Detecting Circulating Maternal Biomarkers to Predict Fetal Size: FLAG 2 (Fetal Longitudinal Assessment of Growth)

RANZCOG SCHOLARSHIP – FINAL REPORT

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I would like to thank the RANZCOG research foundation for this important scholarship funding that has aided in my research towards identifying novel biomarkers to predict infants at risk of stillbirth due to poor fetal growth. I am pleased to report that I have completed studies for this project and have provided an overview of my research findings and extensions below.

PROJECT OVERVIEW:

Every year, three million pregnancies end in stillbirth worldwide. Poorly grown babies are at the biggest risk. Only a fraction of small babies are currently identified before birth. We wish to develop a blood test which identifies small babies. Using blood samples from 1000 pregnant women (Collected January 2018- December 2018) we hope to develop a test that will predict small babies on the same day. We can then plan timely delivery and prevent the deaths of thousands of babies.

This project included recruitment of 1000 samples at the Mercy Hospital for Women on the day of an elective caesarean section. A significant strength of this study is that all samples were characterised by me (a single obstetrician) and classified as small-for-gestational age (SGA) or appropriately grown according to GROW birthweight charts.

Project outcomes:

We are pleased to report that we have now completed studies for this project.

Using the FLAG2 cohort, we have measured numerous proteins and confirmed that indeed molecules we have previously identified as deranged at 36 weeks' gestation in SGA pregnancies are also deranged on the day of delivery. Interestingly, while we hypothesised these markers would be more deranged on the day of delivery in SGA infants, we have not found this to be the case. We continue to explore why this is the case.

Importantly, data from this study is now being included in manuscripts that are under preparation or already submitted and under review:

- Circulating syndecan-1 is reduced in pregnancies complicated by poor fetal growth – currently under-review in EBioMedicine
- SPINT1 is reduced in SGA pregnancies on the day of delivery – currently under preparation

Project extensions:

We are also pleased to report that this funding has resulted in further extensions of the original project.

Novel micro RNAs are deranged in SGA pregnancies
In particular, this funding supported my exploration into micro RNAs as biomarkers for stillbirth. In that work I identified novel circulating micro RNAs as deranged in SGA infants. Excitingly that work was presented at The International Society for the Study of Hypertension in Pregnancy World Congress in Amsterdam 2018, The Australian Reproduction Update 2018, the RANZCOG Victorian Trainees Research awards (where I was awarded first prize) and at the virtual awards session for the Society for Reproductive Biology in 2020.

This work was accepted for publication in 2020 and forms the final chapter of my PhD thesis.
Whigham, CA., MacDonald, TM., Walker, SP., Hiscock, R., Hannan, NJ., Pritchard, N., Cannon, P., Nguyen, TV., Miranda, M., Tong, S., Kaitu'u-Lino, TJ. MicroRNAs 363 and 149 are differentially expressed in the maternal circulation preceding a diagnosis of preeclampsia. Scientific Reports. 2020, Oct 22; 10(1): 18077

Combining biomarkers with ultrasound measures
Our data from the protein biomarkers in the FLAG2 cohort has also given us the opportunity to explore the potential for combining this biomarker information with ultrasound data. Indeed, we have undertaken some preliminary work with our artificial intelligence collaborators that suggests combining such information may improve sensitivity for predicting SGA over either parameter alone. As such, we are now following this potential find up in other cohorts to validate whether indeed this is likely.