Institution: University of Leicester

Unit of Assessment: 5 Biological Sciences

a. Overview: This submission encompasses investigators in the **College of Medicine, Biological Sciences & Psychology** (**CMBSP**), established in 2009 in a major reorganisation of the University into four Colleges. While its 11 Departments reflect teaching activities, research is structured into cross-disciplinary **Themes**, which provide the units from which our submissions to Main Panel A are made. UOA5 also benefits from extensive collaboration and joint appointments with the **MRC Toxicology Unit** located in the University's central campus where clinical and laboratory-based researchers work in close proximity, and with the **University Hospitals of Leicester NHS Trust**.

The emphasis in this unit is on fundamental biological questions addressed in a wide variety of organisms from bacteriophage to humans and higher plants. Our submission is made up of four broad research groupings in which we have critical mass:

• **Genome Diversity & Dynamics (GDD)**: Badge; Bayliss; Beleza; Foster; Heslop-Harrison; Higgins; Hollox; Jeffreys; Jobling; King; Louis; Oggioni; Rajakumar; Royle

• **Regulation of Gene Expression (RGE)**: Bushell; Clokie; Cowley; Drea; Eperon; Morrissey; Revyakin**;** Shackleton; Twell

• **Structural Biology & Biophysics (SBB)**: Carr; Dominguez; Fairall; Kriajevska; Moody; Schmid; Schwabe; Roberts; Vuister; Wallis

• **Receptors & Signalling (RS):** Challiss; Evans; Herbert; O'Hare; Tanaka; Tobin; Willars; Willets

b. Research strategy

Key changes to general research environment during the assessment period

• **Thematic Research**: The core of CMBSP research strategy, and the major environmental change since RAE2008, has been integration of activities into 9 Themes in order to stimulate vital and sustainable research while maintaining a successful Departmental structure. Launched in 2010, these are now mature and effective units that enable strategic targeted investments, support established strengths, and nurture new developments. Each consists of an alliance of researchers sharing broad scientific questions or approaches; investigators can participate in more than one Theme, facilitating collaborations, such as those with clinical researchers. Theme leaders provide strategic and coordinated input to the key CMBSP meetings (Management Board, Research Committee, and Research Implementation Group [RIG; chaired by Prof Mike Barer, CMBSP Research Director]), including allocation of PhD studentships and guidance on new appointments. Three Themes - **Molecular & Cellular Bioscience** (led by Schwabe & Challiss)**, Genome Science** (Jobling) and **Microbial Science** (Morrissey & Oggioni) - form the basis of this submission. Some members of these Themes are allied to clinical medicine, public health or neuroscience, and so are submitted within UOAs 1, 2, and 4. Thematic restructuring means that the groups in UOA5 are very different from those of RAE2008, making direct comparisons difficult.

• **Core Biotechnology Services (CBS):** In 2011 internal investment was used to bring a number of facilities together under unified leadership (Prof Andrew Fry, UOA1) as a virtual department, providing streamlined core services dedicated to supporting research across CMBSP, detailed under section d below. Key to the success of CBS and other research activities has been support from two major funds, described next.

• **Wellcome Trust Institutional Strategic Fund (WTISSF):** The University was awarded flexible funds of £500K p.a. (2011-13) from the Wellcome Trust (WT), 95% of which are disbursed within CMBSP. Funds are prioritised to strategic objectives, e.g. employing a training officer within the bioinformatics service; recruiting two structural biology research fellows; supporting young researchers, e.g. Victoria Cotton (*Royle3*), Rachel Watkins (*Shackleton2*); generating pilot data, e.g. muscarinic receptor work (Tobin), leading to $300K Eli Lilly grant. Bids are assessed by RIG.

• **The University's Research Infrastructure Fund (RIF)**: A £2.5M p.a. fund was established in 2011 to support procurement of research equipment and infrastructure, both as stand-alone requests, and as match-funding for bids to external funders. Bids require CMBSP support before submission, and have brought £1.8M strategic University investment into UOA5 to date.

These developments have greatly enhanced the focus and strategic nature of our research activity, and together with targeted investments in personnel, infrastructure and cross-disciplinary activities, provide a vibrant environment for innovative biological science research.

Activities, operations and achievements of research groupings

(i) GDD, recently reinforced by investments in genomics & bioinformatics, has its roots in Jeffreys' work on minisatellites, which evolved into fundamental studies of normal and aberrant recombination, revealing hotspots and the details of crossover and gene conversion. Researchers use direct and population approaches to study human meiotic exchange, copy number variation, and telomere & transposon dynamics (Badge, Hollox, Jeffreys, Jobling, Royle), and also plant meiosis (Higgins). Genome organisation and diversity are studied in a range of species from bacteria (Bayliss, Oggioni, Rajakumar), to higher plants (Heslop-Harrison).

Louis' appointment represents University investment of ~£1M. He leads the Centre for Genetic Architecture of Complex Traits, studying adaptation, complex phenotypes and epistasis in *S. cerevisiae* and other organisms. The newly appointed Foster studies DNA repair, linking fundamental aspects of genome dynamics to more applied aspects of somatic mutation, and its influence on cancer susceptibility; Beleza brings new expertise in human population genomics.

Key achievements: (i) Demonstration that variation in the human gene encoding a DNA-binding protein, PRDM9, has a profound influence upon normal and pathological recombination (*Jeffreys1*); (ii) Finding that highly active L1 transposable elements are more frequent than previously supposed (*Badge1*); (iii) Use of whole-genome sequencing to understand the phylogeny and domestication history of yeasts (*Louis1*); (iv) Identification of targets of antibiotic-driven positive selection in *M. tuberculosis* via whole-genome sequencing (*Oggioni1*).

(ii) RGE: Members focus on gene expression and regulation, encompassing basic mechanisms and disease-related processes. Work spans the breadth of gene expression, with particular expertise in initiation and maintenance of transcriptional programs in prokaryotes (Clokie, Morrissey) and eukaryotes (Carr, Cowley, Drea, Revyakin**,** Schwabe, Twell), pre-mRNA splicing (Eperon, Dominguez), translational regulation via miRNAs (Bushell) and chromosome organisation (Shackleton). Methodologies range from the biophysical (X-ray crystallography, NMR), single-molecule techniques, high-throughput genomics, to transgenic plants and animals.

Key achievements**: (**i) Collaboration on histone deacetylases (HDACs) including discovery of inositol tetraphosphate as a component of co-repressor complexes, a paradigm shift in the understanding of how signalling is integrated into epigenetic regulation (*Schwabe1,2*). (ii) Identification of regulators of male gamete-specific gene expression in plants (*Twell1*, *3*). (iii) Demonstration that translational inhibition depends on miRNAs impairing initiation complex (eIF4F) function, and that unstructured 5´ UTRs are refractory to inhibition (*Bushell1*). (iv) Use of single-molecule methods to analyse mammalian gene expression complexes, defining RNA splicing complex stoichiometry (*Eperon2*); use of novel chemical biology tools to show that functional interactions between distant sites on the RNA do not involve looping (*Eperon1*).

(iii) SBB: Leicester has established strengths in SBB, reflected in the 2005 foundation of the Henry Wellcome Laboratories of Structural Biology (HWLSB). Investigators share an interest in the mechanisms of action of proteins and protein complexes, investigated through SBB technologies, and including commercial collaborations described in an impact case study. Biochemical, biophysical, cellular and functional assays provide biological context. There is emphasis on complexes involved in gene regulation (Dominguez, Fairall, Schwabe, Carr) in microbial pathogens (Moody, Carr), enzyme mechanisms (Moody, Roberts), and ion channel exchange proteins (Vuister). There are also several associated collaborating groups and fellows (e.g. Wallis, Kriajevska), as well as research into protein structure prediction and modelling (Schmid).

Key achievements: Structures of (i) two HDAC-corepressor complexes (*Schwabe1,2*); (ii) the complex that targets the LDL receptor for degradation (*Schwabe4, Fairall2*); (iii) sclerostin and identification of interaction surfaces (*Carr2*); (iv) complement complexes that are key to innate immune system function (*Wallis1,3,4*). (v) Detailed stereochemical understanding of the ferryl intermediates in haem peroxidase enzymes (*Moody1,2*). (vi) Understanding domain motions in cytochrome P450 reductase and their role in enzymatic activity (Moody, Roberts).

(iv) RS: G protein-coupled receptor (GPCR) (Challiss, Tobin, Willars, Willets) and ionotropic purinoceptor (P2X) (Evans, Mahaut-Smith [UoA1]) research continue to be strengths. Muscarinic acetylcholine and metabotropic glutamate receptors are among the subtypes studied, with an emphasis on the consequences of GPCR phosphorylation. The development of phosphorylation-deficient, knock-in mouse models has been key to determining *in vivo* roles for muscarinic receptor

subtypes in the CNS (Tobin). Mutagenesis, cross-linking and molecular modelling approaches have illuminated purinoceptor ($P2X_1$) structure and function (Evans). Aspects of signalling addressed include bacterial infection (O'Hare), meiotic regulation (Tanaka), and the regulation of pancreatic β-cell insulin release, hypertrophy/hyperplasia and toxicity (Herbert, Willars).

***Key achievements*:** Linking fundamental GPCR research to translational pharmacology, including roles for altered receptor-G protein coupling in fear conditioning and schizophrenia endophenotypes (*Challiss1,2*), and phosphorylation-dependent biasing of muscarinic receptor signalling in brain (learning & memory) and pancreas (insulin release) (*Tobin1,3*). Application of (phospho) proteomic analysis to P2X accessory proteins/chaperones (*Evans3*), receptor "bar-coding" (*Tobin4*) and the phospho-proteome of the malarial parasite *Plasmodium falciparum* (*Tobin2*).

Strategic objectives for research over the next five years

GDD: Studies of somatic genetic diversity and DNA repair will be promoted, to forge links with cancer research in CMBSP. Investment in bioinformatics will facilitate exploitation of genome-wide datasets and approaches. Recruitment of a high-calibre researcher to the Jeffreys Chair of Genetics will strengthen mammalian genome dynamics, and single-molecule approaches to mutation and recombination will be expanded in collaboration with colleagues from SBB and RGE.

SBB: A major development is the 2013 relocation of the **Collaborative Computing Project for NMR** from Cambridge to Leicester, under Vuister. New planned research facilities include a 950 MHz NMR Spectrometer, expanded EM facility, and pioneering single-molecule facilities. Further initiatives will expand translational structural biology, recruiting cancer structural biologists; novel approaches are being developed to study the assembly and function of larger protein complexes.

RGE: The focus will continue to shift from individual transcription factors to complete multi-protein regulatory complexes - studies ranging from the determination of the structures of fully assembled enhancer and epigenetic complexes to single-molecule studies of the assembly and action of the general transcriptional machinery. These will be extended to include the role of lncRNAs, and will utilise genome-wide approaches in both plant and animal models.

RS: Collaborative links with SBB will be strengthened to increase the application of NMR, crystallography and bioinformatics to RS research (*Evans1, O'Hare3*). A new chair appointment will strengthen links to the Centre for Translational Therapeutics and enhance academic drug discovery programmes. Proteomics and advanced live-cell imaging provision will be systematically reviewed to ensure that state-or-the-art facilities (e.g. multiphoton and super resolution microscopy) continue to be available to RS researchers.

Translational integration: Through our thematic structure, interdisciplinary events, co-supervised students, and joint grants we will strengthen the links between basic research in UOA5 and clinically focused research in other Themes in CMBSP. Establishment during this REF period of 3 **NIHR Biomedical Research Units** (Cardiovascular, Respiratory, Lifestyle), a **Collaboration for Leadership in Applied Health Research and Care** and an **Experimental Cancer Medicine Centre** provide opportunities for translation of our basic research, and support our target of establishing an NIHR Biomedical Research Centre. Infrastructure will be further improved with the completion in 2015 of a £30M medical teaching building that will allow a redesign of research space in two major existing buildings (Medical Sciences and Henry Wellcome).

PGR student recruitment: We will recruit additional students from international sources, notably developing countries that are sending junior University staff to the UK for training. We will offer a new format 4-year PhD, with a highly structured and assessed first year involving taught PG-level lectures/seminars and laboratory classes, a modular skills-training programme (including English teaching), and rotational research projects. Passing this first year would be a condition for to progress with the PhD. We will also bid for a WT 4-year PhD programme in the next application round, and better exploit EU sources of support, including Marie Curie Networks. Success of CMBSP's current bid for a CRUK Centre will also provide PhD studentships, accessible to UOA5.

Responsiveness to national and international priorities and initiatives

Our thematic structure provides natural links into the research strategies of major funders. UOA5 connects specifically to the WT strategic challenges 'Maximising the health benefits of genetics and genomics' and 'Combating infectious diseases', the MRC's 'Genetics and disease', and BBSRC strategic priority 'Basic bioscience underpinning health'. Interdisciplinary links are being

forged across the University to exploit opportunities under special calls, and to allow collaborative applications to funders such as the Leverhulme Trust. Collaboration with the Universities of Birmingham and Warwick allowed a successful bid for a £4.5M BBSRC Doctoral Training Programme.

Mechanisms for research development, promotion and dissemination

Our Themes also provide a framework for fostering interdisciplinary research, and a forum for communication, collaboration and research development. They are continuously reviewed by the CMBSP Management Board and Research Committee, and their functions operate under the guidance of steering groups, benefit from central administrative support, and are facilitated through events typically attracting 60-120 researchers from within and outside CMBSP:

• **Regular research days** bring colleagues together for general exchanges of information and ideas, typically including short talks from investigators, post-docs and PhD students, and presentations on facilities, enterprise and career development.

• **Subject-focused research events** include internal and external speakers; examples from the last two years were on Epigenetics (2011), Tuberculosis (2012), and Host-Pathogen Interactions (2013); the bi-annual British Pharmacological Society Cell (BPS) meeting is held in Leicester (its 4th iteration was in 2012). Technical workshops include internal speakers, facility managers, and external companies; e.g. Next-generation sequencing workshops in 2010 & 2012.

• **Seminar series***,* three run in UOA5, with high-quality international speakers - over the last 2 years including Robin Allshire (Edinburgh), Wilbert Bitter (Amsterdam), Hagan Bayley (Oxford), Frank Gannon (Brisbane), Manfred Kayser (Rotterdam), Colin Kleanthous (York), Paul Nurse (LRI), Venki Ramakrishnan (LMB), Timothy Read (Emory), Ed Southern (Oxford).

To strengthen ties with industry and increase commercial income through CASE studentships, research contracts and collaboration, CMBSP has established an Enterprise Committee.

Public engagement: Our press office (and award-winning Newsblog) supports the public dissemination of our research. Members participate in outreach supported by the University's CETL GENIE, e.g.: **Badge**, **Clokie**, **Jobling**, **Tobin**: talks to schools in Leicester, Loughborough, Lutterworth, Hinckley, Coventry; **Bayliss:** talks to Meningitis Research Foundation; **Cowley**: talks to teachers at E Midlands Science Learning Centre; **Clokie**: BBC R4 interview, 'Inside Health'; **Hollox**: 'Breathless Genes' exhibit, Royal Society Summer Exhibition 2012; **Hollox**, **King**, **Jobling**: Leicester New Walk Museum talks for the WT-sponsored 'Inside DNA' exhibition; **Jeffreys**: many public talks, and 'Action for Biology in Schools' Patron; **Jobling**: 32 talks, including annually to 2 x 300 Year-9 students during GENIE 'Dynamic DNA' days; U3A and family history groups; **King**: 31 public events, including talks on the Richard III project, and an annual appearance at 'Who Do You Think You Are?' (London Olympia), the world's largest family history event; **Morrissey/ Rajakumar**: BBC Leicester interviews on *S. aureus* outbreaks, and antimicrobial resistance; **Twell**: Sense about Science participant; **Willars**: Science Link Governor at local Academy.

Interdisciplinary activities

The thematic structure described above automatically promotes interdisciplinarity by bringing together researchers from different Departments and backgrounds.

While the emphasis in UOA5 is on fundamental biological questions, much of our research on humans and model organisms interacts directly with translational activity in other UOAs. The development of these aspects is facilitated by an excellent relationship with the **University Hospitals of Leicester NHS Trust** sustained at the highest level through CMBSP representation on the Trust Executive and R & D Boards, providing an interface for translation of appropriate basic research into the three Leicester hospitals (examples given in [e] below).

Researchers also collaborate with investigators in other Colleges (examples under [e] below). Links to the **College of Science & Engineering** are facilitated by its **Life Science Interface**. Links to the Colleges of Arts, Humanities & Law will be strengthened by planned incorporation of joint seminars with the **Medical Humanities Research Centre** into existing UOA5 seminar programs. The virtual **Alec Jeffreys Forensic Science Institute** promotes interdisciplinary approaches (Chemistry, Genetics [Jobling], Engineering, Pathology, Criminology) and innovation in key areas of forensics.

c. People, including:

i. Staffing strategy and staff development

Relationship of staffing strategy to research strategy and infrastructure

UOA5 strategic recruitment of staff, including succession planning and new posts, is guided by Themes and overseen by the CMBSP Management Board and Research Committee, and has brought in new high-quality researchers (Beleza, Dominguez, Fairall, Foster, Higgins, King, Louis, Oggioni, O'Hare, Revyakin, Vuister). WT (VIP, ISSF) funding has been used to provide bridging funds for excellent Early Career Researchers. Strategic investment from CMBSP is also targeted to establish and develop high-quality permanent staff for our facilities such as CBS (see Section d).

Research Concordat: The University is implementing an Action Plan and timetable for the Concordat to Support the Career Development of Researchers, and was awarded the European Commission's 'HR Excellence in Research' award (2011) in recognition of its commitment. Performance is monitored by a Concordat Steering Group, on which Jobling represents CMBSP.

Equality & diversity: The University proactively manages equal opportunities (EO), as set out in its EO Policy, through its Equalities Unit (including an Athena SWAN coordinator). The CMBSP EO Committee includes Departmental equality officers and student representatives, meets four times a year, and reports to the University EO Committee (chaired by a senior pro-vice chancellor). Gender equality issues and Athena SWAN are standing items. The University holds a bronze Athena SWAN Award, and all CMBSP Departments are working towards silver awards, which the Dept of Health Sciences already holds; three others hold bronze. Women speakers are represented in all UOA5 research events, and in January 2013 a research day 'Celebrating women in Science: Genomic approaches to biological questions' featured female early-career researchers, an equalities presentation, and a lively discussion about the participation of women in SET.

Sustainable staff structure: UOA5's long record in recruiting and developing ECRs, then retaining them as PIs signals a good working environment – examples are Tobin (WT PDRA, 1991), Jobling (MRC Training Fellow, 1992), King (PhD student, 2000), Bayliss (RCUK Fellow, 2007). Our flexible workload policy permits any individual's work balance to shift between research and teaching. Academic careers are thus sustained, yet new research opportunities can be grasped. Staff recruitment considers age and gender balance, and brings on new researchers. Continuous review of research strengths and strategy will ensure scientifically focused yet flexible investments in the future.

Effective development and support of research work: The Research Support Office (RSO) supports grant applications and awards, including: identifying and disseminating funding opportunities; training in applying for grants; providing financial returns and planning**;** advice on costing and submitting grant applications; negotiating contract terms with funders and collaboration agreements with other HEIs and public sector collaborators; providing post-award financial administration of externally-funded projects; submitting invoices, claims and statements of expenditure. A specific team deals with EU funding, and has built up significant expertise.

On-demand grant development sessions are available, with attendees chosen for their expertise, experience with specific funders, or to offer an interdisciplinary perspective. RSO also provides regular opportunities (e.g. the annual 'Research Focus Week') to hear directly from funders, and to attend grant-writing workshops. All grant applications are subject to internal peer review.

Research career development: Mentoring and appraisal by UOA5 colleagues are key parts of career development. In addition, the University's Academic Practice Unit provides professional development training for all staff conducting, supervising and managing research. This includes inductions, and an extensive programme of workshops in research leadership and management, covering funding sources, 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 internal and external experts provide overviews of particular research methods and their benefits and limitations.

Early career researchers (ECRs): The annual Research Staff Forum aims to help ECRs realise their career potential, and includes workshops on transferable skills, enterprise, impact, CV development, and University Research Strategy. A CMBSP Research Staff day (October 2013) aims to build networks and identify issues about career progression. Within CMBSP Prof Ruth Luthi-Carter (UOA4) is responsible for ECR Development and is developing a joint appraisal/

mentorship scheme. Theme research days and workshops provide plentiful opportunities for post-docs to present work to a wider audience. Jobling and Fry (UOA1) run grant-writing workshops, and senior staff offer guidance and review for ECRs embarking on their first grant applications.

ii. Research students

Overview: Current postgraduate research (PGR) population is 98, divided between the research groupings as follows: GDD - 33.5, RGE - 19.5, SBB - 21.5, RS - 22.5. A total of 21.5 PGR students graduated from UOA5 in 2012/13. Studentship funding consists of:

• **BBSRC** Midlands Integrative Biosciences Training Partnership (total ~£4.5M; 2012-14), supporting 15 x 4-yr studentships p.a. across Leicester, Warwick, and Birmingham. Research areas include gene expression and molecular mechanisms.

• **MRC** Doctoral Training Grant (~£0.9M; 2011-13) supporting 3 x 3- or 4-yr studentships p.a.

• **NERC** Doctoral Training Grant (~£0.3M), supporting 1 studentship p.a.

• **CMBSP** Scholarships; 8 x 3.5-yr PhD studentships p.a., allocated strategically (e.g. *O'Hare3*).

• **CASE studentships**: including (in REF period), Carr (UCB Celltech), Herbert (AstraZeneca; *Herbert2*), Tobin (Heptares, *Tobin4*), Novartis, Eli Lilly), Willars (AstraZeneca; *Willars1*).

• **Individually-secured studentships** including (in REF period): Boehringer-Ingelheim Fonds (*Jeffreys1*); Leverhulme Trust (*Eperon1*); NWO (*Vuister1*); British Heart Foundation (*Evans1*); Diabetes UK/Kidney Research UK (*Herbert4*); Commonwealth Scholarship Commission (*Rajakumar4*); Mexican (*Herbert1, Royle1*), Chilean (*Louis4*), & Libyan governments (*Twell3, 4*).

• **Self-funded students**, contributing to the following outputs: *Badge3*; *Bayliss3*; *Jeffreys1, 4*; *Jobling1*; *Rajakumar3*; *Tanaka4*; *Twell4.*

CMBSP 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. 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 in the supervisor's lab. General training in the first year includes 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 PGR committees. CMBSP pioneered the online system PROSE to manage and record training.

To broaden their experience, PGR students also participate in: tutorials and demonstrating to UG students; the annual competitive University Festival of PG Research in which 50 students present to academics, employers, and the public; residential Graduate School programmes and other Vitae training; 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 in public and private sectors from past students, and to network with visitors and exhibitors. Students are fully integrated into the thematic programmes of events, attending seminar series and presenting talks and posters during research days.

Progression & recognition: Students are initially registered as Advanced PGs, and around month 9 write a report and give a seminar. These form the basis for a viva with a Thesis Committee, decisions on progression to PhD student status being approved by the Graduate Office. A second review before the end of year 2 checks that the student is progressing and will complete lab 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 PhD graduates who are outstanding academically and able to present their work to a wider audience, and an annual prize for the two best students graduating each year. Recent UOA5 winners are King (supervisor: Jobling) and Gabriel Lam (Jeffreys) in 2008, Ian Wilkinson (Carr, 2010) and Sophie Bradley (Challiss, 2011). In the 2013 PGR experience survey 82% of CMBSP students were satisfied with their experience, a figure in line with Russell group universities and supporting

our philosophy. Student quality is reflected in the fact that 49% of the 142 UOA5 outputs include authors (total 102) registered as PhD students during the REF period. Many PhD graduates gain excellent post-doctoral/industry positions, e.g. Raheleh Rahbari (supervisor Badge; to Sanger Inst., Cambridge), Oliver Dovey (Cowley; Sanger); Charles Foster (Cowley; CRUK London); Yi Wen Kong & Ian Cannell (Bushell; MIT); Shripana Sarbajna (Jeffreys; CRUK London); Michelle Graciotti (Tobin; EPFL, Lausanne); Ian Wilkinson (Carr; Medimmune).

d. Income, infrastructure and facilities

Research awards commencing in REF period (NB *not* spend, as shown in REF4b)

• **GDD grouping**: Total: £4.4M, including: Jobling (WT SRF, £1.9M), 2 MRC Project (Royle, Hollox); 2 WT Proj (Hollox, Jeffreys); Bayliss (Meningitis Research Fund, £180K).

• **RGE grouping**: Total: £12.8M, including: Bushell (MRC Prog, £3.6M, SRF, £1.8M); Cowley (MRC SRF, £2.1M); 7 BBSRC Proj (Bushell, Cowley, Drea, Twell); 4 WT Proj (Bushell, Clokie, Eperon, Shackleton), 3 Leverhulme Proj (Clokie, Drea, Eperon), MRC Proj (Cowley).

• **SBB grouping**: Total: £9.5M, including: Carr (UCB Celltech, total £2.1M; MRC Tech Structural Biology Partnership - £650K); Schwabe (WT prog, £1.4M, Investigator Award, £2.4M); Dominguez (MRC-CDA, £830K); 5 BBSRC Proj (Kriajevska, Moody, Schmid, Schwabe, Vuister).

• **RS grouping**: Total: £2.9M, including: £490K total British Heart Foundation; O'Hare (MRC Proj , £360K); Tobin (WT Proj, £500K); MRC & WT Capital funding totalling £1.2M (Tobin, Evans).

Research infrastructure

We are supported by University Research Support & Enterprise offices, with a Pro-Vice Chancellor for Research and Enterprise (Prof Schürer) responsible for developing and delivering strategy. He chairs the University Research Policy Committee, of which the CMBSP Director of Research is a member, providing a conduit for coordinating strategy at theme, College and University levels.

CMBSP Research Office: CMBSP has a dedicated Research Office led by an Assistant Registrar with 3.7FTE support, which manages applications for external and internal funding, operates the internal grant peer review system and organises CMBSP committees. It also provides 0.5FTE support to each Theme and aids organisation of events, and website management. An annual CMBSP budget of ~£2M is available for research support, in addition to WTISSF and University funds described above, and mostly distributed via competitive bidding.

Research facilities: We are well equipped with all standard research equipment in excellent premises, including the Henry Wellcome Building (completed 2006), and here highlight five key developments that have improved infrastructure since RAE2008:

1) **CBS**, including**: 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 proteomics (LTQ-Orbitrap and high-sensitivity validation via 4000Q-Trap mass spec) and the PROTEX protein expression laboratory; Sanger sequencing, Roche GSFLX next-generation sequencing, SNP typing and transcriptomics including Illumina bead station and C-Scanner [£142K URIF invest-ment], Q-PCR, robotics, DNA clean rooms; **ES Cell Facility** offering a complete 'DNA to mouse' service; four containment level 3 laboratories; **Bioinformatics and Biostatistics Support Hub**, established in 2010 under Badge, and employing a bioinformatician, biostatistician, and training officer to support experimental design and data analysis; **Biomedical Workshop** with 45 years' experience with specialist research equipment. These facilities are supported by 15 full-time Grade 7/8 and 13 technical posts, from University funds. CBS operates a flexible charging scheme that aims to recoup costs, but allows PGR students ready access. 38% of the 149 papers submitted here used CBS facilities.

2) **Central Research Facility (CRF):** This £17M building, opened in 2012, was part-funded by a £3.9M WT Capital Award, centralises all our animal holding space and houses 4 premium suites managed by CBS. It allows advanced transgenics, behavioural studies and *in vivo* imaging, including a URIF-funded (£355K) IVIS Spectrum Quantitative 2D and 3D optical imaging system.

3) The **Centre for Translational Therapeutics**, led by Tobin, provides a coordinated means to promote the design of novel therapeutic agents. 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.

4) **HWLSB**: Includes 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.

5) 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 bioinformatic analysis. The system is complemented by centralised secure research data storage.

Development of research infrastructure: We will continue to develop CBS and to purchase state-of-the-art equipment via the URIF, including third-generation sequencing platforms to give unbiased access to genetic variation at the single-molecule level. We will obtain a 950 MHz NMR Spectrometer, expand our EM facility, and enhance our single-molecule facilities. Proteomics and advanced live-cell imaging provision will be updated over the next five years.

Cross-HEI use of facilities: Leicester is part of the **M5 group** of Midlands research-intensive universities, including Aston, Birmingham, Loughborough, Nottingham, and Warwick, that is exploring how to boost research collaboration and improve use and sharing of specialist equipment. The M5 online equipment-sharing database (the UK's first, and including facilities within UOA5 laboratories) was launched in December 2012, and the group is now developing mechanisms for cross-institutional booking, and shared maintenance contracts across sites. A joint Leicester-Nottingham-Birmingham microscopy bid is planned to the Wellcome Trust (2014).

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.

All projects involving human subjects undergo ethical review, by an NHS research ethics committee or a University committee as appropriate. Use of genetically modified organisms is monitored by the Genetic Modification Sub-Committee of the University's Biological Safety Office. We are committed to achieving a Concordat on principles of openness in animal research. This is exemplified by the opening of the CRF, to which the media were invited, and about which the CMBSP Research Director was interviewed on BBC Radio 4's Today programme, leading to a Gold Award in the Higher Education (HEIST) Advocacy Campaign.

e. Collaboration or contribution to the discipline or research base

Participation in the peer-review process

All members regularly review grants, and thirteen have been funding committee members:
• **Research Councils:** Eperon - BBSRC Genes & Dev Committee to 2009; Louis - BBSRC Research Committee C (from 2012); Moody – BBSRC Pool of Experts Panel B (from 2009), ESRF Beamline Assessment Panel to 2010; Royle - MRC College of Experts (2006-09)
• **Royal Society**: Jeffreys - Awards and Nominations Committees (2007-10); Louis - International Exchanges Scheme Panel (from 2013)
• **WT**: Tobin / Jobling: Molecules, Genes & Cells Funding Committee (2004-08 / 2007-11), Peer Review College (2011- / 2012-); Schwabe - Interview panel, Senior Investigator Awards (2013)
• **Other UK bodies**: Herbert - Steering committee, Juvenile Diabetes Research foundation; Heslop-Harrison - Sub-panel member, HEFCE Research Excellence Framework (REF2014); Moody – Diamond Light Source Funding Panel 1 (from 2012)
• **Overseas committees**: Dominguez – ANR Funding Committee (France); Louis - AERES Review Committee (Strasbourg 2012); Roberts - Chairman, Selection Panel, Frank Knox Memorial Fellowships, Harvard U**;** scientific advisory board, Institute for Molecules & Materials, U Nijmegen (2005-12); Vuister - NWO (Netherlands) Equipment & Competition Grant Committees (to 2011)

Wider contributions

• **Bushell**: Member, Biochemical Society Gene panel
• **Clokie**: Council member, British Phycological Society
• **Dominguez**: Member, 'Therapeutic strategies targeting the spliceosome' network (SMSDrug.net)

• **Eperon**: Scientific advisory board, Muscular Dystrophy EXon skipping Consortium
• **Heslop-Harrison**: President, Society for Experimental Biology, (2009-11); Council Member, European Cytogenetics Association; Management Committee, Global *Musa* Genomics Consortium
• **Hollox, Jobling**: Textbook, *Human Evolutionary Genetics*, 2nd ed. (2013), Garland Science
• **Jeffreys:** Patron, Children's Cancer and Leukaemia Group (2011)
• **Louis**: Management Committee, EU COST Action on Bioflavours; Trustee, Frozen Ark Charity
• **Moody**: Collaborative Computing Project in Protein Crystallography Working Group (from 1999)
• **Oggioni**: Board member, Italian Society of General Microbiology (from 2013)
• **Roberts**: President, Intl Union of Pure & Applied Biophysics; Fellow, Intl Society of Magnetic Resonance, and Academy of Medical Sciences; Committee Member, British Biophysical Society
• **Vuister**: Executive committee member, Collaborative Computing Project for NMR
• **Willars**: Chair, Neuromedin U receptor family subcommittee for the International Union of Basic and Clinical Pharmacology Committee on Receptor Nomenclature and Drug Classification

Fellowships and other personal awards

• **Bayliss**: RCUK Fellowship 2007-12
• **Bushell**: BBSRC David Phillips Fellowship 2005-10; MRC Senior Fellowship 2010-15
• **Cowley**: MRC Senior Research Fellowship, 2012-19
• **Dominguez**: MRC Career Development Award, 2010
• **Jeffreys**: FRS; Lifetime Governor, Lister Institute of Preventive Medicine; Honorary Fellow, Royal Society of Chemistry (2012); 8 prizes, including Millennium Technology Prize (2008), Croonian Lecture (Royal Society, 2010), European Society for Human Genetics Award (2010), Edinburgh Medal (2010); 4 honorary degrees and 18 named lectures in REF period
• **Jobling**: WT Senior Research Fellowship, second renewal, 2009-14
• **Louis, Schwabe**: Royal Society Wolfson Research Merit Awards, 2008-13 and 2013-18
• **Moody**: Royal Society of Chemistry Cornforth Prize, 2011
• **Schwabe**: WT Programme, 2008-13; WT Senior Investigator Award, 2013-20
• **Wallis**: Lister Institute Research Prize 2012

Involvement in scientific journals

All unit members review manuscripts, and 49% (20/41) sit on the editorial boards of 38 journals, including: **Bushell**: *Cell Death Disease;* **Challiss**: *Br J Pharmacol*, *Biochem Pharmacol;* **Clokie**: *Bacteriophage;* **Dominguez**: *BMC Biochem;* **Drea**: *Front Plant Sci;* **Evans**: *J Biol Chem;* **Herbert**: *Biochem J;* **Heslop-Harrison**: *Theor Appl Genet*; Chief editor, *Annals Bot*; **Jobling**: *Ann Hum Genet*, Advisory Panel, *Nature Comms*; **Kriajevska**: *Clin Cancer Drugs*; **Louis**: *Funct Integr Genomics*; *Chrom Res*, *Yeast*, *PLoS ONE;* **Moody**: *Res Lett Biochem*; *Enz Res*; **Oggioni**: *Infect Immun*; **Roberts**: *Eur Biophys J*, *Biophys Rev;* Chief editor, Encyclopaedia of Biophysics; **Schmid**: *ISRN Bioinf;* **Tobin**: *J Biol Chem, Mol Pharmacol;* **Twell**: *Plant Reprod*, *BMC Plant Biol*; **Vuister**: *ISRN Struct Biol;* **Wallis**: *Immunobiol;* **Challiss**, **Drea**, **Heslop-Harrison**, **Tobin** - F1000 members.

Key collaborations

Members collaborate widely; selected major external collaborators include:

• **UK:** Allan Bradley, Sanger Inst. (*Cowley3*, *4*); John Doonan, U Aberystwyth, (*Drea2*); Chris Tyler-Smith, Sanger Inst. (*Jobling1*); Richard Durbin, Sanger Inst. (*Louis1, 4*); Steve Smerdon, NIMR (*O'Hare2*); Mark Blaxter, U Edinburgh (*Schmid1, 4*); Carol Robinson, U Oxford (*Schwabe2*); Duncan Smith, U Manchester (*Tanaka2*); Peter Doerner, U Edinburgh (*Twell4*); David Scanlan, U Warwick (*Clokie1, 2*); Chris Smith, U Cambridge (*Eperon2*); Francesco Muntoni, ICH (*Eperon3*).

• **USA:** John Moran, U Michigan (*Badge1*, *3*), Evan Eichler, U Washington (*Badge1*), José García-Pérez, HHMI (*Badge2*); Vivian Irish, Yale U (*Drea4*); RK Jayaswal, U Illinois (*Morrissey4*); David Calderwood, Yale U (*Roberts2*); Peter Tontonoz UCLA (*Schwabe4*); Maurizio Pellecchia, La Jolla (*Tanaka3*); Jürgen Wess, NIH (*Tobin1, 3*); Gert Vriend, U Wisconsin-Madison (*Vuister1*).

• **Europe:** Anders Blomberg, U Gothenburg (*Louis1, 3*); Oscar Kuipers, U Groningen (*Morrissey1*); Christiane Wolz, U Tübingen, Jürgen Heesemann, LMU, Munich (*Morrissey3*); Pedro Alzari, Past-eur Institute (*O'Hare1*); Jean-François Riou, Muséum National d'Histoire Naturelle, Paris (*Royle2*); László Nagy, U Debrecen (*Schwabe3*); Gisèle Bonne, U Paris 6 (*Shackleton1*); Claude Antony, EMBL Heidelberg (*Tanaka2*); Anastassis Perrakis, Netherlands Cancer Inst (*Vuister2*); René Bindels, Joost Hoenderop, U Nijmegen (*Vuister3*); Wolfgang Hess, U Freiburg (*Clokie1, 2*).

• **Asia:** Zixin Deng & Hong-Yu Ou, Shanghai Jiaotong U (*Rajakumar1-4*); Keiko Yamamoto, Showa

Pharmaceutical U, Tokyo (*Schwabe3*); Masayuki Yamamoto, U Tokyo (*Tanaka1, 2*); Hong-Gil Nam, Postech, Korea (*Twell1*).

• **Australia:** Brian Dean, U Melbourne (*Challiss2*); Christian Doerig, Monash U (*Tobin2*).

• **Africa:** Getachew Aderaye, Addis Ababa U; Ferdinand Mugusi, Muhimbili U, Tanzania (Hollox).

Interdisciplinary activity at Leicester

• **Clinical collaborations**: Irene Gottlob, Ophthalmology (*Shackleton2*); Chris Brightling, Respiratory Medicine (Challiss – oxidative stress in asthma); Maciej Tomaszewski, Cardiovascular (Jobling – Y chromosome and heart disease); Martin Dyer, Oncology (*Royle3*). Justin Konje, Obstetrics & Gynaecology (*Willets3,4*); Killian Mellon, Urology (*Kriajevska1*).

• **Dept Chemistry**: Dominguez, Eperon, Moody, Schwabe, Tobin, Vuister - projects with Emma Raven, Andrew Jamieson, Andrew Hudson (*Eperon4*), Sandeep Handa, Paul Cullis, including structural studies of haem enzymes; electron paramagnetic resonance studies; developing biologically active peptide mimics and novel spliceosome inhibitors; single-molecule fluorescence studies of splicing dynamics; design of mammalian and malarial protein kinase inhibitors.

• **College of Arts, Humanities & Law**: Jobling - co-investigator on £1.4M Leverhulme programme 'The Impact of Diasporas in the Making of Britain' (PI, Jo Story, Historical Studies), funding a 14-strong group of geneticists (incl. King), historians, archaeologists, linguists, place-names experts and social psychologists; PhD co-supervision with Simon James (Archaeology). King – genetics lead on interdisciplinary Richard III project – *Curr Archaeol* Research Excavation of the Year, 2013.

Collaboration with external non-academic bodies, and patents

• **Bayliss**: Meningococcal carriage studies (*Bayliss3*), used by Novartis to design phase III study on effects of new MenB and MenY-conjugate vaccines
• **Carr**: Structure-based drug discovery and development partnership with UCB Celltech (2 research fellows, 5 PhDs [4 CASE] over REF period); Associated patents and papers (*Carr2*, *4*); New structure-based drug discovery partnership with MRC Technology (1 research fellow, 1 RA)
• **Challiss**: GlaxoSmithKline (*Challiss2*); Heptares (*Challiss4*)
• **Clokie**: Scientific advisory board, Fixed-Phage Ltd.; Patent licenced to Ampliphi, and £200K research contract, for PCR-based *Clostridium difficile* diagnostics
• **Herbert**: Collaboration and CASE studentships with AstraZeneca
• **Morrissey**: Consultancy, VRI Plc on *Staphylococcus aureus* vaccines
• **Oggioni**: BASF Grenzheim, contract research on triclosan resistance (2011); Unilever R&D Colworth, biocide resistance collaboration (2013); Patent - *S. pneumoniae* antigens
• **Schwabe**: Patents PCT/GB2012/052055, UK 1109913.2 and US 61/496,840 (*Schwabe2, 3*)
• **Tobin**: Collaborations with Heptares, Novartis, Eli Lilly (incl. Lift Industrial Grant, 2012-15, $300K)
• **Vuister**: Scientific advisory board, Spronk NMR
• **Wallis**: Patent US SN 13/306,874 (*Wallis1*) sponsored by Omeros Biopharmaceutical
• **Willars**: Consultancy and CASE studentships with AstraZeneca (*Willars1*)

Mechanisms to promote collaborative research with academia and users

• **Louis**: Scientific advisory board chair, Centre for Genomic Research, U Liverpool
• **Rajakumar**: Participation in Royal Society-National Science Foundation of China and Sino-UK Higher Education Research Partnerships for PhD Studies grants (*Rajakumar1-4*)
• **Twell**: Gatsby Charitable Foundation Plant Science Mentor

Conference organising, session chairs

• **Bayliss**: Organiser, Microbial Genome Maintenance Meetings, 2008 & 2013
• **Challiss, Tobin, Willars**: BPS Cell Signalling Meetings, Leicester 2009, 2012
• **Evans**: Symposium organiser 'Purines 2012', Fukuoka
• **Herbert**: Session chair at 'Diabetes UK', Glasgow, 2009
• **Hollox**: Session chair, 'Copy Number Variation', ASHG meeting, San Francisco, 2012
• **Louis**: Organiser, EMBO Conf Series 'Comparative Genomics of Eukaryotic Microorganisms', 2009-13; Organiser & Chair, Royal Society meeting on Subtelomeres, 2011
• **Roberts**: Chair, Scientific Committee, 17th Intl Congress of Biophysics, Beijing, 2011
• **Schwabe**: Organiser, EMBO Conference on Nuclear Receptors, Sorrento, 2013
• **Shackleton**: Organiser, Biochem Soc Meeting on Nuclear Envelope Disease, Cambridge, 2011