2016/2017 Summer Studentship Project Application Form

Send to: Research Office, University of Otago Christchurch, PO Box 4345, Christchurch, by 5pm on **4 July 2016**

Supervisor Information (First named supervisor will be the contact):	
First Supervisor's Name and Title: Gloria Evans, Dr	
Department - UOC &/or CDHB (if applicable): Laboratory for Cell & Protein Expression (LCPR), Obstetrics & Gynaecology, UOC.	
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First Supervisors Mailing Address: LCPR, Department of Obstetrics & Gynaecology, UOC	
Co-Supervisors Name and Title(s): John Evans, Professor	

Research Category (Choose one category only – to be used for judging the students' presentations):		
Clinical	**Laboratory** √	**Community**

Project Title (20 words MAXIMUM):

The effects of oestradiol and progesterone on the expression of Focal Adhesion Pathway and proliferation markers in Ishikawa cell culture.

Project Description:

Introduction: This team from the LCPR research group has been collaborating with Fertility Associates, New Zealand for the last decade in an attempt to increase the success rates of IVF. Testing of endometrial tissue has been the focus of this work. Current projects are concentrating on the adequacy of proliferation of the endometrium in order for the tissue to be receptive to implantation at embryo transfer. We have identified several markers that are associated with a positive IVF outcome and established a reference database of immunohistochemical staining patterns in the endometrium. Women for whom successful IVF has never occurred experience a condition called Recurrent Implantation Failure (RIF); we found these women exhibit a reduction of expression of some of these markers. Some of these markers are associated with proliferation while others are featured in the Focal Adhesion pathway. This pathway leads directly into the Cell Cycle pathway resulting in mitosis. The Cell Cycle pathway has been well profiled by our group (1-3). Reduced expression of those markers will thus affect the downstream rate of proliferation and thence implantation. The Focal Adhesion pathway has also been reported by others (4) to be important in order for the endometrium to become receptive to implantation. However, that group concentrated on other proteins in this pathway.

Using this information we wish to investigate the effects of female sex steroids (oestradiol and progesterone) on the expression of the Focal Adhesion pathway by using endometrial epithelium cell culture. Oestradiol and progesterone are the two most influential steroids during the menstrual cycle. For example oestradiol stimulates endometrial proliferation in the first half of the cycle while progesterone controls implantation in the second half. This study will assist in understanding effects of oestradiol and progesterone on the expression of markers involved in implantation. Identification of markers that mediate steroid activity is a much under-studied area of fertility treatment.

Aim: To determine the effects of oestradiol and progesterone on expression in the uterine endometrium of markers previously identified as being involved in embryo implantation. Implantation, rather than fertilisation, is an area that frequently fails in the IVF process.

Possible impact (in lay terms): In the majority of IVF cycles performed by Fertility Associates, the woman's cycle is completely controlled by the administration of hormones, including oestradiol and progesterone, to create an 'artificial' cycle. Should we find that oestradiol and progesterone increase

the expression of markers present in the Focal Adhesion pathway then there is the very real possibility of using this information to improve the clinical scenario.

Method: Ishikawa epithelial cells, a validated in-vitro model for embryo implantation (5), will be cultured on cover slips using steroid free media. Control cells without treatment will be included. Test coverslips will be exposed to a range of physiological levels of oestradiol and progesterones. Initially, concentration response and time courses will be performed. The coverslips will be mounted onto slides for immunohistochemistry, as previously published, to ascertain expression of markers of proliferation e.g. MKI67 and PCNA and in the Focal Adhesion pathway e.g Insulin-like growth factor 1, Transforming Growth Factor α, Vascular Endothelial Growth Factor A and Focal Adhesion Kinase, as well as receptors IGF1RA, PDGFRα, PGR and KDR. Other endometrial cell lines (e.g. RL952, HEC1A) will assist in substantiating the findings.