SRF VACATION SCHOLARSHIP REPORT 2017

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Degree Title and year of study:	Medicine, Year 3		
Supervisor's Name:	Amanda Sferruzzi-Perri	**Supervisor's Department and Institution:**	Centre for Trophoblast Research, Physiology Development and Neuroscience
Project Title:	The role of placental endocrine IGF2 in regulating placental morphogenesis and fetal growth.		

Briefly outline the background and aims of the project *(max 200 words)*

The placenta is essential for fetal growth. It controls substrate transport and secretes hormones that favour maternal nutrient allocation to the fetus. Previous work has shown that the paternally-expressed imprinted gene, insulin-like growth factor-2 (*Igf2*) is widely expressed by the conceptus and is critical for placental formation and function. In mice, constitutive loss of *Igf2* or just from the transport region (Lz) results in feto-placental growth restriction, whereas ubiquitous *Igf2* over-expression causes overgrowth. In these mutants, the functional capabilities of both the Lz and the endocrine region (Jz) of the placenta are altered. However, the significance of *Igf2* expression in the Jz for conceptus growth and placental function is unknown. This study determined the effect of Jz *Igf2* over-expression (Igf2OE) on placental structure, functional capacity and fetal growth.

Did the project change from that proposed in the application? If so, what changes were made and why? *(max 100 words)*

The original proposal was to undertake histological assessment of the size of the Jz and its abundance and distribution of the three endocrine cell types (trophoblast glycogen cells, giant cells and spongiotrophoblast cells) in placentas with normal, loss or over-expression of Jz *Igf2* during pregnancy. However, due to time constraints, only the Igf2OE placentas were analysed. Also, due to the unexpected finding that in the fetuses were not growth enhanced even though maternal glucose levels and placental weights were increased, we wondered whether the formation of the placental transport region, the Lz was affected by Igf2OE. Thus, I assessed gross placental structure and the composition of the Lz instead, looking at the abundance and distribution of the three Lz cell compartments; maternal blood spaces, fetal capillaries and trophoblast.

What were the main results/findings of the project? *(max 300 words)*

TpbpaCre males were crossed with *H19DMR*-floxed females to produce whole litters with *Igf2* overexpression (Igf2OE) in only the placental Jz. On days (D) 16 and 19 of pregnancy, maternal glucose concentration was determined and dams were culled according to HO regulations. Fetuses and placentas were weighted and placentas were processed for histological analyses. Age-matched dams from the reverse cross were used as controls. Significance was set at $p<0.05$ using *t* test.

On both D16 and D19, dams were hyperglycaemic and fetal growth was unaltered by Igf2OE. However, the Igf2OE placental weights were larger at both gestational ages for the same fetal weight, indicating reduced placental efficiency in the Igf2OE model compared to controls.

Interestingly, there was an increase in the Jz absolute volume in Igf2OE placentas at D16 but on D19, the Jz volume had decreased. There was, however, no change in the volume of the Lz at either age. Although, the composition of the Lz had changed in the Igf2OE placentas. At D19, the Igf2OE placenta had fewer maternal blood spaces but a greater density of fetal capillaries compared to controls. The Lz trophoblast was unaffected by Igf2OE.

What do you conclude from your findings? *(max 150 words)*

Collectively, these data suggest that Jz *Igf2* may prevent overgrowth of the fetus when maternal glucose levels are increased by Igf2OE, through altering the structure in the Lz and thus the placental transport capacity. These data also suggest a role for Jz *Igf2* in the paracrine control of the Lz during mouse development.

How has this experience influenced your thinking regarding your future/ongoing studies, and/or career choice? *(max 150 words)*

Yes, as previously I was unsure what subject I was interested in. I knew that I wanted to gain more experience in research, so that I can use the skills gained in a PhD project and a future research career. However, since this opportunity in the Sferruzzi-Perri lab I have realised that I want to specialise in research surrounding women's health and in particular, the placenta. Also, as a medic, this lab placement has influenced my choice of clinical specialty into Obstetrics and Gynaecology. I hope to increase my experience in this specialty in the future, and also increase my knowledge surrounding its clinical research.

Please use the space below to add any other comments/thoughts about the SRF Vacation Scholarship *(max 100 words)*

Student: I am very grateful for this scholarship, for allowing me to have this opportunity and for helping me develop my skills in the lab and develop my interest in women's health and the placenta. Thank you!

Supervisor: Eman has generated novel and exciting data on the control of mouse placental development and functional capacity. Data generated will contribute to paper/s currently being prepared for publication.