UNIVERSITY OF BIRMINGHAM

# Job description

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| **Post title and post number** | Clinical Lecturer in Endocrinology and Diabetes - 1009 |
| **Organisation advertising Description** | School of Clinical and Experimental Medicine<br>College of Medical and Dental Sciences |
| **Post number** | 1009 |
| **Full-time/Part-time** | Full time |
| **Duration of post** | 5 years or 6 months following completion of CCT |
| **Post is open to:** | Internal and external candidates |
| **Grade** | AC |
| **Salary** | £30,992 to £53,663 a year |
| **Terms and conditions** | Clinical Staff |
| **Closing date** | 17 May 2013 |

## Job summary

This HEFCE funded Clinical Lecturer in Endocrinology & Diabetes post is available for 5 years or until CCT plus 6 months (whichever is sooner). The post provides the opportunity for higher and advanced sub-specialist training in endocrinology & diabetes alongside pursuing an academic research career and contribution to teaching in the endocrine specialist module of the established teaching programmes (MBChB, BMedSc, MRes). The clinical duties of the post will rotate between the Queen Elizabeth Hospital, University Hospital Birmingham NHS Foundation Trust (UHBFT), and Birmingham Heartland's Hospital, Heart of England NHS Foundation Trust.

The postholder will have responsibilities for the care of inpatients and outpatients with the full range of endocrinology & diabetes and general medical problems, and teaching and assessment of medical students and postgraduate students.

Research & Teaching is a key component of these lecturer appointments with 50% of the timetable allocated for this purpose. It is anticipated that the successful applicant will undertake a programme of research in line with the current research interests in the Centre for Endocrinology, Diabetes and Metabolism (CEDAM; http://www.clinexpmed.bham.ac.uk/research/cedam.shtml) within the School of Clinical and Experimental Medicine, College of Medical and Dental Sciences, University of Birmingham. CEDAM houses a significant number of internationally and world leading researchers and has one of the nation's leading track records at obtaining prestigious fellowships by major funders, including clinician scientist and senior clinical research fellowships by MRC and Wellcome Trust.

The College houses state-of-the-art technologies and expertise to facilitate the research career of the successful applicant. These include the £28M Institute of Biomedical Research, with access to core technologies including DNA sequencing, proteomic and metabolomic facilities, and advanced imaging facilities. In addition, the Centre for Endocrinology, Diabetes and Metabolism (CEDAM) has state-of-the-art facilities for laboratory research, including realtime platforms, metabolomics, and a steroid mass spectrometry core unit.

The Wellcome Trust Clinical Research Facility (WTCRF) at QEHB provides a broad range of clinical research facilities including dedicated inpatient and outpatient accommodation, staffed by trained personnel and soon to be linked to an HTA approved tissue bio-repository. The WTCRF includes a state-of-the-art metabolic, DXA for body composition/bone density assessment, and exercise and energy metabolism diagnostic equipment that is partly housed in a WTCRF satellite in the School of Sports & Exercise Sciences. The WTCRF also comprises a paediatric satellite in the Birmingham Children's Hospital and a recently launched mobile research facility, the Health Research Bus, for outreach to the community. The University of Birmingham Human Biomaterial Resource Centre is a state-of-the-art Biobank facilitating translational research; HBRC is immediately adjacent to the WTCRF in the same building as the recently opened gene therapy and cell based therapy pharmacy. The Birmingham Clinical Trials Unit is one of the largest in the UK and provides access to essential skills (statistics, trial design, randomization and outcomes) for clinical trial activity, supported by world class clinical trialists at the University of Birmingham.

## Main duties

| A | ACADEMIC | % (of academic time) |
|---|---|---|
| 1. | Individual and Group Research Projects<br>• To perform clinical and/or laboratory based research studies complementing the academic activities of the Centre for Endocrinology, Diabetes and Metabolism.<br>• Attendance at research group meetings and the weekly seminar programme at the Centre for Endocrinology, Diabetes and Metabolism is anticipated. | 55 |
| 2. | Analysis of data from experimental models and subsequent presentation and publication<br>• To apply statistical methods to analyse scientific study data.<br>• To prepare study findings in a format appropriate for speech or poster presentation.<br>• To write research papers based on the findings of the studies performed in a format appropriate for publication in scientific and medical journals. | 10 |
| 3. | Participate in writing grant and research ethics application<br>• To prepare applications to the Research Ethics Committee for the approval of proposed studies.<br>• To prepare grant applications for the funding of proposed future studies, to bodies such as the Medical Research Council and the Wellcome Trust. | 20 |
| 4. | Contribute to undergraduate and post graduate teaching programmes for a variety of courses including the MB ChB, BMedSc and BDS courses | 15 |

| B | CLINICAL | |
|---|---|---|
| | 50% w.t.e. as clinical registrar in Endocrinology & Diabetes at the Queen Elizabeth Hospital, University Hospital Birmingham BHS FT, or Birmingham Heartland's Hospital, part of the Heart of England NHS FT.<br>It is anticipated that the Clinical Lecturer will rotate across the two sites, probably annually with other Clinical Lecturers in Endocrinology & Diabetes, to provide maximal clinical experience. | |

**PROPOSED JOB PLAN**

The exact timetable will provide 50% research and teaching time (including undergraduate teaching in SGTs and occasional lectures) and 50% NHS service (including bedside teaching).

CEDAM includes four academic clinical lecturers in endocrinology & diabetes, with two at UHB FT and two at HEFT at any given time. This facilitates cross-cover between the two lecturers located at the same site, thereby securing cover for the academic time allocation (50%). The exact split (week by week, month by month) will be agreed jointly by the two lecturers with the academic lead mentor, Prof Wiebke Arlt (Head of CEDAM), and the clinical educational supervisors.

**DESCRIPTION OF CLINICAL COMPONENT OF THE PROGRAMME**

The post attracts academic specialist trainee status (academic NTN), with the clinical components of training being delivered in rotation across the University Hospital Birmingham (UHB) NHS FT and Birmingham Heartland's Hospital, Heart of England NHS Foundation Trust (HEFT).

Clinical placements will be determined in discussion with the West Midlands Higher Speciality Training Committee for Endocrinology & Diabetes, currently chaired by Dr Sailesh Sankar (email: sailesh.sankar@uhcw.nhs.uk) and will provide all the necessary training requirements in endocrinology & diabetes and in general internal medicine, when appropriate. Unless there are exceptional circumstances, the lecturer will undergo rotation around endocrinology & diabetes training posts within the Queen Elizabeth and Birmingham Heartland's Hospital in Birmingham only. This is unlike other specialist trainees in endocrinology & diabetes who may rotate to hospitals much further afield including North Staffordshire, Coventry, Wolverhampton, Hereford and Worcester.

On call duties will be shared between the lecturers, the duties of two lecturers similar to the work load of one specialist registrar whilst at QEHB or Heartland's, and are resident at both sites.

**Status**

The post is non-resident. Accommodation may be available at these hospitals although this cannot be guaranteed.

**Out of Hours commitment**

The basic working week is 40 hours. In addition, the postholder will be expected to undertake out of hours on-call commitment that will vary depending on the duties of the post, but will not exceed the limits defined in the Terms and Conditions of Service paragraph 20.

**UHB Rotation – Clinical Lecturer posts 1 and 2**

The Queen Elizabeth Hospital is the main teaching hospital of University of Birmingham College of Medical and Dental Sciences with which it shares a campus. It houses Endocrinology & Diabetes, which provide the full range of adult endocrine services at the secondary and tertiary care level, including a significant number of general and specialist endocrine and diabetes clinics (see weekly plan below). Alongside are a range of other secondary/tertiary care services including Surgery, Renal Medicine, Hepatic Medicine, Radiotherapy and Oncology, Rheumatology, Haematology, Neurology and Neurosurgery, ENT Surgery, Ophthalmology and Transplantation, Vascular Surgery, Respiratory Medicine, Care of the Elderly, Accident and Emergency and Trauma. The new Queen Elizabeth Hospital Birmingham recently opened in June 2010 and represents a single, £545m facility.

Queen Elizabeth Hospital, University Hospital Birmingham NHS Foundation Trust (Endocrinology: Professors JA Franklyn, PM Stewart, W Arlt, Drs N Gittoes, A Toogood, M Cooper, J Ayuk, JW Tomlinson, K Boelaert; Diabetes: Drs J Webber, W Hanif, P Narendran, S Ghosh, M Saeed).

Local meetings at the Queen Elizabeth Hospital include Grand Rounds, clinical audit, clinical endocrinology & diabetes and research seminars.

The Lecturers in posts 1 and 2 based in UHB Trust will be expected to rotate through "blocks" of clinical training opportunities in endocrinology/diabetes, each lasting four months. There are 4 NHS SpR posts and 2 Clinical Lecturers who together fulfil one attachment, typically working clinically alternate weeks to allow commitment to research and teaching, though different splits are agreeable.

**Block 1: Speciality Diabetes** – Antenatal, Foot, monthly multidisciplinary (e.g. renal adolescents etc). and involvement in the reproductive endocrinology clinic. This post will be involved in improving care of in-patients with diabetes.

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| Monday | am | **Reproductive Endocrinology clinic (weekly)** |
| | pm | **Diabetes Complications clinic (weekly)** |
| Tuesday | am | **Antenatal diabetes (weekly)** |
| | pm | In-patient diabetes referrals |
| | | 5-6 pm, **Clinical Endocrine Meeting** |
| Wednesday | am | **Foot clinic or renal clinic (weekly)** |
| | pm | **1**-2 pm, **Clinical Diabetes Meeting**; Admin/Audit/research |
| Thursday | am | Grand Round 1-2 pm, **Speciality diabetes** (adolescent, lipid, renal, pre-natal) |
| | pm | **Type 1 diabetes clinic (weekly)** |
| Friday | am | In-patient diabetes referrals |
| | pm | **Monthly ED clinic** /Admin/Audit |

**Block 2: Speciality Endocrine** –This post will be involved in **care of inpatient endocrinology and endocrine referrals across UHBFT** covered by the consultant endocrinologist on call. This will involve **weekly supervision of day case and in patient investigations** such as ITT's, water deprivation tests and preparation of cases for the Tuesday 5 pm clinical endocrine meeting.

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|---|---|---|
| Monday | am | **Thyroid clinic (Prof Franklyn)** |
| | pm | **Late effects clinic (Dr Toogood)** |
| Tuesday | am | **General Endo (Dr Ayuk)** |
| | pm | Admin/Audit**; 5-6 pm, Clinical Endocrine Meeting** |
| Wednesday | am | **Pituitary clinic (Dr Ayuk)** |
| | pm | **Thyroid cancer (Prof Franklyn) Fortnightly** |
| Thursday | am | **Bone clinic/Osteoporosis (Dr Gittoes)** |
| | pm | Grand Round 1-2 pm, Admin |
| Friday | am | **Growth hormone clinic (Dr Toogood)** |
| | pm | Admin /Audit |

**Block 3: General Medicine.** At any time 2 of the 5 posts will be attached to this block covering **in-patient medicine in the New Queen Elizabeth Hospital.** With weekday/night on calls often only 1 SpR will be available for ward cover. Rather than full ward rounds they will focus on reviewing new patients, sick and complicated patients and those needing input to facilitate discharge.

**BHH Rotation – Clinical Lecturer posts 3 and 4**

Birmingham Heartlands Hospital, Heart of England NHS Foundation Trust (Prof AH Barnett, Prof M Stevens, Drs A Bates, P Dodson, P Dyer, A Jones, W Malik, M Clarke, A Kamal, A Rahim, J Shakher, S Taheri).

Firm 1 at Heart of England is run by Professor M Stevens, Dr W Malik, Dr M Clarke and Dr S Taheri. Firm 2 is run by Dr J Shakher, Dr A Rahim and Dr A Jones. Both admitting firms participate in a 1 in 4 "split" medical "take" on a rota basis which lasts for approximately 12 hours commencing at 9am or 10pm. The Lecturer is also supported by a SpR, SHO and HP on each firm. Each firm has one medical clinic a week.

Both firms provide diabetes/endocrine services and are responsible for the diagnosis and management of diabetes patients referred by general practitioners from a wide area or by other consultants in the hospital on an outpatient and an inpatient basis. At present there is a comprehensive range of new patient, follow-up patient, diabetes and endocrine clinics together with a combined speciality clinic involving a diabetic/renal clinic, two diabetes/antenatal clinics, a diabetes/erectile dysfunction clinic, a diabetic/foot clinic, diabetes/retinal clinic and diabetes/adolescent clinic. Outpatient diabetes care is based on a community approach and 5 Diabetes Liaison Sisters are employed together with a full time Asian Link Worker, Nurse Facilitator and two GP Facilitators.

A major advance has been the development of a dedicated Obesity Service. A bone and pituitary clinic also operate alternate weeks. The Trust / Directorate is now also a Regional Centre for bariatric surgery. A Diabetic Neuropathy Service has also been established.

| | Monday | Tuesday | Wednesday | Thursday | Friday |
|---|---|---|---|---|---|
| am | Diabetes Clinic<br>Metabolic Journal Club | Undergraduate Teaching/Admin | Specialty clinics (in rotation) | Consultant Ward Round<br>Grand Round | Research |
| pm | Research | Endocrine Clinic/Foot and Neuropathy Clinic | Research | Research | Research |

The post holders at BHH have on call duties three times per month plus post-take ward round.
The BHH post holders rotate through speciality clinics including diabetic-antenatal, renal, foot and neuropathy, medical eye, erectile dysfunction, obesity and lipids, depending on training requirements. The BHH post holders attend reproductive endocrine, weight management, pituitary and bone clinics as required. The post holders will attend between 3.25 and 3.5 outpatient sessions per week

## DESCRIPTION OF RESEARCH COMPONENT OF THE PROGRAMME

The Clinical Lecturer will develop and carry out translational research in endocrinology and/or diabetes, building on the existing themes of the Centre for Endocrinology, Diabetes and Metabolism (CEDAM), with the aim of further enhancing endocrinology & diabetes research in Birmingham.

Birmingham has an immaculate track record in obtaining nationally competitive fellowships, including research training fellowships, clinician scientist and senior clinical fellowships. The Clinical Lecturer will choose an appropriate academic mentor and supervisor that matches his previous research profile and will help to enhance it to become competitive for clinician scientist fellowship applications. The broad research themes within CEDAM include the following:

- steroid endocrinology including the regulation of glucocorticoid, mineralocorticoid and sex steroid synthesis, metabolism and action,
- obesity, diabetes and metabolism
- fetal and reproductive endocrinology
- endocrine cancer with a major focus on thyroid tumourigenesis and molecular investigations of endocrine and hormone-dependent cancer predisposition and pathology.

**Pre-receptor regulation of glucocorticoid and mineralocorticoid action**

A long-standing focus of research is the 11β-hydroxysteroid dehydrogenase (11β-HSD) enzyme system. During the tenure of his MRC Senior Fellowship (1992-2002) Paul Stewart established the physiological significance of 11β-HSD2 as a major regulator of mineralocorticoid action and blood pressure. More recent advances have focused on the type 1 isozyme of 11β-HSD (11β-HSD1) that converts inactive cortisone to hormonally active cortisol. These studies have provided the basis for an integrated translational programme of research funded by consecutive Wellcome Trust Programme Grants, an NIH programme and most recently also by a prestigious European Research Council Advanced Grant.

Patients with glucocorticoid excess, Cushing's syndrome, develop a classical metabolic phenotype characterized by central **obesity, insulin resistance, hypertension, fatty liver disease** and in some cases **type 2 diabetes**. However, in the vast majority of patients with metabolic syndrome, circulating glucocorticoid levels are not elevated. Research within the group has demonstrated that pre-receptor activation of cortisol by 11β-HSD1 represents a mechanism of major significance to the development of the metabolic syndrome. Other research activities within the group have identified a novel endoplasmic reticulum redox mechanism that dictates the metabolic function of 11β-HSD1. Within its subcellular location, the endoplasmic reticulum (ER) lumen, 11β-HSD1 is a bi-directional enzyme. However, the activation of cortisol from cortisone only occurs when NADPH is donated by the redox enzyme hexose-6-phosphate dehydrogenase (H6PDH) that is also located in the ER lumen.

Proof of this concept in man has come from studying the putative 11β-HSD1-deficient state, Cortisone Reductase Deficiency, which in fact is explained by mutations in the *H6PD* gene. Patients manifest with polycystic ovary syndrome (PCOS), the reproductive phenotype of the metabolic syndrome. This is now a principal focus of research for the group with the aim of dissecting the true impact of H6PDH and 11β-HSD1 on glucose metabolism and insulin sensitivity.
Experimental strategies include *in vitro* and *in vivo* studies, the latter comprising novel transgenic and knock-out animal models (BBSRC David Phillips Fellowship to G.G. Lavery). These studies have also shed new light on the more general role of **ER stress in the regulation of energy metabolism**. In particular, the recent discovery by the group that provision of the H6PDH substrate glucose-6-phosphate (G6P), which is dependent on the G6P transporter (G6PT) for import into the ER, impacts on 11β-HSD1 activity, has been exemplified by patients with G6PT mutations (PM Stewart, GG Lavery).

Based on these seminal studies, many pharmaceutical companies have developed selective 11β-HSD1 inhibitors as a novel therapeutic strategy to reverse features of the metabolic syndrome. Stewart and Tomlinson, through industrial collaboration (Pfizer, Exelixis, Roche, Astra Zeneca) and a MRC Experimental Medicine grant are at the forefront of phase I+II studies in this exciting development.

**Obesity, Diabetes and Metabolism**
The metabolic syndrome is defined by distinct regulation within key target tissues of glucocorticoid and insulin action: adipose tissue, liver and muscle. Supported by a recent MRC Senior Clinical Fellowship Award (JW Tomlinson) another strand of research is currently exploring the role of an additional pre-receptor system regulating glucocorticoid availability within metabolic target tissues, 5α-reductase isozymes 1-3, which are involved in local inactivation of glucocorticoids as well as activation of androgens. This program of research extends form laboratory based assessments of glucocorticoid and insulin action, through to the generation and characterization of rodent models and finally translating these observations into clinical studies using state-of-the-art imaging and metabolic assessments including hyperinsulinaemic euglycaemic clamps with stable isotopes and adipose tissue microdialysis.

Diabetes research interests include autoimmunity and type 1 diabetes, with an active collaboration with MRC Centre for Immunology scientists. This includes exploring the phenomenon of peripheral immune tolerance to type 1 diabetes antigens and investigating how insulin resistance and autoimmunity interact in the development of type 1 diabetes – an understanding that may help delay the onset of this disease.

**Pre-receptor regulation of sex steroid action**

The major focus of the sex steroid research group (W Arlt, N Krone) is pre-receptor regulation of androgen action, namely the synthesis, metabolism and action of the crucial adrenal androgen precursor dehydroepiandrosterone (DHEA) and its sulfate ester DHEAS, the most abundant steroids in the human circulation. Primary translational targets are **androgen excess disorders** including **polycystic ovary syndrome** that affects 5-15% of women, representing the leading cause of **infertility** and, importantly, associated with an increased incidence of the **metabolic syndrome**. Therefore, the elucidation of molecular mechanisms underlying PCOS-related androgen excess is of significant importance for improving the management of a common disease that places an increasing demand on health care provision.

Recent prominent achievements include the discovery of two novel monogenic disorders, P450 oxidoreductase and PAPS synthase 2 deficiencies, which have highlighted the significance of co-factor enzymes in the pre-receptor regulation of androgen action. This research has been facilitated by an MRC Senior Clinical Fellowship to W Arlt, with follow-up funding by a MRC Programme Grant, and is synergistically complemented by a Wellcome Trust Clinician Scientist Fellowship (N Krone) on the molecular pathogenesis of **congenital adrenal hyperplasia** (CAH). P450 oxidoreductase (POR) has a pivotal role in facilitating electron transfer from NADPH to all microsomal cytochrome P450 (CYP) enzymes including steroidogenic CYP enzymes. Mutant POR causes a remarkably variable phenotype comprising glucocorticoid deficiency, ambiguous genitalia in both sexes, and skeletal malformations.

Crucially, we have demonstrated that distinct POR mutations can differentially affect electron-accepting CYP enzymes, likely to explain the variability in clinical presentation. Uniquely, POR deficiency may result in disordered sex development (DSD) in both sexes, i.e. virilised genitalia in girls and undervirilisation in boys. Diminished androgen synthesis due to mutant POR readily explains the latter, but is incongruous with the observation of virilisation in female newborns. We have proposed that this apparent contradiction can be explained by the existence of an alternative androgen pathway in early human life and this is a current focus of our research.

DHEA is the principal precursor of androgen synthesis via the classic androgen synthesis pathway. Unconjugated DHEA can be converted directly to androgens, while DHEA sulfate (DHEAS) first requires cleavage of the sulfate group. Previously it had been assumed that circulating DHEAS serves as a pool for continuous regeneration of DHEA for androgen synthesis in peripheral target cells. However, we have demonstrated in vitro and in vivo that the conversion of DHEA to DHEAS by DHEA sulfotransferase (SULT2A1) is the predominant direction of DHEA/DHEAS interconversion. We have provided conclusive evidence for this concept by uncovering inactivating mutations in the co-factor enzyme PAPS synthase 2 (PAPSS2) in a patient with androgen excess, who presented with premature pubarche, subsequently progressing to PCOS. PAPSS2 generates the universal sulfate donor PAPS required by all sulfotransferases including SULT2A1. Consequently, impairment of PAPS provision decreases DHEA sulfation and increases the conversion of DHEA molecules to androgens. Current research examines the role of DHEA sulfation in the pathogenesis of androgen excess disorders, including **premature pubarche and early-onset PCOS**. Significantly, POR and PAPSS2 provide co-factors not only to enzymes involved in androgen synthesis and metabolism but also to enzymes involved in **hepatic drug metabolism**. Thus we are currently investigating whether POR and PAPSS2 represent major determinants of in vivo differences in human drug metabolism and response.

**Pre-receptor regulation of thyroid hormone action and Endocrine Cancer**

The group of CJ McCabe and JA Franklyn has a long-standing interest in the pathogenesis of thyroid hyperplasia and neoplasia, as well as thyroid hormone action. A major focus is the pituitary tumour transforming gene (PTTG) and its interacting partner PTTG binding factor, PBF. Both PTTG and PBF are over-expressed in differentiated thyroid cancer; induce tumours in nude mice, and their expression correlates with tumour behaviour. Critically, recent data indicate that both genes are able to repress the sodium iodide symporter (NIS), responsible for the cellular uptake of iodide. This has a very direct clinical implication. Thyroid tumours with high PTTG and PBF expression will have reduced ability to uptake and concentrate ablative radioiodine via NIS, thereby reducing the efficacy of treatment. Overcoming this inhibition of treatment in **thyroid cancer** is the focus of a current MRC Project Grant, a recently funded translational CRUK grant and a MRC Clinician Scientist award to Dr Kristien Boelaert.

NIS activity is the rate limiting step in iodide uptake by thyroid cells prior to thyroid hormone biosynthesis. NIS mutations have been identified as causes of congenital iodide transport defect (ITD); thyroid stimulating hormone (TSH) upregulates NIS, causing increased iodide uptake and enhanced production of thyroid hormones, linking NIS activity to thyroid function. Given that thyroid hormones exert extremely broad and pleiotropic physiological effects, this pre-receptor mechanism has to be considered of major clinical relevance. To this end, the group are currently characterising transgenic mouse models of thyroid-specific over-expression of PBF and PTTG. Preliminary data indicate that transgenic PBF mice have grossly enlarged thyroid glands, thyroid cell hyperplasia and repressed NIS expression, supportive of a critical role for PBF in the control of thyroid cell growth and iodide uptake.

We have recently identified a role for PBF in **breast cancer**. Oestrogen-mediated stimulation of PBF results in enhanced cell invasion in vitro, and oestrogen receptor positive breast tumours show enhanced PBF levels. We are currently characterising the interaction of PBF with aromatase, the enzyme responsible for the local (re)generation of oestrogen in breast tissues.

**Materno-fetal endocrinology**

Maternal thyroid dysregulation is associated with adverse pregnancy outcomes including miscarriages, pre-eclampsia, intrauterine growth restriction and neurodevelopmental delay. Evidence suggests direct effects of thyroid hormones on fetal development, regulated by the monocarboxylate transporters MCT8 and MCT10 that facilitate thyroid hormone uptake during fetal growth and development; patients with MCT8 mutations suffer from severe neurological deficits. Recent work from the group (MD Kilby, CJ McCabe, JA Franklyn, TG Barrett, Health Foundation Fellowship to SY Chan) has demonstrated that MCT8 and MCT10 are expressed in early gestational fetal brain, adding to our previous data showing changes in neuronal cell MCT8 expression as associated with altered thyroid hormone uptake and cell proliferation. Of note, recent data indicate that PBF binds to MCT8 and regulates its subcellular localisation. The impact of thyroid function on fetal development is currently investigated by a Birmingham-led EME-funded clinical trial (TABLET) assessing the efficacy of thyroid hormone treatment in TPO antibody positive women in preventing miscarriage and preterm birth.

**Diabetic Neuropathy and Cardiovascular Disease**

Diabetic neuropathy (DN) is the most common and often the most disabling complication of diabetes mellitus resulting in great morbidity, mortality and significant economic burden. DN is the leading cause for non-traumatic amputations secondary to foot ulceration. DN can affect different aspects of the peripheral (DPN) and the autonomic (DAN) nervous systems and they usually coexist. DPN and DAN have a wide spectrum of clinical manifestations. DN can range from an imperceptible reduction in foot temperature perception to sudden cardiac death. Recent work by the group (MJ Stevens, P Narendran, A Wagenmakers, RP Steeds, JN Townend, National Institute for Health Research Fellowship to Dr Taheri) has identified sleep apnea as an important contributing factor to diabetes complications. Specific abnormalities of cardiac function (increased left ventricular torsion) and metabolism (impaired cardiac energetics) have also been identified in subjects with type 1 diabetes which may ultimately contribute to heart failure. In the diabetic foot, specific skin structural and functional deficits have been identified which may contribute to lower limb complications. Ongoing research relationships have been established with the University of Michigan in these areas.

## DESCRIPTION OF TEACHING COMPONENT OF THE PROGRAMME

The post holder will be expected to play an active role in delivering bedside and small group teaching to clinical medical students (no more than 2 hours per week).

In addition they will be required to regular delivery of small group teaching sessions (and occasional delivery of lectures) on endocrine or diabetes topics on the undergraduate MBChB (Years 1-3) and also BMedSc and BDS courses. The Endocrinology and Reproductive Endocrinology MBChB courses have an innovative style of teaching and assessment, in line with GMC's Tomorrow's Doctors. The post holder will have also take on responsibilities in formal assessment of teaching delivery including the development of exam questions and exam marking. There may be additional duties in helping with FY2 teaching and in the organization of training for SpRs.

Overall teaching load will amount to approximately one undergraduate teaching session per week. The lecturer will have the opportunity to obtain a postgraduate teaching qualification certificate (PGCert) including active mentorship and peer observation.

## Person specification

| | Essential | Desirable |
|---|---|---|
| Education | Full General Medical Council registration<br>Membership of Royal College of Physicians, or equivalent | Higher degree (MD/PhD) |
| Research Experience | Postgraduate research experience in endocrinology and/or diabetes | Knowledge of research methodology, statistics and trial design<br>Experience of laboratory science incl. basic cell and molecular biology techniques<br>Original research contributions |
| Teaching Experience | | Experience and appropriate qualifications in teaching |
| Skills and Knowledge | Minimum of six months experience in endocrinology & diabetes | |
| Personal Attributes | Determined to pursue a career in academic medicine | |

The organisation

The University of Birmingham is a thriving and dynamic institution that combines over a century of heritage with one of the most compelling and ambitious agendas in higher education. Ranked amongst the world's top 100 institutions, the University is structured to promote faster decision making and to enable it to capitalise on its academic range and financial strength. The University is organised into five academic colleges, with a University Executive Board, led by our Vice-Chancellor, Professor David Eastwood.

Central to our agenda is the development of the University's five year strategic plan 'Shaping Our Future: Birmingham 2015', that builds upon an existing and ambitious programme of change, 'Sustainable Excellence', developed to establish Birmingham as a leading global university.

The strategic plan is based around five mutually supportive goals: enhancing research power; providing students with a distinctive, high-quality experience; sustaining and utilising financial strength; enhancing performance as an engaged university; and becoming the destination of choice amongst our peers. The confidence of the University's ambition is, in part, underpinned by one of the strongest financial positions in the UK HE sector. The University is currently forecasting a turnover of £450 million for the financial year 2011/2012 and carries significant cash surpluses with no borrowings. This is enabling it to invest in high quality research and to enhance still further the educational experience for its students, as well as to continue to improve its estate and infrastructure, despite the prevailing economic conditions.

Over 90% of Birmingham's research was rated as world leading or of international quality in the 2008 UK Research Assessment Exercise (RAE). With world leading activity across a range of subjects, it remains one of the UK's most broadly-based research-led universities.

The University's cultural and intellectual assets include the Shakespeare Institute at Stratford-upon-Avon, the Barber Institute of Fine Arts on campus and the Ironbridge Institute in Shropshire. The University also boasts the internationally-renowned Lapworth Museum of Geology and Winterbourne House and Garden, a unique Edwardian heritage attraction that is home to over 6,000 plant species from around the world. In total the University's economic value to its region is £780 million.

Founded in 1900 and believed to be the UK's first redbrick university, Birmingham established a new model for higher education, breaking away from the Oxbridge tradition. Through the foresight of our founders we have inherited one of our greatest assets – our beautiful parkland campus, which is currently undergoing a £175 million enhancement programme that includes the new Bramall Music Building, a new sports centre containing the city's first 50m swimming pool and a proposed library

development to provide outstanding facilities for students and researchers alongside an open access cultural hub with facilities available to the public.

The University was founded through philanthropy and fundraising. This is just as important today. Birmingham's 'Circles of Influence' campaign has raised over £60 million since its launch in 2009 and continues to provide funding for five priority areas – Health and Lifestyle; Children and Young People; Heritage, Culture and Sport; Student Support; and Innovation and Immediate Impact.

With 28,000 students from 150 countries, the quality of the student experience offered at the University of Birmingham remains of paramount importance. The University is one of the leading members of the Russell Group in terms of the size of its graduate school and the quality of its student experience as shown by the National Student Survey. As well as high quality teaching, students also enjoy an enriched experience through other activities such as sport, for which Birmingham is ranked second in the UK.

As Birmingham seeks to extend its global footprint further it is investing in its international strategy, having established overseas offices in India, China and Brussels. These new offices are developing existing contacts and forging new partnerships with academic colleagues and businesses across the Asia Pacific Region and into Australasia. Birmingham is also building strategic partnerships in North America (notably Chicago) and through its membership of Universitas 21.

The city of Birmingham

Birmingham is a major European centre and the second city of the United Kingdom. It is a city of business and ballet, canals and world class concerts, jewellery and jazz, historical interest and cosmopolitan atmosphere. Birmingham is also the ideal base for exploring one of Britain's most fascinating regions for tourism, being within an hour's drive of Stratford-upon-Avon, Warwick, the Potteries, and the Cotswolds.

The new heart of Birmingham is symbolised by Symphony Hall, considered one of the greatest concert venues in the world. Symphony Hall forms part of the impressive International Convention Centre, which overlooks attractive canals at the hub of the UK's canal network. This setting is a very suitable venue for the CBSO, the globally-respected symphony orchestra. At the magnificent Hippodrome Theatre is the internationally-renowned Birmingham Royal Ballet, adding further cultural depth to the city. Apart from London's West End, Birmingham boasts the highest concentration of live theatre in the UK, including regular tours by the major opera companies.

The City Museum and Art Gallery houses the world's finest collection of Pre-Raphaelite paintings, alongside a major collection of Old Masters, Modern and Contemporary pictures. The Barber Institute of Fine Arts houses one of the best UK university collections of Impressionist and Renaissance art. The restored Gas Hall

Gallery has international touring exhibitions, while the Halcyon and Ikon galleries feature innovative contemporary works. National landmark sites abound, including the National Indoor Arena, the National Exhibition Centre, National Motorcycle Museum, National Car Heritage Museum and the National Sealife Centre.

The iconic Bullring Centre is the largest dedicated shopping facility in Europe. Sports and recreation are well served; the city offers international Test cricket, top-flight football, International Championship golf and top class rugby. The International Convention Centre and National Indoor Arena have spawned a whole new Downtown area at the centre of the city. The National Exhibition Centre, on the outskirts to the city, remains one of the largest exhibition facilities in Europe.

Birmingham is at the crossroads of the UK's motorways. From Birmingham International Airport, more than a dozen different airlines operate scheduled services to 60 destinations worldwide. The University is the only mainland UK university to have its own railway station, while 50 million passengers a year use Birmingham New Street Station, which will be at the centre of the proposed high speed rail network. London is 90 minutes away by shuttle service, with trains every 20 minutes until the evening. There is a high standard of all types of private accommodation, with high quality affordable family housing in several attractive residential suburbs. Public parks and large domestic gardens are a special feature of this greenest of European cities. Quality public and private schools are widely available, with several consistently rated in the top 10 on examination performance in annual league tables of England and Wales.

The College of Medical and Dental Sciences

The University's structure is one of Colleges and Schools, and the College of Medical and Dental Sciences contains five Schools that cover the whole range of pre-clinical and clinical disciplines:

- School of Cancer Sciences
- School of Clinical and Experimental Medicine
- School of Dentistry
- School of Health and Population Sciences
- School of Immunology and Infection

Interdisciplinary research is encouraged, as are links between the clinical and basic science groups. The principle base of the College lies immediately between the main campus of the University and the Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, with other key NHS Trusts on the same campus including Birmingham Women's and The Barbery (Psychiatric) Hospital, giving a coherent basic and clinical academic whole. Each year the College trains 400 medical students including the Graduate Entry course, over 70 dental students, over 65 bachelor of medical sciences students (plus a further 25 medical students who

intercalate into the third and final year of the course), 130 nursing and 80 physiotherapy students.

There are also approximately 400 postgraduate students in the College, managed by a cross-College Graduate School. The College has excellent library and reference facilities. Medical student teaching takes place at all hospitals in Birmingham, but has recently expanded into many of the hospitals in the Black Country. The College is the only undergraduate (preclinical and clinical) school in the West Midlands Region of 5.5 million people. It is the focal point for academic leadership in the Region.

The College has invested more than £73m in an ongoing programme of works to improve and expand its research and teaching facilities, with the aim of advancing its position at the forefront of developments in medical science. This includes a £35m Institute of Biomedical Research, a new state-of-the-art £11.8m Wolfson Centre for Medical Education and a new £500K prosectorium facility for anatomy teaching incorporating 10 ventilated tables and high tech AV teaching aids.

The College created a new £1m phantom head teaching laboratory facility within the School of Dentistry during the summer of 2009. In 2009-10, the College continued to participate in the Centre for Innovation and Training in Elective Care (CITEC) collaboration, which aims to develop Inter-Professional Learning (IPL). CITEC has now funded the installation of a small clinical skills suite with video recording and feedback equipment and a series of successful pilot half day sessions of simulation-based IPL have been held. Work is under way to make these facilities available to wider groups of students and to develop the range of simulation activities available. In 2010, the College launched the Health Research Bus, a mobile clinical research facility funded via Birmingham Science City via Advantage West Midlands, the first of its kind and a great development for clinical research in the College.

From 2010 onwards the College plans to deliver high quality laboratory and clinical research facilities within the new University Hospitals Birmingham NHS Foundation Trust (UHBFT) building. In partnership with Advantage West Midlands, a new purpose built HTA-compliant biorepository, gene therapy pharmacy, and commercial spin out laboratory is also planned. In addition we are looking to expand our clinical trials activity by refurbishing an existing facility. Alongside these developments, the Wellcome Trust Clinical Research Facility (CRF) has received an extra £9.9 million of funding to support expansion of the current facility as well as creating a unique paediatric CRF at Birmingham Children's Hospital. A technology hub will be established within the medical school building in order to bring together high-end technologies and provide access to the latest scientific equipment for research staff from within the College and wider University community. The Medical School building foyer area will also be developed by autumn 2011 to incorporate better student services and improved library facilities.

The School of Clinical and Experimental Medicine

The School of Clinical & Experimental Medicine was created in 2008 as part of a new College structure within the University. The objectives of this reorganisation were to bring together extensive expertise in a wide-ranging field of medical sciences and to develop a highly motivated School with an integrated clinical and basic science portfolio, associating excellence in research, education and clinical leadership. The School plays a major role in the wider portfolio of research and teaching carried out by the College of Medical & Dental Sciences.

A diverse but highly collaborative and interdisciplinary grouping, the School of Clinical & Experimental Medicine has well over 200 research-active staff who together have been awarded more than a quarter of the College's total external funding (and around an eighth of total University research funding). There are also over 500 honorary staff and 100 support staff embedded within the School. These staff are grouped into five major academic Sections, each encompassing education and research in a particular theme:

***Cardiovascular & Respiratory Science:*** Encompassing disciplines including Cardiology and Cardiovascular Sciences, as well as Respiratory Medicine, this Section focuses research on myocardial diseases, vascular research, and lung injury and immunobiology. In myocardial diseases, key areas of study are the pathophysiology of heart failure, novel techniques for cardio-protection during surgery and following ischaemic reperfusion injury, the role of thrombosis and haemostasis in atrial fibrillation, and new approaches to management of life-threatening cardiac arrhythmias. Vascular research includes three main areas: vascular control of blood flow; angiogenesis; haemostasis and thrombosis. Vascular and angiogenic responses to hypoxia are linked, for example, with pathogenesis and treatment of pre-eclampsia. Studies of signalling by receptors in platelets are allied with analysis of the roles of haemostatic, thrombotic and inflammatory processes in vascular diseases. In the field of respiratory science, research centres on inflammatory mechanisms underlying lung injury and fibrosis in disorders including chronic obstructive pulmonary disease, vasculitis and interstitial lung disease. With 70 staff (both clinical and basic scientists) and live funding of over £13 million, translational, therapeutic and basic scientific studies in all of the above areas are funded by the British Heart Foundation, Wellcome Trust, MRC, BBSRC, NIHR and the pharmaceutical industry.

***Endocrinology, Diabetes & Metabolism:*** With around 50 researchers who together hold more than £24 million in live funding, together with Reproduction, Genes & Development researchers in this Section were the major contributors to achievement of our ranking 4$^{th}$ nationally in the 2008 RAE ("hospital based clinical subjects") (75% research rated world or internationally leading), with a strong portfolio of translational research underpinned by large clinical datasets. Current initiatives are supported by major awards from MRC, the Wellcome Trust and the European Commission to study a range of topics including glucocorticoid, gonadal steroid and thyroid hormone

actions and pre-receptor regulation, as well as pathogenesis of endocrine autoimmune diseases and endocrine cancers. A range of programme grant funded research is being undertaken in diabetes, obesity and metabolism; fetal and reproductive endocrinology; thyroid tumourigenesis and molecular investigations of endocrine and hormone-dependent cancer predisposition and pathology.

***Neuropharmacology & Neurobiology:*** Encompassing neurology, psychiatry and neurosciences, research within this Section of the School brings together expertise covering aspects of neuroscience ranging from cellular and molecular, to the whole brain, through to the extensive network of neuronal connections across the body, and how these biological underpinnings interact with psychological and social factors to cause neurological and psychiatric disease. The new Queen Elizabeth Hospital and National Centre for Mental Health that adjoin the Medical School are facilitating our focus on translational neuroscience so that we can apply insights gained through fundamental research on brain structure and function to develop novel pharmacological and cellular therapies for neural damage and psychiatric disease, with a clear goal to promote continuous interaction amongst fundamental and clinical neuroscientists to rapidly translate research from bench to bedside. With around 50 research-active staff, major research teams are neuropharmacology; neurodegeneration and repair; neuronal networks; and psychiatry.

***Reproduction, Genes & Development:*** Covering Obstetrics, Gynaecology and Paediatrics as well as a significant portfolio of clinical genetics, activity in this Section reflects three broad areas of research, education and clinical activity: Obstetrics and Gynaecology; Paediatrics and Child Health; and Medical and Molecular Genetics. The complementary interests of each of these areas enable the theme to make a unique contribution through its research and teaching, to the healthcare of mothers and children in the whole of the West Midlands region. Multidisciplinary reviews and trials on numerous aspects of care (both diagnostic and therapeutic) have been undertaken in aspects of Reproduction, Genes & Development. The School is home to the WHO Collaborating Centre for Reproductive Health, the only centre of its kind in the UK. In addition, translational research is performed within the Wellcome-funded Clinical Research Facility within the University Hospitals Birmingham NHS Foundation Trust and the Paediatric Clinical Research Facility within the Birmingham Children's Hospital, the first of its kind in the UK. With around 60 staff and over £14 million of live funding this is an active research section within the School.

***Medical Science & Education*****:** Home to research within clinical pharmacology and therapeutics, the newly developing initiative of clinical pharmacy, as well as anaesthetics and intensive care medicine, this Section plays a major role in both the research and teaching carried out within the School. Research in basic and clinical sciences is integrated, along with expertise in clinical trials, to advance the understanding and treatment of a spectrum of human disorders. Teaching takes advantage of state-of-the-art research expertise in these areas to deliver the highest standard of instruction.

***School Infrastructure:*** Research in basic and clinical sciences in these areas is fully integrated in the School, which offers training in state-of-the-art facilities, including the Institute of Biomedical Research (IBR) and the Wellcome Trust Clinical Research Facility (WTCRF). The IBR is a £30m JIF-funded facility, the largest of its kind in the UK. In addition to extensive tissue culture and biochemistry laboratories, the IBR includes resources for proteomics and genomics together with containment facilities for work with micro organisms up to category 3. It also provides support for such key technologies as flow cytometry, Mo Flo cell sorting, confocal microscopy, laser capture dissection, sequencing and construct production, GC/MS platforms, array technology and real time qPCR, as well as extensive modern facilities for *in vivo* animal work and mouse breeding and an in-house service for embryonic stem cell work and the production of genetically modified mice. The WTCRF **(www.crf.bham.ac.uk)** is a flagship facility and one of five originally established in the UK, funded by a Wellcome Trust Millennial grant of £3.2 million in 2001. It was further awarded approximately £10m to extend its facilities to include gene therapy/pharmacy facilities, cardiovascular and metabolic research suites and to create the only dedicated children's WTCRF in the UK at Birmingham Children's Hospital. The School also has significant links with major NHS Trusts in the region including University Hospitals Birmingham NHS Foundation Trust (with the new Queen Elizabeth Hospital opened in June 2010 adjacent to the College, a 1200 bed, £50+ million initiative, representing a major opportunity for clinical translation of basic science research), and within a number of other NHS Trusts, including Birmingham Women's and Children's Hospitals, as well as Heart of England, Sandwell and West Birmingham and Birmingham and Solihull Mental Health NHS Trusts, ensuring that our research, practice and strategy are well linked in with all of our neighbouring NHS Trusts (including the Birmingham Women's Foundation Trust).

Teaching takes advantage of the range of research expertise available to deliver the highest standard of instruction to both undergraduates and to postgraduates. Birmingham academic staff works closely with honorary staff with NHS appointments to contribute to undergraduate teaching across the MBChB and BMedSc programmes, as well as postgraduate programmes. Postgraduate qualifications are available in the form of MPhil / PhD by research, MD by research and taught Masters (MSc).