Institution: University of Aberdeen

Unit of Assessment: 1 - Clinical Medicine

a. Overview

Research in Clinical Medicine has international recognition and is a major investment priority at the University of Aberdeen. Our vision is to conduct leading research that focuses on key challenges in health and medicine which addresses the two gaps of translation of biomedical science to healthcare identified in the Cooksey Report. The first gap (translating basic and clinical research into ideas and products) is addressed here whilst the second gap (introducing those ideas and products into clinical practice) is addressed in our return for UoA2.

There is an international profile in both fundamental and translational research which aligns with *Pathways to a Healthy Life* - one of the four highlighted foci of the University's strategic plan. (The contributing groups in this submission are all located in the College of Life Sciences and Medicine, one of three Colleges in the University's Collegiate structure.

This submission comprises a number of interdisciplinary research programmes, which are located in the Institute of Medical Sciences (IMS) and the Rowett Institute of Nutrition and Health (RINH), supported by management structures of the Schools of Medicine and Dentistry and Medical Sciences. Integration and close collaboration have been promoted by the establishment of cross-College research programmes, sharing of core facilities and integrative centres, joint seminar programmes and a College-wide Graduate School which oversees postgraduate activity.

The IMS houses more than 400 active researchers providing a vibrant environment delivering world-class research. It is situated on the Foresterhill Health Campus, which includes the regional acute, maternity and children's hospitals and the medical school, making it one of the largest single-site medical complexes in Europe. The IMS blends basic, preclinical and clinical research to encourage interdisciplinary interaction. Research in the IMS is highly integrated enabling the work of some of our staff to be returned in UoA5. To achieve this, research is organised into six programmes of research – **Immunity, Infection and Inflammation; Musculoskeletal; Cardiovascular Medicine; Cell, Developmental and Cancer Biology; Translational Neuroscience;** and **Microbiology**. Each programme consists of 15-25 PIs and their research staff who are aligned to its research strategies.

These programmes build on areas of strength and deliver high quality research and innovation addressing key societal challenges through: (i) disease prevention and healthy living, and (ii) understanding mechanisms of, and developing treatments for disease. Underpinning the programmes are Integrative Centres, which offer expertise and front-line core technological support. The Integrative Centres include the Aberdeen Biomedical Imaging Centre, a newly established Centre for Genome Enabled Biology and Medicine, the Kosterlitz Centre for Therapeutics (which facilitates translation of biological innovation into new diagnostics and treatments and understanding disease), Systems Biology, a Core Facilities Centre (with e.g. advanced light and electron microscopy imaging, proteomics and FACS), and a Medical Research Facility - for *in vivo* biology and pre-clinical research.

We have major expertise in understanding the role of nutrition in the prevention of disease and maintenance of health. This is embedded in the work of the RINH - internationally renowned over its 100 year history for its work in nutrition. RINH became part of the University of Aberdeen in 2008 in order to fully exploit complementarities with the University's wide-ranging capacity in medicine and life sciences. It will be relocated in a new building adjacent to the IMS on the Foresterhill Health Campus in 2015. RINH has three major programmes addressing key challenges in nutrition; (i) lifelong health, (ii) obesity and metabolic health and (iii) gut health. This provides a broad base to foster collaborative interactions. RINH staff contribute to Scottish Government's strategic research programmes on *Food, Land and People* especially in Theme 7, *Healthy Safe Diets* which is aligned with the UK Global Food Security Programme.

b. Research strategy

Our research success is built on a clear strategy to ensure vitality, long-term development and capacity building and competitiveness. The premises of this strategy are:

1. Promoting focused programmes of research excellence, building on the achievements of RAE

2008, consolidating areas of excellence and strategically growing new areas addressing important clinical questions.
2. Recruiting the best researchers to add capacity to existing areas and develop new areas.
3. Provision of the best technological infrastructure to enable innovative research.
4. Strong leadership, management and effective administrative support, policies and procedures to enable researchers to undertake their work effectively.
5. Strong development opportunities for research staff at all levels to fulfil their potential and develop the next generation of researchers and leaders including a vibrant postgraduate student community, and mentoring and development of early career researchers.
6. Effective means for the dissemination and translation of our research to a range of stakeholders (e.g. the public, patients, policymakers, government, clinicians, academics) through a variety of mechanisms.
7. Active pursuit of economic and societal benefits from our research through proactive knowledge exchange, translational research, and commercialisation activities.
8. Partnership with NHS Research and Development to maintain focus on clinically important issues.

Research Culture

Research strategy, direction and leadership are supported by our Head of College (**Greaves**) and designated IMS Directors (**McCaffery** and **Heys**) within the College of Life Sciences and Medicine. The overall research activities of this College are coordinated by the College Director of Research (Gow-UoA5), who leads the overarching College Research Committee. An underpinning IMS Research Committee meets monthly to manage, to identify research opportunities, to horizon scan, and to ensure co-ordination of activity within the context of the IMS research vision.

Research programmes and groupings

Our research programmes foster and stimulate research within cognate areas that have critical mass. They develop cross-disciplinary collaborative research or become global partners of choice for international collaborations. Each research programme has its own Programme chair and deputy who provide leadership, drive research direction and provide mentoring and support. Each programme has a budget to facilitate strategic developments, encourage collaboration with leading international scientists and host symposia and journal clubs. Also organised each year are cross-programme meetings and retreats for PIs to promote cross-disciplinary research.

These structured research programmes co-ordinate activity from the postgraduate level upwards, and provide peer review support of research grant applications through to help in the execution and dissemination of research outputs.

Our research is complemented by collaborations from other interdisciplinary research groups in other Units of Assessment (UoA), in particular 2 and 5, providing extra breadth and capacity. The programmes represent our international strength and will continue to be a focus for future investment. NB: Our Microbiology programme has been submitted to UoA5.

<u>1. Immunity, infection and inflammation</u>

This programme led by **Brown-G** has major expertise in a number of clinically relevant disease areas including, mycology (the Aberdeen Fungal Group), ocular, gastroenterology, haematology, renal and respiratory immunology.

Brown-G and **Willment**'**s** work has led to a series of publications revealing significant new insights into the biology of C-type lectin receptors, and identification of novel receptors, including Dectin-1, CLEC9A and CLECSF8, and determining their cellular functions. Further work identified C-type lectins that collaborate with other pattern recognition receptors (e.g. Toll-like receptors), leading to the discovery that a chronic fungal skin infection, chromoblastomycoses, could be ameliorated therapeutically by augmenting this receptor collaboration and with a subsequent clinical trial. Their work identified polymorphisms in CLEC7A, the gene for Dectin-1, which increases susceptibility of humans to fungal infections. The role of Dectin-1 in antifungal immunity was originally discovered by **Brown-G,** and this work has transformed the field of innate immunity.

This work been underpinned by MRC and Wellcome Trust programme and project grants and a Wellcome Trust Strategic Award, of £5.1 million in medical mycology and fungal immunology collaborating with Gow and Brown-A (both UoA5) who co-ordinate this pan-UK activity of interdisciplinary training and international capacity building (appointment of **Warris**) in medical

mycology and fungal immunology, e.g. cell biology of *Candida* phagocyte interactions (**Erwig**). The Aberdeen Fungal Group is one of the largest medical mycology centres in the world, holding £16.6 million of research funding.

The ophthalmology immunology research programme (**Liversidge, Kuffova** and Forrester (recently retired)) has delineated control mechanisms in immune and inflammatory eye disease. This led to the development of biologically active scaffolds for corneal transplantation and age-related macular degeneration. Forrester's work was recognised by a prestigious Alcon Research Institute Award for outstanding research in 2013.

El-Omar and **Hold** have made major contributions to understanding the role of chronic (microbial induced) inflammation and regulation in gastrointestinal malignancy. Their work demonstrated that autophagy protects against infection with *H. pylori* and mechanisms underlying this have furthered our understanding of inflammation and eventual carcinogenesis. **Lochhead's** work focuses on the use of epigenetic parameters as predictive biomarkers in colorectal cancer, Similarly, **Kelly**'s work with gut microbiota has led to novel findings on immunity and maintenance of health e.g. in inflammatory bowel disease, and led to the establishment of the spin-out company GT Biologics to develop novel treatments for Crohn's disease and will be starting clinical trials.

Studies by **Barker** in both animal models and patients have improved understanding of the underlying causes of immune-mediated disease (e.g. immune cytopenias) and led to the development of novel treatments, with major, on-going collaborations with **Vickers** at the Scottish National Blood Transfusion Service (SNBTS). This group has characterised the lymphocytes that drive and regulate pathogenic responses to red blood cells and platelets. Work in the laboratory has been underpinned by funding from the Wellcome Trust, most recently as a Programme Grant to **Barker, Erwig** and **Vickers** to study the immune consequences of red blood cell ageing, death and disposal. In collaboration with other staff in the SNBTS, **Vickers'** work also focuses on the immunology of lymphoma, and has led to the manufacture, to GMP standards, of cytotoxic lymphocytes directed against Epstein-Barr virus for the treatment of post-transplant lymphoproliferative disease. This is now used internationally in patient care of EBV infections.

Erwig's group has focussed on the signals that activate macrophages *in vitro* and in glomerulonephritis *in vivo* and more recently on *Candida*-phagoctye interactions. This research led to the development of the concept of macrophage programming to explain macrophage function. **Wilson's** research is directed towards understanding the role of macrophages in the progression and healing of inflammation in human disease, particularly nephritis. She has uncovered novel signalling pathways/mechanisms that regulate macrophage activation.

Studies led by **Devereux** have focused on understanding relationships between maternal allergen exposure and neonatal immune function. His results have led to alterations in dietary advice given to pregnant women by the Department of Health (see relevant Impact Case Study). Clinical trials are evaluating dietary supplementation and immune function in pregnancy.

2. Musculoskeletal

The Musculoskeletal Programme led by **Helfrich** has made major insights in the biology and (patho)physiology of bone, cartilage and muscle, as well as novel approaches for diagnosis and treatment of disorders such as osteoarthritis, osteoporosis, sarcopenia, Paget's disease and osteopetrosis. The programme was awarded European League against Rheumatism (EULAR) Centre of Research Excellence status (2010-2015), under the direction of **Helfrich**.

Crockett, Helfrich and **Coxon** contributed to seminal studies identifying mutations in the gene for RANK (*TNFRSF11A*) and resultant signalling defects responsible for severe cases of osteoclast-poor osteopetrosis. They discovered that different mutations in RANK led to early onset Paget's disease and related conditions, and provided new knowledge on RANK and its ligand which is relevant to the understanding of osteoclast activity in bone disease in general. **Hocking** and **Helfrich** have studied mutations in the protein p62 (Sequestosome 1) in relation to Paget's disease of bone and discovered a novel isoform of p62 lacking the PB dimerisation domain.

De Bari's work has centred on the fundamental biology of mesenchymal stem cells spanning from developmental ontogeny to postnatal niches in health and in diseases such as osteoarthritis and rheumatoid arthritis. He has, for the first time, identified functional mesenchymal stem cell niches in the joint. A key development has been the establishment of an Arthritis Research UK Tissue Engineering Centre, based at four sites, with **De Bari** as Aberdeen lead.

The pharmacology of bisphosphonates (BPs) is a longstanding area of strength in Aberdeen.

Crockett demonstrated that zoledronic acid, the most potent BP in clinical use, is metabolised to the pro-apoptotic ATP analogue ApppI. **Coxon** and **Roelofs** reported the first detailed microscopical analyses of the skeletal distribution of different fluorescent BP analogues *in vivo*, revealing new information about the relationship between BP pharmacology and affinity to mineralised bone and, with international colleagues, **Roelofs** showed for the first time the anti-tumour effect of ZA *in vivo* is independent of osteoclast activity. **Thompson** identified the cellular mechanism by which γδ T cells are activated by ZA treatment and provided new insights into the interactions of γδ T cells and osteoclast and BP penetration into the osteocyte canalicular network.

Lurie is a world leader in the new technique of fast field cycling (FFC) MRI and, supported via EPSRC programme funding, has developed novel imaging equipment in this area. FFC-MRI has now entered the clinical research arena. **Barr** has found that joint shape predicts osteoarthritis progression. These studies are closely aligned to work on genetics of pain and genetics of falls (**Hocking)** and epidemiological studies (Jones, Macfarlane-G in UoA2). **Reid-D, Barr, Macdonald** focus on translational aspects with large scale clinical trials (5,000 women) evaluating the effect of dietary supplementation with fruit and vegetables. Aberdeen's latitude (57 °N) enables exploration of vitamin D status in northerly compared with more southerly latitudes, seasonal variations and contributions of sunlight and diet. **Reid-D** has also taken the lead in international Phase III pharmaceutical trials in osteoporosis.

Miedzybrodzka is a clinical geneticist who has a particular interest in the pathogenesis of talipes equinovarus (club-foot). She is identifying the aetiology of this condition with linkage studies of genetic associations and has developed the largest database of children with talipes in order to identify genetic markers and aetiologically distinct sub-groups.

3. Cardiovascular Medicine

There is a strong programme of translational cardiovascular science bringing together expertise in vascular biology, nutrition, thrombosis and haemostasis, imaging, endothelial and mitochondrial function and cardiac function. The focus is on the understanding of bioenergetics and treatment of cardiac failure, cardiac risk assessment and management of patients with peripheral vascular, cardiac and cerebrovascular disease.

Specific examples include the work of **Frenneaux's** team in understanding cardiac energetic impairment in patients in collaboration with **Dawson** who has developed bespoke advanced imaging techniques. Recently they found that amelioration of energetic impairment by the metabolic agent Perhexiline resulted in improved symptoms and exercise capacity in heart failure and non-obstructive hypertrophic obstructive cardiomyopathy (HOCM). This world-leading work has led to the designation of Perhexiline as a first line therapy for non-obstructive HOCM by the US FDA. **Dawson** has developed and evaluated advanced cardiovascular imaging techniques; cardiac energetics in diabetes mellitus; cardiac resynchronization therapy in patients with heart failure, focussing on significant improvements to personalized medical approaches. **Frenneaux** is collaborating with Hoppler (UoA5) to investigate the role of the Wnt pathway in signalling in cardiomyogenesis to identify novel drug targets.

Mutch's team has focused on the role of factors XII and XIII in thrombosis and has defined platelet polyphosphates as a new class of mediator having fundamental roles in platelet-driven pro-inflammatory/pro-coagulant disorders. This links with Nixon (UoA5) who is evaluating roles of sphingolipids, calcium, zinc on endothelial and smooth muscle cells in vascular disease.

MacLeod leads a group investigating cerebrovascular disease, with clinical trials addressing stroke prevention related to reduction in cholesterol levels (SPARCL trial) and the identification of sequence variants on chromosome 9p21.3 which confer risk for atherosclerotic stroke. They have also identified a new association for large vessel stroke within HDAC9 on chromosome 7p21.1, which has suggested distinct genetic profiles for different stroke subtypes. In terms of cardiovascular disease prevention, Myint was appointed to UoA2 with expertise in the identification of risk factors for stroke and cardiovascular disease to develop this area with **MacLeod** and **Frenneaux**. His work has identified the effect of behaviour on the risk of stroke in large cohort studies and the first identification of lower vitamin C as an independent risk factor for hypertension, and as a risk factor for stroke. Further large cohort studies identified physical functional health as a predictor for coronary heart disease.

In terms of reducing the incidence of vascular disease, **Thies'** team has shown that the consumption of 3 portions of whole-grain foods is effective. In contrast, he demonstrated the lack

of protective effects of omega-3 fatty acids and lycopene dietary supplementation on platelet and endothelial function in large scale human dietary intervention trials - important for nutritional advice.

4. Cell Developmental and Cancer Biology

Fowler has studied the effects of exposure to complex cocktails of environmental chemicals on foetal development and adult health facilitated by access to a unique range of normal second trimester foetal tissues. His work has highlighted potential risks posed by foetal exposure to sewage sludge, smoking, narcotics and other environmental toxins, with adverse effects persisting into adulthood. As an example, his work has identified, for the first time, a human testis developmental gene (*DHH*) disrupted by maternal cigarette smoking. **Sekido**, whose work has highlighted a number of gene pathways critical for normal sex determination and cell fate programming has published key insights into the control of normal reproductive development. Further research links **Fowler** and **Sekido** in understanding such mechanisms.

Work by **Murray-G** on lung and colon cancer has made a substantial contribution to the determination of prognostic markers, including annexin profiling, matrix metalloproteinase/tissue inhibitors and individual cytochrome P450. He has collaborated with Hoppler (UoA5) to demonstrate how cell-to-cell signalling regulates embryonic development, stem cell differentiation and how the Wnt signalling pathway drives cancer progression.

Collie-Duguid and **Heys** have focused on biomarker discovery in neoadjuvant therapy in both breast and lung cancer. This has led to an understanding of mechanisms of resistance to chemotherapy involving serpin B3 and macrophage activation. This links to research within the Immunity and Disease programme (**Wilson, Liversidge**). Further research investigating the role of nutrient-gene interactions in malignancy has linked with Pertwee's team (UoA5), defining the role of endocanabinoids in breast and prostate cancers and linking to McEwen's work on androgen receptors and prostate cancer (UoA5). New research funded by the EU (**Heys** with Bond from UoA2) is investigating health care in eight countries to understand optimal delivery of care.

Welch and his medical imaging team have significant expertise in positron emission tomography (PET), focusing on novel analysis techniques and novel tracer development in models of cancer. This work links closely with the expertise of Zanda (UoA5) in medicinal chemistry and drug discovery. For example, the team has developed 18F-fluoro-deoxy-ribose (FDR) as a new efficient prosthetic group for the radiofluorination of many molecules for the pre-clinical PET imaging of tumours. Translational studies with breast, oesophageal, stomach and lung cancer patients have linked with NHS clinicians to demonstrate clinical utilities of PET.

The role of nutrition in epigenetic regulation and DNA damage has been facilitated by the expertise from the RINH (**Haggarty**, **Duthie**). For example, **Haggarty** has examined epigenetic imprinting in health, pregnancy and disease identifying links between diet, birth outcome and imprinting signals influencing disease risk. **Wallace's** expertise in polyamine metabolism has led to a shift in the understanding of selective cytotoxic drug delivery using a putrescine-anthracene conjugate. In collaboration with Stansfield (UoA5), polyamine biosynthesis regulation has been dissected using the first systems level analysis of a feedback control system.

Cruickshank's expertise in cervical neoplasia, utilising the cross-disciplinary expertise of Cotton and Gray (UoA2) facilitated the Tombola study (MRC and NHS funded) – a unique study embedded within a national screening programme in England and Scotland. This has determined the most appropriate way to deal with low-grade cervical neoplasia in the context of a national screening programme, and has led to changes in UK clinical practice.

5. Translational Neuroscience

The work of this Programme's researchers focuses on neuroimaging and involves collaborative research with neuroscientists from UoA5 and clinical researchers (radiologists, psychiatrists, psychologists) with an interest in ageing and dementia illnesses.

The PET expertise of **Welch**, working with Platt (UoA5), has led to the development of novel PET tracers and has demonstrated that [^{18}F]-barbiturates identify β-amyloid over-expressing cells in transgenic "tau" mice and that [^{18}F]-barbiturates are very promising for the diagnosis of Alzheimer's disease. Development of a method for non-invasively measuring changes in mouse brain metabolism using preclinical FDG PET CT has been used to study changes due to genotype, ageing, activation and the response to novel Alzheimer's disease therapy (and to validate PET CT, EEG and sleep phenotypes as translational biomarkers for research in Alzheimer's disease).

Murray-A has focused on neuroimaging using MRI with special reference to ageing and dementia. Structural magnetic resonance imaging research in the Aberdeen Birth Cohort of 1936 demonstrated that education compensates for subclinical dementia related neuropathology and that early life socioeconomic environment influences hippocampal volume in the seventh decade of life, reflected in a more complex brain structure that allows retention of cognitive ability into later-life. This work will feature in a BBC2 science series in late 2013.

Collaboration between **Reid-I** and **Schwarzbauer** has recently led to a major breakthrough, showing for the first time that the brain is functionally hyperconnected in severe depression and that this hyperconnectivity is removed following successful treatment with electroconvulsive therapy (ECT). This work was featured by *Science*, *JAMA* and *TIME*. An international collaboration with **Schwarzbauer** and the Universities of Tubingen and Heidelberg, led to the development of functional connectivity imaging as a novel diagnostic tool for consciousness. **Waiter,** with collaborators, identified the neural correlates of Autism Spectrum Disorder resulting in a number of highly cited publications. Work with **Murray-A** on normal cognitive ageing demonstrated that ageing is associated with retaining youthful functional anatomy for information processing. Their collaborative research has demonstrated functional correlates of social stereotyping and, with **Reid-I** and Steele (in Dundee), they identified prediction error abnormalities in depression and schizophrenia. With colleagues in Edinburgh and Dundee, they have also demonstrated abnormal neural responses to social exclusion in schizophrenia.

c. People:

i. Staffing strategy and staff development

The University of Aberdeen promotes a staffing policy of excellence through mentoring, and development and promotion of internal staff and external appointment of new staff at the highest levels of academic excellence. Newly appointed staff are selected specifically to strengthen existing areas of research or develop new programmes. For example, we recruited **Brown-G** and **Warris** to further strengthen fungal immunology and clinical mycology, **Frenneaux** and **Dawson** to develop our cardiovascular research programme and **Sekido** to link with **Fowler** studying sex determination in embryos and **Haggarty** and **Rochford** in nutrition and epigenetics. **Groening's** expertise in biomechanics further strengthens musculoskeletal research. Furthermore, **Parson's** appointment, with his expertise in neurological growth mechanisms, allowed us to develop the spinal cord regeneration research programme in translational neuroscience. **Rochford's** expertise in the genetics and epigenetics of obesity and lipogenesis is allowing new research in cardiovascular medicine and cancer research and **He's** expertise in image analysis has strengthened the area of neurological research. Further appointments in our complementary UoAs, in particular 2 and 5, include; Zanda (Medical Technologies) to develop PET ligands for use in experimental and clinical trials, Carabeo with expertise in signalling pathways in relation to chlamydial infections, Heisler in human nutrition. These and other new appointments in systems biology, health economics, psychology and social science add value to our research.

Our postdoctoral mentoring programmes have assisted successful fellowships for **Gregory**, **Thompson**, **Coxon** and **Crockett** in the musculoskeletal programme, with the last two having been guided through to senior lectureship positions. **Hocking**, **Wilson** and **Mutch** have also come through postdoctoral mentoring to senior lectureships. In addition, **Erwig** and **Devereux** have been mentored though clinical fellowships to senior lectureships and now to Chair positions

As well as these appointments, teaching fellows have been appointed to enhance strategic areas. These non-research positions allow research active current staff to devote more time to develop their research programmes, grant applications and outputs.

Those who have been newly appointed to academic positions are required to develop a three-year plan with an assigned mentor during their probationary period, which is reviewed annually as part of their mentoring provision. They are also given a restricted teaching and administrative load in the first two years of their post to facilitate research development. Appointees are provided with dedicated laboratory research space and are given priority when resources and PhD studentships are allocated by the Research Committees and programme leads. All staff have an annual, and structured, appraisal, and clinical academics have a joint clinical appraisal with the NHS. In 2011 a Framework of Academic Expectations was introduced as an integral part of the reflective appraisal process, where staff set their own objectives using the Framework as a benchmark to understand how their work is progressing. The ethos of appraisers and line managers is one of support and

encouragement to help researchers perform to their best and set standards of achievements.

Research excellence is promoted by the University through supporting professional and career development of research staff, in accordance with the UK-wide Concordat to support the career development of researchers. We have fully embraced this developmental agenda, ensuring that policies and procedures reflect its principles including supporting researchers in relation to suitable career opportunities and where appropriate, to become leaders in their fields.

From 2009 onwards all staff have been made aware of the Concordat and a key aspect of the implementation plan for this emphasises that the University, through its Researcher Development Unit, focuses on both early career and established researchers. Four researchers from UoA1 (since 2008) have participated in an award winning International Leadership Development Programme for future leaders and all managers receive high quality training and coaching.

Specific projects to do this have been supported by an "Achieving the Best" award, funded by the Leadership Foundation in Higher Education. The University of Aberdeen has been recognised by the European Commission for positive actions to support the career development of researchers and its plans to implement the Concordat. The University is one of 38 institutions in the UK to receive the 'HR Excellence in Research' badge from the European Commission.

The development and advancement of independent research staff to core positions and senior posts (as above) illustrates our support for Early Career Researchers (ECRs). There is an established scheme to support ECRs applying for external fellowships, develop their CVs and ensure alignment with our strategy. An award of £96,000 from the Scottish Universities Life Sciences Alliance (SULSA) Leaders programme is being used to develop their academic or industrial research careers.

The Scottish Clinical Research Excellence Development Scheme (SCREDS) provides an integrated training and career development pathway for clinicians to obtain a senior clinical academic appointment and a Certificate of Completion of Training (CCT). The scheme is operated in partnership with NHS Education for Scotland and 20 posts are held in the School of Medicine with appointments a clinical fellow, senior clinical fellow, clinical scientist and clinical lecturer levels.

The University Court oversees the implementation of equality and diversity policy. The University applies this policy to all aspects of employment. All staff have access to specific training in equality and diversity which is mandatory for those involved in selection and management. The University has achieved Investors in People (IiP) status across the institution. It achieved bronze Athena SWAN recognition of good employment practice for women in science, technology, engineering and medicine, and is preparing for silver. **Galley, Wallace** and **Helfrich** have established the "Esslemont Group" to promote equality, diversity and gender balance, highlighting women's roles in science and medicine. The roles of women in medicine, science and business are highlighted by national/international leaders in these fields. The careers of all females appointed to lectureships and above are profiled as role models.

We achieve integration of clinical academics and NHS-employed active researchers through our Head of School of Medicine and Dentistry who is also the Director of NHS R&D (**Reid-D**). All NHS specialities have a "clinical speciality lead" to enable involvement of NHS staff in research. The National Health Service Research Scotland (NRS) fellowship scheme (commenced 2011 and funded by the Chief Scientist Office Scotland) has made three awards to NHS consultants to allow time in research. These are in areas which strengthen our research (e.g. geriatrics, emergency medicine and pharmacy) by developing new areas with NHS support. The equivalent of approximately 9 additional full-time clinical academic posts is funded by the NHS to develop areas where research and clinical service will benefit from clinical academics (e.g. oncology, orthopaedics, rheumatology, general and vascular surgery).

ii. Research students

Research students are trained in research-intensive environments with 200 doctoral students currently in training. Our PhD student population (numbers in brackets) has been achieved though success in Research Council awards (MRC, BBSRC) (14), Doctoral Training Grants (5), Industrial CASE awards (2) and funded overseas students(31), European Union including Marie Curie training awards (2), Oliver Bird awards (6), different charitable foundations (26), from The Chief Scientist Office, Scottish Government and the NHS (10), as well as members of staff (22), and self-funded (13). We have 10 PhD studentships from the SULSA and the Scottish Imaging Network: A Platform for Scientific Excellence (SINAPSE) pooling initiatives in Scotland and we have co-founded posts with other partners to stimulate new joint research activity across disciplines (57).

The recent award of the Wellcome Trust's Strategic Award to **Brown-G**, with Gow and Brown-A (from UoA5) will fund 10 international PhD studentships and 3 clinical PhD studentships of which 4 will be in Aberdeen with all the international PhD students undertaking an MRes in Aberdeen initially. A newly established MSc in Stratified Medicine (up to 50 students annually commencing 2013) has been established in Aberdeen and Glasgow.

The Graduate School of the College of Life Sciences and Medicine is responsible for overseeing their appointment, training and progress. High-quality training is delivered to support the academic, professional and personal development of our students.

The development of research skills occurs with bespoke training for anticipated needs according to the student's Personal Development Plan (PDP), which is discussed regularly between student and supervisor. There are mandatory courses in the initial three months of training, including induction on scientific conduct, research ethics and governance, project design and monitoring of progress. Other mandatory courses include Health and Safety Training, Home Office courses for those working with animals and courses in scientific writing, data handling, statistics, presentational skills, entrepreneurship and knowledge exchange. All students have access to funding for specialist courses they require if not provided locally.

Each student has a minimum of two supervisors and an advisor who is there to give independent advice. Supervisors have recorded meetings monthly with the student and there are compulsory progress reports made at six-monthly intervals which are reviewed by College Postgraduate Officers. There is a nine month review with a written report, viva and presentation with two members of staff. In the second year, there is a written report and a poster presentation, and in the third year a presentation made at the annual postgraduate symposium. After 27 months of study students submit a thesis plan and progress is reviewed until completion. This management programme has contributed to a high completion rate of 87%. Since 2008, a total of 94 doctoral research degrees have been awarded.

In addition to providing students with excellent training in their chosen research area, a "flagship leadership programme" has been established which provides bespoke leadership training and mentoring, to position talented individuals as leaders in the near future. This unique programme cultivates strategic thinking and leadership skills through cross-disciplinary activities over and above the generic skills training provided for all PhD students. The programme has workshops, public engagement events, and visits, involving different stakeholders in research (e.g. the public, media, NHS, government advisors, policymakers, pharma, venture capitalists, and entrepreneurs). Novel elements include a 2 day *Bio-business Made Simple* course, research commercialisation, leadership style and management training, team working, 360^{o} feedback, and interpersonal skills. Training quality control is overseen by the Director of the Graduate School.

d. Income, infrastructure and facilities

Members of this submission currently hold grants totalling £43.3 million, with research spend since 2008 totalling £56.6 million. The RINH has a Scottish Government Research and Science Directorate (RSD) programme grant. We attract funds that cut across traditional discipline boundaries from a wide diversity of funding agencies. Examples of major awards in the assessment period include £5.1 million Wellcome Trust award for the "Medical Mycology and Fungal Immunology Consortium" with a further investment of £1.5 million by the University and £1 million from the FSA to support biomarker discovery.

The Foresterhill Health Campus (FHC) is a 125 acre site for the University of Aberdeen and a wide range of NHS Grampian facilities, including Aberdeen Royal Infirmary (approx 1,000 beds), Emergency Medical Care Centre (£110 million new build opened in 2012), Royal Aberdeen Children's Hospital, Aberdeen Maternity Hospital and adjacent Royal Cornhill Hospital (Psychiatry).

The University and the NHS have invested heavily in the FHC site with approximately £100 million invested in recent years, including a £3.5 million Life Science Innovation centre (LSI) for development of spin-out companies in partnership with Scottish Enterprise Grampian which houses successful spin-out companies (e.g. GT Biologics, TauRx), and the Suttie Centre for Teaching and Learning which supports pedagogic research (£21 million, opened in 2010). A major development in progress is a new Rowett Institute of Nutrition and Health building project which will be completed in 2015 at a cost of ca. £40 million. In support of this capital build project Scottish Government has given £12 million towards the building and a grant of £250,000 has just been awarded by the Wolfson Foundation towards the project, reflecting the importance of the

development to outside stakeholders.

Investment in core facilities that underpin our research activities, equipment and staff, has been extensive. All facilities are administered by a technology manager and an academic manager to plan for next generation equipment and future needs. We ensure open access to our communal facilities for all funded research. The economies of scale we enjoy ensure early replacement of aging equipment and timely investment in new technology. New and enhanced facilities include:

[1] *The Centre for Genome-Enabled Biology and Medicine*, with next generation sequencing facilities that include Illumina HiSeq 1000 (2012), Illumina MiSeq (2012), and Roche GS Junior454 Sequencer. A next generation sequencing Bioinformatician expert assists with data analysis while Biomathematics and Statistics Scotland, based in RINH, provide further bioinformatics support.

[2] *FACS facility*, a state-of-the-art multi-user facility with a full range of analytical and sorting capacities. It includes a wide-range of equipment with the most recent additions being a BD Fortessa Next generation (2011) and Bio-Rad Luminex 200 (2010).

[3] *Microarray facility*, based on the Affymetrix GeneChip Microarray platform with qPCR verification of results.

[4] *Proteomics facility* for electrospray and MALDI-TOF mass spectrometry analysis of protein separated by a variety of 20 gel separation methods. Proteomics robots for mass spectrometry have been upgraded and a new Orbitrap LC/MS purchased.

[5] *Microscopy facility* provides equipment for microscopical imaging at tissue, cellular and subcellular resolution. Systems for advanced microscopy include laser-based and spinning disk confocal imaging, live cell imaging, and laser microdissection. Electron microscopy (EM) with a new transmission EM (Jeol 1400 PLUS with tomography) and Scanning EM (EVO) and a fully equipped histology laboratory.

[6] *Mass Spectrometry facility* that includes Gas isotope ratio mass spectrometry, three instruments for liquid chromatography/MS/MS for the quantification of metabolites by Multiple Reaction Monitoring and a new ICPMS.

[7] *The Aberdeen Biomedical Imaging Centre* provides preclinical facilities for animal CT, MRI and PET. The last uses a GE eXplore Vista PET/CT, with excellent expertise and facilities provided for new PET tracer development in a recently expanded (£1 million) centre.

[8] *Medical Research Facility* for rodent models, located on the Foresterhill Health Campus with £6 million barrier and transgenic wings.

[10] *The Human Nutrition Unit*, a metabolic research facility equipped to perform human phenotypic and physiological measurements, and staffed by nutritionists, dieticians and medical staff to perform a broad range of human nutrition studies.

[11] *High-performance computing facility* analyses and archives burgeoning datasets from 'omics' analyses and modelling applications.

Cross-cutting Integrative Research Centres are also key for our translational research, including *The Kosterlitz Centre for Therapeutics,* set up to encourage and facilitate translation of discoveries into disease therapeutics and diagnostics by providing expertise and industrial links not readily available to biomedical and clinical scientists. The Kosterlitz Centre oversees a portfolio of over 20 drug discovery projects and has attracted >£2.5 million funding. Examples in the pipeline include new cannabinoid receptor enhancer and inhibitors for pain and depression, fungal diagnostics/therapeutics, antibody-based treatments for cancer, drugs for neuro-degenerative disorders, hypertension, diabetes and prostate cancer and novel PET tracers.

Our research programmes are facilitated by administrative support and robust governance processes. Research and Innovation (R&I) consists of a team of specialist advisors for peer-reviewing and supporting applications with additional support from our finance and governance teams. They aim to maximise University research income, identifying intellectual property opportunities and successfully exploiting innovative ideas in partnership with our researchers. The University Advisory Group on Research Ethics and Governance advises on research governance policy and ethical issues. The Framework for Research Governance provides a detailed overview of research governance arrangements in place, with the CLSM Committee for Research and Commercialisation and its senior management having over-arching responsibility for day to day

governance of the College's research activity.

The University of Aberdeen Development Trust was established in 1982 to raise funds for the sole benefit of the University of Aberdeen (registered charity SC002938) with its Trustees and staff supporting researchers in UoA1. Since 2008 the Trust has raised a total of £15.0 million for the College of Life Sciences and Medicine with UoA1 researchers receiving awards of £4.5 million.

A joint NHS Grampian and University of Aberdeen Clinical Research Steering Group exists to drive collaborative research with 100 commercial studies with industry underway and a further 543 non-commercial studies. The R&D Director has a budget of approximately £8 million per annum to support clinical research including 80 research nurses and a biorepository.

e. Collaboration or contribution to the discipline or research base

In the REF period, UoA1 staff have published over 1,000 ISI listed scientific publications. Evidence of research-based contributions to the discipline include:

A number of submitted staff holding awards and fellowships of professional organisations and societies – Fellowship of the American Academy of Microbiology, Fellowship of Royal Society of Edinburgh and Fellowship of the Royal Society of South Africa (**Brown-G**); Chair Board of the National Osteoporosis Society and Chair Metabolic Bone Disease Clinical Studies Group of ARUK (**Reid-D**); Trustee British Society of Immunology (**Barker**); Senior Clinical Fellowship, Chief Scientists Office (2009-2013, **Erwig**); MRC Clinician Scientist Fellow (2005 to 2010, **De Bari**); Wellcome Trust International Senior Research Fellowship (2004-2009, **Brown-G**); Chief Scientist Office, Clinical Academic Fellowship (2010 – 2013) and Frank Knox Memorial Fellowship, Harvard University (2011-2012) (**Lochhead**); Alcon Research Institute Award for outstanding research globally (2013, Forrester, now retired); Chair, Society for Reproduction & Fertility (2009-2013, **Fowler**).

Researchers are involved in a wide range of peer review and consultation activities with Unit researchers on 19 grant awarding bodies and have peer reviewed applications internationally.

Participation in the peer review process

ARES evaluation committee [French REF equivalent] (**Fowler**), Arthritis Research UK (**Barker**), Arthritis Research UK Fellowships panel (**De Bari**), BBSRC Molecules, Cells and Industrial Biotech Committee Chair (**Brown-G**), BHF Chairs and Programme Grants committee, BHF Regenerative Medicine and Research Excellence panels (**Frenneaux**), BHF Project Grants committee (**Mutch**), Breast Cancer Campaign (**Heys, Haggarty**), CRUK Biological Sciences Committee (**Murray-G**), Chief Scientist Office, Experimental and Translational Medicine research committee (**Collie-Duguid**), Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (**Wallace**), European Calcified Tissue Society Board (**Helfrich**), CRUK Biological Sciences committee and CRUK Centres Quinquennial Review panel (**Murray-G**), Food Standards Agency T07 Food Allergy Expert Advisory Panel (**Devereux**), MRC Infections and Immunity Board (Brown-G), MRC Population and Systems Medicine Board, MRC Experimental Medicine Challenge Panel and MRC/Wellcome UK Biobank Imaging Panel (**Frenneaux**), MRC NC3Rs grants panel for CRACKED-IT and Maths and Science (**Wallace, Fowler**), MRC/NIHR Evaluation Board (**Reid-D**), National Institute of Academic Anaesthesia (**Galley**), Wellcome Trust College (**Brown-G**), NCRI PET Methodology (**Welch**), Royal College of Surgeons Research Committee (**Heys**), Osteoarthritis Research Society International (**De Bari**), Scientific Advisory Committee on Nutrition UK (**Haggarty**), Scottish Translational Medicine and Therapeutics Initiative **(Reid-D, El-Omar),** Swedish Research Council, Agence National de la Recherche, France (**Fowler**), UK Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (**Devereux**).

Journal Editorships and Assistant Editorships

Amino Acids (**Wallace**); Biochemical Journal (**Wallace**); British Journal of Anaesthesia (**Galley**); Gut (**El-Omar**); International Journal of Surgical Oncology (**Heys**), Reviews editor Frontiers in Brain Imaging (**Schwarzbauer**); Journal of Pathology (**Murray-G**), Journal of Thrombosis and Haemostasis (**Greaves**); Frontiers in Genetics, Nutrition in Epigenetics, Population Epigenetics (**Haggarty**); Osteoarthritis and Cartilage (**De Bari**); PLoS One (Academic Editor) **Hold;** Journal of Innate Immunity, Journal of Immunology (**Brown-G**); Therapeutic Advances in Musculoskeletal Disease (**Reid-D**).

Editorial Boards

UOA1 researchers are also members of 49 editorial boards for national and international

journals and almost all act as peer reviewers for these journals.

Collaborations with external bodies (i.e. governmental, regulatory, industry)

Greaves chaired SIGN guidelines for prevention and management of venous thromboembolism and antithrombotics indications and management and chairs the Clinical Trials Data Monitoring Committee for NHS Blood and Transplant in England; **Heys** chaired the SIGN guidelines for breast cancer treatment, and led the GMC national review of Clinical Academic Training (UK); **Miedzybrodzka** (ovarian cancer) and **Macdonald** osteoarthritis therapy SIGN guidelines member; **Fowler,** member of the European Food Safety Authority Expert Working Group on Bisphenol A; **Haggarty**, member of Scientific Advisory Committee on Nutrition; **Duthie** and **Haggarty**, members of Advisory Committee on Novel Foods and Processes; **Fowler**, Chair of the Society for Reproduction and Fertility; **Reid-D**, Scottish Stratified Medicines Innovation Centre Board; **Wallace**, Paediatric Medicines Expert Advisory Group (Committee for Human Medicines).

Staff are encouraged to collaborate with industry via science advisory boards, consultants, and as collaborators through multinationals and SMEs. Examples include, **Johnstone's** work with Marks and Spencer and CNP Professional Ltd for development of nutritional products, **Hold** providing specialist food microbiological support to DM Training Consultants Ltd, and **Devereux's** food trials with Baxters (international food producers).

Responsiveness to national/international priorities and initiatives

The University has responded to Scottish pooling initiatives and is a major partner in SULSA. This is a research pooling partnership supported by the Scottish Funding Council and established in 2007 between the Universities of Aberdeen, Dundee, Edinburgh, Glasgow, St Andrews and Strathclyde and has funded premier researchers and facilities across Scotland. In Aberdeen this has allowed development of systems biology research expertise, antibody/peptide libraries, developments in the PET facility and research projects in the Kosterlitz Centre. The Kosterlitz Centre also has utilised as number of on-going SULSA projects which have been funded from the "High Throughput Screening" fund and the "Catalyst" chemistry fund from SULSA. In addition, "SINAPSE" *(*Scottish Imaging Network: A Platform for Scientific Excellence)", a pooling initiative has enabled us to further enhance our imaging facilities and is part of the Scottish Stratified Medicines Innovation Centre. The Unit's researchers within the Scottish Translational Medicine Research Collaboration, (TMRC) have worked with Wyeth (latterly Pfizer), and Scottish Enterprise to support a variety of research projects worth £4.3 million, since 2008.

Many researchers are involved in multicentre EU funded projects where our involvement ranges from co-ordination to participation. For example, at the RINH there are 4 active major EU projects, with **Heys** and **Fowle**r (co-ordinator) co-applicants on FP7 collaborative projects and **Kelly, Wallace,** and **Helfrich** in Marie Curie Training networks**.**

Mechanisms to promote national/international collaborations with academic community or users of research collaborations

Effective academic collaboration is facilitated from local to global scales. Among programmes within the unit of assessment, there is a fully integrated research environment based upon a strategy overseen by a University Vice-Principal for Research and Knowledge Exchange and a College Director of Research, supported by a generic administrative centre for research and innovation. Multidisciplinary collaboration involving UoA1 has been enhanced by University-wide investment in cross-cutting research themes described above, and international collaboration is exploited through our Centre for Sustainable International Development.

Markers of effective of collaboration

The effectiveness of mechanisms for international collaboration is reflected in the 2012 Times Higher University world rankings which received an "international outlook" score of 84.8/100. In the Leiden University rankings (2011-12), the University of Aberdeen was ranked top university in Scotland and second in the UK for scientific collaboration with other institutions. In addition, we were sixth in the table for international collaboration, with UoA1 researchers fully represented within these collaborations.

In June 2013 the latest Praxisunico Spinouts UK Survey annual report ranked the University of Aberdeen as 6th in the UK for success in 'spinning-out' research into commercial company formation for the three year period 2010-2012.