Institution:
University of Ulster

Unit of Assessment:
3B Allied Health Professions, Dentistry, Nursing and Pharmacy – Biomedical Sciences

a. Overview

The Biomedical Sciences Research Institute (BMSRI) is composed of eight Research Groups, with staff mainly drawn from the School of Biomedical Sciences, but also some from the recently established School of Pharmacy & Pharmaceutical Sciences (9 FTE), and from the School of Psychology (3 FTE). In the current period we have delivered on our RAE commitments and continued our financially sustainable expansion for the benefit of the health of the general population, clinical treatment of patients, and economic development.

The Table shows the staff in each Research Group.

	GROUP	GROUP STAFF / *NEW STAFF
(A)	Diabetes	Flatt (Leader): Abdel-Wahab, Gault, Irwin, S McClean, McClenaghan, McKillop, O'Harte
(B)	Human Nutrition & Dietetics (Northern Ireland Centre for Food & Health, NICHE)	Strain (Leader), Dooley, Gallagher, Gibney*, Gill, Hoey* (ECR), Kerr* (ECR), Livingstone, Magee, McAnena (ECR), McCann*, McCormack, D McDowell, McMullan, McNulty, McSorley, Mulhern* (ECR), Pentieva, Pourshahidi* (ECR), Price* (ECR), Ternan, Ward, Yeates* (ECR).
(C)	Molecular & Translational Medicine	Mitchell (Leader), Clauss*, Kim, Leslie, Shaw.
(D)	Nano-Systems Biology	Downes (Leader), Barnes* (ECR), Dubitzky, Howard, McKerr, O'Hagan* (ECR), Saetzler, Soto.
(E)	Pharmaceutical Science	J Callan* (Leader & Norbrook Pharmaceutical Science Chair), Banat, B Callan*, Fetherston*, Matoussi*, McCarron*, McHale, Tambuwala*, Webba da Silva.
(F)	Stratified Medicine	Bjourson (Leader), Atkinson*, Blayney*, Conway*, Gibson*, Kelly*, P McClean*, A McDowell*, McGeough*, McGilligan*, Murray*, Politis*, Watterson*.
(G)	Transcriptional Regulation & Epigenetics	Walsh (Leader), Lees-Murdock, McKenna* (ECR), McKeown, Thompson, Worthington.
(H)	Vision Science	Moore (Leader), Anderson, Beirne, Breslin, Little, McClelland, Nesbit*, O'Donoghue, Saunders, Vidinova.

b. Research strategy

We undertake research in biomedical science, nutrition and dietetics, optometry, and pharmaceutical science. Our strategy has been to concentrate on key degenerative diseases, including those with a nutritional aspect, that affect an increasingly ageing population. We have worked from the basic molecular level as far as to human clinical trials, with translation to clinical and commercial benefits. Our basic and applied research into disease development has led to improvements in disease prevention, diagnosis and therapy, and we have ensured a wide audience for our outputs with a focus on societal benefit and global impact. Our approach to research over the last 20 years has been outstanding: we achieved 5* ratings in both the RAE1996 and RAE2001 and we were ranked in second place in terms of grade point average in RAE2008.

Our research priorities have been to deliver on RAE2008 commitments; and to re-examine and to modify our focus where necessary, in order to ensure that our research areas are optimally aligned with future major external funding drivers for continued sustainability. In order to increase competitiveness and grow external research grant income along with staff and PhD student numbers, we have striven to develop new initiatives during this current five year period. Our overall approach has been to build and develop further on the RAE2008 strategy, by deepening existing areas of strength, maintaining research quality, and selectively expanding in related clinical areas in terms of both infrastructure and staff.

Evaluation of Research:

i <u>Achieving RAE2008 strategic plans</u>: All key commitments have been delivered. At the Coleraine campus in 2008, we opened as planned the **4,000m^2 SAAD Centre for Pharmacy & Diabetes** (**£1.84M** from the SAAD Group, **£3.2M** from the SRIF3 programme and **£1.3M of** university funding) to accommodate the **Centre for Metabolomics,** the **new Pharmacy & Pharmaceutical Sciences School**, and a new suite of laboratories to accommodate the Diabetes Research Group. We also opened **four new major clinical research centres:** (1) In 2008, **a £2M 1,000m^2 multi-use flexible facility for the Clinical Translational Research & Innovation Centre** (**C-TRIC;** formerly **ABC-RIF)**; a not-for-profit Company, wholly owned by the BMSRI, the Western Health & Social Care Trust and Derry City Council, located at Altnagelvin Hospital, Derry~Londonderry. (2) In June 2013, the **£5.5M Invest NI-funded (Regional Development Agency) Functional Brain Mapping Facility**, a multidisciplinary cross-faculty initiative led by the Intelligent Systems Research Centre (Faculty of Computing & Engineering), in partnership with the BMSRI, the Institute of Nursing and Health Research and C-TRIC. (3) In September 2013, the **£4M Wellcome Trust-Wolfson Foundation Northern Ireland Clinical Research Facility (NICRF)** in Belfast City Hospital, a partnership between University of Ulster, Queen's University of Belfast, the Health & Social Care R&D Office and Belfast Hospital Trust. (4) In October 2013, the **£11.5M Northern Ireland Centre for Stratified Medicine** based in C-TRIC, with funding for 22 new posts including 15 new lectureships and 5 Research Associates with agreement for clinical input from 10 Consultants based in the Western Health & Social Care Trust (funded by Invest NI/Public Health Agency R&D grant and the University). This last Centre will contribute to two of our planned strategic objectives from 2008: systems-biological studies and identification of biomarkers. It may eventually assist in one deferred proposal, the creation of a cross-border medical school.

ii Growth. This success in maintaining a dynamic, internationally competitive, financially sustainable infrastructure has enabled the BMSRI to grow and thrive, reflected by a **<u>23% increase in research staff</u>** numbers (60.7 FTE submitted in RAE2008, 74.1 FTE in REF2014), recruited from Centres of Excellence in Ireland, Scotland, England, and elsewhere in Europe, Asia and the US. We have delivered a sustained year-on-year increase in **<u>research income, which has increased by >30%</u>** (average annual spend £3.1M in RAE2008, £4.07M in REF2014). This growth was supported by our policy of making funded PhD studentships an institutional commitment in grant applications over £250K (see also section c. People). This policy ensures expert external peer review of all internally allocated PhD projects, adequate PhD funding, and an element of competitive advantage in our research applications.

iii Core Facility Units (CFUs) were established with a **£2.7M University investment** to update and replace specialist equipment, and to organise our previously dispersed infrastructure into a more efficient and sustainable model. Researchers and industry pay for use of CFUs at full economic costing or market rates, and unsustainable infrastructure has been replaced by outsourcing and collaborative initiatives. This initiative has been strategic and highly successful: CFUs now operate with an overall surplus retained for reinvestment in new equipment/services, and we have dramatically reduced reliance on recurrent BMSRI budgets; 90% of CFU income is derived from external research grants or industry consultancy. The bulk of the BMSRI recurrent budget now supports PhD students, ECRs and new staff, and pump-primes new strategic initiatives. A proportion of our recurrent budget is also used to leverage match funding from outside organisations (see section e. Collaboration or contribution to the discipline or research base).

iv We have continued to make **a major contribution to health and well-being, economic prosperity, and the expansion and dissemination of knowledge** by undertaking internationally agenda-setting research that is disseminated in major interdisciplinary journals and in international specialist journals outstanding in their fields *(*Lancet, Nature, Proc. Natl. Acad. Sci. USA, Science, Am. J. Clin. Nutr., Blood, Circulation, Diabetes, Invest. Opthalmol. Vis. Sci., JACS, J. Natl. Cancer Inst.*,* Nucleic Acids Res., and others).

v We have had excellent success in **creating and protecting Intellectual Property (IP)** arising from our research: since 2008, we have filed **48 Technology Disclosures** through Innovation

Ulster Ltd (IUL - a University owned Knowledge Venturing Company), maintained **25 active patents (three of which have been granted)**, and **filed 28 new patents**.

vi We have transferred knowledge and skills into useful products for patient benefit, and we have helped drive economic growth regionally, nationally and internationally through a diversity of routes including via IUL. Since 2008, we have undertaken **22 Fusion projects (£419K)** (Fusion is the all-Island of Ireland equivalent to KTP) and **19 Invest NI Proof of Concept (PoC) projects (£2.14M)**. In addition, IUL has supported 15 BMSRI Proof of Principal (PoP) projects (>£100K). We have two active spin-out companies: Diabetica Ltd, and the newly established Jennaron Therapeutics Ltd. We have provided bio-incubation and mentoring via C-TRIC's innovative Bio-entrepreneur Programme. We have completed licencing agreements with major industries such as Sanofi Aventis, Randox, Nestec, and Domain Therapeutics and have received licence income on our IP. Through our initiative known as the BMS Campaign we have engaged with major pharma, diagnostics and the food industry. We have also increased consultancy income and mentorships schemes for small enterprises in C-TRIC.

vii Our staff have provided leadership and established influential networks regionally, nationally and internationally (see section e. below, membership of networks and committees, which regulate and inform public health and policy, and our Impact Case Studies).

Research Groups and their priority research activities, which have enabled the BMSRI to achieve these successes, are outlined in paragraphs A-H below. As would be expected, staff members from the different Research Groups frequently collaborate on diseases that have shared environmental or genetic determinants. Post RAE2008, BMSRI's strengths, weaknesses, opportunities and threats were reviewed and the structures revised; some Groups were strengthened by provision of new staff and resources, and new groups were created through strategic initiatives and investments described above.

(A). Diabetes: The Group has continued to conduct research of therapeutic importance, through development of novel antidiabetic agents; this has proved to be highly relevant for treatment of both obesity and neurodegenerative disease. Translation of research through IUL and Diabetica Ltd has enabled the generation and grant of valuable IP resulting in impressive commercial exploitation and international impact. Research is divided in five key areas: (A.1) Engineering of pancreatic islet beta-cells providing *in vitro* models of glucose-responsive insulin secretion, as a tool to understand beta-cell function, uncover drug targets and test novel therapies and has yielded new therapeutic targets, aspects of beta-cell signal transduction; established electrofusion-engineered rodent and human beta-cells that are currently utilised commercially by pharmaceutical partners and demonstrated incretin hormones as effectors of stem cell differentiation towards the beta-cell phenotype (McClenaghan, Flatt). (A.2) Anti-diabetic and anti-obesity effects of structurally modified brain-gut peptides which has led to commercially viable enzyme-resistant, long-acting forms of GIP, GLP-1 and CCK-8 for treatment of diabetes, obesity and metabolic disease (resulting in an impressive series of 14 granted patents). Such research has led to three new IP filings focused on xenin and novel dual-acting incretin analogues (Flatt, Gault, Irwin, O'Harte; GB1200509.6, GB1214493.7, GB1313108.01), which have received >£130K in development funding. (A.3) Previous research involving the discovery and actions of new insulin-releasing agents from amphibian skin secretions (resulting in two granted patents, EP1590458, US8003610) has led to development of a novel concept of beta-cell drug desensitization which is the current focus of a £100K Invest NI PoC (Abdel-Wahab, Flatt, McClenaghan, P McClean). (A.4) Elucidation of the mechanisms of pancreatic islet beta-cell dysfunction, and actions of glycated regulatory proteins: aspects of beta-cell gluco-lipotoxicity and long-term modulation by amino acid exposure; the detrimental and novel role of beta-cell insulin glycation in diabetes, and its utility as a biomarker (one patent granted in EU, EP1540352) (Flatt, McKillop, O'Harte). (A.5) Effects of antidiabetic drugs and brain-gut peptides on behaviour and neurodegeneration in diabetes and Alzheimer's disease (Gault, P McClean, Flatt) collaboration with the Molecular Medicine and Stratified Medicine Groups, and GIP and GLP-1 analogues have shown utility as potential anti-neurodegenerative agents (one granted, EP2197475 and seven pending patents) (Gault, Flatt).

(B). Human Nutrition and Dietetics: The Northern Ireland Centre for Food & Health (NICHE) was established as a Centre of Excellence (EU structural funds) in 1996, to provide greater understanding of diet-related health issues, with a predominantly disease-preventive emphasis. Research programmes have been very successful at identifying food components or dietary regimes likely to benefit human health, particularly for prevention or treatment of cardiovascular disease, immune disorders, stroke, cancer and obesity. Research has been structured into seven priority areas organised in key Sub-Group teams led by senior Group members: (B.1) Energy balance, appetite regulation & nutrition education (Livingstone, Gallagher, Kerr, McCann, Pourshahidi, Price). (B.2) Folate & related B-vitamins in health & disease, (Hoey, McAnena, McNulty, Pentieva, Strain, Ward). (B.3) Phytochemicals & gut microflora in health & disease (Gill, Magee, McSorley). (B.4) Micronutrient modulation of immune & inflammatory responses (McNulty, McSorley, Mulhern, Pourshahidi, Strain, Ward, Yeates). (B.5) Psychological factors associated with food & nutrition (Gallagher, Gibney, Livingstone, McCormack, Strain). (B.6) Nutrition, toxicology & child development (Strain, McSorley, Mulhern, Yeates). (B.7) Microbiology group was relocated to NICHE to progress diagnosis, surveillance and examine links with microbiome and health (Dooley, Gill, D McDowell, McMullan, Ternan). An important and remarkably successful aspect of NICHE is the development and validation of biomarkers for chronic disease to facilitate dietary intervention studies in healthy subjects at risk of disease. Ground breaking work has demonstrated that hypertensive patients, who inherited a specific *MTHFR* genotype, uniquely respond to riboflavin supplementation, an exemplar of stratified medicine and gene-nutrient interactions. Volunteers for intervention and other studies are drawn from the local community. The Group exploit the Human Intervention Studies Unit CFU. Studies in healthy humans, and specific patient groups, through collaborations with clinicians in the specialised areas of cardiology, gastroenterology, respiratory medicine, and paediatrics. In delivering such work, NICHE projects are also undertaken at our hospital centres based at C-TRIC (Altnagelvin Hospital) and the NICRF (Belfast City Hospital) in partnership with Health & Social Care Trusts. In addition to research in Ireland, NICHE also has numerous collaborations with other centres of excellence in the UK, Europe, USA, Australia and New Zealand. Research from NICHE has had major international significance and impact in countries such as the Seychelles, India and Malawi.

(C). Molecular & Translational Medicine: Strategic investment in neuroscience (dementia) has continued since REF2008, the Group was strengthened by relocation of researchers from Psychology (Leslie, Kim, Shaw) working in partnership with new appointments in Stratified Medicine (P McClean). The Group has continued to successfully develop promising new treatments for Alzheimer's disease (AD) and now has a strong patent position in this area (which is further developing with partner diagnostics). The Group uses preclinical animal models to conduct research into neurodegeneration and psychiatric disorders. The Group examines biological processes of stress, anxiety and dementia with recent success in the development of promising new treatments for AD. (C.1) Alzheimer's disease Research has involved the analyses of the processes in the brain that are associated with AD, especially the connection between type 2 diabetes and AD. This work led to the discovery that novel modified incretin hormone drugs (developed by the Diabetes Group) to treat type 2 diabetes, show remarkable effects in reducing degenerative symptoms in transgenic animal models of AD, including a normalisation of the vasculature. Leads developed by the Group have progressed to human clinical trials for the treatment of AD in collaboration with pharmaceutical partners (P McClean, Kim). Behavioural tasks and *in vivo* recording are used to analyse neuronal activity in the working brain. Anatomical studies of neurons in the cortex are under way to identify dendritic changes after learning and in disease. (C.2) The role of nanoparticles in neurodegenerative diseases has been the focus of EU Framework 7 funded research; this is in collaboration with the Nano-Systems Biology Group (Kim, Howard). (C.3) The psychiatric disorders research (funded by the BBSRC, previously funded by Wellcome and Merck Neuroscience) examines behavioural and biological processes in stress and anxiety, and has traced the links between anxiety-reducing drugs and the fundamental behavioural processes of extinction and memory following learning, and developing links to mouse models of AD. A distinctive feature of provision is a substantial and well-equipped operant conditioning laboratory which is used alongside other behavioural methods, surgical, pharmacological and neurochemical techniques (Leslie, Shaw). (C.4) Vascular research expertise in the Group includes

the morphological, cellular and molecular determinants of pattern formation in the vasculature and the development of mathematical models of vascular growth. Using vascular casting, this work has shown that incretin hormone analogue drug therapy can dramatically prevent vasculature defects and/or possibly restore the vasculature in preclinical models of AD (Mitchell, P McClean, Gault). Vascular research also has a strong interdisciplinary component and involves research into wound healing, characterisation of Akt inhibitors for the treatment of malignant gliomas, and bone regenerative medicine (Mitchell).

(D). Nano-Systems Biology: a multidisciplinary Group with expertise in molecular cell biology, nanotoxicology, tissue engineering, systems biology and advanced imaging techniques. The Group has access to real time, beam scanning, and two-photon confocal microscopy; laser capture microscopy; atomic force microscopy combined with confocal microscopy; image processing for 3D stereological measurement and for Comet DNA analysis; a Dualbeam cryo FIB-SEM, capable of nano-milling frozen biological samples and then imaging the exposed surface; an environmental SEM capable of imaging hydrated living tissue; a high resolution TEM; and a newly installed two-photon Stimulated Emission Depletion (STED) super resolution fluorescence microscope with an environmental chamber that enables dynamic imaging of delivery systems within cells and deep tissues in three dimensions, over hours to days. Research areas include: (D.1) The long term effects of nano-particles *in vivo* are investigated using specialist imaging methodologies. Research of low-dose minimal change toxicology, nanotoxicology and nanoparticle fate, including the potential neuro-toxic effects of nanoparticles induced by protein misfolding in the brain, and the possible link with neurodegenerative disease, is conducted in collaboration with the Molecular & Translational Medicine Group (Howard, O'Hagan, McKerr; Kim). (D.2) Cell signalling disruption in the foetus by low doses of environmental pollution, leading to adult oncogenesis by inducing tissue dysgenesis (Howard, Downes, Soto). (D.3) 3D culture of models of human tissue funded by the MRC (Howard, Barnes, McKerr, Soto, Downes), and stereological analysis of tissues (Howard, Saetzler) have been developed. (D.4) Advanced Bioimaging, including atomic force microscopy of the surfaces of living cells, and EM imaging of a range of biological samples (Howard, McKerr, O'Hagan). (D.5) Development of Comet techniques for measuring DNA damage, repair, replication and methylation at the single-cell level (Downes, Howard, McKerr, McKenna (Transcriptional Regulation): nutritional aspects of this work in collaboration with Strain and McNulty (NICHE). (D.6) Protection of corneal surfaces from DNA damage (Downes; Moore (Vision Science). (D.7) Data analysis: data mining with Grid computing (Dubitzky), 3D reconstruction of microscopic images (Saetzler, McKerr), and data analysis of effects of Vitamin D (Dubitzky, with Strain (NICHE)).

(E). Pharmaceutical Science & Practice: The strategic investment, outlined above, facilitated the establishment of this new Group in the SAAD Centre for Pharmacy & Diabetes, with the appointments of six new staff members (McCarron, J Callan, B Callan, Fetherston, Matoussi, Tambuwala) and relocation of others (Banat, McHale, Webba da Silva) to the Group. Research covers laboratory-based investigations into formulation design, through to pharmacy practice-based work into specialised services and medicines management. Research is active in: (E.1) The use of novel hydrogel materials and dressings for drug delivery and management of chronic ulceration and acute laceration currently being commercialised by a new University spin-out company (McCarron). (E.2) The use of nanotechnologies in advanced drug delivery involves the application of supramolecular chemistry to the development of luminescent sensors and switches as well as new photosensitiser conjugates for use in Photodynamic Therapy (J Callan, Matoussi, McCaughan). (E.3) Stimulus-responsive drug delivery systems, including ultrasound-mediated gene transfer and exploitation of the effects of electric and ultrasonic fields for therapeutic purposes (McHale). (E.4) Programmable DNA nanostructures examining the mechanism governing the self-assembly of four-stranded DNA, its role in the regulation of gene expression and how these nanostructures may be utilised in sensing and in therapeutic applications (Webba da Silva). (E.5) Isolation of microbial components that have utility as bio-surfactants in wound healing and other biomedical applications (with other cross-disciplinary applications such as the oil industry) (Banat). (E.6) Development of controlled-release microbicide vaginal ring drug-delivery systems for the treatment of HIV (Fetherston). (E.7) Development of novel therapeutics for the treatment of Inflammatory Bowel Diseases and colorectal cancer (Tambuwala).

(F). Stratified Medicine: A new Group established in July 2013, with the appointment of 12 new lecturers with an investment of £11.5M. The focus is the accelerated translation of biomarker discoveries into clinical utility with tangible benefits for degenerative diseases of ageing. Research is centred on the development of prognostic and theranostic biomarker panels aligned to therapeutic interventions for key degenerative diseases of ageing including: hypertension, bone health, inflammatory disease, diabetes, mental health & AD, breast/prostate cancer and blindness. Key successes to date include the development and grant of new IP (EP2232268 A2) for stratifying rheumatoid arthritis patients into responders and non-responders to anti-TNF therapy (under commercial development in partnership with the Technology Strategy Board and Randox Laboratories Ltd). A breast cancer diagnostic (WO 2010/063454) aimed at identifying lymph node negative breast cancer patients who are at high risk of developing metastases has been developed as a diagnostic platform with Randox Laboratories Ltd. Multidisciplinary links exist with the new £5M Northern Ireland Centre for Functional Brain Mapping (Faculty of Computing & Engineering's Intelligent Systems Research Centre) focused on the development of stratified medicine biomarkers of diagnosis and treatment response for dementia and mental illness.

(G). Transcriptional Regulation & Epigenetics: Research focuses on classical and non-classical mechanisms of transcriptional control (MRC funded) with an emphasis also on prostate cancer (Prostate Cancer Charity funded). (G.1) The Group has an established profile in examining epigenetic changes in cell differentiation and de-differentiation (Walsh, Lees-Murdock). (G.2) Expertise in steroid hormone receptors, particularly Vitamin D and Androgen receptors, their target genes, and discoveries relating to modulation of their activities by coactivators and corepressors which modify chromatin structure or cause changes in DNA methylation (Thompson). (G.3) Research is specifically focused on prostate cancer, and the changes in gene activity (Worthington), including (G.4) the role of microRNA (McKenna) and (G.5) epigenetic marks (Walsh) which take place during tumorigenesis, particularly in the anoxic cell (Worthington). Collaborative links with the pharmaceutical sector include strategies to maximise the effect of bicalutamide for treatment of androgen-sensitive prostate cancer (McKeown, Worthington).

(H). Vision Science: This Group brings together vision scientists, optometrists and molecular biologists who perform laboratory-based investigations, develop preclinical human and animal models of disease and undertake optometry and ophthalmology practice-based research within hospitals and in the community. Specifically; (H.1) Clinically relevant psychophysical investigations of visual function with ageing in order to better understand the fundamentals of neural and optical changes in the normal and diseased eye (glaucoma and AMD) (Anderson, Beirne, Vidinova). Application of psychophysical, electro-diagnostic and imaging techniques to better understand how retinal structure relates to functional change in the development of myopia and in retinitis pigmentosa (Anderson). (H.2) The Northern Ireland Childhood Errors of Refraction (NICER) study: a robust population-based analysis of the distribution and determinants of childhood refractive error in the UK informs eye care practitioners, commissioners and government agencies as they develop evidence-based strategies for paediatric eye care (McClelland, O'Donoghue, Saunders). (H.3) Clinically relevant molecular biology and immunological investigations of the ocular surface, improve diagnosis and treatment in the ageing or diseased eye. This work has resulted in discovery of the NLRP3 inflammasome in the eye and development of preclinical models allowing assessment of gene therapy in a mutation or gene specific approach, paving the way for cutting edge therapeutics to be applied to the cornea. Application of next generation sequencing technologies to genetic eye disease enhances diagnostic acumen, while identifying new targets for therapy. Assessment of cataract and refractive surgery visual outcomes within the ophthalmic community informs best practice (Beirne, McGilligan, Moore). (H.4) Investigating visual processing and optical performance of children with developmental disabilities including Down's syndrome and autistic spectrum disorders using objective refraction, advanced imaging, electrodiagnostic and clinical techniques influences diagnosis and clinical management of visual disorders in this Group. On-going studies will further refine understanding of the impact of developmental disability on visual function, maximize visual outcomes and optimize clinical care (Little, McClelland, Saunders). (H5) Investigations into the role of the calcium-sensing receptor (CaSR) in regulation of ionic

homeostasis in the lens and functional analysis in the ageing and cataractous eye have the potential to prevent disease onset (Moore, Nesbit).

Future Objectives & Plans: Over the next 5 year period, we plan to deepen our basic science research base at Coleraine and Clinical research in Derry~Londonderry and Belfast hospital sites. We will strategically target Research Council, Major Charity and EU funding in line with the University's corporate objectives, and our plans are to increase research income by 5% annually with a minimum of at least 40% of our research income derived from Research Council, Major Charity and EU funding initiatives. We are well placed to achieve these objectives as our investment strategy and expansions are **perfectly aligned with the major priorities areas of these funders**. By exploiting our expanded basic research and new clinical resources described above, we aim to further increase our pipeline of innovations and expand translation of outputs to clinical utility and commercial ventures, all underpinned by a focus on publication in the highest impact journals. We will achieve these innovations by building on our recent achievements in the area of stratified medicine with the objective of becoming the leading Centre for Stratified Medicine over the next 5 years. We plan to create **a new £20-25M Institute for Health & Wellbeing** in partnership with hospitals in Derry~Londonderry and Letterkenny in the Irish Republic. This will integrate our new Stratified Medicine Centre, new Centre for Functional Brain Mapping, and the University of Ulster Bamford Centre for Mental Health (reported in the Ulster Psychology submission). We will develop a **new multidisciplinary Clinical Data Analytics and Health Economics Centre** as a partnership between BMSRI and the Faculty of Computing & Engineering's Intelligent Systems Institute, the Health Trusts, global industry and the regulatory stakeholders. We will also seek to establish **a new TSB Catapult Centre for Diagnostics in Stratified Medicine initiative** (£200M initiative announced in Oct 2013) in partnership with Queen's University Belfast, Randox, ALMAC, other Centres in the UK and across Ireland. We seek to become the major rallying Centre linking pharma, diagnostics and healthcare systems, in the UK and Ireland and enable businesses in these Islands to exploit stratified medicine. The BMSRI and the University are leading the development of a new Veterinary School and Research Institute, and the BMSRI plans to integrate research of zoonotic disease and human health. We intend to develop our Stratified Medicine Centre as a Postgraduate Medical School.

c. People, including:

i. Staffing strategy and staff development:

The University of Ulster received the **European Commission's HR Excellence in Research Award** in 2013 in recognition of the strong Institutional commitment to the principles laid out in the Research Staff Concordat, and our CPD framework includes all domains and subdomains of the VITAE UK (Research Development Framework). The University is a member of the Athena Swan Charter (Bjourson and Moore represent the BMSRI). We strongly support **equality and diversity** and staff are able to reduce their FTE contracts consistent with individual personal circumstances. In addition, staff members avail of career breaks or variations in contract without disadvantage. The University has a policy of affording equality of opportunity to all irrespective of gender, sexual orientation, religion or race. The BMSRI **gender profile is 50:50 female:male** and we provide support systems for staff returning from maternity leave or other leave of absence**.**

In RAE2008 the BMSRI submitted 60.75 FTE Category A staff, and since RAE2008 we have successfully **expanded our FTE staff significantly by 23%** to 74.1 FTEs. We recruited **6.2 FTE lecturers to the School of Pharmacy & Pharmaceutical Sciences** and **12 FTE lecturers to the new Northern Ireland Centre for Stratified Medicine** (strategic priority initiatives), with the remaining new appointments being made to replace staff retirements or vacancies in the existing BMSRI Research Groups. Professorial promotions have included J Callan, Gault, McCormack, McKillop, Moore, Saunders, Walsh, Ward. J Callan was awarded the **Founding Norbrook Chair in Pharmaceutical Science** and appointed Group Leader. Losses within NICHE (Welch, Thurnham, retirement; Wallace, deceased; Stewart-Knox, resigned) and imminent retirements were addressed by appointment of six new staff (Drs Hoey, McCann, Mulhern, Price, and Prof Gibney) and relocation of the microbiology team to NICHE to develop microbiome research. We are also recruiting two additional staff at professorial level to NICHE ensuring continuity of leadership. The BMSRI age profile is approximately 28% aged 25-35yr; 31% aged 36-45yr; 21% aged 46-55yr; 18% aged 55-65yr; and 1% aged 66-75yr; a profile which is highly consistent with

sustainability. We also appointed a Quality Assurance Officer, a Clinical Trials Manager and an IT Officer to enhance research support already provided by 22 research technicians.

Effective development and support of the research work of staff: At University level, research performance and targets are set by the PVC (Research & Innovation) and the Dean of the Faculty, and monitored by the University Research Office. The BMSRI Director (Bjourson) manages the overall research strategy and priorities for the BMSRI. All staff contribute to teaching and administration but **individual workloads are carefully reviewed** and agreed between the RI Director and the appropriate Head of School. Individual teaching and administrative workloads are reduced and carefully managed to assist researchers achieve their full potential, while maximising research outputs and impact across the BMSRI. Research areas are formally managed through eight Research Groups led by Research Group Leaders recruited by a competitive process serving 4 year terms with opportunity for reappointment. The role profile of Group Leaders requires international research experience and standing, a sustained record of securing major external grants and substantial successful experience of **managing and mentoring staff and PhD students**. All Research Institutes are set **research income targets** by the University, and the RI Director sets individual staff external grant income targets, benchmarked against the RAE2008 National UoA metrics, and publication targets which are monitored at bi-monthly BMSRI Directorate meetings. When appointing new academic staff, we recruit junior researchers with exceptional promise and established scientists of substantial achievement with many coming from international Centres of Excellence.

The BMSRI pays particular regard to **supporting the careers of Early Career Researchers**, who on appointment, are assigned a personal mentor and submit a 1-2 year research development plan. New appointments are allocated appropriate generous start-up funds for generation of preliminary data for strategically identified research grant application(s). Start-up packages also include the allocation of a PhD research studentship, co-supervised by an experienced staff member. **Formal mentoring policies include:** undertaking the research module of the PgCHEP incorporating the preparation and review of first research grants, and papers are reviewed by expert panels with feedback at every stage. The extensive network of external academic, health policy bodies and industrial collaborations into which new staff are introduced dramatically enhances their own opportunity to work on an international level. Our commitment to implementing the Concordat on Contract Research Staff (see above) means that such researchers are afforded the same opportunities as academic staff, to develop independent research careers.

To stimulate engagement and collaboration with NHS end-users, the BMSRI Director and the Research Director of the Western Health & Social Care Trust offer ten **annual match funded clinical pump-priming projects** (up to £10K) each specifically for projects which are co-supervised by an **academic staff member and a Health Trust Clinician**. These awards form the basis of more substantial joint grant applications involving health service end-users and develop the research career of Trust staff.

Most research staff are based at the Coleraine Campus in the Centre for Molecular Biosciences and the new SAAD Centre for Pharmacy and Diabetes. In 2013 we **recruited 12 new permanent Lecturers** (with 4 additional Lecturers, 5 Research Associates, a Business Development Manager and an additional Technician to be appointed by October 2014) in our newly established £11.5M Centre for Stratified Medicine, in the Clinical Translational Research & Innovation Centre (C-TRIC), embedded in the heart of a major acute hospital site. This strategic partnership between the Western Health & Social Care Trust and the Derry City Council is located in the Altnagelvin Hospital site in Derry~Londonderry . We appointed Prof Ward as Deputy Director of our £4M Wellcome Trust-Wolfson Foundation Northern Ireland Clinical Research Facility, a partnership between University of Ulster, Queen's University of Belfast and the Health & Social Care R&D Office and Hospital Trust), in the Belfast City Hospital Campus.

Integration of NHS staff has been very successful overall. We have appointed Visiting Professors from the NHS and ten clinicians from Altnagelvin hospital, all of whom are aligned with new academic appointments in the Stratified Medicine Centre. The C-TRIC CEO is also Director of Research in the Hospital Trust and the C-TRIC Board is composed of an equal number of NHS staff and University staff (including representatives of the Trust Governance staff). The BMSRI Director is a member of the Steering Committee of the NI Pathology Network Board, and the

Northern Ireland Biobank along with Queen's University representatives and Trusts. All BMSRI-affiliated staff from the NHS, industry and public bodies have access to the full range of training and mentoring courses and support packages of the University and such staff contribute to our advisory panels, including some of the following:
Visiting Profs/Honorary Positions: from **the NHS:** D. Alexander, M Edmondson (Patient Client Council), W A Coulter, W Dickey, H McGavock, M O'Kane, J E Moore, P J Morrison, S Shah; Trung Do (Partners Health Care USA); from **Food & Policy Organisations:** M Flynn, (FSAI R. Ire), J R Rao, (AFBI, UK), H Verhagen, (RIVM Netherlands); from **Universities/Institutes:** A Flynn (Univ. College Cork), I McClean (Univ. Dundee), I Rasko (Hungarian Academy of Sciences), I Rowland (Univ. Reading); from **Private Companies/Industry:** C Short (McNeill Nutritionals), J O'Brien (Nestlé), J Haughey (Norbrook Labs, Pharma), J Moore (Cathedral Eye Clinic), A Leccisotti (Siena Private Eye Clinic, Italy); S Whoriskey (Ex Entrepreneur in Residence MIT,USA), G W Meijer (Nestlé). **Advisory Panels & Boards of Directors:** C-TRIC board members, C Duffy (EU Horizon 2020), A Sherrard (BiobusinessNI), L Williams (Derry City Council), J Lusby (Deputy Dir. WHSCT), A Kilgallon (Medical Dir. WHSCT).

ii. Research students:

The BMSRI has completed an average of 24 PhD awards per year (**118 since 2008**), including four CAST awards with industry. Since **21.4 new FTE Category A staff have been appointed in the last 18 months,** they have not yet had the time to supervise PhD students to completion within the BMSRI: therefore the number of completed PhDs per FTE Category A staff in the BMSRI has been reduced in REF2014.
Postgraduate research student registration is undertaken by the University Research Office (RO) which administers student records and grants; and works with faculty-based Research Graduate Schools (RGS) to allocate research studentships through fair and transparent competition. The RO maintains research databases and makes data returns to HEFCE. PhD studentships have been financed internally through Vice Chancellor's Research Studentships (VCRS) and externally through research grants and awards, such as the Department of Agriculture & Rural Development awards, and more extensively the Department for Employment & Learning NI (DEL) awards; DEL awards are accepted by HEFCE as equivalent to RCUK awards (note: NI Universities are not eligible for RCUK DTAs). Each year, a number of these DEL and VCRS PhD and MRes awards are allocated to the BMSRI.
All PhD proposals are reviewed by the BMSRI Postgraduate Committee and the RI Director to ensure alignment with RI strategic priorities, feasibility, affordability, academic rigour, technical training, and potential clinical/societal/economic impact. Our policy is to also allocate DEL/VCRS funded studentships as an institutional commitment in major external grant applications (see also section b. Research Strategy) providing an additional level of expert external peer review of all internally allocated PhD projects, and ensuring adequate PhD consumable funding. The RGS responsible for PhD students, is managed by a Board, including staff and student representation, which reports to Faculty committees and to the University central Research Degrees Committee. The BMSRI Postgraduate Tutor - organises 100-day, 9-month and final year assessments, and monitors supervision.
PhD students have the opportunity to engage in journal clubs and staff/student presentations, and are also encouraged to attend in-house events at which we host a diversity of external speakers. The University's Staff Development unit works with RGS for a **Generic and Research Skills Training programme**, available on line for all PhD students and complemented by Personal Development Portfolios. PhD students also undertake project specific training such as Good Clinical Practice, phlebotomy training and animal handling as required. Each PhD project is allocated **£1000/year from the BMSRI recurrent budget** for conference attendance and/or career development visits. Funded students are also allocated £1,000/year through the RGS to support their research project. Institutional Audit by QAA in 2010 commended the "comprehensive support, training and supervision of research students", noting the following good practice: comprehensiveness and clarity of the documentation provided; availability of seminars for experienced supervisors; planning of the research and personal development training. Technology generated by research students also features significantly in the BMSRI patent portfolio.

d. Income, infrastructure and facilities

The BMSRI has **increased annual external research grant income spend by >30%** (**£20.36M since 2008**), up from £3.1M/year (RAE2008) to £4.1M/year (REF2014). This increase includes income from the BBSRC, MRC, TSB, EU, major charities and industry.

Infrastructure and Facilities: The BMSRI building infrastructure includes the **£14.5M 6,200m^2 Centre for Molecular Biosciences** (CMB) at Coleraine (constructed in 2003). The Research Strategy section describes the substantial investments including the £2.7M to establish formal Core Facility Units, the £2M C-TRIC (the Clinical Translational Research & Innovation Centre) in Derry~Londonderry, the £5.5M Functional Brain Mapping Facility the new £4M Wellcome Trust-Wolfson Foundation Northern Ireland Clinical Research Facility (NICRF) and the £11.5M Northern Ireland Centre for Stratified Medicine. Equipment across this building infrastructure has been consolidated as Core Facility Units, up to GLP standards. A **Quality Assurance Officer** manages the CFUs assisted by **22 technicians** and a **Clinical Trials Manager** (who oversees clinical trials, ethics and governance). Each CFU Coordinator operates with **agreed business plans** and CFUs retain surplus income for reinvestment in staff support or new equipment. CFU resources are available to researchers and IUL promotes CFUs services to third parties in major industry and SMEs.

The CFU services include:

Bioimaging CFU: comprising the FEI Centre for Advanced Bioimaging (FEI's European demonstration laboratory) and the Leica Centre for Tissue Engineering: a full range of EM and STED microscopes, and other microscopic equipment detailed above (Research Groups, D).

Cell Technologies CFU: provides cell/tissue barcoded computerized storage (1.2 million HTA sample capacity) with full traceability; patch clamp neuronal recording; confocal microscopes; window chamber/skin flap model for *in vivo* imaging of vasculature, neurons and plaques in mouse models of cancer and Alzheimer's disease (AD); suite of tissue culture rooms; flow cytometers; X-ray and caesium gamma sources.

Genomics CFU: includes a DNA sequencer and synthesizer, pyrosequencer; quantitative real-time PCR instrumentation (provides SNP, methylation, gene knockout, data integration and pathway modeling).

Human Interventions Studies Unit (HISU): suite for nutritional intervention trials on human volunteers including residential trials (metabolic measurements), kitchen; an exercise suite, BodPod, ergometer, treadmill, ergospirometer and bone densitometer; a gastrointestinal analytical laboratory, with access to a Category II laboratory for blood and faecal sampling and analysis.

Metabolomics and Proteomics CFU: provides metabolomics and proteomics with a range of mass spectrometers; peptide sequencing and synthesis; NMR with FTS.

Pharmaceutical & Aseptic Manufacture CFU: with instrumentation for early stage product development/characterization, assisting SMEs in initial stages of product development (stability, physical characterization, packaging, drug release and SOP development; and an Aseptic Manufacturing Suite.

Vision Science CFU: fully equipped eye clinic providing specialised visual function tests to the public, including measurement of characteristics of the ocular media and the retina. Resource includes macular densitometry; light scattering meter; specialised lasers and instruments for simulating the ciliary muscle action in the eye.

Clinical Translational Research and Innovation Centre (C-TRIC): includes clinical consultation rooms, blood processing and physiology labs, and access to clean room for preparation of medicinal formulations; staffed with 6 clinical trials nurses, technician and assisted by formal networks across UK and the island of Ireland with access to accredited diagnostic labs and pharmacy services in the Trust.

Biological Behavioral Research Unit (BBRU): A large fully equipped small animal unit now under the management of the BMSRI since December 2012.

e. Collaboration and contribution to the discipline or research base

Network grants from a diversity of sources were a strong feature and some examples include**:**

£1.37M US National Institute of Health (NIH) (to Strain) for an international study on mercury toxicity from fish consumption; an award (to McNulty) of **£1.24M from NI Department for Employment & Learning (DEL)** through its 'Strengthening the all-Island Research Base' initiative: Irish Universities Nutrition Alliance Project- Building additional and sustainable research capacity in nutrition and bone health. The Nanosystems Biology Group (Howard) secured **£450K EU FW7** to study the impact of nanoparticles on protein misfolding in the brain, the Group were also awarded a **£360K MRC** NC3RS grant to develop 3D tissue culture models of cancer. Stratified Medicine Biomarker projects with Industry Networks include a **£324K TSB** grant (Bjourson) part of a total £900K Randox Inflammatory biomarker project; and a **£322K DSM Nutritional Products Ltd grant:** Blood pressure lowering effect of riboflavin in genetically predisposed hypertensive adults; The Pharmacy Group (Webba da Silva) was awarded **£290K BBSRC** to study DNA quadruplexes; The Transcriptional Regulation & Epigenetics Group were awarded **£378K MRC** funding (Walsh) to study methylation. This is not an exhaustive list, but rather a snapshot of the funding secured in the period.

Exemplar Networks/MOU's: **Bjourson**: Northern Ireland Pathology Network. **Dubitzky**: EGI-InSPIRE and MAPPER; University of Modena and Reggio Emilia, Modena, Italy. **McHale:** Sonidel Ltd/Ireland; **Livingstone**: Adjunct Professor, Monash Univ., Australia. **McNulty**: International Biomarkers of Nutritional Development (BOND) coordinated by USA NIH; European Micronutrient Recommendations Aligned (EURRECA) Network; Joint Irish Nutrigenomics Organisation (JINGO): Trinity College Dublin, Univ. College Dublin, Univ. College Cork.

Exemplar Panel Memberships: **Bjourson**: Northern Ireland Biobank Steering Committee; CRUK (Belfast) Steering Committee 2012-2013; Council Member Irish Soc Clinical Genetics 2008-2013. **Downes**: Panel member, UCD School of Biomolecular Sciences Quality Review, 2010; REF 2014 subpanels 3&6. **Dubitzky:** Evaluation panel for FP7 programs (HEALTH and ICT). **McCormack**: HUCBMS National Executive Committee; Healthcare Science Advisory Committee NI. **McNulty**: Expert Panel Member (Folate) for the international Biomarkers of Nutrition for Development (BOND) project at the US NIH. **O'Harte:** Chairman of Academy of Finland, International Health Sciences Grant Committee, Helsinki, (2011 and 2012); EU Assessor Panel Member, Innovative Medicine Initiative (IMI), Brussels, 2009. **Pentieva**: Working Group of Dietary Recommended Values for Vitamins, European Food Safety Authority (EFSA). **Strain**: Chairman of Working Group on Health Claims and Vice-Chair of the NDA (Dietetics, Nutrition and Allergies) Panel of the European Food Safety Authority (ESFA), Parma, Italy; President of the Board, European Nutrition Leadership Programme (ENLP); Member of VLAG International Advisory Board (Wageningen and Maastricht Universities, The Netherlands). **Webba da Silva**: European Research Council (ERC) referee in peer review evaluations

Exemplar Collaborations: Univ. of Amsterdam; Arizona State Univ.; Univ. of Bergen, Norway; Università di Bologna, Italy; Univ. of British Columbia; Univ. of California, San Diego; Univ. of California San Francisco; McDonald Institute for Archaeological Research, Cambridge; Chinese Academy of Sciences, Shanghai; Univ. of Colorado; CNRS-Univ. Paris Diderot, France; Univ. College Dublin; Dublin City Univ.; Univ. of Dundee; Univ. of Edinburgh; MRC Human Genetics Unit Edinburgh; Harvard Medical School; Univ. of Helsinki; Imperial College, London; Indiana Univ.; Karolinska Institute, Sweden; Univ. of Konstanz; Korea Advanced Institute of Science and Technology, Daejeon, South Korea; Ludwig Boltzmann Inst., Vienna; Univ. of Mainz; Univ. of Massachusetts; Univ. of Milan; NUI Maynooth, Ireland; Moorfields Eye Hospital/UCL; Ludwig Maximilian Univ. of Munich; Univ. of Miami; Purdue Univ; Penn State College of Medicine, PA; Queen's Univ. Belfast; Univ. of Rochester, NY; St Louis Univ., MO; Univ. of Rostock, Germany; Rutgers Univ., NJ; Hungarian Academy of Sciences, Szeged; Teagasc Ireland (Irish Department of Agriculture); Steno Diabetes Research Centre, Denmark; Trinity College Dublin; US Department of Agriculture.

Company Founder/Directorships: **Bjourson**: Director, Innovation Ulster Ltd; C-TRIC. **Flatt, McClenaghan, O'Harte**: Co-Founders of Diabetica Ltd. **Leslie**: Director, New England Center for Children UK Ltd. **T Moore** Director of OMG3s. **Strain**: Member, Board of Directors, ILSI Europe.

Exemplar Professional Body Interactions: **J Callan**: Royal Society of Chemistry, Member Academy of Pharmaceutical Science. **Flatt**: International Working Group of Juvenile Diabetes Research Foundation. **Gibson**: American College of Rheumatology, American Society of Mass Spectrometry, Human Proteome Organisation. **Little** General Optical Council Educational Visitor Panel. **Saunders**: Vice-Chair UK College of Optometrists Research Committee. **Strain**: 24th President, The Nutrition Society.

Exemplar Prizes, Awards, Honours: **J Callan**: Founding Norbrook Chair in Pharmaceutical Science. **Flatt, McClenaghan & O'Harte**: Academic Enterprise Awards Europe Life Sciences award, 2008. **Gault**: EASD Rising Star Award (Vienna, September 2009). **McNulty**: Member of the Royal Irish Academy. **O'Donoghue**: College of Optometrists Neil Chairman medal for outstanding research, 2012. **Strain** British Nutrition Foundation Annual Prize 2012. **Webba da Silva**: Global Centre of Excellence Award, University of Kyoto, Japan

Exemplar Editorial Boards:
Volumes: **Dubitzky**: Senior editor-in-chief: The Encyclopedia of Systems Biology, Springer.
Journals: **Dooley**: Appl. Environ. Microb. **Irwin** BMC Endocr. Disord., PLoS ONE. **Magee**: Food Chem. Toxicol. **O'Harte**: Brit. J. Pharmacol. **Walsh**: Genomics, **Webba da Silva**: Int. J. Mol. Sci.

Exemplar Conference Organising Committee: **Anderson**: European Academy of Optometry and Optics (EAOO). **Dubitzky**: 2012 IEEE International Conference on Bioinformatics and Biomedicine (BIBM 2012), Atlanta, USA. **Gault**: Diabetes UK Annual Professional Conference Organising Committee. **Webba da Silva**: Conformational Diversity and Applications of G-Quadruplexes, Barcelona, Spain 2012; National Organizing Committee, EUROMAR 2012.

Exemplar Invited/Key Lectures: **J Callan**: Invited Lecture: Molecular Sensor & Molecular Logic Gates, Antalya, Turkey, 2010, Invited Lecture: Royal Society of Chemistry, Macrocyclic & Supramolecular Chemistry Conference, Birmingham, UK Dec 2008; Invited Lecture: Royal Society of Chemistry, Macrocyclic & Supramolecular Chemistry Conference, Bath, Dec 2011. **Downes**: Plenary lecture, 75th Anniversary Szentgyörgyi Conference, Szeged, Hungary 2012. **Flatt**: Ernst Friedrich Pfeiffer Memorial Award Lecture of EASD; **Livingstone**: 16th International Congress of Dietetics: Sydney, Australia. **Leslie**: Keynote speaker, European Association of Behaviour Analysis Crete, Greece 2010; Keynote speaker, Brazilian Association for Behavioural Medicine, Salvador, Brazil 2011. **McNulty**: Invited speaker, International Speaker Lecture Programme, 'Folic acid supplementation and optimal health: getting the balance right', National Institutes of Health, Washington DC, 2008. **Strain**: Keynote speaker - Friedman School Symposium, Boston 'Health Claims in Europe' 2008; Keynote lecture, The Nutrition Society of Australia and Nutrition Society of New Zealand; Joint Annual Scientific Meeting 2009, Newcastle, Australia Nutrition in the 21st Century, 'Seychelles Islands study (Child Development)'; Keynote, 'Building a National Nutrition and Genetics Database' Nutrition Society of Taiwan 2012. Keynote, "DRVs in Europe",11th China Nutrition Science & International DRIs; Contributed to series: World Famous Scientists Lecturing in Hubei, China; William Evans Visiting Fellowship, University of Otago, New Zealand 2013. **Webba da Silva**: Science Foundation Research Conference, 'Self-assembly of Guanosine Derivatives: from Biological Systems to Nanotechnological Applications', Innsbruck, Austria 2009.