APPLICATION FOR A GOSHCC SURGICAL SCIENTIST PHD STUDENTSHIP

Academic Supervisors
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1. Title.
Bladder, renal and bowel development in open spina bifida

2. Portfolio summary.

Aims: To compare urinary tract and bowel phenotype in fetal mice with open spina bifida to control embryos, using morphometric, histological and immunohistochemical analyses. Is it a primary or a secondary phenomenon? Or is it a combination of both? Is there a progressive change during gestation?

Background: Myelomeningocele is a neural tube defect and affects 0.3-4.5 of every 1000 children born worldwide. Renal damage and renal failure are among the most severe complications of spina bifida. These complications have been important issues in spina bifida literature over the years, with reported death due to renal failure up to 20% in the first year of life. It is thought that Children born with spina bifida can probably use their own kidneys for a lifetime if they start to receive adequate early urological treatment soon after birth.

A preliminary study in a murine model overexpressing the grainyhead-like gene at ICH showed that renal abnormalities were present in late gestation but no significant difference was seen in morphology in the detrusor smooth muscle when compared to a control group. The numbers in this group were too small to make valid conclusions and further studies are needed.

Proposed methodology to be adopted:
The generation of Grhl3 transgenic mice at UCL Institute of Child Health. The morphological characteristics urinary tract (bladder, ureter and renal unit) and the bowel will be processed and analysed as well as immunohistochemical analysis of nerve and smooth muscle expression. The contractile properties of smooth muscle tissue in relation to its activation by motor nerves and agonists will be preformed in-vitro and the relative importance of different neurotransmitters in regulating smooth muscle function will be elicited.

Significance of this project
This study will equip the appointee with first-rate experimental and analytical skills to take forward into future academic surgical training. It will also increase understanding of aberrant bladder development and should lead to funded studies in larger animals - both supervisors
have worked with fetal sheep and Professor Cuckow is part of a porcine research group at the University of Aarhus. Ultimately, we hope that this area of research will inspire new therapeutic approaches to improve outcome for human conditions in patients with neuropathic bladder.

References:

