

Further particulars

The project

The project is funded by a three year project grant from Action Medical Research.

We have identified that systemic up-regulation of a putative anti-oxidant (paraoxonase 3, Pon3) takes place in late gestation in the fetal rat, sheep and human. However, there is currently no direct evidence for an antioxidant effect of Pon3 in the perinatal period. The aims of the project are to determine: (1) is absence of Pon3 associated with oxidative stress in neonatal life? (2) is absence of Pon3 associated with oxidative stress in fetal lung explants exposed to elevated PO₂? (3) can oxidative stress associated with absence of endogenous Pon3 be reversed by recombinant Pon3? We have established a breeding colony of heterozygous Pon3 null mutant mice. The project will involve analysis of flash frozen samples of lung from het/het matings in late gestation and in the early neonatal period. It will also include study of explants of fetal lungs from late gestation fetuses in low oxygen tension and exposing them to a rise in partial pressure of oxygen in the range physiologically observed in the perinatal period. In both cases, indices of oxidative stress (principally lipid, protein and DNA oxidation; and gene expression) in wild type and Pon3 null mutants will be compared. Explants of fetal lungs from Pon3 null mutant late gestation fetuses will be exposed to increased PO₂, and measures of oxidative stress in the presence and absence of rPon3 will be compared. Finally, the effects of rPon3 in explants from preterm and term wild type fetuses will be compared. We have data to support the feasibility of this proposal.

Specific essential requirements for the candidate.

- PhD in relevant subject.
- Ability to conduct complex laboratory procedures
- Ability to analyse data to publication standard
- Ability to work independently but addressing overall aims of project
- Extensive previous relevant laboratory experience
- Good communication skills
- Ability to interact effectively and appropriately with other staff
- Ability to learn and employ new techniques, where appropriate
- Computer literate
- Work according to University regulations, including Health & Safety, use of radio-isotopes etc.

Desirable qualities in candidate

- Previous experience of the methods to be employed in the project (i.e. study of fetal tissue explants, gene array, qRT-PCR/TLDA, Western blot, in situ hybridisation and immunohistochemistry, microscopy)
- Expertise in bioinformatics
- Previous experience in studies of the rodent fetus
- Ability to prepare manuscripts for publication

The Department of Obstetrics & Gynaecology

Professor Gordon Smith Head of Department and Honorary Consultant
Dr Andrew Prentice University Senior Lecturer and Honorary Consultant
Dr D S Charnock-Jones University Reader (Non-clinical) in Reproductive Biology
Dr Francesco Colucci University Reader (Non-clinical) in Immunology
Dr Miguel Constância University Lecturer (Non-clinical) in Reproductive Biology

The Department of Obstetrics and Gynaecology has programmes of basic, translational and clinical research addressing the determinants of pregnancy complications. Dr Charnock-Jones and Dr

Constancia both use transgenic mouse models to identify key genes involved in murine placentation with the aim of better understanding normal reproductive function. Dr Constancia has a major interest in placental epigenetics, in particular genomic imprinting (i.e. selective epigenetic silencing of genes according to parent of origin). Other basic work in the department addresses preparative changes in gene expression in the fetus for post-natal life. Dr Colucci is an immunologist whose main area of interest is the biology of the natural killer cell. His research programme includes the role of a sub-type of this cell type, uterine natural killer cells, in the control of murine and human trophoblast invasion of the maternal uterine resistance vessels. Translational research in the department focuses on the control of uterine smooth muscle (myometrium) and on placentation. Prof Smith and Dr Charnock-Jones lead a group studying the basic biological mechanisms controlling human myometrial quiescence and contraction. They have also conducted studies around fetal preparation for birth. Prof Smith also leads a large scale prospective cohort study of unselected women in their first pregnancy where placental function is studied by assessing circulating markers in maternal serum, by serial Doppler ultrasound of the utero-placental circulation and by assessing placental gene and protein expression following birth. This project involves collaboration with translational researchers from multiple departments in the clinical and pre-clinical school. Finally, clinical research in the Department uses secondary analysis of diverse data sources to study determinants and predictors pregnancy outcome. Recent studies have shed light on the major public health issue of rising rates of caesarean section. The research component of the post can, therefore, be selected on the basis of the successful candidate's previous experience and interests and could extend from analysis of clinical data, translational research using human samples, through to relevant animals studies.

Additional information

On site amenities include childcare facilities and the Frank Lee Sports and Social Club.

Project supervisors:

Professor GCS Smith, MD PhD.

Professor of Obstetrics & Gynaecology

Dr Stephen Charnock-Jones PhD.

Reader in Reproductive Biology.

To apply please email your letter of application, CV and CHRIS 6 form

<http://www.admin.cam.ac.uk/offices/hr/forms/chris6/> to Joanne Hackett, jh483@medschl.cam.ac.uk – informal enquiries are also welcome

Or post to:

Joanne Hackett

Administrator

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Closing date: 4 December 2011.