Institution: King's College London

Unit of Assessment: UoA5

a. Context

The UoA5 return within King's College London (KCL) comprises three research divisions working in the general area of biomedical science within a "Health School" environment. The divisions are the Randall Division of Cell and Molecular Biophysics (Randall), the MRC Centre for Developmental Neurobiology (CDN) and the Wolfson Centre for age-Related Diseases (CARD). The **Randall** brings together cell and developmental biologists, structural biologists, biophysicists and chemists working collaboratively to elucidate the molecular mechanisms of cell function. The **CDN** scientists work on the molecular and cellular mechanisms underlying development of the nervous system in both invertebrate and vertebrate model organisms. The **CARD** picks up from development by aiming to restore function to the damaged nervous system with a focus on pain, hearing loss and neurodegeneration. Importantly, there are extensive interactions across the divisions as evidenced by, for example, shared infrastructure and our long established tri-divisional annual postgraduate day symposium. Likewise, there are extensive interactions with colleagues in the Medical School and the Institute of Psychiatry at KCL as well as with other HEIs.

Much of the activities in UoA5 are basic sciences that do not in themselves lead to impact. However, we do have considerable impact at the level of the development of new medicines and treatments, and our impact also extends to influencing policy and engaging with society. The beneficiaries of this research and related activities in non-academic communities include patients, industry and health care providers.

b. Approach to impact

Our *approach to impact* involves encouraging and supporting our staff to engage and collaborate with our stakeholders at an early stage of the research process to ensure that our activities are relevant, and will produce useful results for the end-users and non-academic communities.

Industrial beneficiaries. We are working on molecules and mechanisms implicated in a wide range of diseases including allergy and asthma, cardiovascular disease and age-related conditions including stroke, dementia and pain – these are areas of considerable unmet need with no restorative treatments for many of them. We bring academic expertise to several stages of the drug discovery pipeline including target identification, target validation and the development of new drugs – and then work with companies to translate these findings. For example two of our submitted impacts (McMahon and Walsh/Doherty) detail our role in identifying NGF and the myelin associated glycoprotein (MAG) as novel therapeutic targets for pain and stroke respectively. This work underpinned the development of anti-MAG antibodies by GlaxoSmithKline for stroke and anti-NGF antibodies by a number of companies for pain. These are currently in late stage clinical trials and listed as major assets by the various companies. Another submitted impact (Doherty) highlights how an academic collaboration underpinned the development of highly innovative new treatment for cancer by a small biotechnology company (Adherex Inc). Finally, the submitted Corcoran impact highlights the establishment of a new company called CoCo Therapeutics Ltd in partnership with the Wellcome Trust and Advent to commercialise new drugs that we have developed for Alzheimer's disease.

Benefits to patients. We actively seek out and encourage collaborations with clinicians with expertise in the conditions associated with our areas of interest, particularly when we see therapeutic opportunities for our work. Many of our applications for external funding have a combination of academics and clinicians as named investigators, and we ensure that relevant results are presented at clinical meetings and in journals that reach a clinical audience. We are also careful to ensure that for clinically-related studies involving patients and health service providers we establish from an early stage of planning that the research is not only feasible, but of potentially significant value to end-users. Three of our submitted impact studies, one from Band and two from Marshall, highlight how basic science/clinical partnerships can lead to the development of new treatments or procedures and these are Lithium Dilution as an indicator for

cardiac output, laser eye surgery to improve vision, and short pulsed laser treatment for the treatment of macular degeneration.

Influencing Policy and Practice. A number of our staff have influenced Government policy on the safe and effective use of medicines. For example, Marshall has sat on a number of committees reporting on the safety of Laser eye surgery. Ballard is a key advisor to UK & international health providers on political action to reduce antipsychotic prescribing in dementia and a member of NICE. In the UK Ballard's work has contributed to a 50% reduction in antipsychotic prescribing to people with dementia – and we have submitted this as an impact. We contribute to national policy in additional ways, for example Francis directs Brains for Dementia Research which supplies human tissue to researchers in the UK and overseas and co chairs the UK Brain Bank Network's User Group involved in setting standards and policy for all UK Brain Banks. Finally, Malcolm Irving is the KCL academic lead and executive member of the Francis Crick Institute that oversees this £650M investment. This reflects our close involvement in perhaps one of the most significant developments in UK biological sciences for a generation (http://www.crick.ac.uk/).

Public Involvement. We have taken a number of approaches to increasing public knowledge and awareness of all aspects of our work. This is designed to engage teachers and school pupils in thinking about how research is conducted, the value that it has to society as a whole and the ethical issues that surround this area. Several staff members participate in externally organised events, for example Wardle is a STEMNRET ambassador and has recently presented at the London (2011) and Cheltenham (2012) Science Festivals. Others are active within charities to inform lay members about disease and potential therapies, for example Zammit for Muscular Dystrophy. In addition we are actively engaged with the media, with for example Ballard conducting more than 350 radio and TV interviews commenting on dementia. The "How Not To Get Old" Channel 4 series filmed in our labs and used an interview with one of our post-docs in a program, and Robbins was involved in recreating Galvani's frog experiment for "Shock And Awe: The Story Of Electricity" for BBC4.

Importantly, we go to considerable efforts to explain how and why animals are used in research. For example, in July 2008 and 2011, Roger Morris joined the Home Office Chief Inspector to present their Annual Report on the statistics on experimental animal usage at a press conference, which led to subsequent radio and press interviews. Indeed, Roger Morris and King's are cited in the Science and the Media Expert Working Group's report (2010) to the Dept of Business, Innovation and Skills thus: "It is important to acknowledge that there has been a dramatic increase in the number of scientists speaking to the media about animal research and organizations like UAR, and funding agencies like Wellcome and the MRC have worked hard to change this defensive culture. In King's College London, Professor Roger Morris, Head of the School of Biomedical & Health Sciences, has spearheaded a process of change that he says has 'changed the default from refusing to allow a journalist into a lab unless there is a very special reason to do so to allowing science reporters into a lab unless there is a very special reason not to."

c. Strategy and plans

A plank of our strategy is to actively engage with our researchers to further develop non-academic research impact in addition to the usual academic indicators of excellence. Our submitted impacts were built on a platform of excellent research, informed by early engagement and dialogue with key stake holders. Our current scientific partnerships with big pharma, biotech and technology companies, as well as ongoing work on public engagement with bodies like the Wellcome Trust, will underpin our future impacts. We will first discuss a couple of examples of how we support impact, and then provide a brief description of the Pfizer Pain lab, the Nikon Imaging Centre and the IMI Europain program as examples of activities that will generate future impact.

Supporting staff to generate impact. We support staff to generate impact in numerous ways. For example at the level of the Institution, the Business and Innovation facility at KCL provides expertise on Intellectual Property, patenting, technology transfer, industrial partnerships and commercialism. At the level of the research divisions, considerable technical and infrastructure

support is provided by way of core facilities that underpin our ability to work with industrial partners. For example, support and for drosophila and zebrafish work with the CDN has allowed us to develop a number of novel disease models that are attracting the attention of colleagues in industry. Within the Randall, this type of support has led to the opening of a KCL/Nikon imaging centre and fostered a series of grants to develop new "super-resolution" imaging applications. Pharmaceutical companies are more reliant than ever on outsourcing some drug discovery activities, and within the Wolfson core support for animal technicians allows us to maintain several sophisticated animal models of pain and regeneration that are accessed by several companies on a collaborative or contract basis. Also, core histopathology and bioinformatics support within the Wolfson has underpinned several industry funded drug discovery programs – largely pursued on a collaborative basis.

Early stage engagement with Industry. The conventional methods of drug discovery have largely failed for many areas of neuroscience, and the pharmaceutical industry is looking towards new models including "open innovation" and "academic partnerships" to reenergise this process. We see direct engagement with colleagues in industry as central to the development of new relationships that lead to impact. We facilitate this in several ways. Firstly, we invite numerous colleagues from industry to lecture on our "Drug Discovery Skills" masters developed in partnership with GSK, AstraZeneca, and Pfizer, and our students also spend 5 months in the industry partner's labs (recently extended to include Eli Lilly). Next, we put considerable effort into open competitions for industry sponsored CASE studentships – 45 students are currently funded by various research council schemes (MRC,BBSRC,EPSRC) with 10 of these supported by industry sponsored CASE awards (supported by UCB, Novartis x2, Eli Lilly x4, AstraZeneca, GSK and Pfizer). We have also appointed individuals with outstanding records in industry as visiting Professors. These include Frank Walsh, currently CEO of the biotechnology company Ossianix Inc. Before this Frank served for seven years as Executive Vice President and Head of Discovery Research Worldwide for Wyeth. Mike Owen is a more recent "recruit" – Mike has also had many leadership roles including Senior Vice President and head of Biopharmaceuticals Research and Development at GlaxoSmithKline (2001-2009). Both visit regularly and provide help and advice on many of our programs.

The **KCL/Pfizer Pain Lab** is an excellent example of the "open innovation" strategy that is being pursued by some of the major pharmaceutical companies**.** During the review period the Wolfson CARD partnered with Pfizer to create an open innovation laboratory for pain research that involved a team of up to 5 Pfizer staff being based in our KCL labs to conduct research in pain biology. This integration of academic and industry teams has led to synergies in research strategies and has developed new methodologies that have been adopted by both partners.

The **Nikon Imaging Centre** is another excellent example of the synergies that arise when academics work with an industry partner. This is a partnership between KCL (led by the Randall) and Nikon Instruments UK. Our photonics physicists (e.g. *Ameer-Beg*, *Cox* and Heintzman) and biophysicists (*Ewers*, *Owen*) are working with Nikon to develop new applications in Super resolution microscopy with EPSRC programme and MRC Strategic award support. In turn Nikon have provided 10 state-of-the-art instruments including N-SIM and N-STORM Super Resolution microscopes housed in space adjacent to the Wolfson CARD.

The **Innovative Medicines EUROPAIN** project is a third example that highlights how we work within large consortia to tackle big problems. Scientists within the Wolfson, led by McMahon are working with three renowned academic pain consortia from Germany, Denmark and the UK, a Spanish SME and with Europe's most active pharmaceutical companies to search for changes in the nervous system that contribute to pain, in order to fill the gaps in the current knowledge of chronic pain. The group aim to elucidate the mechanisms of pain, using novel experimental models, human volunteers and clinical data of pain patients The identification of CXCL5 receptor as a molecule that causes the pain of sunburn (more details below) has been highlighted as an early success for this program (http://www.imi.europa.eu/content/europain).

Recruiting for Impact. During the past five years there have been strategic appointments of new researchers at all levels to consolidate and advance existing research areas. Importantly, research impact is central to our recruitment strategy with several appointments designed to enhance our activities in the area of disease model development, drug discovery and imaging. For example, Karen Steel (FRS) was recruited from the Sanger to further develop genetic mouse models of hearing impairment; Corcoran was appointed to develop new drugs for Alzheimer's disease and has founded a spin-out company to take this forward (CoCo therapeutics); McNaughton's very recent appointment has brought a third Wellcome Trust Seeding Drug Discovery award to the Wolfson, this time for the development of new pain treatments. Eggert has given us new capabilities in chemical biology. Finally the appointments of Parsons/Ameer-Beg/Cox/Heintzman/Ewers and Owen underpins on our collaboration with Nikon.

Over the next 5 years our work will continue to provide impact in several areas and we highlight 3 priorities. In pain and regeneration research we have several programs that aim to identify and validate novel therapeutic targets, a recent high impact success in this area being widely commented upon is the identification of the CXCL5 receptor by McMahon's Wolfson CARD group as a molecule that causes sunburn pain. This was highlighted in several press releases – e.g. see http://www.aaas.org/news/releases/2011/0706sp_sunburn.shtml. The development of drugs to novel pain targets is a priority area for the Wolfson CARD that will be facilitated by our recent investment in a Drug Discovery Unit, and also the recruitment of McNaughton. This drug discovery unit is led by Corcoran and has already had one major impact evidenced by the formation of CoCo Therapeutics. Within the Randall Sutton is leading a program in collaboration with UCB to develop small-molecule inhibitors of the IgE/FcεRI interaction using virtual screening approaches made possible by the units seminal work on solving the crystal structure of the complex. A related phase I clinical trial of the anti-IgE therapeutic antibody omalizumab in non-atopic asthma (with Novartis) will also be undertaken. Within the MRC Centre, a major effort will be made to fully model neurodevelopment disorders such as autism all the way from the generation of mouse mutants to in vitro and in vivo characterisation, including behavioural testing of phenotypes. This is ambitious but essential work if we are to understand these complex disorders.

d. Relationship to case studies

We have selected eight impacts that represent the broad range of our activities and these are listed below, and placed in context above.

(1) David Band –. LiDCO: Minimally invasive measurement of cardiac output and haemodynamics by pulse contour analysis and lithium dilution
(2) John Marshall – Laser eye surgery and its regulation.
(3) John Marshall - Retinal Rejuvenation Therapy.
(4) Doherty – The development of a 'first-in-class' N-cadherin antagonist for cancer
(5) Walsh/Doherty – Anti-MAG antibodies to treat stroke.
(6) McMahon – Identification and validation of nerve growth factor (NGF) as a peripheral pain mediator
(7) Ballard – Reducing Harmful Use of Antipsychotics in People with Dementia
(8) Corcoran – Establishment of CoCo Therapeutics to take forward new drugs for Alzheimer's disease.