



## RACP Foundation Research Awards

### FINAL REPORT

<b>Project / Program Title</b>	Maternal hyperoxygenation - a potential new fetal treatment for hypoplastic left heart syndrome	
<b>Name</b>	Dr Flora Wong	
<b>Award Received</b>	2016 Fellows Research Establishment Fellowship	
<b>Report Date</b>	8 August 2018	
<b>Chief Investigator / Supervisor</b>	Dr Flora Wong	
<b>Administering Institution</b>	Monash University	
<b>Funding Period</b>	Start Date:	1 April 2016
	Finish Date:	1 Oct 2017

#### PROJECT SUMMARY

Hypoplastic left heart syndrome is a severe congenital heart disease. Babies with hypoplastic left heart syndrome require very complex cardiac surgery shortly after birth with high mortality and morbidities in survivors. There is a lack of a suitable animal model of hypoplastic left heart syndrome for testing new therapy.

Using the fetal lamb and a novel fetal cardiac catheterisation technique, we aimed to create a fetal lamb model of hypoplastic left heart by closing the fetal foramen ovale (a small hole in the wall between the two upper chambers of the fetal heart). The fetal lamb model is useful for testing new treatments such as maternal hyperoxygenation (giving the mother, in this case the pregnant ewes, supplementary oxygen during pregnancy) to mitigate the development of the hypoplastic left heart before birth.

Our results showed that our fetal lamb model developed structural and cellular features of hypoplastic left heart. We have also applied maternal hyperoxygenation in pilot studies. Our results demonstrate the utility of the fetal lamb model of hypoplastic left heart for testing new treatment for this severe heart disease.

#### PROJECT AIMS / OBJECTIVES

The aims of the project are:

- 1) To develop a fetal lamb model for hypoplastic left heart syndrome (HLHS) by occluding the fetal foramen ovale via fetal cardiac catheterisation

2) To perform a proof-of-concept study using the fetal lamb model of HLHS to test the new treatment of maternal hyperoxygenation (with mother breathing supplementary oxygen via mask) to reduce progression of HLHS in utero

We have performed 12 fetal lamb studies and produced 6 fetal lambs with occluded foramen ovale. The 6 fetuses all survived well until delivery at near-term. We applied maternal hyperoxygenation in 2 fetal lambs as pilot studies. Another 9 normal fetal lambs were used as controls for comparison. Morphological analyses demonstrated that our fetal lamb model of occluded foramen ovale had structural and histopathological

changes of hypoplastic left heart. Further studies and analyses are underway to investigate the changes with maternal hyperoxygenation.

### **SIGNIFICANCE AND OUTCOMES**

Babies with hypoplastic left heart syndrome currently are only offered complex and risky cardiac surgery after birth with significant long-term problems. There is a lack of a suitable animal model of hypoplastic left heart syndrome for testing new therapy.

Using novel catheter-deployed techniques, we have created a fetal lamb model which is the first mammalian model of hypoplastic left heart. We have applied maternal hyperoxygenation (mothers breathing in supplementary oxygen for 4 hours per day) in pilot studies to the pregnant ewes, as a potential fetal treatment to reduce progression of hypoplastic left heart syndrome in-utero.

Our proof-of-concept study has demonstrated feasibility of using the fetal lamb model to test new treatments. This paves the way for a larger animal study to confirm the efficacy and optimal treatment regime, and to fully evaluate the potential benefit and risk of maternal hyperoxygenation for both mother and fetus, before human trials.

### **PUBLICATIONS / PRESENTATIONS**

Manuscript is being prepared using this data for publication in a peer-reviewed journal.