Institution: King's College London

Unit of Assessment: UoA5

a. Overview

K**ing's College London** (KCL) is a multi-faculty research-led University ranked in the top 20 worldwide. It has more than 24,000 students (including 10,000 postgraduates) and more than 6,100 employees. It is a member of the Russell Group, and a partner in the Francis Crick Institute (http://www.crick.ac.uk/), a world-leading biomedical research institute opening in 2015. King's Health Partners (KHP - http://www.kingshealthpartners.org) links the College to three local Foundation NHS Trusts and is one of five accredited Academic Health Sciences Centres in the UK. King's also hosts two NIHR Biomedical Research Centres, with total funding of £113m over 5 years. An independent survey carried out by Rand Europe in May 2013 for the UK Department of Health (see http://www.rand.org/pubs/research_reports/RR318.html) showed the following national metrics for the *overall health research activities* at King's: RAE average 4* ratings: 6th; Number of highly cited publications: 5th; Mainstream HEFCE QR funding: 3rd; Income from research grants and contracts: 5th; Number of PhDs: 5th; ARWU in clinical medicine and pharmacy: 6th. We have recently been rated 13th in the world in clinical, pre-clinical and health (see Top 100 universities for Clinical, Pre-clinical and Health 2013-14 - Times Higher Education). Our return in **UoA5** has a health focus with almost 100 research teams populating three interactive research Divisions within the School of Biomedical Sciences and located in close proximity of each other on the Guy's campus. The **Randall Division of Cell and Molecular Biophysics** (Randall) brings together cell and developmental biologists, structural biologists, biophysicists and chemists working collaboratively to elucidate the molecular mechanisms of cell and tissue function using innovative imaging, structural and biophysical approaches. The **MRC Centre for Developmental Neurobiology** (CDN) studies the development of the nervous system in both invertebrate and vertebrate model organisms. Its aim is to understand how the processes of embryogenesis, orchestrated by the spatio-temporal regulation of developmental control genes, form this most complex of structures. The CDN benefits from interactions with the Randall in developing its imaging technology and addressing the cell biology of neurons. Its achievements directly impact on the understanding of disease mechanism as the vast majority of the genetic orchestrators of brain development are now found as key players in neurodisorders. The **Wolfson Centre for Age-Related Disease** (CARD) picks up from development and normal brain function by aiming to understand pathophysiology and to develop strategies to restore function to the damaged nervous system. The focus is on pain, hearing loss and regeneration largely within the context of brain injury, neurodegenerative disease and ageing. Extensive interactions between these Divisions are illustrated in section B2.

b. Research strategy

The past five years have been used to renew our staff, our facilities and above all our scientific reach, to enable us to reposition our science at the cutting edge of important new areas. We initially focus on the three research Divisions, their achievements and plans.

The Randall Division for Cell and Molecular Biophysics *takes an integrated multidisciplinary approach to biomedical research at the molecular, cellular and whole animal levels, with an active interface with associated clinical studies. The Division is housed in ca 2500m^2 of research space on the 3rd floor of New Hunt's House designed specifically for its needs, and includes specialized facilities and infrastructure to support five core research areas described below. Much of the research in the Randall crosses UoA boundaries; thus although its centre of mass lies in UoA5, some of the embedded staff have joint appointments with other Schools and some are being returned in other UoAs (Medicine, Physics, and Maths) as indicated below. The five core areas are organized as Research Sections; two of the Sections are technically-defined (structural biology and molecular biophysics; cell imaging) and three are biologically-defined (cell motility and cytoskeleton; muscle signaling and development; allergy and asthma).*

(a) Structural biology and molecular biophysics. Protein structures are determined by X-ray crystallography and NMR, supported by other biophysical techniques and computer-aided molecular modelling. Current research interests include: antibody-receptor interactions in allergy (*Beavil, Gould, McDonnell, Sutton;* see section *e* for detail); antibiotic resistance (*Sanderson*); enzyme structure and mechanism (*Steiner*); protein-RNA and protein-DNA interactions (*Conte*); anti-viral drug design (*Sanderson*); muscle protein structure (*Pfuhl; UoA1*); tail-anchored membrane proteins (*Isaacson*); single molecule force spectroscopy (*Garcia-Manyes; UoA9)*, structural bioinformatics and molecular dynamics simulations (*Fraternali*). Major achievements of members of the Section during the assessment period include structures of topoisomerase target enzymes in complex with clinically important anti-viral drugs, protein domain interactions involved in muscle assembly and dynamics, protein-RNA interactions in the mechanism of transcription initiation, mechanical folding/unfolding of proteins, various structures of the IgE network of protein-protein interactions in allergy (see section *e*), and the prediction of regions of protein instability and of protein-protein interaction networks in cancer biology. Plans for the next five years are characterized by further collaboration between members of the Section and clinical scientists (in allergy and asthma, cancer, cardiovascular, imaging sciences, immunology, virology) as well as other groups within the Randall (cell signaling, cell migration, muscle signalling) and also with the new King's Institute for Mathematical and Molecular Biomedicine. Links with the new Chemistry Department will be further developed, as will those with Physics in studies of protein folding/unfolding, measurement of inter-molecular forces, and the use of single-molecule FRET to investigate protein dynamics, track molecular interactions in cell membranes and measure protein-protein interactions and cell-cell adhesion.

(b) Cell imaging. Advanced optical imaging techniques are developed and applied to unravel the biological processes at work when molecules interact in living cells. Bioactive molecules are used for functional imaging of live/fixed cells, cellular organelles, tissues and whole organisms. New techniques have been developed for super-resolution imaging (*Cox, Ewers, Heintzmann, Owen*), fluorescence lifetime imaging (*Ameer-Beg, Suhling (UoA9), Vojnovic*), single molecule imaging (*Ameer-Beg*), multiphoton-based intravital imaging (*Ng (UoA1)*, *Vojnovic*) improved by adaptive optics and applied to image pathophysiological processes in live animals *in vivo*, and high-content imaging of cancer cells and tissues for drug/siRNA screens and prognostic disease marker discovery (*Ameer-Beg, Ng)*. Biological processes are imaged in the context of diseased states to develop new ways of monitoring and manipulating them and help to predict drug target effects and their translation to organ and organism level physiology. Within KCL the section has strong links and joint appointments with the Division of Cancer Studies, the Division of Medical Imaging, the Richard Dimbleby Department of Cancer Research, the Physics and Maths departments, and with the Cancer Research UK/EPSRC/DoH/MRC-funded KCL-UCL Comprehensive Cancer Imaging Centre. Plans for the next five years include: high content imaging of cancer cells and tissues for drug/siRNA screens and prognostic disease marker discovery; multiscale (whole body and nanoscale) imaging of pathophysiological processes, coupled to quantitative analyses developed within the Institute for Mathematical and Molecular Biomedicine, and super-resolution imaging of protein network organisation, coupled to genomic analyses, of both normal and disease states. These will be supported by a recent MRC Strategic Award for development of super-resolution and functional imaging on live cells.

(c) Cell motility and cytoskeleton The coordinated migration and adhesion of cells is a prerequisite for the establishment and maintenance of multi-cellular organisms and is essential for development, wound healing and immune responses, and also contributes to the progression of various diseases including chronic inflammatory diseases and cancer. PIs in the section *(Csikasz-Nagy, Dodding, Eggert, Jones, Krause, Linker, Oliferenko, Parsons, Ridley, Sanz-Moreno, and Stramer*) share a common interest in the role of the cytoskeleton in cell polarity, cell shape, axon guidance, cell adhesion, cell migration and cytokinesis, and there are many interactions and collaborations. Major achievements in the REF period include: identifying new phosphorylation sites that regulate key proteins involved in migration, including lamellipodin and fascin, and demonstrating the importance of new and unexpected links between integrin adhesion receptors and cell migration regulators such as Cdc42, N-WASP and RIAM. Plans for the next five years include using *in vivo* models to visualize the activity of cell migration regulators at high resolution in living cells during development and cancer progression. This will be complemented by development of improved 3D environments to

study interactions between different cell types involved in inflammation and cancer. We also plan to use biophysical approaches to study forces underlying cell adhesion, motility, protein-protein interactions and developmental processes in collaboration with biophysicists at KCL and in the Mechanobiology Institute (National University of Singapore), and build systems models of cell motility with the KCL Institute for Mathematical and Molecular Biomedicine.

(d) Muscle signalling. Section members study the genetic regulation of the development of the musculo-skeletal and cardiac systems (*Hughes, Logan*, *Wardle, Zammit*), the pathways controlling the assembly and turnover of contractile structures (*Gautel (UoA1), Ehler (UoA1)*) and the molecular mechanisms underlying muscle contraction and its regulation (*Irving, Pfuhl (UoA1), Sun*). We use genetic, cell biological, biophysical and structural approaches. These methods enable us to analyse the proteins responsible for signalling, and the structural integrity of muscle, its renewal from endogenous stem cells, and the impact of mutations that underlie the pathology of muscle. Some section teams are also members of the Cardiovascular Division in the School of Medicine and the British Heart Foundation Centre of Research Excellence, renewed in 2013 for a further 5 years. Major achievements in the review period include: proof of the essential roles of activity, intracellular signals, translational regulators, gene regulatory networks in vertebrate heart, head, limb and trunk myogenesis and remodelling, the role of cytoskeletal proteins like formin, titin and obscurin in cardiac myofibril formation, maintenance and in cardiomyopathies, and identification of a mechanosensory pathway in striated muscle linked to autophagosomal protein turnover. Plans for the next five years include the analysis of the role of activity, force and regulated translation in muscle growth; muscle-connective tissue interactions; mechanisms of myogenic specification by identifying transcriptional complexes and gene regulatory networks required to drive heart and skeletal muscle progenitor cell fate; novel regulatory mechanisms in contraction of skeletal and cardiac muscle; and translational work on myopathies caused by sarcomeric, cytoskeletal and autophagy pathway gene mutations.

(e) Allergy and Asthma. Section members *(Beavil, Gould, Sutton, McDonnell)* aim to elucidate the molecular mechanisms underlying allergic disease and facilitate the development of new therapies. Combining techniques in structural biology, molecular genetics and cell biology, they study the allergic response from the control of IgE antibody gene expression to the various protein-receptor interactions that mediate the physiological allergic responses. The Section has close links with the Division of Asthma, Allergy and Lung Biology in the School of Medicine, and all four PIs are members of the MRC and Asthma UK Centre in Allergic Mechanisms in Asthma (joint with Imperial College; renewed in 2011 for a further five years). Major achievements in the review period include elucidation of the crystal structures of IgE-Fc in complex with the high-affinity mast cell receptor FcεRI, and with the low-affinity B cell receptor CD23. The former is a target for therapeutic intervention, and collaboration with a pharmaceutical company (UCB) has been initiated to discover small-molecule inhibitors. The role of CD23 in the mechanism of IgE regulation by B cells has also been elucidated, together with a detailed understanding of the structure of CD23 and the role of calcium. The group's discovery of the importance of local synthesis of IgE in allergic tissue has opened the way to trials of anti-IgE therapy in "non-atopic" asthma, and single B cell cloning and IgE expression techniques developed by the group have enabled functional and structural studies of allergen recognition by specific allergic and non- allergic antibodies. Plans for the next five years include further development of a small-molecule inhibitor of the IgE/FcεRI interaction (with UCB), a phase I clinical trial of the anti-IgE therapeutic antibody omalizumab in non-atopic asthma (with Novartis), and pre-clinical trials of an anti-ovarian cancer IgE (together with the Imaging Sciences Division and the KHP BRC on the Guy's campus), thus advancing this new field of "allergo-oncology". Fundamental studies of IgE dynamics and interactions at the cell surface will be pursued using single-molecule FRET, and the IgE/CD23 interaction will be pursued as a target for intervention. The nature of allergenicity and the human B cell response to allergens will be studied in the case of peanut allergy in collaboration with clinical colleagues (St. Thomas' Hospital), and similarly the molecular mechanisms associated with viral exacerbations of asthma will be studied collaboratively through the MRC & Asthma UK Centre (St. Mary's Hospital). A small molecule drug discovery unit, based on a structure led virtual screening model adopted by the Wolfson CARD, will be extended to the Randall.

The MRC Centre for Developmental Neurobiology (CDN) *was established by an MRC Centre grant in 2000, and has been successfully renewed for two additional 5 year periods. It houses 24 HEFCE-funded faculty and five MRC or Wellcome Trust Fellows in state-of-the-art contiguous research space on the 4th floor of New Hunt's House. In an ethos of extensive intra- and extra-mural collaboration, CDN scientists seek to understand how the brain works by studying how sequential layers of complexity of cell specification, connectivity and network formation transform an epithelial sheet into an adult brain. Development is studied in cell-based systems (primary cultures, neurons derived from mouse embryonic stem (ES) cells) and whole animal models (principally Drosophila, zebrafish and mouse, but also C. elegans, Xenopus and chick). Critical to the development of a functioning brain is the formation of connectivity as synaptic activity sculpts out dynamically responsive circuitry to produce the neural substrate for complex brain function. Immediate proximity to the Randall, a shared history with key PIs in the CARD and a joint seminar program, have fostered strong links across these divisions. CDN members also collaborate with other neuroscientists and neuroclinicians at KCL, especially those in the Institute of Psychiatry (IoP) and, more recently, Pediatrics at St Thomas Hospital*. The CDN research is organized around five main areas.

(a) The genetic control of neural development. Our work of piecing together the pathways and networks of gene action through exhaustive analysis of genetic gain- and loss-of-function phenotypes is allowing us to reconstruct essential generative stages in brain development: neural induction (*Bell*), regional specialisation (*Chambers, Houart, Kiecker, Lumsden, Sahara*), cell fate acquisition (*Graham, Houart, Larsen, Lieberam*), neurogenesis (*Clarke, Lumsden, Sahara, Sousa-Nunes*), neuronal migration (*Formstone, Lumsden, Wingate*), and axon guidance (*Drescher, Gordon-Weeks, Guthrie, Hindges, Tear*). This has used range of novel transgenic and gene delivery systems and high resolution imaging developed during the review period. Highlights include *Clarke's* discovery of the factors controlling the asymmetric division of neuronal precursors, the first evidence in vertebrate embryos; *Guthrie* and colleagues' identification of alpha2-chimaerin as responsible for Duane syndrome; *Houart's* identification of the first direct target of the Rett syndrome gene Foxg1 and *Lumsden's* discovery and characterization of novel cell groups and circuits in the mammalian thalamus, crucial to luminance detection and diurnal rhythm entrainment. Our progress in understanding the molecular cascades driving the key developmental processes led to impact in neuro-developmental disorders (*Drescher, Guthrie, Houart, Wingate*). Future plans in the next 5 years in this area include a genome-wide functional study of genes involved in neuro-developmental disorders and the initiation of a major effort in understanding Human brain development. Groundwork for these goals has been achieved this year. Houart is co-heading a major UK-wide collaborative Wellcome Trust Strategic Award (Deciphering Mechanisms of Developmental Disorders), obtained in January 2013, involving clinicians and geneticists and providing high quality phenotyping of mice produced by the Sanger mutagenesis program, carrying loss of function mutation in genes linked to developmental disorders. The CDN also initiated a close collaboration with KCL Pediatrics to further ascertain translation of the CDN extended knowledge of brain development and Houart is organizing a London-wide consortium to develop a programme of research focused on understanding the development of the human brain.

(b)Synaptic-activity driven circuit maturation. We have invested over the past five years in studying how neural activity refines circuitry by the selective reinforcement or elimination of synapses (*Andreae*, *Burrone, Ch'ng, Grubb, Hindges, Keck, Lowe, Meyer, Thompson, Williams*). The Centre contains an exceptionally strong research team in visual development and plasticity (*Drescher, Hindges, Keck, Lowe, Meyer, Thompson*) as well as in vitro systems (*Burrone, Grubb, Hindges, Lieberam*), who are together exploiting the visual system and its diverse connectivity with the superior colliculus, thalamus and neocortex. In addition, in vivo and in vitro systems are being used to both fine-tune these new technologies and exploit them to characterise the development of neuronal connections in the hippocampus (*Burrone*), olfactory bulb (*Grubb*), telencephalon/neocortex (*Clarke, Houart, Sahara*), thalamus (*Lumsden*) and neurons derived from ES cells or human induced pluripotent stem cells (*Lieberam, Burdakov*). Highlights so far include the discovery of a novel mechanism for neuronal homeostasis that involves reversible displacement of the axon initial segment away from the cell body (*Grubb* and *Burrone*), and the use of advanced optogenetic tools to explore functional connectivity in the visual pathway (*Meyer* and *Thompson*). The next 5 years will focus on identifying the connectivity and functional input/output relationship

between neurons in specific neuronal network with a special attention to cognitive, motor and visual circuits. Complementation of conventional electrophysiology by two-photon microscopy, new live imaging techniques using optogenetic tools, and advanced transgenic approaches in mouse and zebrafish, including reliable trans-synaptic tracing methods, now present unprecedented opportunities to study the assembly of neural circuits at combined structural and functional levels. Our planned studies will combine rabies-variant virus trans-synaptic tracers to label interconnected neurons with the genetically encoded reporters of synaptic activity, combined with optogenetic modulators of neuronal activity, which can be activated within even individual dendritic spines. By using these light-sensitive proteins to modulate activity we are able to interrogate defined neuronal circuits to establish the role of neuronal activity in circuit formation.

(c) Cell biology of neurons and glia. Underpinning much of the work above is the need to understand the molecular mechanism of cellular function, particularly if we are to design effective therapeutic interventions. Our focus is on a cell (the neuron) with exceptional nanometer-scale compartmentalization that is dynamically regulated on millisecond time scales, requiring very high resolution tools to measure activity of specific neurons, induce or repress neuronal activity and manipulating the key proteins involved. Our interests include primary culture and in vivo studies of protein trafficking in healthy and degenerating neurons and synapses (*Fanto, Houart, Tear, Burrone*), the molecular interactions regulating apico-basal polarity during neurogenesis and axogenesis (*Clarke*), microtubule dynamics during axogenesis, synaptogenesis and axon/synapse degeneration (*Gordon-Weeks*), dynamics of adhesion complexes during forebrain morphogenesis, neuronal migration and synaptogenesis (*Guthrie, Houart, Wingate*), and the molecular behavior of RNA processing proteins in and outside of the nucleus in developing and diseased neurons (*Guthrie, Houart, Makeyev*). The identification of Drebrin as key regulator of microtubules dynamics in neuronal migration and neurite outgrowth (*Gordon-Weeks*), the fine-tuned regulation of RNA processing proteins in neurogenesis (*Makeyev*) and the importance of PTEN/PI3K function in neuronal differentiation (*Eickholt*) are amongst our achievements of the review period. The next 5 year will see the increase of our effort in understanding the role of endocytosis, vesicular trafficking and sub-cellular regulation of RNA processing in the developing and diseased neuron.

(d) Molecular and cellular mechanisms of neurodegeneration. We have adapted our experimental systems to investigate molecular mechanisms of neurodegeneration. *Fanto* studies toxicity in a polyglutamine neurodegenerative disease, DRPLA, caused by a PolyQ mutation in atrophin-1 and initiated collaboration with scientists at the CARD (*Bateman, Lalli*). *Houart* has established a zebrafish model for the neurodegenerative disease Human Spastic Paraplegia and is collaborating with Shaw (IoP) and eight other UK labs on an MRC/Wellcome Trust initiative to dissect the molecular mechanism leading to neurodegeneration in ALS patients. The current work includes the initiation of a small molecule screen in zebrafish and the future use of the small-molecule drug discovery facility through collaboration with the KCL new Chemistry Department. Working in Drosophila, *Tear* studies the effects of Tau phosphorylation at high resolution in an Alzheimer's model; *Pini* has discovered a novel pathway involving extracellular histones, released by dying cells, which are selectively neurotoxic in the nanomolar range while causing astrocytes to become reactive; he has two patents on potential therapeutic agents for use in AD and stroke. The next five years will see an increase in cohesion between the IoP, CARD and CDN scientists in dissecting the mechanisms of neurodegeneration as well as increased links with the main UK players in the field. At the CDN in coordination with Randall (*Gautel UoA1*), St Thomas and IoP partners, research will have a strong focus on understanding the role of vesicle trafficking, endocytosis and RNA processing proteins in degeneration (*Burrone*, *Fanto, Guthrie, Houart, Makeyev*).

(e) Environmental factors: Influence of the environment upon the development and maintenance of neuronal circuits is becoming a significant interest of the CDN. *Ch'ng* who joined 6 years ago, investigates the genetic network regulated by insulin-like peptides in modulating homeostasis and aging. The next 5 years will see the development of this research area. To this aim, we have recruited this year Drs. *Sousa-Nunes* who is dissecting the molecular players in environmental regulation of neurogenesis, and *Burdakov* who evaluates environmental effects on modulation of synaptic activities (electrophysiology, synaptic networks).

The CDN will pursue two major aims in the next quinquennium. One of these is to seek renewal of MRC funding as a *Centre for Neural Circuit Development*, with the mission to explore the mechanisms involved in genesis of both normal and abnormal/disordered circuits. The CDN is already well equipped for this work at molecular and cellular levels and needs to acquire expertise in animal behaviour, to measure the impact of any change in network connectivity. This will be achieved by developing extramural collaborations (including the IoP), and specifically recruiting in this area. Collaboration is also underway with St Thomas CDB to understand how imaging of brain activity in human neonates can be used to delineate the onset of psychiatric syndromes. The other new focus will be human brain development, coupling observation in fixed tissue, in utero imaging and tissue engineering from iPS and NS cells. This timely programme will be build together with key partners across London, including the Tissue Engineering unit of Imperial College.

The Wolfson Centre for Age-Related Disease (CARD). *Progress in understanding age-related diseases, and in translating these findings into new medicines, is urgently needed. The **CARD** was founded in 2004, expressly to develop strategies aimed at restoring function to the damaged nervous system. To achieve this we need to understand how the normal adult brain functions, how it responds to stress and injury, and why repair mechanisms often fail. To this end we have ~20 principal investigators working across a number of highly interactive groups in a self-contained building close to the CDN/Randall. Much of what we do is driven by studies on molecules first identified as playing major roles in the developing nervous system. Phenotypic characterization of mouse mutants drives a considerable part of our efforts in understanding dysfunction in cognitive, motor or hearing loss and pain, with a large number of pre-clinical models used to evaluate therapeutic interventions in pain, Alzheimer's and Parkinson's disease, spinal injury and stroke. We have also recently established a drug discovery unit to help translate our efforts in these areas, and have hosted a KCL/Pfizer open innovation pain lab.* The CARD is organized in 5 research areas.

(a) Neurobiology and Pharmacology of Pain Chronic pain is prevalent in aging populations and its clinical treatment remains limited. We have made considerable progress over the review period in understanding the basic neurobiology of pain and in designing and evaluating novel treatments. The core group of senior scientists working in this area (*McMahon, Bevan, Malcangio, Gavazzi*) has been complemented by the recruitment of *Peter McNaughton* from Cambridge where he served as Head of the Pharmacology Department. The appointment of a group of younger scientists (*Andersson, Flatters, Grant*) who held junior or fellowship appointments during the review period, and by the recent recruitment (May 2013) of *Raouf* from Pfizer ensures critical mass. Considerable progress has been made in the review period in the identification of novel pain mediators, with highlights including *McMahon's* identification of CXCL5 as a key mediator of irradiation-induced pain in humans; *Malcangio* providing key insights into the nature of the microglial derived mediators of chronic pain and *Bevan's* and *Andersson's* identification of important thermosensitive ion channels. We have identified three main challenges for the next 5 year period. Firstly, we will used our established "gain and loss of function" and pre-clinical mouse models to determine how the various cytokines, chemokines and ion channels that we have recently identified as pain mediators contribute to the establishment and maintenance of a wide range of pain states. Secondly, we will use a variety of methods (including virtual screening) to develop small molecules and/or biologicals as novel therapeutics against the most promising candidates (e.g. CXCL5 and associated ligands and receptors), a goal that will be supported by our new drug discovery lab (details below). Finally, we will develop and refine *in vitro* models to allow us to better understand at the cellular level how the pain state is generated and maintained. To this end the recruitment of *Raouf* is highly strategic as he adapted a microfluidic based compartmentalized culture model to study the neurobiology of nociceptive nerve endings; future studies will include the development of optogenetics to allow for highly controlled patterns of activation of these neurons. *Robbins* and *McMahon* are working with colleagues in Bath and asking the bold question as to whether we can replace dysfunctional parts of the nervous system with semiconductor devices. To this end neuroprothetic devices are being developed and we have proof of concept obtained both in vitro and in patients.

(b) The Genetics of Age Related Hearing Loss. Our above strengths in sensory neuronal function have provided a foundation to extend our research efforts to another major area of unmet need, and this is age-related hearing loss. To this end we have recently (Oct 2012) recruited Karen *Steel*

and her team. A mouse genetic screen has been used to identify several molecules involved in progressive hearing loss, and led to the discovery of two primary mechanisms underlying deafness, one involving lipid signaling that affects homeostasis of the cochlea and the other involving maintenance of the afferent synapses of sensory hair cells, and over the next 5 years these and other mutants will be characterized to determine the molecular basis of the condition. The effect of human mutations in these genes on age-dependent development of deafness will also be studied in collaboration with Williams/Spector (Dept Twin Research & Genetic Epidemiology at King's). Collaborative opportunities are also starting to be developed between this group and the pain groupings.

(c)Neurodegeneration and ageing. There is perhaps no bigger "age-related challenge" facing society than the increase in the number of individuals living with dementia, particularly Alzheimer's and Parkinson's diseases. During the current review period the core group of senior scientists working in this area (*Ballard, Francis, Duty*) have made key observations in models that range from mice to man. For example, Ballard's clinical trials and reviews in Alzheimer's disease have underscored the limited benefits and potential harms of antipsychotic drugs with immediate impact upon prescribing practice and *Francis* has proposed a new mechanism for the newly approved drug "Memantine", and identified changes in tau phosphorylation in the post-mortem brains of patients treated with this drug. In Parkinson's disease, *Duty's* group provided preclinical evidence that validates type III metabotropic glutamate receptors as targets to relieve symptoms and offer neuroprotection. The grouping has identified a number of new challenges for the next quinquennium. A major new initiative between this grouping and the "pain" grouping is being undertaken. The question of pain in the context of Alzheimer's disease had largely been ignored despite considerable evidence suggesting that it is a major debilitating factor in the ever increasing population of people living with this dementia, over the coming 5 years *Ballard* and pain scientists in the Wolfson will start to investigate this at both the clinical and pre-clinical level. *Ballard* is also leading our efforts in a large EU program that will determine the efficacy of stem cell therapies in preclinical models of dementia, and with others in the drug discovery lab contribute to a substantial bioinformatics led "drug re-purposing" program to new treatments for Alzheimer's disease. *Francis* is undertaking a major initiative to understand the biochemical basis of cognitive and behavioural symptoms in Lewy body dementias with aim of identifying new treatment targets for this under-researched group of diseases. *Duty* will work with colleagues at Lundbeck testing the translational potential of drugs that target type III metabotropic glutamate receptors using clinically-relevant, systemically-active agents in her preclinical models.

(d) Neural Regeneration and Adult Neurogenesis. The ability of the prenatal and to some extent young postnatal mammalian brain to recovery from injury is in sharp contrast to what we see in the adult brain. The ability of adult rat CNS to recover from injury is being studied in Stroke by *Moon,* who has identified neurotrophin-3 as a potential treatment, and for contusive injury of spinal cord by *Bradbury*, who has demonstrated the efficacy of virally expressed chondroitinase ABC in promoting regeneration. Their work in the coming period will be aimed at translating this work to man, *Moon* evaluating clinically-relevant routes of delivery towards starting Phase I clinical trials, *Bradbury* collaborating with Eugene Redmond (Yale) to develop a primate model of the injury/treatment paradigm as a prelude to human studies. *Doherty* has established a key role for DAG Lipase-dependent endocannabinoid signalling in regulating neurogenesis in the adult hippocampus and sub-ventricular zone, and in the coming years will investigate how DAGLs are activated and test the hypothesis that the age-related decline in adult neurogenesis reflects loss of endocannabinoid tone. *Lalli* has identified, and is defining the mechanism by which a number of candidate molecules control adult neurogenesis (including Ras-like GTPases and cytoskeletal regulators), and will use our high resolution in vivo imaging to identify how disease and age impact on their function. The *Bateman* group discovered the important role of insulin/mTOR signalling in neurogenesis and has recently identified several novel genes that regulate this process. In the next five years they will elucidate the molecular mechanism by which these novel mTOR pathway genes control neurogenic processes.

(e) Drug Discovery Unit. The CARD has invested in appropriate screening equipment, bioinformatics support with a molecular modeling and virtual screening capability to create a neuroscience Drug Discovery Unit directed by *Corcoran*. Highlights include his development of retinoic acid receptor(RAR)α agonists for Alzheimer's disease and RARβ agonists for spinal cord

injury supported by two independent Wellcome Trust SDDI awards. *Corcoran* (with Advent, The Wellcome Trust and KCL) has founded a spin-off company (http://cocotherapeutics.com/) to take the RARα compounds into Phase 2a clinical trials. *Williams and Doherty* are using virtual screening to identify small drug-like molecules with similar actions. For example, several hits against both the Nogo receptor and the TrkB receptor have been identified in programs funded by Wyeth and by Auris Medical respectively. *Williams* has also developed the first searchable platform-independent microarray expression database (SPIED - www.spied.org.uk) and together with *Ballard, Doherty* and *Corcoran* is using a meta-analysis-based strategy to curate novel disease transcriptional signatures to probe the Broad Institute's connectivity map to reposition drugs to treat Alzheimer's disease and Parkinson's disease (supported by Wellcome Trust). *Cox* pursues pharmacological studies in gut on neural regulation of satiety, and curative mechanism of bariatric surgery that similarly translate through to translational outcomes, via EU-funded collaborations involving Zealand Pharma, Novo Nordisk A/S and others.

Effective dissemination of research: Apart from the obvious communication to other scientists, in combination with the Wellcome Trust and the MRC we have increased public understanding of how the brain works. In 2012, the CDN provided scientific content, scientific advisors and events content for "Brains: Mind as Matter" at the Wellcome Collection. Brains reached a direct audience of over 100 thousand visitors. The exhibition generated across-the-board national and international media coverage (press, radio, BBC television) and a successful book (Kwint and *Wingate*, 2012). A single-day live event, featuring scientists from the CDN, attracted 5000 visitors to the Wellcome Collection. This year, MRC funding was obtained to support public events to celebrate 100 of MRC funded research in developmental neurobiology and 60 years since Gosling and Franklin's Photo 51 demonstrated the double helix of DNA. This year's series of public events involves collaboration between Randall and CDN and exemplify our continuous activity in public engagement by PhD students up to Professors, from outreach activity in our local schools to engagement with the wider public and the scientific press, particularly through the future KCL Science Media Centre.

Multidisciplinarity*:* Since 2000 our research has been organized and managed through inter- and multi-disciplinary research Divisions rather than in traditional discipline-based departments (which we retain for teaching), so that inter- and multi-disciplinarity now pervades our research. Within the biomedical sciences themselves, this has resulted in seamless combinations of molecular, cellular, tissue or whole animal approaches in many labs. The interface between basic biomedical science and experimental medicine has been developed through our Academic Health Sciences Centre, King's Health Partners, with its Clinical Academic Groups that provide a set of translational and reverse-translational pipelines linking basic science and clinical medicine. New links at that interface have also been stimulated by our NIHR-funded Comprehensive Biomedical Research Centres (£113m over 5 years) and translational PhD studentships (10/year). The interface with physical sciences, engineering and maths is equally well developed, through different mechanisms. The Physics/Biology interface has been a research focus for King's since the 1950's, following Franklin and Wilkins contribution to the discovery of the structure of DNA, and this biophysics tradition continues with its hub in the Randall. Currently, the major growth area in King's biophysics is in biophotonics and the development of novel optical microscopies for super-resolution, functional imaging, screening and diagnostics, recently stimulated by an MRC Strategic Award. Highlights of the recent and planned work in this area were described in section B2 above, as was some of our other research at the bio/physics interface. Links to chemistry were paradoxically stimulated by the temporary closure of the King's undergraduate Chemistry department from 2003 to 2011, when it was re-created as Chemistry with Biomedicine by the recruitment of a team of new lecturers with research interests at the chemistry/biomedicine interface. Chemistry research continued in the interim, but was embedded in biomedical Divisions, greatly strengthening the interface. Links to maths, computer science and informatics have been stimulated recently by joint appointments, research grants and studentships, and notably by the formation of the Institute for Mathematical and Molecular Biomedicine.

c. People, including:

i. Staffing strategy and staff development

Our recruitment strategy is designed to maintain and strengthen existing areas and to develop new teams to address emerging questions. In the CARD, Lalli, Andersson, Flatters and Moon moved

from junior fellowships to HEFCE funded positions, with Bradbury moving to an MRC senior fellowship. New programs have been developed with the recruitment of Corcoran (CDN), Raouf (Pfizer), Steel (The Sanger) and McNaughton (Cambridge). In CDN, Ch'ng, Fanto, Grubb, Keck and Meyer moved from fellowships to tenured posts; current fellowship holders are Alexandre (Royal Society), Formstone (Wellcome), Larsen (MRC) and Sousa-Nunes (Cancer Research UK). Since 2008, CDN recruited Ch'ng (Harvard), Keck (MPI, Tuebingen), Lieberham (Columbia), Sahara (Salk). In the Randall, Krause and Parsons moved from fellowships to tenured positions; current fellowship holders are Cox (Royal Society), Dodding (Wellcome), Fornili (BHF), Robertson (Canadian Heart), Sanz-Moreno (CR-UK), and Sun (BHF). Since 2008 we recruited Csikasz-Nagy (from Microsoft Italy; 0.25FTE), Eggert (Harvard), Ewers (ETH Zurich), Garcia-Manyes (Columbia; joint with Physics), Logan (NIMR), Linker (CR-UK), Oliferenko (Singapore), Owen (Sydney; joint with Physics) and Wardle (Cambridge).

As indicated above, our new recruits are now predominantly through the fellowship track, and we provide long-term support to our research fellows with the goal of facilitating transfer to a HEFCE-funded position when their research group is well established and funded. This support includes mentoring and regular progress development reviews, advice with funding applications, initial embedding in established host labs where appropriate, and access to shared research facilities and infrastructure. In addition to the fellowship track, we have made strategic appointments at senior as well as junior levels, and the majority of these recruits came with an established research group supported by fellowships and grants. The minority of appointees at lecturer level who need to build a research group on their arrival are supported to do so in the same way as described above for fellows, with protected time for research. Each Division hosts weekly seminars for internal and external speakers, and we jointly host prestigious "International Seminars" across the Divisions, as well as international symposiums.

Concordat for support of Researchers, equality and Diversity. All early career researchers participate in our performance development review system, which focuses on the personal career development of the ECR. In addition we are introducing a mentorship programme in which ECRs are supported by experienced PIs in other groups. A 'post-doc champion' represents the ECRs at Divisional and School management level and helps the ECRs develop bottom-up initiatives, like the Guy's Researchers' Society, which has organized seminars and workshops on many topics including careers and entrepreneurship as well as science talks. Appropriate School and College committees now have direct ECR representation. Our PhD students and post-docs are encouraged to teach (tutorials and laboratory practicals) for up to 30h a year, for which they receive accredited training (10 credits on the 180 credit level 7 Postgraduate Certificate in Academic Practice (PGCAP). Senior post-docs are encouraged to increase and diversify their teaching from the 30h norm and gain the first 60 credits of their PGCAP. Research fellows normally take on gradually increased teaching to reach the level of a first year academic. All our researchers are supported in preparing for wider career opportunities (Principles 3-5 of the Concordat) with generic, science specific, and post-doc specific courses (http://www.kcl.ac.uk/study/pg/school/training/training-courses/index.aspx). We also promote Equality and Diversity through Divisional and College Level participation in Athena Swan led activities, and notably whilst one of our scientists chairs the KCL Athena Swan committee (Dr Susan Duty), another (Dr Marzia Malcangio) Chairs the British Society for Pharmacology "Women in Pharmacology" committee KCL provides a wide range of strategic programmes and networks to promote equality of opportunity and achievement, e.g. the *B-MEntor* scheme for Black and Minority Ethnic group staff, the *Career Break Fund* for academic staff returning from a career break (e.g. maternity, paternity, adoption leave), the *Women's Network*, and the *Springboard Women's Development Programme* for research staff.

ii. Research students

New academic staff must pass a course on PhD supervision and developing graduate students (https://internal.kcl.ac.uk/student/help/grad-school/s-visor/train/index.aspx). Selection of students is based on a competitive interview by a committee – with guidelines laid down by our graduate school All students have a 1st and 2nd supervisor. Each Division has a Postgraduate Advisory Committee (PAC) chaired by its Postgraduate Coordinator to oversee student progression. Progress reports, co-ordinated by the graduate school, are completed online every three months by the student and supervisor. At the end of their first year, each student writes a substantial research report including a

literature review that is examined by the Divisional committee before upgrading from MPhil to PhD. All students must attend programmes on scientific management (risk assessment, project design, data handling, ethics, radiation and genetic hazards, human subjects, legal aspects of animal experimentation, presentation skills and the use of computing and statistics), basic IT skills and more generic life skills (personal effectiveness, communication, networking, team working, giving and receiving constructive criticism, talking to scientific audiences, publication, and teaching).

Of the students who were in their first year in 2008 all 30 successfully submitted their PhD's within 4 years. We currently have 90 full time and 5 part-time students in the tri-divisional program with a new cohort due in Oct 2013. 54 of the full-time students are on 4-year funding programs. 45 students are funded by various research council schemes (MRC, BBSRC, EPSRC) with 10 on Industrial CASE awards (supported by UCB, Novartis x2, Eli Lilly x4, Astra Zenica, GSK and Pfizer). Our ethos is open and collaborative research, with the students taking full advantage of the communal lab philosophy and open access to shared equipment and core technical support. In addition to developing a close working relationship within their own group (based on regular lab meetings and presentations), they also have their own PhD seminar/journal club program that they operate independently of their supervisors. A highlight of the year is our tri-divisional annual postgraduate day symposium where the final years students give talks and the others present posters. All students are encouraged to present their work at national and international conferences, with designated funds available for this. Finally, during the visit of external speakers (world leaders in their field) we set aside time “to meet the students” to help develop networking skills and build confidence.

d. Income, infrastructure and facilities

Research income for the review period was stable at £13-14m per annum over the REF period. Within this UK Research Council income was also stable at £5-6m p.a. with MRC as our major funder. Income from UK Charities was also stable at £5-6m p.a. The remainder is accounted for by income from EU and industry. These figures do not include major cross-School funding initiatives like NIHR funding (total £113m over 5 years) and the BHF Centre for Research Excellence (£9m in the REF period, recently renewed for an additional £6m) of which we are major beneficiaries.

Our multidisciplinary organization into Research Divisions and Centres facilitates a culture of maximal sharing of infrastructure and facilities, both within and between Divisions, and more widely across the College. CORFU, our centralized Core facilities planning and management team, co-ordinates such facilities across the College. Increasingly, we are partnering with other London-based Universities and with the Francis Crick Institute in major investments and initiatives in research facilities. Locally, our policy is use such shared facilities to disseminate critical mass in specialist fields and to exploit synergies that arise from multidisciplinary approaches. There is a high level of exchange between labs - of technologies, practical expertise, reagents, and ideas. Infrastructure is available to support the very wide range of work that we undertake, from detailed studies on molecules to whole animal models, using a range of biophysical, structural, cell and molecular biology techniques. Our open-access policy allows early career researchers to obtain key preliminary results ahead of submission of grant applications.

Facilities for optical microscopy are probably unmatched in the UK. We have led the development of the Nikon Imaging Centre at King’s, the only such Center in the UK, which provides 10 state-of-the-art instruments currently including N-SIM and N-STORM Super Resolution microscopes in a partnership agreement (2010-2020) that allows continuous upgrading and replacement as new instruments are developed. 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. Many other microscopes are located within the Divisions, including for time-lapse video microscopy, including 2 spinning disc and ten additional confocal microscopes. An electrophysiology lab and a multiphoton microscopy facility for in vivo imaging of synaptogenesis in mouse cortex have recently been completed in the CDN and the Randall continues to pioneer cutting edge developments in optical imaging (e.g. FRET and FLIM). In other areas, we also have state-of the art facilities for single cell iontophoresis, electroporation, sonoporation, laser cell ablation, oocyte injection, ES cell culture, laser-capture microscopy, Affymetrix gene chip analysis, and DNA sequencing. We have a in-house zebrafish TALEN-induced mutagenesis platform, funded by the Wellcome Trust (led by

CDN, in collaboration with Randall), housed in a new zebrafish facility (co-funded by KCL and Wellcome Trust) providing the largest and most modern UK facility (holding up to 47,000 fish) to support our zebrafish users. We also led on the establishment of the core ultrastructural-imaging facility, including two scanning electron microscopes, resolution 3nm (field-emission FEI instrument) and 10nm (Hitachi instrument), both with full elemental X-ray spectral analysis and ability to image hydrated specimens, three transmission electron microscopes including cryostage and full tomographic reconstruction capacity at nm resolution. Another recent initiative led by the Randall and funded by the Wellcome Trust is the Biomolecular Spectroscopy Centre, which is equipped with 400 and 500MHz NMR's plus a new 700Mhz instrument, high-throughput Surface Plasmon Resonance, Chiroscan spectrophotometers and mass spectrometry. Animal facilities in close proximity to our labs are available for full phenotypic characterization of mutant zebrafish and mice and for all of the surgical procedures required for gain and loss of function studies (e.g. in utero electroporation in mice). Mice have been moved into IVC's to secure a much higher level of biosecurity. We have access to transgenic mouse facility. We have several fly rooms, and a *Xenopus* room.

e. Collaboration or contribution to the discipline or research base

Essentially all of our returnees are heavily involved in the peer-review process for journals and grant awarding bodies and attend conferences often as invited speakers. All are external examiners for BSc courses and PhD theses. Several sit on advisory boards and collaborate extensively with companies. The above sections provide evidence for the multidisciplinary and collaborative nature of our research, and our Industrial collaborations. Due to space constraints we simply highlight some of our other achievements and responsibilities, collaborations, invited talks and reviewing for journals and funding bodies not included.

Fellowships of national and international learned societies, prizes and awards: FRS: *Irving, Lumsden and Steel*. Fellow Acad Med Sci: *Irving, Ridley, Lumsden and McMahon*. Fellow, Society of Biology: *Ridley*. Fellow of the Higher Education Academy: *Wingate*. W. Maxwell Cowan Prize for Outstanding Contributions in Developmental Neuroscience: *Lumsden*. Lister Prize: *Burrone* and *Wardle*. European Molecular Biology Organization (EMBO): *Lumsden* and *Ridley*. Wellcome Trust Young Investigator Award: *Burrone*. Royal Society University Research Fellowships: *Cox* and *Parsons*. Wellcome Trust Career Development Fellowship: *Dodding*. CRUK Career Development Fellowship: *Sanz-Moreno*. HFS Young Investigator Award: *Eggert*. BHF Fellowships: *Fornili* and *Sun*. R. Laura and H. Wekerle Foundation Award: *Keck*. NUS Partnership Awards: *Williams*. HHMI Visiting Scientists Janelia Farm: *Heintzmann* and *Williams*. Discovery Fellowship and Development Early Career Research Award, Australian Research Council: *Owen*. London Law Trust Medal: *Andersson.* MRC Senior Non-Clinical Fellowship: *Bradbury*. Schellenberg Prize and Robson Award: *Bradbury*. The Brain Prize, awarded by the Grete Lundbeck European Brain Research Foundation and The Award of Merit, Association for Research in Otolaryngology: *Steel.*

Examples of Funding Bodies Board and advisory board memberships: Wellcome Trust Molecular Neuroscience Grant Committee: *Graham*. AERES national Funding Agency, France: *Houart* and *Doherty*. ANR Grant Panel, France: *Houart*. Scientific Advisory Council, Leibniz-Institute for Molecular Pharmacology, Berlin; *Eggert*. EU-Cofund Postdoctoral programme DTI-IMPORT Evaluation Committee: *Fanto*. IBENS, Ecole Normale Superieure: *Houart*. IDBML, Marseille: *Houart*. CIRB, College de France, Paris: *Lumsden*. Fondation Francqui Stichting Prize Jury for Biological and Medical Sciences, Karolinska Institute, Stockholm: *Lumsden*. National Committee for the Selection of Research, Italian Ministry of Research (MIUR): *Fraternali*. SAB of Research Complex at Harwell: *Irving*. SAB, Biochemistry Department, Natl Univ Singapore: *Jones*. Panel Member for Biology 2014 RAE, University Grants Committee of Hong Kong: *Jones*. Royal Society URF Award Panel: *Parsons*. *Nature* policy focus group: *Parsons*. Chair, Life-Sciences Panel, The *Nature* Index: *Sun*. DFG Excellence Initiative Review Panel, Germany: *Ridley*. MRC Molecular and Cellular Medicine Panel: *Ridley*. European Research Council Advanced Grants, Chair of LS3 panel: *Ridley*. EMBO Annual Meeting committee: *Ridley*. Royal Society Newton International Fellowships Committee: *Ridley*. Research Excellence Framework UK 2014, subpanel member for UoA5: *Ridley*. Association for International Cancer Research: *Sanz-Moreno*. Agencia Nacional de Evaluación y Prospectiva Spain: *Sanz-Moreno*. Ramon y Cajal Programme Spain: *Sanz-Moreno*. Research Grants Review Board, Asthma UK: Sutton. MRC Developmental Pathway Funding Scheme: *Bevan*. MRC college of Experts: *Cox*. DEFRA TSE panel: *Morris*.

Examples of Editorial Board memberships: Cell: *Ridley***.** Developmental Cell: *Ridley*. Developmental Dynamics: *Graham*, *Guthrie* and *Logan*. EvoDevo: *Graham*. Journal of Anatomy: *Graham* (Editor in Chief). Development: *Graham*, *Guthrie*, *Houart*, *Logan*, and *Lumsden* BioMed Research International: *Bell*. Developmental Neurobiology: *Guthrie* and *Lumsden* (Section Head); Faculty of 1000: *Houart*, *Hughes*, *Kiecker*, *Graham*, *Logan* and *Lumsden*. F1000 Research: *Lumsden* (Advisory Board). Frontiers in Synaptic Neuroscience: *Keck*. BioMed Research International: *Kiecker*. Mechanisms of Development: *Lumsden*. BMC Developmental Biology; *Hughes*, *Logan* and *Lumsden*. Neural Development: *Lumsden* (Founder and co-Editor-in-Chief). PLoS Biology: *Hughes*. PLoS One: *Fraternali*, *Parsons* and *Tear*; Frontiers in Neurodegenerative Diseases: *Tear*. Invertebrate Neuroscience: *Williams*. Scientific Reports (Nature Publishing Group) – Neuroscience: *Wingate*. Interdisciplinary Science Research special issue: *Wingate*. Molecular BioSystems: *Eggert*. Journal of Current Proteomics*: Fraternali*. Frontiers in Bioinformatics and Computational Biology: *Fraternali*. Biophysical Journal: *Irving*. Journal of Muscle Research & Cell Motility: *Irving*. Frontiers in Membrane Physiology and Biophysics: *Owen*. International Journal of Biochemistry and Cell Biology: *Parsons*. Open Biology: *Parsons*. Journal of Visual Experimentation: *Parsons*. International Reviews of Cell Molecular Biology: *Parsons*. EMBO J and EMBO Reports: *Ridley*. Journal of Cell Biology: *Ridley*. Skeletal Muscle, Bone and Tissue Regeneration Insights: *Zammit*. Committee member and Communications Officer. British J Pharmacology: *Bevan* and *Duty*. Pain: *Gavazzi*. Open Journal of Pain; CNS and neurological disorders -Drug targets: *Malcangio*. Textbook of Pain: (Co-editor) *McMahon*. Editor - Journal of Pharmacology & Toxicological Methods: *Robbins*.

Examples of Research consortia leadership roles; advisory roles and Courses and Conference organisors: MRC Centre Director: *Lumsden*. Director of the London Pain Consortium (www.lpc.ac.uk): *McMahon*. Academic Director of EuroPain (www.imieuropain.org) supported by €6M grant from the EU-IMI and >€12m from Pharma: *McMahon*. Co-lead of MRC/Wellcome Consortia, "Neurodegeneration": *Houart*. "Deciphering Mechanisms of Developmental Diseases": *Houart*. EU-AIMS (European Autism Interventions - A Multicentre Study for Developing New Medications), an IMI-funded multicentre collaboration between academia and industry across Europe: *Andreae* and *Burrone*. ZF-Health (Fish models for diseases): *Clarke* and *Houart*. EU consortium on the neuronal cytoskeleton: *Gordon-Weeks*. KCL Coordinator for The Minority Health and Health Disparities International Research Training (MHIRT) Program – KCL/UC Irvine, USA: *Hindges*. Executive committee of the Thomas Young Centre: *Fraternali*. Executive Committee and HEI Co-ordination Committee, Francis Crick Institute: *Irving*. Collegium Internationale Allergologicum: *Sutton*. Co-Director of Biomedical Research Unit for dementia: *Ballard*. Director of Research for the Alzheimer's Society: *Ballard.* Member of MRC Brain Bank Network Steering Committee: *Francis*. Chair Women in Pharmacology Committee: *Malcangio*. Member of the UK-wide “Concordat” Steering Group convened by “Understanding Animal Research” and Working Group convened by the National Centre for Replacement, Refinement and Reduction of the use of animals in research (NC3Rs): *Moon*. Advisor to UK & international health providers on political action to reduce antipsychotic prescribing in dementia: *Ballard*. Member of NICE: *Ballard*. SfN mini-symposium organizer 2011: *Grubb*. EMBO Practical Course Organziers: *Houart* and *Hindges*. Summer Course ‘Zebrafish Genetics’, MBL, Woods Hole: *Houart*. European Symposium on Imaging Structure and function in the Zebrafish Brain: *Meyer.* International Society for Developmental Biology Conference: *Tear*.

Examples of Public Engagement: *Wingate*: Wellcome Trust Arts Funding Committee (2011 – present). Scientific Advisor for “Brains: The Mind as Matter” at the Wellcome Collection (2012); Curator of “Between” at the Inigo Rooms, East Wing Somerset House (2012), Norwegian Museum for Science and Technology, National Medical Museum, Oslo: Video interview and photomicrographs for “Inaccessible World” (2009); Documentary “The good, the true and the beautiful”: collaboration between Anwar Saab (1001 films) and *Inside out. New images and imagination about the body* (Professor Merte Lie, Norwegian University of Science and Culture). *Bateman* – Outreach activities including Keynote speaker National Science week (March 2013). *Morris* -public engagement on the use of animals in research, including a speaker at "the scientist" Wellcome Trust Workshop