Institution: King's College London

Unit of Assessment: 3B - Pharmacy and Nutritional Sciences

A. Overview

King's College London (KCL) is a multi-faculty research-led (Russell Group) institution with 24,000 students (~10,000 postgraduates) and is ranked in the top 25(QS) universities in the world. It is a member of King's Health Partners (KHP) – one of five Academic Health Sciences Centres (AHSCs) accredited by the Department of Health. The constituent members of KHP are King's College London, Guy's and St Thomas' Foundation NHS Trust, King's College Hospital Foundation NHS Trust, South London and Maudsley NHS Foundation Trust. The School of Medicine and the School of Biomedical Sciences will merge in 2014 to form a Faculty of Life Sciences and Medicine, to further enhance inter-disciplinary activities and deliver our strategic aim of translating basic science discovery into clinical impact.

PHARMACY research (~52 FTE) within the Institute for Pharmaceutical Sciences (IPS) has a *Molecules to Medicine* research strategy in which novel medicines are discovered and new formulations evaluated in patients through the inter-related themes: (1) Drug discovery, (2) Medicines Development and (3) Medicines Use. In **NUTRITION**, within the School of Medicine's Divisions of Diabetes & Nutritional Sciences and of Women's Health (~42 FTE), the research themes are (1) Diabetes, (2) Diet and Cardiovascular Health, (3) Diet and Gastrointestinal Health, (4) Metal Metabolism, (5) Early Life Origins of Disease and (6) Pregnancy, Fetal Well-being and Childbirth. These contribute to the discovery and development of medicines, and to the modification of diet and lifestyle from conception through to old age, with the aim of disease prevention and management.

B. Research strategy

PHARMACY: Our *Molecules to Medicine* research strategy is summarised by research themes.

In **Drug Discovery**, we seek to identify new biological targets and chemical entities to develop as drugs using a range of chemical biological, biochemical, biophysical and natural products-based methodologies. We are using the nematode *C elegans* to identify genes and gene products with potential as novel drug targets (**Dolphin, Sturzenbaum**) and conducting biosynthetic studies in *Streptomyces* bacteria (**Long**) and cytochrome P450-catalysed L-tryptophan nitration in *thaxtomin* phytotoxin (**Barry**) for potential drug discovery. We have established strengths in peptide (**Bansal**), carbohydrate (**Wagner**) and heterocyclic (**Rahman, Thurston, Wagner**) synthesis, and other chemistries for the production of new chemical entities, together with expertise in low-, medium- and high-throughput screening (**Rahman, Parsons, Thurston**) and *in silico* design (**Barlow, Rahman, Thurston**). Traditional Chinese medicines are also investigated for new drug leads, and as models for innovative analytical approaches for the standardisation of complex matrices (**Hylands**).

Biomarker discovery and development underpins drug discovery. Our expertise ranges from the development of new instrumentation and methodologies (**Smith**) to the detection of pharmaceutical agents in diverse matrices, and the development of novel mass spectrometric, NMR spectroscopic metabolomic and proteomic methodologies (**Legido-Quigley/Mason**). Our translational approach centres on the discovery of small-molecule biomarkers for clinical diagnosis, and further expansion of this programme is anticipated through collaboration with the MRC-NIHR National Phenome Centre, a legacy of the Olympic Drug Testing Centre (Cowan, KCL Drug Control Centre and with GlaxoSmithKline).

Research on ***neurodegeneration*** (**Jenner, Parsons, Salvage**) focuses on drug development for the symptomatic treatment of neurodegenerative orders (mainly Parkinson's disease) and the discovery of neuroprotective compounds. One of our major achievements has been the development of the successful spin-out company Proximagen (**Jenner/Salvage**) (see Impact Case). In ***pulmonary research***, we study the cellular and molecular basis of inflammatory cell recruitment, airway remodelling and airway hyper-responsiveness using a variety of *in vitro* and *in vivo* models of pulmonary dysfunction (**Page and Spina**). A key achievement has been the development and clinical evaluation of a novel inhaled mixed phosphodiesterase (PDE) 3 & 4 inhibitor, RPL-554, a bronchodilator with anti-inflammatory activity now in clinical use (see Impact Case). Our *anti-infectives initiative* (**Bruce, Harvey, Mason, Page, Rahman**) focuses on

discovering new classes of anti-infective agents by studying microbial ecology in the airways of patients with cystic fibrosis and other respiratory diseases. **Rahman** has designed novel DNA quadruplex-binding agents with antibiotic properties. We also using genetic and pharmacological approaches to identify novel drug targets involved in ***inflammation, sepsis and endothelial function,*** for example, the enzymatic processes regulating nitric oxide bioavailability in endothelial cells. In the ***cardiovascular area***, **Curtis & Heads** are evaluating potential candidate compounds for the management of ventricular arrhythmias and atrial fibrillation. ***Anticancer drug discovery*** is now a growing research activity with a focus on the discovery of small molecules (**Nikolova, Panaretou, Rahman, Thurston**), and on nanoparticle-based chemotherapies (**Al-Jamal/Thanou**). Drug targets suitable for high-throughput screening campaigns (both physical and virtual) are also being explored in p53 (**Nikolova**), Hsp90 and lipid oncogenic signalling pathways (**Panaretou**). **Thurston** has developed a novel anticancer agent (SJG-136) which has reached Phase II clinical trials in ovarian cancer and leukaemia. Our 5-year CRUK Small Molecule Drug Discovery Initiative Programme Grant (**Thurston**, 2008-2013, £2M) has discovered novel lead protein-protein and transcription factor inhibitors. Of these, a novel NF-κB inhibitor (TSG1301) is progressing to Phase I clinical trials through a new KCL-based spin-out company, Transcriptogen Ltd (**Rahman, Thurston**).

Medicines Development focuses on the ***formulation*** of medicines and the translation of ***drug delivery*** concepts to the clinic. One group (**Barlow, Chan, Dreiss, Harvey, Kudsiova, Lawrence, Mason**) focuses on understanding the physicochemical and biological properties of supramolecular, macromolecular, polymeric and colloidal systems through advanced analytical techniques. For example, **Dreiss** focuses on cross-linked polymeric gels for tissue engineering, and structural studies of the intermediates involved in protein amyloid formation. Work on membrane biophysics and antimicrobials (**Harvey, Mason**) has involved metabolomic profiling of microbes in response to challenge with antibiotic peptides, along with systematic studies of antimicrobial peptide-lipopolysaccharide interactions. **Chan** is applying Fourier transform infrared spectroscopy to monitor metabolic changes in whole cells. Research in membrane biophysics and surfactant systems (**Lawrence, Kudsiova**) has focused on the structural characterisation of non-viral vectors for the delivery of DNA and RNA, and other research is concerned with the mathematical and computational modelling of drug-membrane interactions (**Barlow**). Inventive research has to led to novel devices and formulations notably around topical drug delivery systems (**Jones**) and oral dosage forms (**Martini**). For example, Solaraze Gel™, currently marketed for the skin disorder *actinic keratosis* by MedPharm Ltd, a successful spin-out company, resulted from this research programme. New analytical methods (**Royall**) have enabled quality-by-design approaches in product formulation. The group is also designing delivery systems for new and established drugs for clinical trials with KHP. These include the formulation of a novel central blood pressure lowering drug (**Forbes, Martini**), the design of a rescue medicine for use in narcosis (**Forbes, Royall**), and a new patient-controlled analgesia medication (**Forbes, Whittlesea**). The study of ***nanomedicines*** ranges across all of these activities with formulations being developed for lung targeting (**Dailey, Forbes, Jones, Kudsiova, Lawrence Mason**), CNS targeting (**Begley, Thomas, Preston, Al-Jamal**), and anticancer applications and theranostics (**Al-Jamal, Mason, Lawrence, Kudsiova**). Examples include nanotoxicology (**Dailey**), CNS-targeted nanomedicines for sleeping sickness (**Thomas**), nanocarriers to deliver proteins/enzymes to the CNS (**Begley**), and the design and evaluation of carbon nanotubes as drug carriers and imaging agents (**Al-Jamal**). For ***inhaled medicines*** (**Jones, Dailey, Forbes, Spina, Page**) further inroads have been made into inhalation toxicology (*e.g.,* mechanisms of macrophage responses) and lung targeting (*e.g.,* pulmonary retention of inhaled medicines). Nanotechnological approaches are also key to our islet transplantation programme in diabetes (see below).

Medicines Use focuses on ***treatment adherence***, ***medication risk***, ***substance abuse*** and ***herbal medicines***, and the ***evaluation of psychotropic medicines***. The Anticoagulation Reference Centre (a joint venture led between KCL and the Thrombosis Centre, King's College Hospital) undertakes pharmacokinetic-pharmacodynamic modelling research to inform and refine national and international guidelines on the optimal use of novel oral anticoagulants (**Patel**). **Auyeung** and **Weinman's** pioneering work has identified key predictors of non-adherence to medicines and other recommended treatments as a basis for developing interventions which are

being tested across KHP and then commercialised in conjunction with Atlantis Healthcare. Our diabetes research programme (see below) also studies treatment compliance using unique approaches such as neuroimaging and psychological therapies (**Ismail, Amiel**). In the area of ***medication risk***, we investigate professional and patient factors, which play a role in the development of adverse drug events, such as the nature, extent and cause of dispensing errors (**Whittlesea**). Psychometrically valid models to predict the adverse effects of medicines in the elderly (**Davies**) and in neuropathic pain (**Cornelius**) are also being developed. We are also investigating potential health risks associated with Chinese herbal medicines (**Barlow, Hylands**). **Taylor** and **Weinman** focus on key stages in the use of medicines, from efficacy trials through to prescriber- and patient-factors, which can result in sub-optimal use and the misuse of medicines. **Taylor's** research centres on the efficacy and safety of psychotropic medication, informing the use of these medicines (see Impact Case). There is an on-going programme of research on the use of biomarkers of substance misuse in different populations (*e.g.,* high-risk drivers, smokers, those receiving methadone treatment including pregnant women) to aid assessment by healthcare practitioners (**Wolff**). Our work in high-risk drivers has resulted in a change in national policy for the re-licensing of high-risk drink drivers by the Driver Vehicle Licensing Agency (see Impact Case), and we contribute substantially to research for the DVLA recommendations around fitness to drive in diabetes (**Amiel, Choudhary**).

NUTRITION: Our overall strategy is to prevent and manage non-communicable diseases (*e.g.*, diabetes, obesity, hypertension, cardiovascular disease, gastrointestinal disease, anaemia and iron overload) through effective manage of diet and lifestyle with a specific emphasis on improving prevention, early detection and treatment in people of black ancestry. Our strategy is summarised below according to research themes.

The **Diabetes** theme brings together a multidisciplinary team of scientists, clinicians and psychologists to target improvement of outcomes in diabetes care, focussing on the causes and prevention of diabetes and its complications. We investigate cell biology, human metabolism and behaviour *in vitro* and *in vivo* to explore the pathophysiology of, and find better treatments for, two major diabetes-related problems: (1) treatment-related hypoglycaemia, and (2) the global pandemic of obesity-related diabetes and insulin resistance, of particular relevance to our local community. Inter-disciplinary work using neuroimaging to investigate hypoglycaemia unawareness pioneered by **Amiel** is now being applied to appetite control in insulin resistance, obesity and its treatments. Translational studies in hypoglycaemia prevention (see Impact Case) include: a) targeting the achievement of good glycaemic control (including improvement of pregnancy outcomes); b) preventing the vascular complications of diabetes through structured education (a major achievement from the last assessment period has been the development and on-going investigation of our structured education programme in Type 1 diabetes, DAFNE, now used by 30,000 UK patients); c) the use of novel continuous glucose monitoring technologies; d) the use of psychological techniques (**Ismail**); e) and islet cell replacement (**Amiel, Choudhary, Ismail, Pickup**). A programme of research concerned with glucose sensing (fluorescent biosensors) is also underway supported by EPSRC (**Pickup**) with the aim of developing a non-invasive glucose sensor. Work on beta cell biology investigates the function, growth and development of islets, and the potential for new therapies. An overarching aim is to improve the outcomes of islet transplantation (now an NHS-supported service for intractable hypoglycaemia) as a therapy for Type 1 diabetes using cell therapies (**Jones**, **King**) and the nano-encapsulation of islet molecules to inhibit clotting and immune responses (**Jones**, **Pickup**). This research is facilitated by access to the King's College Hospital Human Islet Isolation and Transplantation Unit (**Amiel, Choudhary**), and through collaborations with the KCL MRC Transplantation Centre, Liver Transplantation at KCH and Diabetes Immunology at Guy's Hospital. The strategic appointments of **Behrens** and **Bornstein** will strengthen the islet transplantation programme. **Behrens** will develop stem cell methodologies for generating functional beta cells/islets, and **Bornstein** will build on our nanotechnology expertise, including plans to incorporate new molecules into the islet coat and the use of oxygenated chambers (developed by **Bornstein** in Dresden) to protect islets in order to allow transplantation of minimal islet mass and to increase recipient numbers for clinical trials.

The beta cell biology group aims to identify novel therapeutic targets for Type 2 diabetes through genomic-wide profiling of G-protein coupled receptor expression in human islets (**Persaud**). The

identification of the kisspeptin receptor (GPR54), and its expression and function in β-cells, underpins the clinical investigation into the role of placental kisspeptin in gestational diabetes (**Bowe, Jones**), supported by the large local diabetic pregnancy services) and its potential use in enhancing islet survival.

Our strategic aim to enhance our focus on obesity and Type 2 diabetes is supported by ~2 million NIHR funding (RP-PG-0606-1142). This research on new-onset disease in our ethnically diverse local community (the South London Diabetes Study) includes a focus on the mechanistic interaction between depression and poorer outcomes in diabetes *via* inflammatory pathways, and on psychological therapies to increase therapeutic compliance (**Amiel, Ismail, Pickup**) and has potential global relevance. So far, this research has revealed a much higher prevalence of Type 2 diabetes in the black population and we are now engaged in phenotyping studies to understand their unique metabolic derangements, with a view to more personalised therapeutic approaches. The newly started NIHR-funded MOVE-IT study (**Ismail**, NIHR £2 million) will provide support to diabetic patients at high risk for cardiovascular disease. Insulin resistance and obesity research will be enhanced by the appointment of **Rubino**, an expert in the mechanisms underpinning the improvement in glycaemia following bariatric surgery, including the role of incretins, and our technical ability to examine the impact of bariatric surgery on beta cell function. We aim to further investigate the role of this surgical procedure in the prevention and treatment of Type 2 diabetes. On-going research in this area supported by the MRC (**Howard**; £505,392) relates to pathways of immune cell mediated inflammation in adipose tissue and their role in insulin resistance. Here, a major achievement has been **Howard's** demonstration that genetically modified mice deficient in the immune cell transcription factor T-bet have lower energy expenditure and increased visceral fat compared with wild-type mice, yet paradoxically are more insulin sensitive.

The **Diet and Cardiovascular Health** aims to develop effective lifestyle advice for the prevention of cardiovascular disease (see Impact Case). It investigates how diet and obesity can modify surrogate risk markers for cardiovascular disease (*i.e.*, blood pressure, lipid profile, metabolic syndrome and Type 2 diabetes, haemostasis and parameters of vascular function), as well as trying to understand the underlying physiological processes involved. Over the period of assessment this group, led by **Sanders**, has completed four randomized controlled trials of longer term dietary intervention in older men and women funded by the Food Standards Agency/Department of Health: RISCK (£579,876), DRFRUITNVEG (£463,176), MARINA (£1,169,325) and CRESSIDA (£908,210). The landmark study RISCK demonstrated that a reduction in saturated fatty acid (SFA) intake did not improve insulin sensitivity as previously believed, but showed favourable reductions in total cholesterol:HDL cholesterol by replacement of SFA with mono-unsaturated fatty acids (MUFAs) compared with carbohydrate (both high and low glycemic index forms). We have shown that endothelial function and pro-coagulant activity are more influenced by diet in the post-prandial phase, with implications for Type 2 diabetes complications. Importantly, the DRFRUITNVEG study (**Berry**) challenged the view that increasing potassium rich fruit and vegetables to five or more portions a day lowers blood pressure and improves vascular function. We are now investigating the effects on vascular function of compounds such a nitrate, polyphenols and sulforathane (**Siow**, BBSRC Case studentship BB/I532137/1) in green vegetables and vitamin D (**Sanders**, BBSRC Case studentship BB/I53267X/1). For example, **Siow** has identified mechanisms by which polyphenols and sulforathane influence endothelial cell function, and **Hall** has shown that isoflavones acutely affect endothelial function measured in human subjects *in vivo*. This work is being extended to polyphenolic material in fruit with Technology Strategy Board funding through GlaxoSmithKline. Our strategy is to continue investigating the effects of dietary modification on vascular function and blood pressure with increasing focus on the mechanisms of arterial stiffening. The recently completed CRESSIDA study, an integrated dietary approach to modify cardiovascular risk, comparing a diet conforming to dietary guidelines with a conventional UK diet, found a 4 mm reduction in ambulatory day systolic blood pressure and reduced arterial stiffness, as well as favourable changes in lipid profile and inflammation in men and women aged 40-70 years at average risk. These important results now form the evidence-base for integrated dietary advice.

KCL research strongly supported the advice to decrease salt intake, both in normotensive and hypertensive subjects, and especially in ethnic minorities with a focus on people of black ancestry. While obesity and physical inactivity impair sensitivity to insulin, our findings suggest that diet

composition exerts a smaller influence. **O'Dell** has identified a diet-gene interaction for adiponectin, an adipocyte-derived protein that plays a key role in insulin resistance, with the favourable effects of a high MUFA diet compared to a low fat diet particularly with increasing age. With the growing evidence that insulin resistance is more strongly affected by early life influences rather than obesity in adult life (see Early Life Origins of Disease theme below), we are addressing the impact of childhood and adolescent factors in modifying the risk of adult cardiovascular disease in people of black and Asian ancestry. The DASH study (**Cruickshank**) obtained information from >6,000 schoolchildren aged 11-13y, and 96% of these again at 14-16y, stratified to 5 major ethnic groups (European; Black Caribbean; Black West African; Indian; Pakistani/Bangladeshi) and is now studying the participants at ages 21-23y. Working with colleagues in Jamaica, **Cruickshank** found that formerly malnourished children show evidence of increased systemic vascular resistance and that maternal malaria in pregnancy results in increased blood pressure in the offspring, supporting the view that early malnutrition may 'programme' hypertension in later life.

The **Diet and Gastrointestinal Health** theme addresses how modification of the diet can manage gastrointestinal disease and improve gastrointestinal health. Coeliac disease (CD, or gluten-sensitive enteropathy) affects 1% of people in the UK, Europe and US, and KCH has a major treatment centre. **Ciclitira**, a gastroenterologist and authority on CD, is developing sensitive assays (including bioassays using biopsies from patients with CD) to detect coeliac toxic peptides and apply this information to the testing of foods suitable for patients with CD. The group has also identified novel microbiota in patients with Crohn's disease, and has shown that modification of gut microbiota may affect pouchitis. It has also discovered that dietary modification by exclusion of cinnamates and related compounds can result in symptomatic improvement in oro-facial granulomatosis. **Whelan** focuses on the effects of modifying the gut microbiota on gastrointestinal disease, including the first clinical trials of pre-biotics in the treatment of Crohn's disease, and on the low FODMAP (Fermentable Oligo-saccharides, Di-saccharides, Mono-saccharides and Polyols) diet for the treatment of irritable bowel syndrome. The basis of this diet is that restriction of foods containing carbohydrates that undergo colonic fermentation may relieve symptoms of irritable bowel syndrome. **Emery** focuses on protein turnover in patients with trauma and sepsis, and investigates nutritional support requirements in severely ill hospital patients. This has demonstrated a surprising lack of benefit of nutritional support (*e.g.*, sip-feeds) in hospital patients with cancer in a meta-analysis, consistent with the concept of "ebb and flow" in response to tissue injury. Colorectal cancer is now a leading cancer that appears to be related to diet, and **Emery** has been investigating the hypothesis that hypomethylation of DNA induced by folate insufficiency may increase the risk of developing the disease, while **Pott** has been investigating the effects of oily fish intake on apoptosis and mitosis in colonic crypts. **Ellis** is studying the bioaccessibility of nutrients from plant foods, in particular the effects of cell wall material (the physical structure of plants foods) on nutrient bioavailability in the gut and the effects on gut microbiota: the research supported by a BBSRC DRINC award (BB/H004866/1 394,663; and 3 case studentships BB/H531994/1, BB/L502650/1).

Metal Metabolism. This theme takes a multidisciplinary approach to study the nutritional and metabolic role of biometals, particularly iron, copper and zinc. The absorption and transport of these metals, present in food and water at low concentrations, are tightly regulated by a number of recently discovered proteins. Zinc (Zn) has emerged as the most prevalent metal co-factor present in at least 3000 human proteins, and it is only recently that Zn insufficiency has been recognised as a major nutritional global problem contributing to growth stunting and increased infant mortality from diarrhoeal disease, pneumonia and malaria. Supported by the BBSRC (BB/K001442/1 £347,029), NERC (£122,405), NC3Rs(£383,312) and the EU (F6 Programme), **Bury, Hogstrand** and **Maret** have made major contributions to the concept that Zn(II) ions control many aspects of signal transduction, and that perturbations in Zn homeostasis can have pathological sequelae. **Jones** and **Maret**, funded by Diabetes UK, are investigating the role of Zn in insulin target tissues and on insulin release. We also address the interactions of Zn with other metals (Ag, Cd, Cu, Hg, Zn), and how these may act as environmental stressors. **Bury** has also made advances into understanding the evolution of the glucocorticoid (stress) receptors (GR1, GR2) which are important regulators of metal metabolism (*e.g.*, the metallothioneins). An innovative model for the study of metal transport, a fish gill cell culture system (FIGCS), developed by **Bury** and

Hogstrand, has been used to identify zinc transporters. This system is undergoing adaptation to predict metal toxicity in natural waters and, potentially, as an alternative to animal toxicity tests to assess safety of pharmaceuticals and xenobiotics in the environment (supported by a BBSRC case studentship BB/J500483/1).

Iron deficiency and associated anaemia, as well as iron overload resulting from genetic disorders such as haemochromatosis or thalassaemia, are both global health problems. KCL researchers have been world leading in this area and have developed the iron chelator deferiprone for clinical use (**Hider**, Pharmacy recently retired – see Impact Case study), and have identified regulatory pathways for iron absorption and regulation. **Mckie** first identified ferroportin, the target of the hormone hepcidin and the only protein which stimulates iron efflux in cells, and **Bansal** (Pharmacy) has developed an assay for hepcidin. These researchers (**Bansal, Hider, Mckie, Sharp,** and Srai and Porter at UCL]) are now focusing on how hepcidin regulates iron homeostasis, and have been supported by BBSRC (£438,860, 206-11; £379,430, 2007-11; BB/J008060/1, £211,660, 2012-14), Wellcome Trust (£356,915, 2011-13), EU and industry (BASF, Shire Pharmaceuticals, Vifor) funding. Mouse models (dietary, mutant and knockouts) and *in vitro* cell culture systems are employed to identify factors involved in iron sensing to investigate how these factors influence hepcidin production. Using this approach, promising targets for hepcidin regulation have been identified including bone morphogenetic protein-binding endothelial cell precursor-derived regulator (BMPER), along with the transcription factor ATOH8.

Early Life Origins of Disease. This theme links all activities, particularly with regard to maternal and fetal nutritional status and established risk for raised blood pressure, obesity and Type 2 diabetes in children and in later life. The research programme focuses on understanding the aetiology and underlying mechanisms of reproductive dysfunction, obesity, risk of Type 2 diabetes and cardiovascular disease. The interaction of genes and the early life environment is a central focus, with particular reference to the impact of nutrition and metabolic states on both pregnancy outcome and early life origins of disease (funded by BBSRC case studentship BB/G01709/1, the British Heart Foundation and EU Framework 6 and 7 programmes). **Poston** and **Taylor** address the influence of maternal obesity on the offspring with regard to risk of obesity, diabetes and cardiovascular disease. Using a rodent model of overfeeding in pregnancy, KCL researchers have shown that the offspring become insulin resistant, obese, and hypertensive in adult life**.** Following a successful pilot, the UPBEAT trial (35% participants of black ancestry), which involves a diet and lifestyle intervention in obese pregnant women, has been rolled out into a national trial funded by NIHR (RP-PG-0407-10452; £2.1M). The trial aims to reduce the prevalence of maternal gestational diabetes and fetal macrosomia, conditions associated with increased risk of Type 2 diabetes in later life. Ongoing work includes an EU FP7 *EarlyNutritio*n Programme (**Poston** co-PI, 2012-2016, £930K) which focuses on the developmental origins of obesity, including a translational programme using the animal models, and a follow-up study of the metabolic health of children from the UPBEAT trial to assess the influence of maternal diet and obesity on metabolic risk in the child. Our research is relevant to our strategy to focus on health inequalities, especially among those of black ancestry who reflect our local population. Additional funding for follow-up studies of the cardiovascular health of UPBEAT children has been obtained (**Poston**, BHF PG 13/38/30289; £203K) and also for investigating, using biomarker approaches, determinants of maternal gestational diabetes in UPBEAT women and of obesity in their children (**Poston**, MRC; MR/L002477/1, £825,398K; 2014 start). **Coen** (BBSRC BB/H008845/1; £688,303) and **O'Byrne** (BBSRC grant BB/J002232/1 £741,012) investigate the societal, nutritional and hormonal influences *in utero*, and in early postnatal life, on offspring central regulatory pathways of energy balance and reproductive function. Interrogation of the pathways leading to offspring obesity has identified decreased satiety leading to greater food intake, associated with persistent changes in the neurocircuitry of the appetite regulatory centres of the hypothalamus. An important mechanistic role for high concentrations of leptin in early post-natal life has been identified as the origin of increased food intake and obesity in the offspring and in the development of hypertension through increased efferent sympathetic tone**.** These observations informed protocols in the UPBEAT child follow-up study. **O'Byrne's** research on puberty onset has provided insight into the precocious onset of puberty in obese females by demonstrating premature up-regulation of kisspeptin and NKB signaling in the hypothalamus, and the critical role of fetal exposures by demonstrating that an infective episode in pregnancy in the rat can delay puberty in the offspring**.**

Poston and **Sanders**, supported by the UK Big Lottery Fund, have demonstrated an independent association between dietary folate intake and fetal growth restriction in a prospective study of 500 adolescent pregnant teenagers of whom 35 % were of black ancestry. An intervention trial with Tommy's Charity (in Phase 1 of development) is now planned to determine whether folate supplements, if taken throughout pregnancy, can improve birth weight in teenage pregnancy and reduce metabolic and cardiovascular risk in the child.

The overarching goal of our **Pregnancy, Fetal Well-being and Childbirth** is to deliver new diagnostic tools, novel therapies and clinical management guidelines to improve overall outcomes for pregnant women, thereby improving the health of the next generation. A major focus is the detection of fetal abnormalities and medical problems that arise in pregnancy (*e.g.*, anti-phospholipid syndrome, pre-eclampsia, obstetric cholestasis, diabetes), as well as the management of pre-eclampsia, pre-term labour and dysfunctional labour. Advances in clinical management include refined tests for Down's syndrome, a new predictive test for pre-eclampsia (**Nicolaides**), a quantitative biomarker test for the risk assessment of spontaneous premature labour based on the measurement of cervical fetal fibronectin (**Shennan, Tribe**, with HOLOGIC), and a patented biomarker (Elafin) for the prediction of premature labour (**Tribe**). The PELICAN trial (**Chappell, Shennan**, with Alere Ltd) demonstrated that placental growth factor (PlGF) out-performs all current tests for diagnosis of severe pre-eclampsia (see Impact Case). An accurate blood pressure monitor suitable for use in pregnancy in resource-poor settings, trialled in rural Africa, for detection of pre-eclampsia has been developed (**Shennan**) (see Impact Case). **Pasupathy** has established that customised birth weight centiles rather than traditional birth weight centiles identify those infants large for gestational age at greater risk of adverse outcomes. SCOPE, an international consortium led by **North** (**Poston co PI)**, designed to develop new tests for prediction of the common adverse outcome of pregnancy (pre-eclampsia, intrauterine growth restriction and pre-term birth) has finished recruitment (5690 nulliparous pregnant), and has already led to >20 papers published. KHP are internationally recognised for research into adverse pregnancy outcomes associated with systemic lupus erythrematosus (SLE) and anti-phospholipid syndrome (APS). **Khamashta** has identified anti-phospholipid antibodies in pregnant women, and the appointment of Girardi (an international expert in fetal/maternal immunology and in animal models of the anti-phospholipid syndrome) will strengthen this work. **Chappell**, **Tribe** and **Williamson** research obstetric cholestasis, a disorder associated with adverse pregnancy outcome and premature birth. **Williamson** has identified a link between this condition and genetic variation in the genes encoding two biliary canalicular transporters responsible for efflux of bile acids and phospholipids. She has also provided the first evidence, using animal models and analysis of mother–child cohort data, that obstetric cholestasis has long-term adverse influences on the metabolic health of the child. The PITCH trial (**Chappell, Williamson**) provided the evidence base for a new multicentre RCT in obstetric cholestasis commencing in 2014 and will assess the potential benefit of ursodeoxycholic acid on pregnancy outcome (PITCHES, MRC/EME). Our clinical trials team has led or contributed to more than 20 studies during the assessment period, and these were studies facilitated by access to a socially deprived population of pregnant women, especially of black ancestry, in South London with high rates of pregnancy-associated complications.

C. People, Including:

i. Staffing strategy and staff development.

We aim to attract the best researchers by being national and global leaders in our various contributing disciplines, and by placing a strong focus on mentoring, support and career development. We describe common policies and practices in the Institute of Pharmacy and the Diabetes & Nutritional Sciences and Women's Health Divisions. In *Drug Discovery*, a key strategy of KHP has been to improve cancer detection and treatment, and one of the objectives has been to strengthen KCL research capacity in chemical biology and drug discovery in the area of cancer chemotherapy. To this end, we have made two professorial (**Phillips, Thurston**) and four other (**Al-Jamal, Chan, Rahman, Thanou**) appointments in the oncology area, and five early-career appointments in chemical biology **(Barry, Nunez, Orner, Rosta, Sanz**). In the *Medicines Use* area, we have also made a number of new appointments at professorial and other levels in the areas of *Health Psychology* (**Auyeung**, **Weinman**) and *anticoagulant use* (**Patel**). Another

strategic aim of KHP has been to build our capacity to address obesity and diabetes that have a particularly large impact on our local community, which contains a high proportion of individuals of black African descent. To this end we have made five strategic professorial appointments. **Cruickshank** will interrogate the diet and lifestyle aetiology of hypertension in people of African descent, utilising experience in African and Caribbean countries to address the high incidence of Type 2 diabetes and the increased cardiovascular risk in our ethnically diverse South London population. **Rubino** will focus on the mechanisms by which bariatric surgery in obese individuals can "cure" or prevent Type 2 diabetes. **Behrens**, a world-class developmental biologist, will facilitate collaborations with the beta cell biologists to develop methodologies for generating functional beta cells/islets to extend the clinical islet transplantation programme. The appointment of **Bornstein** will focus on translational medicine around cell replacement therapies in diabetes, and the involvement of the stress pathways in diabetes, obesity and their cardiovascular complications. **Whelan** will focus on evidence-based practice amongst dieticians in order to maximise application of research findings into dietetic practice. These appointments have been complemented by three early-career appointments (**Bowe, Harding, Pott**). A new centre of excellence, the KHP Women's Health Academic Centre (CAG), launched by the Chief Medical Officer (Dame Sally Davies) in 2011 brings together the KCL Division of Women's Health and clinical services in our partner KHP Trusts, creating a strategic alliance to streamline research outcomes to clinical practice, with an emphasis on recognising the importance of pregnancy outcome in determining the health of the next generation. New professorial appointments include **Williamson**, to lead our expanding maternal medicine research programme, and **Girardi**, to lead the investigation of the causes of adverse pregnancy outcome in women affected by SLE and anti-phospholipid syndrome.

Staff Development: There is a KCL-wide Staff Development Programme and annual appraisals, and interim reviews that identify specific training needs, which the College responds to by developing and holding specific courses, as well as by offering an annual programme. This programme offers a wide range of opportunities including Leadership and Management, a full Graduate Researcher Development Programme, and language and IT courses. Promotions are considered on an annual basis. The Researcher Development Unit in the Graduate School has responsibility for the provision of central training and development for post-doctoral research staff, postgraduate research students and PhD supervisors. Academic Clinical Fellows (ACFs) benefit from the Integrated Academic Training Course (IAT) supported by the STEM (School of Translational and Experimental Medicine) cluster of the KCL/GSTT BRC, and from a range of courses in research design and management.

Early Career Researchers (ECRs): As outlined above, a large number of our academic appointments have been relatively junior staff. We have an active policy and very good track record of nurturing postdoctoral ECRs towards research fellowships and subsequent independent academic careers in the physical, biomedical and clinical sciences. Early career staff members are provided with start-up funds on appointment, given a light teaching load, and are mentored by an experienced member of staff. They are encouraged to take on the supervision of PhD students in partnership with experienced staff members. KCL adheres strongly to the principles outlined in the Concordat. All PIs are strongly encouraged to promote the careers of postdoctoral researchers, for example through developing independent areas of research, building-up collaborations, and involvement in teaching, management and decision-making.

Equality and Diversity: KCL recognises that *equality of opportunity*, and the recognition and promotion of *diversity*, are integral to its academic and economic strengths. Key principles are: to promote equality of opportunity in all areas of work; to develop the diversity of skills and talents within our community; to ensure that existing and prospective staff and students are treated solely on the basis of merit, ability and potential without any discrimination related to age, disability, gender, marital status, pregnancy, maternity, race, religion, sexual orientation; to provide and promote a positive working, learning, and social environment free from prejudice, discrimination, harassment, bullying or victimisation; and to promote good relations between individuals from different groups. These principles are followed in all areas of work including recruitment, grading of posts, promotions, and appointments to positions of responsibility. Recruitment and other

panels reflect diversity in gender, experience and expertise. KCL provides a wide range of strategic programmes and networks to promote equality of opportunity and achievement. Examples include 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. One third of the staff returned are women, and the retention of female scientists and researchers, and the adoption of Athena Swan principles, is one of our key priorities (KCL has recently been accredited to Athena Swan Bronze status). This starts at the time of recruitment where we ensure that interview panels have appropriate female membership. There is a significant emphasis on a family-friendly work environment (*e.g.*, the timing of meetings and seminars, policies on flexi-working, *etc*). We believe that visible female role models (*e.g.*, **Amiel**, **Ismail, Lawrence, Persaud, Poston**) are very important in inspiring and guiding younger female scientists. We encourage research staff to apply for career development awards, and have been successful in gaining an MRC Career Development Award, 2 NIHR Clinical Training Fellowships and an NIHR Allied Health Professional Fellowship (all women), as well as two NIHR Clinical Lectureships (one starting in 2014). Three female NIHR Academic Clinical Fellows have recently been appointed to Women's Health.

Integration of Clinical Academics and NHS-Employed Active Researchers: The creation of KHP has enabled formal alignment of KCL Research Divisions with relevant clinical services in the partner Trusts. This allows "bench to bedside" Clinical Academic Groupings (CAGs) to facilitate the rapid transfer of new scientific knowledge toward clinical practice and service delivery policy and practice. This strategy is underpinned by two NIHR Comprehensive Biomedical Research Centres (BRC) at KCL/GSTT, and at the KCL Institute of Psychiatry. In addition, the BRC support GMP/GCP-compliant Clinical Research Facilities on all of the major hospital campuses, and our UKCRC-registered KHP Clinical Trials Unit and the KHP Clinical Trials Office (JCTO) support all clinical trials. For our research groups, there is specific additional benefit in closer links with successful (in terms of outcomes) clinical services supporting large cohorts of people with relevant conditions, such as pregnancy, diabetic pregnancy, hypoglycaemia-prone Type 1 diabetes, bariatric surgery and endocrine cancers. KHP are major tertiary referral centres for diabetes (especially problematic Type 1), liver disease, mental health, coeliac and inflammatory bowel disease including oro-facial granulomatosis, for pregnant women affected by Lupus and APS, and for those at risk of pre-term birth or pre-eclampsia. KHP is unique, with CAGs in Pharmaceutical Sciences, Diabetes, Obesity and Nutrition and in Women's Health, which bring together basic scientists, dieticians, midwives, pharmacists, clinical pharmacists and medical practitioners. In addition, the close association with KHP has led to the creation of a range of new honorary clinical academic positions for Trust employees (*i.e.*, 6 Professors, 4 readers, 10 senior lecturers and 16 lecturers), providing appropriate recognition and status, and increased access to clinicians for research and teaching.

ii. Research students

All staff members undergo regular training in research supervision, and each student is allocated a first and second supervisor. A comprehensive research and postgraduate training portfolio across the Health Schools is organized and coordinated through the Research Divisions. KCL has excellent PhD completion rates (91.6%; HEFCE 2013) and graduate employment rates (94%; HESA 2011/12). The College has a Graduate School that provides opportunities for students to broaden their horizons and acquire transferable skills. All PhD students are first enrolled on an MPhil course, and are expected to complete transfer to PhD within the first year. Postgraduate tutors are in place to support and monitor PhD/MD Res student progress, and to ensure that reports are signed off on a timely basis using a College-based on-line reporting system. Individual research groups organise journal clubs, and peer review protocol development and data analysis plans. Clinical research fellows funded by the BRC/NIHR are supported by a STEM cluster training programme which includes advice on fellowship applications. There are regular research seminars organised by the Institute of Pharmaceutical Science, the Diabetes & Nutritional Sciences Division and by Women's Health, as well as by the BRC Biomedical Forum, and a programme of lectures organised by the KCL/GSTT-BRC with outstanding external lecturers. The Library Services allow access to over 25,000 electronic journals and 600 databases. The library

also contains over 1.25 million books, as well as historical collections of nutrition and pharmacy journals, and there is support by information specialists who provide training on information retrieval and management, including bibliographic software (EndNote) and data management and analysis (SPSS, SAS). Annually, a graduate symposium is organised in the summer to allow postgraduate students to showcase their research. The Graduate School also makes funds available for students to present their research findings at national and international conferences. The reporting scheme for PhDs is designed to ensure that all full-time students complete within 4 years of registration, and that interruptions in study due to maternity leave are taken into account. In nutrition, 6 BBSRC Case studentships have been awarded with partners in the food (Tate & Lyle, Premier Foods) and pharmaceutical (GlaxoSmithKline, AstraZenica) industries in addition to a Diet and Health Research Club-BBSRC award. Grants are also available for PhD students to spend time working in one of King's seven strategic partner universities around the world including UCSF, Chapel Hill North Carolina, Renmin University, University of Sao Paulo, JNU Delhi, National University of Singapore and Hong Kong University. Over the period of assessment, 194 doctoral awards have been made.

D. Income, Infrastructure and Facilities

Over the period of assessment, research spend through KCL (REF 4b + 4c) has been ~£50 million. Annual research expenditure has been maintained despite the global economic downturn and is now on an upward trajectory. The main sources of our grant income are from the Research Councils, UK Central Government and charities, but we also receive substantial funding from industry and the European Union Framework Programmes. In addition to the income shown in **4b** and **4c** of the REF Return, we have benefited from NIHR project funding of £6 million channelled through the NHS, as well as support from the NIHR Centres. The value of new awards in the year ending 31 July 2013 was £7.3 million. Our current portfolio with BBSRC includes 9 doctoral training grants and £2,835,196 in project grants. In Pharmacy, recent successful consortium grants include: MRC (**Forbes**, **Page** and others: £654,643, to study the safety and kinetics of inhaled particles), MRC (**Dreiss**, **Thomas** and others: £841,859, to study sleeping sickness treatments) and EU FP-7 (**Forbes** and colleagues in Dentistry: £1,153,401, to study improved microbicide formulations). In Nutrition and Women's Health, recent awards include MRC (**Poston**, MR/L002477/1, £825,398K; 2014 start), EU F7 (**Nicolaides**, ASPRE trial; ref 601852, €5,839,800, 2013), NIHR HTA (**Shennan**, a pre-eclampsia clinical trial, Ref 12/25/03, £1.7M), Bill and Miranda GATES Global Development Grant for blood pressure monitoring in pregnancy (**Shennan;** Number OPP1086183 2013, $IM USD) and EU FP-7 *EarlyNutrition* (**Poston**; 2012-2016, £930K).

KCL recently acquired **Britannia House**, an ex-AstraZeneca facility adjacent to the Guy's Campus, to provide state of the art laboratories for the drug discovery activities (*e.g.,* chemical synthesis, molecular biology and cell culture suites). It also houses a Category 3 facility, one of only three in London. This will support our strategy for strengthening chemical biology and drug synthesis. A new *Anticancer Drug Discovery Initiative* has been established in Britannia House to combine the drug discovery activities of the **Thanou**, **Rahman** and **Thurston** groups, with the cancer biology and clinical oncology activities of Professors Peter Parker and Andrew Tutt in the Integrated Cancer Centre at KCL (Guys Campus). For drug discovery research, the NMR facilities include 400, 500 and 750MHz spectrometers, and there are BiacoreTM, X-Ray Crystallography and molecular modelling facilities on the Guy's campus.

Extensive mass spectrometry facilities are available in the **Franklin-Wilkins Building(FWB)** where the **Mass Spectrometry Centre** offers access to Liquid Chromatography–Mass Spectrometry (LC-MS), Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS), LC-MS/MS/MS, Matrix Assisted Laser Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF), Surface-Enhanced Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (SELDI-TOF), Gas Chromatography/Mass Spectrometry (GC-MS), Negative Chemical Ionization GC-MS and isotope ratio mass spectrometers.

Laboratories in FWB, St Thomas' and Guy's and King's College Hospital Campuses are modern and well-equipped with basic items such as centrifuges, spectrophotometers, safety cabinets, fume hoods, cell culture and minus 80°C storage facilities with emergency backup power. The laboratories in FWB also provide access to specialised equipment for cell counting (5-channel

Fluorescence-activated cell sorting, FACS), confocal microscope imaging, cell culture and a range of analytical equipment including rheometers, 2-D electrophoresis with automated spot picker and an ILAB 650 chemistry analyser. There are also facilities for radioisotope working (gamma and scintillation counters) as well as a dedicated Radioisotope suite. The **Genomics Centre** in FWB is equipped for high throughput sequencing analysis for gene methylation, high throughput real-time PCR, gene expression (Affymetrix™ and custom arrays), and siRNA analyses, and also organises hands-on training for research staff and students. There is also bioinformatics support through a full-time bioinformatics officer, and also access to facilities at the GSTT/KCL/BRC Genomics Centre. The KCL proteomics centre provides access to state-of-the-art mass spectrometry (*e.g.,* ORBITRAP) and technical expertise. A central Microscopy Unit offers comprehensive electron microscopy services. Specialist in-house facilities include multi-modal spectrometers, solid-state NMR spectroscopy, rheometers, infrared imaging, distributed computing systems, and light scattering. KCL is also a partner in the new **Francis Crick Institute**, a world-leading scientific research institution in central London focusing on understanding the underlying causes of health and disease, and in accelerating discoveries from the laboratory into the clinic. We also have access to Central X-ray, neutron and high power laser facilities, and extensively utilise those at the Rutherford Laboratories (evidenced by Office of Science Technology time valued at £4.26M over the census period).

The **Biological Service Unit** has facilities for research on marmosets, normal and transgenic rodents, as well as an aquarium system for fish and *Xenopus*. There are also facilities for measuring energy expenditure and activity in rodents (CLAM; **Taylor**), for remote blood pressure and temperature measurements (radiotelemetry, **Taylor**) and for investigating the effects of hypoxia on iron metabolism (hypobaric chamber, **McKie**). KCL researchers (**Keeble**, **King**, **Nandi**) have contributed to the MRC/BBSRC capacity building initiative in Mammalian Biology.

Research on human tissues is supported by a human islet isolation facility at King's College Hospital, which supplies islets for research studies. Laboratories in the Rayne Institute at St Thomas' Hospital allow for the collection and rapid processing of gastrointestinal biopsies for research investigation. Facilities for conducting research on human subjects are provided across KHP, and include a Metabolic Unit, purpose-built for human feeding studies, and state-of-the-art clinical research facilities (CRFs) which provide services to measure vascular function, insulin sensitivity, visual function, body composition and cognitive function on each of the hospital sites. Specialist clinics in premature birth, lupus pregnancy and diabetes provide unique research focussed clinical environments. Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) facilities for brain imaging are also available within KHP.

A NIHR-accredited Clinical Trials Unit supports clinical trials. Specialised facilities for Phase I oncology clinical trials are in place in the Integrated Cancer Centre (Guy's Campus). Statistical support is provided by a full-time statistician (**Seed**), as well as by statisticians in the KHP Clinical Trials Office. Extensive use is made of the CPA-accredited laboratories at Guy's and St Thomas' Hospital and at King's College Hospital Trusts (Harrington and Sherwood). The Women's Health Division hosts a commercial partner, MedSciNet UK, which provides data solutions to clinical trials. The College has policies on research governance covering research ethics approval, the Human Tissues Act and safety issues such as radioisotopes, biotechnology, risk assessment and occupational health for staff and students, as well as good practice in research. Procedures are in place to ensure compliance with the MHRA regulatory framework, and provision is made for data archiving. Procedures exist for complaints of research misconduct and protection of the anonymity of whistle-blowers. KCL Business and Innovation supports commercialisation of research assets associated with intellectual property generated by researchers.

E. Collaboration or Contribution to the Discipline or Research Base

Industry-Academia Partnerships have been realised through numerous Industry-CASE, Technology Strategy Board, and Knowledge Transfer Schemes with companies such as Archer Daniel Midland, GlaxoSmithKline, MedPharm, Medtronics, Melbourn Scientific, NovoNordisk, Pfizer, Premier Foods, Prosonix, Reckitt Benckiser, Unilever and Vifor. Other industry-academia links include the creation of an industry-academia Open Innovation Network for inhaled medicines

development. KCL researchers collaborate both internally (across the multiple campuses) and externally, both nationally and internationally as illustrated below:

- On-going collaborations in China, funded jointly by the Royal Society and the Chinese Academy of Sciences, have led to the establishment of a King's Centre for Integrative Chinese Medicine (**Hylands** with colleagues in Medicine).
- A strategic link with the Department of Bioengineering and Therapeutics at UCSF in the US, has initiated a joint PhD programme in Pharmaceutical Sciences, alongside faculty and student exchanges (**Hylands, Page**).
- A long-standing collaboration with researchers at the National Cancer Institute (NCI) in the US has led to the NCI to fund and oversee both Phase I and II clinical trials in the US of a novel DNA sequence selective agent, SJG-136, discovered and developed in the **Thurston** laboratory.
- **Long** has research collaborations with the National Marine Institute of Australia and a number of Australian Universities to study the extraction of novel compounds with sun-screen activity from organisms associated with the Barrier Reef.
- KCL diabetes researchers led by **Amiel** participate in international collaborations to improve insulin delivery systems and are part of the international JDRF Artificial Pancreas Program.
- Significant collaborations in diabetes include the MRC Transplantation Centre, the Institute of Psychiatry's Centre for Neuroimaging Sciences, the PET Imaging Centre (for brain imaging and glucose sensing and the UK Islet Transplant Consortium (including Newcastle, Oxford and Manchester). A Pancreas- and Islet-Transplantation-Program with the University of Dresden is planned following the appointment of **Bornstein.**
- The Diet and Cardiovascular group led by **Sanders** collaborates with the British Heart Foundation Centre and the NIHR Comprehensive Biomedical Centre at Guys and St Thomas' Trust for the measurement of vascular function. The RISCK investigators (Reading, Surrey, Imperial, Cambridge, King's) exemplify another active collaboration.
- **Cruickshank** has an active programme of research with the University Accra and the Tropical Medicine Research Institute (Jamaica) on the developmental origins of hypertension.
- **Ciclitira** is involved in collaboration with the Waksman Institute Rutgers University, USA and European investigators in Spain and Italy in developing new tests for coeliac toxic peptides.
- **Whelan** holds a visiting Chair at Monash (a KCL strategic partner), and has a collaborative programme of research on the management of irritable bowel disease.
- The **Metal Metabolism group** forms the hub of the London Iron Metabolism Group which involves collaboration with Oxford, UCL, Cambridge), Australia, Europe and the USA.
- The EU *EarlyNutrition* programme brings together KCL researchers (**Poston**, **Taylor**) with the MRC Metabolic Diseases Unit (Cambridge), the MRC Lifecourse Epidemiology Unit (Southampton), the University of Munich, Abbott Nutrition, the University of Dublin and the University of Adelaide. (http://www.project-earlynutrition.eu).
- The SCOPE collaboration led by **North**, between six universities worldwide is developing algorithms to predict pregnancy outcome (http://www.medscinet.net/scope/).

Examples of Contributions to the Discipline and Research Base

Al-Jamal received the Royal Pharmaceutical Society Science Award at the 2012 APSGB conference.

Amiel chairs the panel revising guidelines for the management of Type 1 diabetes in adults for NICE, and of the European Federation for the Study of Diabetes, China Diabetes Society & Lilly research programme. UN/UNESCO Helmut Mehnert Prize 2009, Diabetes UK's Banting Memorial Prize 2013.

Barlow is Chairman of the Large Scale Structures Facilities Access Panel at the Science and Technology Facilities Council (STFC).

Bornstein is Councillor of the European Society of Clinical Investigation, Member of the German Academy of Sciences (Leopoldina).

Chappell is Editor of PLoS Medicine, and NIHR HTA Board Member (2013-).

Ciclitira is a member of the WHO Codex Alimentarius, and commissioned by the American (2001-2012) and British Societies of Gastroenterology (2000-2012) to write the guidelines for the management of coeliac disease.

Hogstrand is a member of the European Food Safety Authority Scientific Committee, and Vice-Chair of the *FEEDAPP* Panel.
Houslay is Editor-in-Chief of the journal *Cellular Signalling*, and Editor of the *British Journal of Pharmacology*.
Ismail was awarded three prizes in the Integrated Care Winner Quality in Care Awards 2011, a Gold Award for the best community initiative; a Silver Award for best integrated care and best for Health Inequalities.
Hylands is a member of the Expert Advisory Groups on Herbal Medicinal Products of the British Pharmacopoeia Commission and of the Medicines and Healthcare products Regulatory Agency. He is a specialist assessor for the Austrian Ministry of Science natural product research program, and a Senior Scientific Adviser to the Chinese Academy of Medical Sciences for medicinal plant development.
Lawrence is Chief Science Advisor of the Royal Pharmaceutical Society, Science Chair for the 3rd APS UK PharmSci Conference (2012), and awarded Eminent Fellow of APS and Fellow of Royal Pharmaceutical Society.
Long is an Expert Advisor to the UK Government on antibiotic use and resistance;
Maret is Editor-in-Chief of the journal *Metallomics*.
Martini was President of the European Industrial Pharmacists Group (www.eipg.eu) from 2007 to 2013.
O'Byrne is President of the British Society for Neuroendocrinology, and Council member of the International Neuroendocrine Federation.
Page is an Editor of *Pharmacology Reviews* and the *Handbook of Experimental Pharmacology*, and was a recent Editor-in-Chief of *Pulmonary Pharmacology & Therapeutics* (until 12/12). He was chair of the Society of Biology Animal Science Group (until 12/12), Chairman of the Babraham Institute's Babraham Biotechnology Ltd Trustees Joint Board, and was awarded President's Medal from the Society of Biology (2012).
Poston is a NIHR Senior Investigator, Fellow of Academy of Medical Sciences, and MRC Board Member (PSMB), BBSRC Committee A Pool member 2010-2013; RCOG- Chair of Research Committee and President Blair Bell Research Society. Member of Council of the International Society for the Developmental Origin of Disease, Steering Committee Early Nutrition Academy, NICE Guidelines PHAC committee - Weight Management Before, During and After Pregnancy.
Rubino is a member of the International Diabetes Federations Task Force for guidelines for bariatric surgery for obese Type 2 diabetes.
Sanders was a member of the WHO/FAO Joint Expert Consultation of the Role of Fats and Fatty Acids in Human Nutrition 2008, Member of the Scientific Advisory Panel of the Global Dairy Platform, Trustee and Scientific Governor of the British Nutrition Foundation. He chaired the British Nutrition Foundation Task Force Report on *Nutrition and Development: short- and long-term consequences on health.*
Shennan chairs the National NIHR Reproductive Health & Childbirth (RH & C) Specialty Group; Member of the WHO Technical consultation group on pre-eclampsia (2013); expert advisor to the NICE Hypertension Guideline development group (2009), Scientific Committee European Society of Hypertension: Consensus group on home BP monitoring. Top prize winner in the NHS 2013 Innovations Awards.
Taylor is Editor-in-Chief of *Therapeutic Advances in Psychopharmacology,* pharmacology lead for the NICE Guideline group (CG 91; Depression in chronic physical health problems).
Thurston is Editor-in-Chief of the Royal Society of Chemistry's *Drug Discovery* book series, and a recent Senior Editor of *Future Medicinal Chemistry* (until 3/13), awarded Fellowships of the Royal Pharmaceutical Society and the Academy of Pharmaceutical Sciences.
Tribe is a Member of Council of the Physiological Society.
Whelan received the David Cuthbertson Medal from the Nutrition Society (2012) and was a member of the International Life Sciences Institute (ILSI Europe) Expert Panel on Prebiotics.
Wolff is member of the Secretary of State for Transport Honorary Medical Advisory Panel on Alcohol, Drugs and Substance Misuse & Driving (2007 – ongoing), Substance Misuse Skills Consortium: Research and Evidence Work Group, and the National Treatment Agency (2011-2013). She has also Chaired the Department for Transport's (2013) Expert Panel on Drug Driving.