Child Health Research CIO

CHILD HEALTH RESEARCH CHARITABLE INCORPORATED ORGANISATION (CHR CIO)
PROGRESS FORM – VACATION STUDENTS

Student's name:	Isobel Gray
Academic Programme:	Genetics & Genomic Medicine
Project title(s):	Investigating Ift80 expression in mouse models with Jeune Syndrome patient mutations

1. Lay Summary

What are you trying to do in this studentship?

During this studentship I have been working on 3 specific Jeune Syndrome patient mutations which were previously generated in mouse models using CRISPR/Cas9 (*Ift80*^{L549del}, *Ift80*^{A701P}, *Ift80*^{A554fsX}). The *Ift80*^{A554fs} resulted in embryonic lethality, showing total loss of Ift80 is detrimental for development, however it is possible that missense mutations result in tissue specific phenotype. Therefore I have been investigating to see if there is an effect of the mutations on the level of expression of Ift80 in the mutants at both RNA and protein level.

During this studentship I have been working to understand the biology of rare disorder called Jeune Syndrome. Jeune Syndrome is due to mutation in a gene called Ift80. I have been working on 3 Ift80 mutations found in Jeune Syndrome patients. These patient mutations were previously generated in mouse using CRISPR/Cas9 technology to study the syndrome in detail. One of these mutations caused early death of mouse embryos, showing that total loss of Ift80 is detrimental for development. However it is possible that other types of mutations may result in tissue specific phenotype. Therefore I have been investigating to see if there is an effect of the different mutations on the level of expression of Ift80 gene at both RNA and protein level.

Why is this research important?

Jenue Syndrome is an autosomal recessive condition, which significantly shortens individuals' lives and is characterised by a narrow chest, short ribs, shortened long bones and polydactyly. The Ift80 gene is part of the IftB complex, required for the maintenance and elongation of cilia and anterograde transport in cilia. So far in vitro and in vivo studies have shown that Ift80 null mutations results in loss of cilia. Phenotypes of mouse models have also shown polydactyly as well as eye and tooth abnormalities in certain genotypes. In order to characterise the allelic series in more detail the RNA and protein levels must be investigated. It is predicted the missense mutations (*Ift80*^{L549del}, *Ift80*^{A701P}) will have no effect on mRNA production but it is likely that the frameshift mutations will results in transcript instability due to the presence of a premature stop codon.

2. Value of Your Experience

I have thoroughly enjoyed my 8 weeks at the Institute of Child Health (ICH) and have found it extremely rewarding. The collaborative culture, commitment to excellence as well as access to cutting edge technology has provided me with a much better understanding of a research

career. This placement has allowed me to appreciate the time and attention to detail that must be invested in order to obtain meaningful results and that cutting corners is not an option. Having only previously learnt basic laboratory techniques, my confidence has grown immensely and I can now independently extract and quantify RNA, synthesise cDNA, perform a PCR and qRT-PCR, as well as perform a Western blot and understand the process of choosing appropriate antibodies. Additionally I believe I have improved my verbal communication of results, both to colleagues on a day to day basis, and through delivering a presentation as I was given the opportunity to present at the cilia disorders section meeting. These skills will be extremely helpful for the final year research project of my degree and in my future professional career. Being able to talk to colleagues holding different roles (PhD, MSc, Research Assistant, PostDoc, PI) has given me an insight into progression of a research career as well as additional opportunities available with a science degree that I did not know existed. I have learned so much throughout the project and have been provided with invaluable experience that will help to inform my future career choice. I would like to thank all of Dagan Jenkins' group for being extremely welcoming and always willing to help and especially Jeshmi Jeyabalan Srikaran for guiding me the whole way through the project and giving me so much of her time.