **Personalised Medicine through Patient Stratification**. We have a specific objective to coordinate the ITM and the Clinical Immunology Service to be able to provide 'deep' phenotyping of patients involving immunological and DNA sequence analysis. This development will be complemented by the provision through University investment and organisation of 'omics' platforms (deep sequencing, proteomics and metabolomics) and an **integrated cross-campus strategy for bioinformatics**. The bioinformatics initiative will incorporate systems science for analysis of multi-system datasets and facilitate links between UHB electronic medical records and UoB research databases. The University bioinformatics initiative will be focused around a newly created **Centre for Computational Biology**, and will involve a number of appointments, including two at Chair level.

Full realisation of the potential of our translational pipeline will also be supported by two planned developments, for which funding is presently being sought. One will be to create a dedicated facility for the preclinical utilisation of human cells and tissue samples, encompassing cell derivation, cell based diagnostics/assays for high throughput screening, monoclonal antibody production and development, and support for cell based therapies to be conducted in the ATF. The second development will be to provide a suite of dedicated laboratories suitable for thorough longitudinal phenotyping of small animal (largely rodent) models in space contiguous with the BMSU breeding and maintenance facility.

c. PEOPLE, INCLUDING:

i) Staffing Strategy and Staff Development

The University and College systematically pursue an integrated staffing strategy that aims to strengthen our areas of biomedical research excellence and concurrently maximise the chances for synergistic interaction between them. This is exemplified by our **external recruitment success** during the assessment period, which has targeted areas that are likely to facilitate multi-disciplinary collaboration and research progress, e.g. Chairs in the overlap areas of chronic inflammation/steroid biology (Clark), cancer/stem cell biology (Bonifer) and endocrine-related cancer (Mehanna). In addition to recruitment, enhancing excellence also requires **retention of high quality staff** and thus external recruitment is balanced by **internal promotion of high performers** and **the introduction of professorial banding to recognise and reward success at Chair level**. During the period of assessment, we have recruited 15 Chairs, 2 readers and 23 senior lecturers whilst 22, 22 and 23 existing members of staff were promoted to Chair, Reader and senior lecturer, respectively, all within and contributing to our 4 key research themes.

Promoting and embracing equality and diversity is another crucial component of our staffing

strategy and the mix of genders, ethnicities and nationalities amongst members of our staff is testament to this. The career development and success of female staff is systematically nurtured by our staffing policies as well as by the implementation in 2009 of a **'Women in Academic Medicine and Science'** steering group in MDS, recognised by Athena Swan Bronze Awards in 2012 (University) and 2013 (MDS). Nationally, the Chair of this group (Martin) sits on the Medical Advisory Board for Athena SWAN at the Equality Challenge Unit. Activities include regular meetings, a mentoring scheme supporting early stage female researchers, diversity and equality training for all members of staff including induction packs for new starters as well as active input into policies surrounding promotion processes and senior leadership training and development. As a consequence of these activities: **women now comprise 50% of our academic staff and 25% of our professors;** 3 out of 5 Heads of School are female and 37% and 44% of staff at senior lecturer and lecturer level are women.

Integration of international staff members is actively supported by specific induction and welcome packs, regular meetings, surveys and through focus groups. A dedicated Marie Curie Researcher Society supports our international fellows for whom we are a favourite destination, reflected by the 11th position of the University amongst 842 European institutions in winning Marie Curie fellowships, and researchers in UoA1 have contributed to this significantly. 23% of our staff members are non-UK nationals (14% EU and 9% other internationals).

The success of our equality and diversity strategy in helping members of staff to achieve their full potential is also illustrated by the fact that the numbers of female and international staff members applying for internal promotion are entirely reflective of their numbers within overall staff and their success rate in obtaining promotion is identical to men and UK nationals, respectively. Our staffing strategy also aims to maintain the **vibrant mix of clinical and basic scientists** facilitating close interactions that are at the basis of our translational research capacity and strategy. We have systematically created and taken forward a number of activities for effective implementation of the *Concordat to Support the Career Development of Researchers*. Career development of all academic staff is supported by annual staff development reviews, mentorship schemes, coaching and courses offered by the University's Centre for Learning and Academic Development (CLAD). We have also developed a novel **tailor-made career development programme for post-doctoral basic scientists**, focussing on recognition of the postdoctoral training stage as a unique opportunity for making active career choices, with targeted support for those who demonstrate research excellence and aspire to independence. This includes the **Birmingham Fellows Programme**, implemented in 2011, with a second round in 2012 and a third round in 2013. Birmingham Fellows are junior investigators with research achievements of world-leading excellence and evidence of the most promising leadership potential. All Fellows recruited during the 2011 and 2012 rounds were offered a 5-year start-up package, mentoring and the expectation of retention as permanent staff upon continued research success.

During the assessment period we have reached out to the entire postdoctoral researcher base by establishing the **Post-Doctoral/Early Researcher Career development And Training (PERCAT) initiative** (lead Bicknell) that provides a wide variety of training and support opportunities for early career researchers, driven by their active involvement. This includes symposia, research speed dating events and dedicated grant and fellowship clinics providing grant writing advice by senior researchers as well as mock interview panels in support of fellows shortlisted for interview.

These initiatives have contributed to our **outstanding success in supporting researchers of all career stages in obtaining prestigious personal fellowship support**. During the period of assessment 74 junior clinical academics were awarded externally funded Research Training Fellowships (e.g. MRC, Wellcome, NIHR, CRUK, BHF, ARUK), 22 received clinician scientist fellowships and 5 senior clinical fellowships. Similarly, 20 early career basic science researchers succeeded in securing prestigious career development awards from the Wellcome Trust, BBSRC, and Royal Society amongst others and 7 secured a senior research fellowship.

These success rates are also driven by our **highly respected integrated clinical academic training pathway** (Lead Harper) that has been commended by the NIHR and Birmingham is in the top 25% of institutions for NIHR-funded training posts. Our Academic Foundation programme has established a reputation for excellence; 32% of applicants come from other universities and 98% of appointees reported Birmingham as their first choice. We have recruited to 38 academic clinical fellow (ACF) and 40 academic clinical lecturer (ACL) posts within our areas of research excellence.

Success is demonstrated by 75% of our ACFs progressing to competitively funded personal fellowships (national average 35%) and overall success from all our aspirant clinical research fellows exceeds 50%, one of the highest rates in the country. This has resulted in 90% of all our clinical research fellows undertaking PhD/MD training receiving competitive fellowship funding. During the period of assessment, 43% of ACLs have progressed to senior academic positions.

Clinical research activity, involving close integration of Birmingham academic staff and research active NHS-employed clinicians, is led by BHP, in close interaction with other local and regional trusts through the West Midlands Academic Health Science Network. Our success in effectively integrating our research with NHS-based research activities is also reflected by the fact that 16 of 21 NIHR Comprehensive Local Research Network (CLRN) leads for Birmingham & Black Country are University of Birmingham staff.

ii. Research Students

Since 2008 we have enrolled 622 postgraduate research students (PhD, MD, MPhil and MSc by Research). Nearly 150 funded studentships have been made available, driven by our success in obtaining large doctoral training grants (2 BBSRC DTGs in ageing biology, 7 Marie Curie ITNs, a unique Wellcome Trust integrated clinical and non-clinical DTG and studentships associated with the MRC Centres and an MRC Capacity Building scheme for Stem Cell Science). A key element of sustainability is nurturing the next generation of researchers. Increasing PGR numbers and obtaining increased numbers of fellowships for ECR were strategic aims achieved in the current assessment period. The NIHR BRU in Liver Disease also has a major clinical training element linking to our outstanding clinical academic pathway (see above) run by Harper. Looking forward, we aim to increase training further through dedicated studentships in translational medicine linked to the ITM. These will include those funded via industry-linked programmes such as CASE involving small to medium enterprises and big pharma.

The majority of our PGR Students / Doctoral Researchers (DRs) enter programmes that map directly to the research excellence themes relevant to UoA1 and are thus trained within a mature 1+3 Year structure (non-clinical) and with dedicated training platforms for clinical students. Our innovative Combined (Basic & Clinical) Wellcome Trust Training Programme (one of only two awarded nationally) aligns its 30 students to those areas of excellence represented by UoA1 and described above. We have also leveraged university funded studentships to capacity-build in spheres of emerging strength (ageing, stem cells, trauma, epigenetics, tumour immunity) and the bulk of institutional MRC DTA is aligned to DRs relevant to UoA1 where matching from internal funds effectively doubles its power. UoA1 is also populated by relevant Charity-funded DRs (number: 61; sources: WT, CRUK, BHF, LLR).

The University of Birmingham is at the top of UK and European organisations in winning Marie Curie Initial Training Network (ITN) grants offering PhD training with integrated international exchange; the **University of Birmingham is number 1 out of 842 with regard to numbers of coordinated ITNs and within the top 20 of all organisations for ITN grants awarded**, again with a significant contribution of Birmingham UoA1 researchers to this success.

Outside the EU, overseas partnerships and training for our DRs are grown and facilitated through financing Overseas Work Experience Placements and developing Joint Degrees between UoB and U21 partners in areas germane to UoA1: the recently created MDS/University of Melbourne Joint Studentship Programme being one such example. Translational research is a major driver of the postgraduate research delivery and a strong component of the R&KT culture within UoA1 returned areas. Current and recent CASE awards have partnered with the likes of Pfizer, AZ, GSK and Unilever. Knowhow for technology spinout is systematically promoted and an active Medici fellow programme for academia-industry interaction has been taken up by 41 postdoctoral researchers across the College.

Supervisors are appointed on the basis of research excellence and the ability to supervise and mentor students. A tailored supervisor-training programme (for both new and established Academics) was launched by MDS in 2011 to assure quality of supervision. Each DR is guided by a supervisory team made up of at least two individuals. DR training is driven through a process encapsulated in Development Needs Analysis (DNA) forms designed to be in line with the Research Council Joint Skills Statement and the new Researcher Development Framework. Student and supervisors complete an Annual Progress Review (APR) form that is reviewed and monitored by a Progress Panel with action as necessary. A recently introduced annual process

now impels all DRs to provide, direct to the Graduate School, appraisal of their supervision delivery: follow up and action flowing where necessary. Each DR is additionally assigned a separate mentor completely independent of the supervisory team for impartial guidance and confidential advice.

Nearly 50% of our postgraduate researchers stay in research undertaking a variety of postdoctoral/lecturer positions in the UK (86%) and abroad (12%), with over 40% moving into the health/health care/private sector. Three of our recent clinical PhD graduates have gone onto secure prestigious MRC/Wellcome intermediate fellowships whilst one has gained a MRC senior clinical fellowship. Our postgraduate researchers have an excellent track record in publishing their research, with 11 postgraduate researchers going on to be first author on 4* papers.

d. INCOME, INFRASTRUCTURE AND FACILITIES

Research Income: To increase external research income, we have used strategic Institutional investment to support areas where there is a critical mass of internationally leading researchers coming together in University designated Centres. These centres are supported on the expectation that they will obtain national funding to maximise sustainability. These research programmes are underpinned by investment in cross cutting platforms (e.g. technology hub; animal models; clinical trials units; patient focussed research facilities, tissue repository), to deliver advances in translational medicine. This strategy has been highly successful with 10 national Centres awarded or renewed during this assessment period. For example, the CTIR established in the new QEH in 2011 with £8m investment in research labs, 2 new Chairs and a clinical research facility was the driver for the MRC-ARUK Centre for Musculoskeletal Ageing Research (with University of Nottingham), Healing Foundation Centre for Burns Research; NIHR Surgical Reconstruction and Microbiology Research Centre (with Royal Centre for Defence Medicine & Royal British Legion Centre for Blast Injury Studies, Imperial College London), the ARUK Centre for Rheumatoid Pathogenesis (with Glasgow and Newcastle Universities) and the NIHR ECMC. The Birmingham NIHR Liver BRU (£6.5M awarded in 2008 and renewed in 2012) was further supported by significant UoB and Regional Development Agency (RDA) investment in tissue banking and cell therapy. Other centres renewed include MRC Centre for Immune Regulation; CRUK Centre for Cancer Research; CRUK Clinical Trials Unit and the NIHR Wellcome Trust Clinical Research Facility.

Focussing our research strategy on areas where the University is internationally leading has maximised our potential to attract income from research councils, government and charities to underpin Centre level awards. By focussing on priority research areas the College has established a £295m portfolio of live research funding. This together with our success in developing partnerships with industry and the NHS will allow us to sustain and further develop these research areas in the future.

Research infrastructure: Since RAE 2008 a new estates strategy systematically co-located groups according to research themes, rather than departmental alliance, and in new or refurbished high quality space to enhance research productivity. The main locations are:

1) The **Institute of Biomedical Research (IBR),** a £30m JIF-funded facility opened in 2004 which houses laboratory-based research groups including the **MRC Centre for Immune Regulation**. It includes a technology hub, state of the art imaging and laboratories for Category 3 microorganisms. Since 2008 the IBR has been extended into contiguous, high quality space in the Medical School. This substantial investment has increased our basic science laboratory space by 3000m^2 and allowed us to co-localise research groups working on DNA repair and epigenetics and various aspects of tissue repair and regeneration. Over the next few years the IBR will be further extended to co-locate the Clinical Immunology Service and Cancer immunology grouping with the MRC Centre for Immune Regulation to further enhance synergy.

2) The **CRUK Cancer Centre** and the **CRUK Clinical Trials Unit (CRCTU)** are located in contiguous buildings at the west end of the Medical School campus. Since 2008 substantial investment has provided high quality accommodation for the CRCTU allowing the unit to extend its portfolio of academic trials and thereby to increase income to sustain future developments. The CRCTU is the largest cancer trials unit in the UK (134 staff) with expertise in late phase trials, development of novel therapeutics and biomarkers in clinical trials. In 2009 the CRCTU was awarded core funding to become the UK's designated clinical trials unit for paediatric malignancies.

CRCTU has recruited 4478 patients into 56 trials since 2008. The CRCTU also hosts the **NIHR BRU in Liver Disease** extending expertise in early phase trials in cancer into non-malignant diseases an example of how we disseminate skills to maximise delivery. The **NIHR ECMC** focuses on early phase translational activity and includes a paediatric ECMC at BCH leading childhood phase 1/2a trials. The **Centre for Clinical Haematology,** built with RDA funds in 2011, houses the National Leukaemia and Lymphoma Research TAP. Coordination of national trials activity through the TAP has greatly increased recruitment and income allowing us to expand the Centre into adjacent space to increase capacity.

3) The **Institute for Microbiology and Infection** opened in 2011 in refurbished laboratory space in the Biosciences building, co-locating microbiologists and immunologists from the Schools of Biosciences and I&I. This helped to maximise synergy and collaborations and already resulted in a substantial increase in grant funding in support of sustainability.

4) The **NIHR/Wellcome Trust Clinical Research Facility (NIHR WT CRF)** based at UHB and BCH provides high-quality clinical environments for experimental and complex research studies. It was established in 1999 as one of the original Wellcome Trust Millenium facilities. A subsequent £10M Clinical Research Initiative Award from the Wellcome Trust, Wolfson Foundation and DoH funded an extension into the new QEH, a dedicated Gene & Immunotherapy facility and the first paediatric facility in the UK at BCH. In 2012 it received the largest NIHR CRF award nationally (£12.5M) to fund the running of the facility until 2017. The **CRF Health Research Bus** is a unique mobile research facility containing state-of-the-art clinical research equipment and a laboratory that allows studies to be done in the community. Since 2001 the NIHR-WT CRF has studied over 70,000 patients in more than 350 studies. As part of a national CRF network it promotes collaboration between CRFs and hosts conferences and workshops. Since 2008 two major new developments linked through shared governance to the CRF have expanded our translational research capability:

The Human Biomaterials Resource Centre (HBRC) established with RDA funding is one of the first Human Tissue Authority licensed tissue biorepositories. The involvement of senior pathologists ensures material of high quality and linkage to appropriate clinical data. Biobanking is facilitated by standardised collection procedures, generic ethics and consent that apply to all of our affiliated hospitals, allowing comprehensive recruitment from our large and diverse population base. Projects are assessed by a scientific advisory committee without need for additional ethics approval thereby streamlining governance for the individual researcher. This powerful platform provides a national resource accessed by researchers throughout the UK, e.g. as a component of **CRUK Clinical Hubs** and an **EU Innovative Medicines Initiative for stem cell research**.

The Advanced Therapies Facility (ATF) (opened 2013) funded by RDA, UHB and UoB provides state of the art cell and gene therapy suites integrated into the CRF with pharmacy facilities designed for gene, cell and biological therapies and “hatchery space” to co-locate academics and companies to develop commercial ideas. ATF projects have already attracted substantial funding from EU, MRC and NIHR suggesting the facility will be sustainable.

5) The **Centre for Translational Inflammation Research (CTIR)** opened in 2011 within the new QEH. This purpose-built facility brings together researchers working on mechanisms of inflammation biology from two Schools (CEM and I&I) with NHS clinicians and patients, providing high specification lab facilities as well as an integrated satellite of the NIHR WT CRF, a powerful platform for translation and experimental medicine in patients with chronic inflammatory disease. We have developed a strong relationship with the Ministry of Defence and the RCDM at UHB. This has helped to secure the **NIHR SRMRC** allowing us to carry out trauma research in both the civilian and military context, supported by MoD funded PhD students and technical support through the SRMRC linked to the CTIR.

Links with the NHS: The need to deliver translational research led to the establishment of BHP in 2011. The formation of BHP as an AHSC under a strategic alliance model was recently acknowledged by being short-listed as one of 8 national AHSCs to be interviewed for official designation in late 2013 in the 2013 NIHR/DoH competition. In 2012 BHP leveraged matched funding of £12m from government as part of the Birmingham City Deal, to establish the ITM that will serve as the engine for BHP to translate laboratory discovery into improved patient care and commercial activity. The ITM will cover 5 floors of high-quality refurbished space in the old QEH linked to the NIHR WT CRF. It will incorporate clinics for a broad range of well-characterised

patient cohorts including common and rare diseases, a portal for clinical trials and an early drug discovery unit, clinical bioinformatics and a floor of stratified medicine to include genomics and deep immunophenotyping. Commercialisation will be maximised through one floor of industry incubator space and there will be an integrated training programme for clinicians, life scientists and allied health professionals to develop the translational researchers of the future. Analytical capacity will be used to exploit access to some of the world's most complete healthcare data through UHB's state of the art comprehensive Electronic Medical Records (EMR) system, recording data from 800,000 adult patients each year and soon to be extended to BCH. This allows us to map demographic and complex clinical data from patient cohorts onto phenotyping and genomic information providing a unique opportunity to explore mechanisms of disease and develop personalised medicine through stratification. BHP is embedded within the recently licensed **West Midlands Academic Health Sciences Network** and a single West Midlands portal in the ITM will facilitate the involvement of clinicians and researchers from across the region and increase investment from industry. The ITM will provide the final link to deliver translation from basic science through experimental medicine, clinical trials and into the clinic and together with BHP will stimulate growth in the local economy.

Research facilities and equipment:

- The **Technology Hub** was set up in 2008 to bring together key technology platforms (next generation sequencing, high speed cell sorting, protein and antibody production, imaging and transgenic services) into a single structure to improve management, access, support and training. This structure allows us to plan replacement and facilitates investment in new technologies, including through the University **Research Technologies and Infrastructure Coordination Group**, which provides match funding for equipment requests associated with peer-reviewed grant applications and funds strategic investment in multi-user equipment facilities. The Technology Hub also links into M5, which is a group of Midlands universities (Birmingham, Leicester, Loughborough, Nottingham and Warwick, and Aston) that is exploring how to boost research collaboration and improve sharing of equipment.
- The **Biomedical Services Unit (BMSU)** provides facilities for the breeding and maintenance of animal models as well as capacity for investigational procedures. Planned expansion will increase capacity for longitudinal phenotyping (see section b).
- The **Henry Wellcome Building for Biomolecular NMR Spectroscopy** (renewed in 2012) is a national resource with open access to six NMR spectrometers operating at 500-900 MHz, four cryogenic probes and high throughput autosamplers.
- The **Birmingham University Imaging Centre (BUIC)** is a state-of-the-art brain MRI capability including stimulus delivery, eye tracking and limb movement recording and transcranial magnetic stimulation (TMS) with 64 channel simultaneous EEG recording. Cardiology and liver developments are facilitated through the NIHR BRU funded 3T clinical research MRI, based at the QEH.
- The **Systems Science for Health (SSfH)** initiative was launched in 2010 with £1M of University investment across 3 Colleges to coordinate UoB's expertise in metabolomics, analytical and computational workflows. The award of a prestigious **Technological Alliance Partnership** with **Thermo Fisher Scientific** in 2013 provides access to new technologies, scientists and engineers enhancing existing facilities including **Translational Steroid Metabolomics** and the **Biosciences Advanced Mass Spectrometry Facility**.
- The **Birmingham United Molecular Pathology (BUMP)** unit established 2012 is one of three national Technology Hubs which sequence tumours collected through the CRUK-funded Stratified Medicine Clinical Hubs centred on the **Birmingham ECMC** and **HBRC** underpinned by two Technology Strategy Board stratified medicine awards.
- The **Clinical Immunology Service** has developed deep immunophenotyping to stratify patients with blood cancers and identify the basis of complex secondary immunodeficiencies. Such coupling of research with clinical diagnosis improves clinical practice, attracts income for future developments and provides unique research opportunities.

Research student facilities: To ensure they work in a nurturing and challenging academic environment we place students in state-of-the-art laboratories with access to training in the latest technologies through the Technology Hub. The NIHR WT CRF runs courses in all aspects of translational medicine for clinical and non-clinical scientists as well as nurses and other health

professionals. For clinical projects BHP gives unrivalled access to the e-health informatics teams and data related to the 800,000 patients a year seen at the new QEH. All students have excellent information services provided by the Medical School learning hub that was refurbished in 2011.

For information on Research Ethics and Governance please see section b.

e. COLLABORATION OR CONTRIBUTION TO THE DISCIPLINE OR RESEARCH BASE

Our researchers support, influence and enhance local, national and international research activities, through collaboration, and through an extensive portfolio of national and international leadership roles. The majority of returned Birmingham research reflects local, national and international collaboration, specifically with European colleagues and institutions (supported by EU funding), as well as collaborations with researchers in the developing world, supported by WHO and charities. The recent launch of BHP and the development of the ITM are high profile examples of strategic development underpinned by major UoB investment (for the ITM this included £3m matched by £3m from UHB leveraging a further £12m from DoH). Significant national collaborations include membership of Wellcome Trust Case Control Consortia (for autoimmune and for psychiatric disorders) and lead roles in national research consortia for hepatic, rheumatological and renal diseases. Interdisciplinary collaboration in Birmingham research is reflected by a number of strategically supported areas such as trauma and ageing research, examples of successful interdisciplinary research.

The national research agenda and peer review processes are supported by significant roles of Birmingham academics in **UK Research Council and AMRC strategic panels and grants committees** (e.g. Moss, Chair of the MRC Infection and Immunity Board; Jenkinson, Chair of the ARUK programme grants Committee; Lord, RCUK Lifelong Halth and Wellbeing strategy panel and BBSRC Healthy Organism strategy panel; Bonifer, co-Chair of a BBSRC grant panel; Buckley, vice Chair ARUK research committee; Mitchell, Chair of Scottish Infections Research Network grants panel). The local research agenda is supported through extensive CLRN and NHS Trust R&D committee chairmanship (Birmingham Women's and SWBH Trusts) and through lead roles in Birmingham's adult and paediatric NIHR-Wellcome Trust CRFs (Buckley, Barrett, Harper, Martin). Birmingham academics deliver national research strategy through extensive **Royal Medical College and specialist society roles** such as Council membership of the Academy of Medical Sciences (Adams, Franklyn), Royal College of Physicians, Chair of Systemic Lupus Erythematosus group (Gordon), extending to European (Gordon, co-Chair EULAR; Arlt, European Society of Endocrinology executive committee member & POC chair) and US specialist society leadership roles.

Birmingham academics further enhance research quality and peer review through **journal editorship activities**, including associate and senior editorship and board membership of leading journals (such as *Am J Physiol*, *Arthritis & Rheumatism, Aging Cell, Biochem J; J Immunol, J Hepatology*, *Transplantation, J Clin Endorinol Metab, Endocrinology, J Biol Chem* and *EMBO Reports*). Influence of the research agenda, both speciality specific and general, is delivered through interaction of Birmingham academics with a wide array of government and related agencies including the NIHR (Harper, Gordon), NICE (Piddock), UK National Stem Cell Network (Frampton), TSB & HPA (Hawkey) and DoH (Lane), typically through panel chairmanship. Reach is extended through influence on similar **international agencies and grant giving bodies** (European Commission, France, Germany, Norway). Birmingham academics have delivered major influence on **national and international guidance documents through leadership roles in Royal Colleges and specialist societies** in the UK, Europe and the USA. Peer esteem is reflected by **highly prestigious personal research fellowships** and **major national and international research prizes** (e.g. Fellow of the American Academy of Microbiology, Piddock; Lord Cohen Medal, British Society for Research on Ageing, Lord; Heberden Medal, British Society for Rheumatology, Gordon; Michael Mason Prize, British Society for Rheumatology, Raza; Shine Award, Naidu; European Journal of Endocrinology Prize, Society for Endocrinology UK Medal, RCP Graham Bull Prize in Clinical Science and Endocrine Society USA Ernst Oppenheimer Award (1st European-based recipient), Arlt; Pitt Rivers Award, British Thyroid Association, Franklyn; European Society of Paediatric Endocrinology Young Investigator Award, Krone; Mead Johnson Medal, American Perinatal Research Society, Kilby).

Strengthening of regional partnerships is a key strategic aim of the University. In 2011,

Birmingham and Nottingham launched a joint **Concordat** underpinned by a framework agreement for collaboration, thus linking two of the Midlands most successful research-intensive universities in order to build on their complementary research strengths. The successful bid for the MRC-ARUK Centre for Musculoskeletal Ageing Research was the early beneficiary of the concordat. The Birmingham-Nottingham Strategic Collaboration Fund (£400K) was established to pump-prime the overall joint venture, and collectively the two universities will be investing £4M over 4 years to support studentships, fellowships, workshops etc. Projects with the State of Sao Paulo Research Foundation (FAPESP) have been committed £240K of the investment, which is matched by an equivalent amount from FAPESP. Through the **Birmingham Science City Research Alliance** we have strong partnerships with Warwick and Nottingham, e.g. the UoB/Warwick/Nottingham Midlands Imaging Initiative.

Proactive engagement with industry and robust support for translational/commercialisation opportunities is fostered through collaborative links with industry both at an overarching strategic level and through individual researchers. A dedicated senior professional Business Engagement Partner, appointed in 2012, has facilitated the implementation of a focused strategy for promoting and developing academic-industry interactions, in particular longer-term strategic partnerships with major healthcare companies. We have established an academic-led **Business Engagement Operations Group** with academic 'champions' from all Schools to identify new engagement opportunities and intellectual property (IP) potential. This approach has already borne strong results, with exemplars such as the Bioscience Ventures Ltd partnership with Abingdon Health. We use funding streams such as the Wellcome Trust ISSF to support specific **Knowledge Transfer Secondments** of academic staff into industry and NHS settings to increase knowledge and understanding of these translational environments. UoA1 staff have access to a dedicated **Technology Transfer Team** within the College's R&KT Office working with individual academics to assess IP and commercialisation strategies. The College **External Commercialisation Board** comprises top industry experts, including Simon Campbell (Senior VP, World-wide discovery, Pfizer), Malcolm Skingle (Director, European Academic Liaison, Global External Affairs, GlaxoSmithKline), Clive Dix (Chairman of Board, Bioindustry Association), Martin Murphy (CEO, Syncona Partners, the venture capital arm of Wellcome Trust) and Alan Boyd (R&D Director, Ark Therapeutics). Their advice is linked to the University's own dedicated commercialisation company, **Alta Innovations** that support the patent process and drive consulting, licensing and spin-out opportunities for UoA1 academics.

International collaboration is a further key strategic objective. This is evidenced not only by strong partnerships between specific research groups with those in leading international institutions (e.g. Northwestern University Chicago, Mayo Clinic Rochester, Erasmus University Rotterdam) but also by UoB investment to support partnerships such as the **Universitas 21 network** partner University of Melbourne (2 joint studentships annually) and establishment of UoB offices in China (Guangzhou, Shanghai), Brazil and India. The College has an **International Engagement Oversight Committee** with academic champions for different regions (Africa, Australia, Brazil, China, Europe, India, USA), supported by senior academic management and the UoB International Office. This is exemplified by our dedicated **EU Networking Task Force** (lead Arlt) that drives participation in EU-funded research through targeted networking and proactive matching of researchers with FP7 and Horizon2020 research calls. This strategy is systematically supported by the **dedicated EU Funding Support office** within the UoB Research and Innovation Services, further enhanced by the **University of Birmingham EU office in Brussels**, opened in 2010, which provides a venue for UoB academics to meet with collaborators for EU projects. The office facilitates direct input into EU research policy, connections with European institutions including the EU's Joint Research Centre, as well as face-to-face meetings with EU stakeholders, thereby enhancing our ability to form pan-European partnerships and respond to calls in a most timely and effective manner. Reflecting the success of this strategy, the last EU monitoring report (2012) has stated that the University of Birmingham has advanced to 24th place amongst all HEIs taking part in FP7 in terms of signed agreements, with the European Commission making a special note of our progress: 'The biggest jump was demonstrated by the University of Birmingham (UK) - from 37th position in 2011 to 24th position in 2012'.