Institution:	Newcastle University
Unit of Assessment:	UoA5

a. Overview

Newcastle University's REF2014 UoA5 return is composed entirely of staff members of the **Institute for Cell and Molecular Biosciences** (ICaMB), 32 of whom are returned here. A further five ICaMB academics are returned in UoA1 and two in UoA3. UoA5 staff perform fundamental multi-disciplinary research on the molecules and processes that govern cellular homeostasis and pathogenesis. We are also driven by the challenge of ensuring that our research has impact on non-academic beneficiaries (see REF3a for details). There are three major research groupings within UoA5 that map to our research aims and which enhance collaboration and capacity: ***Bacterial Cell Biology*** (*BCB*), ***Proteins: Structure, Function and Evolution*** (*PSFE*) and ***Sensing, Signalling and Expression*** (*SSE*). Since RAE2008 there has been major capital investment in the purpose-built Baddiley-Clark Building (opened in 2010 by Sir Paul Nurse), housing the Centre for Bacterial Cell Biology, and to allow the consolidation of all other research laboratories housing returned investigators into two levels of the Medical School. This rationalisation of space facilitates collaboration and also reflects the three areas of research strength in UoA5 that demonstrate excellence at all academic stages. The increasing strength of our research is reflected by: [1] a 56% increase (78 for RAE2008; 122 for REF2014) in returned publications in the 'Discovery' journals (*Nature*, *Cell*, *Science*, *EMBO J* [and their sister publications]; *PNAS*; *Genes & Dev*; the major *PLoS* journals), contributed by 27 PIs across UoA5, in comparison to 21 staff from the equivalent UoA (UoA14) in RAE2008; [2] the number of Early Career Fellowships won by our staff which has increased from two to five; [3] the numbers of doctoral awards per fte which have grown from 2.24 (RAE2008) to 2.53; and [4] the increase in our total grant spend from ~£26M to ~£32M which has occurred despite a challenging funding climate. Notably, during the current REF period members have been awarded seven individual senior/advanced investigator grants (European Research Council [ERC]/Wellcome Trust [WT]), seven programme grants and two WT Centre/Strategic Awards.

b. Research strategy

Summary of strategy and future plans.

Our research strategy has concentrated on: [1] developing our research groupings through key appointments and appropriate investment (see below); [2] emphasising personal development programmes (see section c "**People**"); and [3] fostering interactions between different research groups (cross-Faculty, intra- or inter-group; see below). Key developments, representative achievements and future plans for the three research groups of UoA5 are detailed below:

(i) The ***Bacterial Cell Biology*** *(BCB) Group* (**Aldridge**, **Daniel**, **Errington [FRS, FMedSci]**, **Gerdes**, **Hamoen**, **Harwood**, **Kenny**, **Khan**, **Murray**, **Vollmer**, **Zenkin**) tackles fundamental aspects of cell biology, biochemistry and pathogenicity of bacteria. Notably, **we have established a critical research mass in *bacterial cell biology***. The *BCB* group has been reinforced and underpinned by significant external and internal investment (~£30M), bringing together research staff into the new Baddiley-Clark building, which is adjacent to the main Medical School building that houses the majority of ICaMB. Together with other colleagues across ICaMB and from Computing Sciences, they form the Centre for Bacterial Cell Biology (CBCB), one of the world's largest research centres to focus on the molecular and cellular biology of bacterial cells. In addition to considerable infrastructure investment, the CBCB has specialised high level facilities for optical bioimaging, housing Nikon N-SIM and N-STORM super-resolution microscopes. Interactions across groupings within UoA5 is evidenced by a BBSRC LoLa to **Errington** et al, which has led to two further joint BBSRC awards to **Vollmer** and **Lewis**, ensuring the integration of our multi-disciplinary research strengths in molecular studies of the bacterial cell wall, combining genetics (**Errington**, *Cell,* 2013), biochemistry (**Vollmer**, *Cell,* 2010) and structural biology (**Lewis**, *EMBO J,* 2009). These PIs have created broad insights spanning these individual disciplines in this topical research area (**Errington, Daniel, Lewis, Vollmer,** *EMBO J,* 2011). **Key achievements** from the *BCB* group in this REF period are represented by the work of **Errington**, **Gerdes** and **Zenkin**. **Errington** has discovered and characterised mechanisms underpinning the formation of cell wall-less L-forms of *Bacillus*, providing new insights into cell wall formation and models for the proliferation of primitive cells (**Errington**, *Cell,* 2013; http://tinyurl.com/je-l-forms). Toxin-antitoxin

(TA) systems, are widely distributed in bacteria and are critically important in how bacteria respond to environmental challenge. **Gerdes,** a pre-eminent authority in this area, has continued his fundamental work on TA loci by demonstrating that they are required for antibacterial persistence against antibiotics (**Gerdes,** *Cell,* 2013; http://tinyurl.com/kg-persister, showcased on BBC1's 'Bang Goes the Theory'; see REF3a). Transcription by RNA polymerase III is the major source of RNA for eukaryotes but gaps persist in our knowledge of how transcription terminates. Recently, **Zenkin** has used insights from his work on bacterial RNA polymerases to solve this mystery, revealing an ancient core mechanism that is likely to have evolved before the divergence of eukaryotes and prokaryotes (**Zenkin,** *Science,* 2013; http://tinyurl.com/nz-rnapol). The broad strength of *BCB* and its research environment is evidenced in this REF period by 54 publications in 'Discovery' journals (*Cell*, eight; *Nature*, three; *Science*, four; *EMBO J*, twelve; *PNAS*, seven; *Nature* sister journals, seven; *Cell* sister journals, four; *EMBO* sister journals, one; major *PLoS* journals, seven; *Genes & Dev*, one;), and well-read review journals (*Nature Rev Microbiol* 2009, 250 citations; *FEMS Microbial Reviews* 2008 [x2], 391 and 238 citations).

Future Research Plans for the *BCB* group:
A major theme for *BCB* expansion lies in the cross-disciplinary domain of ***synthetic biology***. This new discipline aims to characterise and manipulate complex biological systems for commercial, environmental and social benefit (see REF3a). In this regard, most important early applications of this technology will be based on the more tractable bacterial systems where we are extremely strong. We have already generated funding in the field of synthetic biology through two EPSRC and TSB grants (£3M **Errington**, **Harwood**) and are currently applying to become one of the new BBSRC core-funded Synthetic Biology Units (£15.5M bid). **Errington** is co-Director of the newly founded (March 2013) Centre for Synthetic Biology and Bio-exploitation. The University has initiated a trans-Faculty strategy to invest and support the initiative through new appointments to complement or strengthen key areas, in particular in computation and chemical engineering, which underpin synthetic biology. The strategy is exemplified by the recruitment of Krasnogor (UoA11) and his research team by Computing Science, affiliated to the *BCB* group with office and lab space. A new building (planned for 2015) will bring together research teams and consolidate our focus on synthetic biology. Complementing the University's commitment to synthetic biology, the North East is home to a thriving pharmaceutical industry; around 1,000 life science and healthcare companies in the region employ over 35,000 people and are responsible for a turnover of ~£10 billion, or 30% of the UK's pharmaceutical GDP (http://tinyurl.com/ne-pharma). The University is thus ideally positioned to exploit and benefit from the synthetic biology revolution.

We will also extend our interests in natural product chemistry and the search for new antibiotics. With colleagues in the Faculty of Science, Agriculture and Engineering (SAgE), we will exploit a unique actinomycete culture collection established by Prof Mike Goodfellow. Actinomycetes are responsible for a large proportion of natural product-derived drugs, and the collection has been made available to us through a Newcastle University spinout company, Demuris Ltd, with the aim of developing new approaches for antibiotic discovery (see REF3a). There is also substantial potential for basic science in studying the biological and ecological roles of natural product molecules, and the chemical biology of their synthetic pathways.

(ii) The ***Proteins: Structure, Function and Evolution*** *(PSFE) Group* (**Bolam**, **Dennison**, **Embley [FMedSci]**, **Gilbert**, **Hawkins**, **Hirt**, **Lakey**, **Lewis**, **Salgado**, **van den Berg**, **Waldron**) is united by the common goal of seeking to understand the nature of protein:protein and protein:ligand structure/function relationships at the molecular level. Structural biology, led by **Lewis,** is a highlighted cross-Faculty research focus uniting the interests of our research groups. This is evidenced by University capital investment to integrate and house the UoA5 structural biologists on the 3rd floor of the Medical School, through the funding of a Faculty-wide Molecular Interactions Facility (see section d) and by providing funding for new appointments. The new structural biology appointments in ICaMB are **Salgado** (Imperial College, London), **van den Berg** (University of Massachusetts USA) and Davies (Cambridge - a new IRES appointment, see **staff development**, section c below). This investment complements appointments to the Northern Institute for Cancer Research (NICR; Noble and Endicott from Oxford, both UoA1) which strengthen this fundamentally important area. The new appointments have been supported by University-funded purchases of

major automated equipment for the production of high quality crystals. The expansion and investment in the *PSFE* group during the REF period has resulted directly in the following, representative **research achievements**. **First, Gilbert** and **Bolam** have focused on the mechanisms used by the human microbiota to utilise dietary and host complex carbohydrates as nutrients. They work closely with structural biologists to determine structures of target enzymes and glycan binding proteins (**Bolam,** *Cell,* 2010). The evolution of the gene repertoires that underpin nutritional flexibility is a developing interest shared between **Gilbert**/**Bolam** and **Embley**/**Hirt**, who focus primarily on the molecular evolution and pathogenic mechanisms of human intracellular microsporidian parasites. A **second research highlight**, from the evolutionary biologists **Embley** and **Hirt**, concerns the transport proteins used to exploit host cells and the functions of their minimal mitochondria, resulting in two key papers (**Embley, Hirt** *Nature*, both 2008). This work is naturally shifting to focus on structure-function relationships of the relevant parasite transport proteins in collaboration with **Lewis** and **van den Berg**. A **third research highlight** concerns the Wellcome Trust/Royal Society Sir Henry Dale Fellow, **Waldron**, and his interests in the fundamental importance of metals in biology. Through structural and biochemical analyses, he identified that subcellular localisation is crucial for the correct folding of metalloproteins (**Waldron,** *Nature,* 2008). In this REF period, 35 publications in 'Discovery' journals by this group include; (*Cell*, one; *Nature*, five; *Science*, one; *PNAS*, fifteen; *Nature* sister journals, four; *Science* sister journals, one; *EMBO* sister journals, one; major *PLoS* journals, seven;), and well-read review articles in *Nature* 2009 (215 citations) and *Nature Rev Microbiol* 2009 (214 citations).

Future Research Plans for the *PSFE* group:
The University has a strategic vision to further integrate and promote ***structural biology*** across the Faculty of Medical Sciences. As part of the strategy, the Faculty provided funds to recruit new Professorial-level staff (Noble, Endicott, NICR; both UoA1) and **van den Berg**, (ICaMB), an exceptional membrane protein structural biologist who works on essential outer membrane proteins of bacteria including pathogens. Significantly, **van den Berg** was, in 2004 in work published in *Nature,* the first investigator to visualise the structure of a protein-conducting membrane channel and has continued this ground-breaking work to become one of the world's leading crystallographers of membrane proteins (**van den Berg,** *Nature,* 2009). The importance of structural biology to the University is further highlighted by the recruitment of two Early Career Researchers, **Salgado** and Davies, who study host:pathogen interactions and the mammalian synaptonemal complex, respectively. Major investment in ICaMB's structural biology unit will continue to be an aim, to extend already well-defined collaborations between the eubacterial cell biologists (**Errington**/**Vollmer**) and members studying carbohydrate-acting proteins (**Bolam**/**Gilbert**), and to allow further exploitation of our expertise in metals in biology (**Dennison**/**Waldron**). Novel interactions with members of our *SSE Group* and those studying the bacteria:eukaryote interface are already ongoing.

Understanding the inter-relationships and modes of ***communication between microbiota and their human hosts*** is a critical research focus for the 21st Century. The realisation that the human microbiota makes a significant contribution to human health has led to international microbiota metagenomes programmes, and the development of genetic systems for key members of this microbial ecosystem. A future development for UoA5 will be a collaborative research programme between **Bolam**/**Gilbert** and **van den Berg**, focussing on the outer membrane saccharide transporters of the human microbiome. Furthermore, as the human microbiota has a significant impact on the host immune system, we will seek increased interactions with immunologists at Newcastle (Ali, Kirby, Mellor; all UoA1). We will build on the fledgling interactions between the biochemists **Bolam**/**Gilbert** and the molecular evolutionary biologists (**Embley**/**Hirt**) to include **Lewis** and **van den Berg**. This work will focus on the role of gene sharing (lateral gene transfer) between eukaryotes and the prokaryotes that colonise the human mucosa, including important sexually transmitted pathogens. Ageing research and its translation to healthy ageing is a strategic priority for the University and the BBSRC; alterations in the microbiome during ageing combine these two central research priorities. We aim to expand our interest in this area by exploring the microbiota in the diet and in the ageing population (**Bolam**/**Gilbert**), as well as to investigate the role of the metal proteome in cellular ageing (**Dennison/Waldron**).

(iii) The ***Sensing, Signalling and Expression*** *(SSE) Group* (**Brown**, **Connolly**, **Higgins**, **Lightowlers**, **Morgan**, **Perkins, Quinn**, **Rutherford**, **Schneider**, **Watkins**), is concerned with how DNA is replicated (**Connolly**) as cells divide (**Higgins**), how it is expressed (**Brown**, **Lightowlers**, **Schneider**, **Watkins**), and how this expression can respond to changing environments (**Morgan**, **Perkins**, **Quinn**, **Rutherford**; Lydall and Veal, both UoA1). The *SSE* Group has benefited from internal investment to consolidate laboratory space on the second floor of the Medical School and has been strengthened by both internal (Lydall to join the yeast geneticists, **Brown**, **Morgan**, **Quinn**, **Rutherford**, Veal; **Lightowlers** to become the new Director) and external recruitment (**Higgins**, Harvard USA; Kenneth, University of Michigan USA as an IRES recruit; **Perkins**, Bristol; **Schneider**, Edinburgh). **Higgins** strengthens the cross-Faculty interest in the molecular regulation of cytokinesis in eukaryotes. He identified the mechanism underlying a histone modification essential for correct spindle-kinetochore attachment during chromosome segregation and cell division (**Higgins,** *Science,* 2010). Several *SSE* group members use model organisms to investigate fundamental aspects of sensing, signalling and expression and one **key achievement** is represented by **Morgan** who, with Veal (UoA1), demonstrated that the increased sensitivity of ubiquitous antioxidant enzymes to redox stress leads thioredoxin to act on repair pathways critical for survival (**Morgan,** *Mol Cell,* 2012). A further highlight is provided by **Lightowlers**, who brings expertise in the area of organellar gene expression and pathogenesis. With Chrzanowska-Lightowlers (UoA1) **Lightowlers** revealed a fundamental error in the interpretation of the mitochondrial genetic code (**Lightowlers,** *Science*, 2010). This work formed part of the successful case for support in establishing a new £5.8M WT Centre for Mitochondrial Research in Newcastle. The final research highlight concerns **Perkins**, who has discovered fundamental mechanisms linking the pro-inflammatory NF-κB and p53 tumour suppressor pathways (**Perkins,** *Mol Cell*, 2010). This crosstalk allows the cell to integrate NF-κB and p53-dependent signalling to control aspects of cell fate, including apoptosis, autophagy and ATP synthesis. This REF period, the *SSE* Group has published 33 papers in 'Discovery' journals (*Cell*, one; *Nature*, two; *Science*, three; *EMBO J*, three; *PNAS*, six; *Nature* sister journals, four; *Cell* sister journals, nine; *EMBO* sister journals, three; major *PLoS* journals, two), a key review is *Nat Rev Cancer* 2012 (118 citations).

Future Research Plans for the *SSE* group:

In the next five years we will extend our interests in ***eukaryotic cellular homeostasis*** with a particular aim of strengthening links within the Faculty of Medical Sciences. Our current work in higher eukaryotes focuses on key players in the NF-κB and p53 signalling pathways (**Perkins**, **Watkins**, Kenneth). We will shift emphasis from single cell-based studies to designing, producing and analysing relevant transgenic mouse models in order to better establish the significance of these pathways *in vivo* and to determine their relevance to cancer and other diseases. Recent technologies such as ChIP and RNA-Seq will be harnessed to provide clearer insight into the wider perspective of the pathways we are investigating, benefiting from the Faculty's strategy to develop bioinformatics and analyses of large datasets This is evidenced by the recent recruitment of Dr. Diego Miranda-Saavedra (UoA1) to the Institute of Cellular Medicine (ICM) from Osaka University. His research interests combine whole genome analysis of gene expression in mammalian cells with bioinformatics. The University has also provided funds to support the high level appointment of **Higgins**, who will spearhead work in higher eukaryote cell cycle biology and develop small molecule inhibitors of key cell division regulators. The recruitment of **Higgins** and Davies will promote links with **van den Berg**, Madgwick (WT Career Re-entry Fellow to ICaMB), Herbert (UoA1) and NICR staff, through their interests in cell division (Newell, Robson, Endicott, Noble; all UoA1). Crucially, this will facilitate our longer-term goal to provide insights that will support cancer drug discovery, encourage and establish links between ICaMB and the NICR, a major CRUK centre for drug discovery, and integrate the cross-Faculty strength in structural biology.

A related goal is to strengthen the links between the WT Centre for Mitochondrial Research and UoA5 members. We will investigate the signalling processes that monitor mitochondrial function within the cell **(Lightowlers**, **Perkins**) and analyse structure:function relationships in essential modulators of mitochondrial function (**Lightowlers**, **Lewis**; Chrzanowska-Lightowlers, UoA1). We will also build on our expertise in using simple but powerful model systems (yeasts and nematodes: **Morgan**, **Quinn**, **Rutherford**; Veal, UoA1) by harnessing high-throughput technologies (with Lydall, UoA1) and modelling (with Shanley, UoA1) to provide a framework for a

systems-level understanding of cellular biology. Finally, we will build upon the promising research area of RNA biology in UoA5, supporting work on RNA quality control (**Schneider**), ribosomal RNA production, ribosome assembly and ribosomal pathologies (**Brown, Watkins**). This work has natural links to **Zenkin** on RNA polymerase. Our long term aim is to exploit the potential of RNA biology to underpin novel therapies for RNA-associated pathologies, fostering new links between UoA5 and the more clinically-related researchers in the Faculty.

c. People, including:

i. Staffing strategy and staff development

Management structure

All investigators returned here are managed by ICaMB. **Lightowlers** was appointed as the Institute Director (2012) on the completion of **Errington**'s tenure (2006-12). Dedicated administrative teams provide support for all aspects of staff and postgraduate management, progression and development. Day-to-day management is facilitated by the Executive. Research strategy is deployed by the Institute Research Strategy Group (IRSG), which meets monthly, consists of academics at all levels and is naturally focused around our UoA5 research themes (see also REF3a). The structure of the IRSG ensures that decisions regarding the identification of research areas for development/expansion, and for the recruitment of new staff, are made transparently.

Staff development

Over the next REF period we will consolidate and expand upon recent investment to provide a research environment that will address a range of problems relevant to medicine and industry. It is essential that our staffing strategy supports our aim of research excellence and provides a solid foundation to allow us to meet our strategic goals. This strategy is largely facilitated by IRSG, which is also tasked with implementing the 2008 RCUK Research Concordat to support the career development of researchers, ensuring the support of equality and diversity and sustaining staff structure. Consequently, IRSG focuses on all strategic elements of academic staff appointments, from independent research fellowships to the highest levels of appointment with the main emphasis and criterion being research excellence. The IRSG was instrumental in pioneering the design and implementation of the 5 year tenure-track Independent Researcher Establishment Scheme (IRES). ICaMB instigated this scheme as a proactive measure in part to replace academics approaching retirement, but particularly to facilitate the strengthening of research groupings (see section b). To foster career development, IRES Fellows are mentored by an experienced member of academic staff and, following a rigorous probationary examination after three years, successful Fellows will be offered a permanent position at the end of the five year fixed term. Appropriate start-up packages are provided, including a postgraduate studentship from the Faculty of Medical Sciences. After a large number of exceptional applications, the first round of IRES in June 2013 resulted in the appointments of Davies, Kenneth and Rodriguez (from the Gurdon Institute, Cambridge) in areas relevant to our research strategy. An additional round of IRES appointments has been approved by the Faculty for 2015/6 and will again be targeted at our strategic priority research areas. In addition to the IRES positions, staff at all stages of their career have been appointed to UoA5 during the REF period: Madgwick, **Murray**, **Schneider**, **Waldron** (Research Fellows); **Salgado** (Lecturer); **Higgins, Perkins**, **van den Berg** (Professorial).

A key element of our research strategy is graduate student recruitment and development. We will continue to recruit the highest quality students with an emphasis on building capacity within the three strategic research areas of UoA5 (see section b). We have already focussed our current BBSRC-funded doctoral training programme on providing studentships within these areas and this will be continued throughout the next REF period to increase capacity. Future plans include our current bid for a BBSRC Synthetic Biology Centre, which includes funding for ten PhD studentships to support ***synthetic biology***. In addition, Davies, Kenneth and Rodriguez (IRES appointees) have been appointed in ***structural biology*** (Davies) and ***eukaryotic cellular homeostasis*** (Kenneth; Rodriguez).

We have in place a programme of rigorous performance development review (PDR) which is undertaken yearly by all staff in the Institute. All academics are reviewed by **Lightowlers**, who aids in identifying and facilitating development needs. These are often met by referral to the University

Staff Development Unit which provides appropriate workshops. Academics are also strongly encouraged to consider sabbaticals where possible and to contribute to relevant conferences. We are particularly interested in meeting the needs of the junior members of staff. In 2012, the Director established a biannual round-table discussion with Madgwick, **Murray**, **Salgado**, **Schneider** and **Waldron**, which will be extended to include Yuzenkova (newly-awarded Royal Society University Research Fellow) and the new IRES appointees. These discussions informed IRSG's decision (see REF3a) to establish our Institute blog (http://blogs.ncl.ac.uk/icamblog/) and our social media presence (on Twitter, Facebook) and led to a re-evaluation of our digital data storage capabilities.

The **Athena SWAN Charter** is starting to play a central role in the forward planning of UoA5, supporting University policies such as flexible working opportunities, career breaks, parental leave, enhanced maternity and paternity leave. We are working towards opportunities that embrace gender equality, e.g. 3 of the 8 appointments within the REF period were female (**Salgado**, **Schneider**, Rodriguez). Based on our approach to staff management and appointment we aim to apply for silver Athena SWAN status before January 2014.

How does UoA5 discharge its responsibility to postdoctoral scientists?
Our research success depends on the industry and contributions of our postdoctoral and postgraduate (PGR) scientists. In this REF period, a Postdoctoral Association (IPA, http://tinyurl.com/ICaMBlog-IPA) has been formed. All postdoctoral scientists are encouraged to take an active part in the IPA (Academic lead **Murray**), which focuses on research and careers advice. Postdoctoral researchers are an important part of our seminar series and annual Away Days. Our academics offer career advice to all postdoctoral scientists through annual PDR and through Career Pathways Reviews which are offered at the 4-year postdoctoral stage. In the last 6 months of all postdoctoral contracts, a meeting is offered where every attempt is made to confirm and discuss career aspirations and to identify new sources of funding. In this regard bridging funds, partly provided by the Wellcome Trust (WT) Institutional Strategic Support Fund, can allow, for example, completion of research and seamless movement to new funding when in place. This is well evidenced by Dr. Victor Emelyanov, a postdoctoral researcher with **Embley**, who was bridged for 6 months, providing data underpinning a successful WT programme grant application.

ii. Research students
Evidence of sustainable doctoral training and of an integrated student research culture
We value our PGR students extremely highly and we are committed to increasing student numbers and quality of research training. Indeed, this REF period has seen us increase our doctoral awards per fte from 2.24 (RAE2008) to 2.53. Furthermore, our members have secured for the Faculty four external doctoral training awards over the REF period totalling £7.35M (BBSRC DTA 2004-8; 2 x DTG 2009-12; £4.25M BBSRC DTP 2012-15). In the first cohort (2012-13) of the current BBSRC DTP, ten of fourteen studentships available to Newcastle were taken by students who selected UoA5 projects and supervisors, further emphasising the strong role we play in postgraduate training within the University. In addition, our outstanding training reputation has been recognised during the REF period by the award of significant PhD training awards from other major sources, including funding from the National Institute for Health Research (NIHR) and the WT (see below). A key University research priority is in ageing research, and the NIHR Newcastle Biomedical Research Centre (BRC) was awarded in 2011 (£16.6M) to improve treatments for age-related disease. In 2012, in open competition across the Faculty's 300 plus academics, 50% of PhD studentships from this initiative were awarded to UoA5 PIs. The multi-centre, £5.1M WT Strategic Award led by Aberdeen University, of which Newcastle University is a component, will fund thirteen PhD fellowships and six postdoctoral fellowships. Notably, the first funded PhD studentship was awarded to **Quinn** in 2013. The WT Centre for Mitochondrial Research (**Lightowlers**) has attracted funding for 8 postgraduate students. Further significant sources of PhD funding include pan-EU training schemes (Marie Curie ITN or ERC) held by **Dennison**, **Embley**, **Errington**, **Gilbert**, **Hamoen**, **Harwood**, **Vollmer**. During this REF period we have also focused on the application of technology and impact generated by our research students. **Staff secured 23 CASE awards, a 25% increase from RAE2008**. Details of these CASE studentships and their major contributions towards our current impact are described in REF3a, sections b and d.

We are committed to ensuring a high quality student experience for our PGR students. In the 2011 HEA PRES survey UoA5's PGR student body responded very positively about their experience, with a satisfaction rating of 97%. A strong commitment to research student culture is evidenced by: (i) the annual expenditure of Institute funds to support PGR (e.g. matching funds for PhD studentships, bridging funds to enable papers to be written after thesis submission, annual symposia for 2nd/3rd year PhD students, social events) is second only to support staff costs; (ii) our performance indicators, which reveal Faculty and RCUK PGR targets are routinely met or exceeded; as a representative snapshot, in 2010-2011, our PGR student progression, 4-year submission and completions rates were 92%, 91% and 87%; (iii) our students consistently author research papers in Discovery journals, frequently as first author, and win prizes. For example, Yanping Zhu (supervisor **Gilbert**), *Nature Chemical Biology* (2010); Anastasios Tsaousis (**Embley**, **Hirt**), *Nature* (2008x2); Graham Scholefield (**Murray**), Erkam Gundogdu (**Hamoen**), Kathryn Schirner (**Errington**), Ricarda Richter (**Lightowlers**) *EMBO Journal* (2012, 2011, 2009, 2010, respectively); Lauren McKee and Fiona Cuskin (**Gilbert**), Kristoffer Winther (**Gerdes**), Monica Olahova (Veal), *PNAS* (2012, 2011, 2008, respectively). In 2008, two Newcastle University teams, composed of UoA5 PGR students, were awarded prizes at the BBSRC Biotechnology YES competition (http://tinyurl.com/icamb-yes); (iv) following a Research Degree Programme Quality Assurance and Enhancement Audit visit to ICaMB (2009), we were nominated as an exemplar for other Institutes at Newcastle University for PGR practice; (v) in 2012 we introduced an 'Exit' seminar scheme in which students give an open oral presentation before their *viva voce*. The event has become a celebration of the student's doctoral research, and its success is such that from 2012-13 the scheme was rolled out by the Faculty across all Research Institutes. Finally, due in large part to enthusiasm from the PGR students, we have established a PGR student society termed PAN!C (http://tinyurl.com/icamb-panic). This Society, managed and run by UoA5 PGR students, organises research and career symposia, and social events for all our PGR students. The success of PAN!C is demonstrated by the fact that it is financially self-sufficient due to their successful application to the University PGR Innovation Fund, an application that was singled out for 'enhancing the research environment and student experience'.

Examples of career destinations for PGR students

Evidence of the strong training culture and broad skills acquired by our PGR students is provided by examples of their first career destinations. These include prestigious national and international research institutions (e.g. Universities of Cambridge, Oxford, King's College London, Edinburgh; NIH, Bethesda, USA; University of North Carolina, Chapel Hill, USA; CNRS Montpellier, France; Dalhousie University, Canada; UCB-Celltech, Belgium; Universities of Gröningen and Cologne, Germany), industry (e.g. Angel Biotechnology, AstraZeneca, Avecia Biotechnology [now Fuji Film], Cobra Biomanufacturing, GlaxoSmithKline, Marakon Management Consultants), the NHS (Consultant in Renal & General Medicine, Nottingham; Clinical Biochemist, London), the Home Office (Forensic Science Laboratory), and medical charities (The Wellcome Trust).

d. Income, infrastructure and facilities

The standing of our research is again illustrated by the funding granted to our academics at all stages of their careers. UoA5 investigators have been awarded £39.32M across all three research themes since 2008. Despite the challenging financial climate over the REF period, there has been a major increase in success, particularly in the form of major, long-term funding from the WT and European funding agencies. We have been successful in obtaining three WT Senior Investigator awards (**Errington, Gilbert, Vollmer**) worth a total of £4.58M, and three other significant WT awards; programme grants to **Embley** (£1.5M) and **Perkins** (£1M) and, in association with members from UoA1, one of only 8 WT Centres in the UK (£5.8M, **Lightowlers,** co-PI). **Quinn** is a senior co-PI on a £5.1M WT Strategic Award that is co-ordinated by Aberdeen. We have also been awarded four ERC Advanced Grants (**Embley**, **Errington**, **Gerdes, Gilbert**), each worth around £2.5M, and a £0.8M ERC Starting Grant (**Zenkin**). Indeed, we have a **60% success rate** in applying for WT Senior Investigator awards and ERC Advanced Grants. National funders have also supported our bids for larger grants, for example, in 2009 we received a £3.2M BBSRC LOLA to **Errington**, **Daniel, Lewis** and **Vollmer**. **Bolam** and **Gilbert** are co-PIs on two BBSRC Bioenergy Centre programme grants with Nottingham and Cambridge (£1.4M) in the BBSRC-funded Bioenergy Centre, the largest public investment in bioenergy in the UK. Further major BBSRC funding has been secured by **Harwood** and **Lewis**, who are both members of a pan-

European systems biology consortium, SysMO2 (£0.6M). **Perkins** has been awarded a £0.75M CRUK programme grant. **Van den Berg** was awarded a Royal Society Wolfson Research Merit Award, is a co-PI on an Integrated Medicine Initiative award (£0.6M) and collaborates with the University of Virginia on a $0.6M NIH award. Several Early Career Fellowships have been awarded to staff during the REF period; a WT/Royal Society Henry Dale award (**Waldron**), 2 Royal Society University Research Fellowships (RSURF; **Murray**; **Schneider**) and a WT Career Re-entry Fellowship (Madgwick). A third RSURF was awarded to Yuzenkova (Aug 2013), outside the time restrictions of this return.

Other major funding has also supported UoA5 research. For example, a third consecutive BBSRC DTG was awarded in 2009 (£3.1M in total over the periods 2004-08 and 2009-12). The successful £9M bid (£4.25M to Newcastle) for the BBSRC DTP (2012-15), shared with Durham and Liverpool Universities, was led by Newcastle UoA5 staff in which we are the consortium lead and budget holder. The impact of these studentship awards over the past 9 years has enabled us to substantially increase our postgraduate student numbers. We have also been effective in our collaborations with other Institutes within Newcastle University and other Institutions (see section e below), resulting in successful grant applications. For instance, a cross-University bid between members of ICaMB (**Errington**, **Harwood**) and Computing Science (Wipat, Hallinan; both UoA11) for a £0.8M EPSRC Award provided the seedcore funding to launch our new research strategy into ***synthetic biology*** (see section b and REF3a).

Infrastructure and facilities

Following the rationalisation of space, UoA5 investigators occupy two floors of the main Medical School Building as well as the CBCB. Though split, the sites are adjacent and are fully integrated through the emphasis on overall management, PI meetings, joint supervision of graduate students and post-docs, Institute seminars, Away Days and the annual Institute events. Technical, support and workshop staff are also shared across the two buildings. Faculty and FEC funds have been combined for the rationalisation and upgrading of laboratory space in the Medical School building, maintaining pre-existing facilities and for providing new capital equipment. Although smaller in footprint and staffing, the CBCB offers up to date laboratory facilities for up to 100 researchers and postgraduate students, is supported by a £6M WT Capital Award, and represents a significant investment by the University into bacterial cell biology. New CBCB equipment (value £1.4M) includes Nikon N-SIM and N-STORM super-resolution microscopes. The CBCB was also successful in a BBSRC REI bid (2008), which led to the purchase of a flow cytometry unit and a spinning disc confocal microscope. In order to expand structural biology during the REF period, the University has also invested in automated facilities for setting up crystallisation plates and for their storage and visualisation. Investment in the *PSFE* and *SSE* groups is evidenced by the expansion of the Molecular Interaction Facility, funded by the Faculty Headroom Funds to include new BIAcore X-100 and Microcal ITC200 devices (**Lakey, Lewis**) and the training of a specialist technician. These funds have also supported updating of spectroscopy in the upgrade of the SLM polarisation fluorometer (**Connolly**), the purchase of a new UV spectrometer (**Dennison**), and maintenance/upkeep of the ICP-MS (ECR, **Waldron**).

Several other facilities which were established by members of ICaMB over the current REF period have proved successful. These include our proteomics and mass spectrometry centre (previously referred to as PiNNACLE, now NUPPA http://tinyurl.com/ncl-nuppa see REF3a) and the high throughput robotics facility; both are now managed centrally by the Faculty. The Protein Purification and Characterisation Unit (PPCU) is managed by **Hawkins** and provides expertise in protein chemistry to University members. The PPCU is underpinned by a legacy to the value of £0.5M in the form of lab infrastructure and equipment released to the University from the sale of Arrow Therapeutics (**Hawkins** co-founder - see REF3a) to AstraZeneca.

e. Collaboration or contribution to the discipline or research base

Our research has led to many examples of major contribution to the discipline by staff, with significant impact on academic (see below) and non-academic beneficiaries (see REF3a). Furthermore, our major published research findings (122 'Discovery' publications), our research income (£39.32M) and commercial interactions, demonstrate clear evidence of collaborations that have made significant contributions to many topical research fields. Internal and external

collaborations are extensive and involve every investigator returned here, and are highly successful as evidenced in joint grant income and publications. All staff contribute to peer review and have given invited lectures in the REF period, irrespective of their seniority. Many sit on scientific advisory panels, act as editors or associate editors for learned journals and speak at, or organise, international meetings. Further, we promote mobility of young researchers as evidenced by exchange of research students between UoA5 returned staff and their collaborators.

The following are notable examples of UoA5 member contributions to the discipline:-
Several UoA5 staff contribute to government, European and industrial strategies. For instance, **Errington** served on Sir John Beddington's Government review on biodetection and the BBSRC Health portfolio working group (see REF3a). **Embley** is a panel member of the Genetics, Cellular and Developmental Biology, Microbiology and Immunology Committee for the Academy of Medical Sciences. Several UoA5-returned investigators have served as members of RCUK funding panels (BBSRC **Brown, Daniel, Gilbert**; MRC **Khan**; BBSRC BRIC, **Lakey**). Panel members on international research councils include **Gilbert, Harwood** and **Lightowlers**; **Embley** is vice-Chair of the Marie Curie Environment panel, evaluating Fellowship applications from young scientists. Some of our highest profile staff have received significant personal honours during the REF period, including: **Embley**, who was elected to an **EMBO membership** (2010) and made a **Fellow of the Academy of Medical Sciences** (2011); **Errington** was awarded the Biochemical Society's **Novartis Medal** (2013), and **Zenkin** the Society of General Microbiology's **Fleming Prize** announced in 2013. **Gilbert** was awarded the **Bruce Stone Medal** (2011) for polysaccharide research and was the recipient of an **honorary PhD** from the Technical University of Lisbon (2009). **Perkins** was awarded the **Tenovus Scotland Medal** (2009) for biomedical research.

External collaborations have been established both nationally and internationally by UoA5-returned staff. **Bolam** and **Gilbert** have established national (Nottingham/Cambridge Universities) and international (Novozymes) collaborations in the BBSRC-funded Bioenergy Centre. **Lightowlers** and others have formed the new WT Centre for Mitochondrial Research, focusing on the genetics of mitochondrial gene expression and disease, collaborating with groups in the UK and abroad, based for example in Cambridge, Munich, Paris, Koeln, Melbourne and New York. **Quinn** is a key member of a multi-centre, WT-funded Strategic Award, led by Aberdeen University, focusing on the prime cause of life-threatening fungal infections. Several staff fostered strong collaborations in the EU, contributing to integrated projects (**Lightowlers**, EUMITOCOMBAT), the Integrative Medicines Initiative (**van den Berg**, New Drugs for Bad Bugs) and multiple Marie Curie research initiatives (**Embley**, **Errington**, **Gilbert**, **Hamoen**). **Errington** was a director and member of the scientific advisory board of Biota Holdings Ltd (Melbourne), is a director of Demuris Ltd (see REF3a), and collaborates with **Gerdes** and **Vollmer** in the EU FP7 project, DIVINOCELL.

Finally, our staff have organised international meetings and given keynote oral presentations world-wide. **Gilbert** was Chair of the Gordon Research Conference (GRC) on cellulosomes, cellulases and other carbohydrate modifying enzymes (2009); **Errington** co-chaired the GRC on Bacterial Cell Surfaces (2008); **Gerdes** was convenor at the 5th (2011) and 6th (2013) FEMS congresses. **Errington** gave the Kluyver Lecture of the Dutch Microbiological Society (Arnhem, 2008), the Fred Griffith Prize Review Lecture, Society for General Microbiology (Edinburgh, 2009), the Inaugural Joel Mandelstam Memorial Lecture (Oxford, 2009), the Mendel Lecture (Brno, 2011), and the Sir William Dunn Lecture (Cambridge, 2011). **Embley** has given the Svedberg Lecture (Uppsala, 2009) and the opening, plenary lecture of the Society for Molecular Biology and Evolution (Dublin, June 2012). **Lewis** gave an invited presentation at the 37th Lorne conference (2012) on protein structure. **Lightowlers** was an invited speaker at the Howard Hughes Janelia Farm Research Campus (2011) and gave the Pasteur Institute - Cenci Bolognetti Lecture at the Sapienza University of Rome (2011). **Lakey** was an invited speaker at the Biennial European Workshop on Bacterial Protein Toxins in Germany 2013 (alternates with GRC). **Gilbert** gave a plenary lecture at the GRC on cellulases (2011); **Bolam** (2009, 2013) and **van den Berg** (2009, 2010x2) between them gave five invited lectures at GRCs in their respective fields.