Child Health Research CIO

CHILD HEALTH RESEARCH CHARITABLE INCORPORATED ORGANISATION (CHR CIO)
VACATION STUDENT REPORT - 2018

Student's name:	Peter Polgar
Primary supervisor:	Dr Dagan Jenkins
Subsidiary supervisor (where applicable):	Grace Freke
Project title(s):	Investigating the role of BBS1 in cell junction regulation

Summary

What are you trying to do in this studentship?

The eukaryotic human cells contain numerous different organelles – subunits with varying form and function. One such organelle that can be present on these cells are primary cilia – protuberances of the cells surface which are thought to play a part in signalling between cells and the control of cell growth. Primary cilia are non-motile and are commonly found in mammalian cells – almost each cell is thought to possess a single primary cilium at a point in its life.

Disorders affecting the function of cilia are known as ciliopathies. An example of these is Bardet-Biedl syndrome (BBS), a rare human genetic disease which has multiple symptoms including obesity, kidney problems, polydactyly (an increased number of fingers or toes) and vision impairment. Mutations in multiple human genes are linked to the disease, including those in the *BBS1* gene, responsible for the creation of the BBS1 human protein. BBS1 acts in a complex with seven other proteins. This octameric complex, known as the BBSome, is thought to play a part in intracellular trafficking to the primary cilia, though could potentially have other, currently unknown functions.

Previous research on a *BBS1* knockout (a cell line incapable of making functional BBS1 proteins) has found that these cells formed fewer and shorter primary cilia. They were also found to have disturbed tight junctions (multi-protein complexes which are normally found between neighbouring cells, responsible for holding cells together). The research done in this studentship aims to confirm these observations in another *BBS1* knockout cell line, to show that the observed phenotypes are related to the loss of *BBS1* expression.

Why is this research important?

While BBS is relatively rare (it affects approximately 1 person in 150000), it has very severe symptoms which can include kidney failure and blindness, and it currently lacks a cure. As mutations of the *BBS1* gene are linked to Bardet-Biedl syndrome, studying its function can further the understanding of the underlying mechanisms of BBS. This knowledge, in turn, could help in creating a cure for the disease, which otherwise can only be treated with physical, speech and visual therapy. An extended knowledge of the molecular background and the causal mutations of BBS could also aid in better predicting and explaining the expressivity, penetrance and heritability of the disease.

In addition to the clinical aspect, the research project can further the understanding of the function of the BBSome and BBS1 in particular. Data from this research could be used by other studies on the BBSome, primary cilia, epithelial cell polarity or tight junctions.

Value of Your Experience

Please comment on the value of your experience undertaking this CHR CIO vacation studentship.

I believe this studentship greatly helped my professional development. Through my experiments, I learnt key laboratory techniques related to immunofluorescence assays, including the seeding, fixing and staining of cell samples, the mounting of cover slips and the imaging of the slides. By maintaining and regularly passaging my cell lines, I improved my aseptic technique, and became more confident in working in a biological safety cabinet, using light microscopy and counting cells with a haemocytometer. As these skills are highly transferable and useful in science, I believe they will provide me with a good foundation for a career in research and an edge in the competition for PhD positions.

Working independently in the laboratory boosted my confidence in a research environment. While following pre-written protocols made me better at reading and executing instructions, adapting them to different situations made me more flexible and improved my decision making skills. Through discussing previous and current results, as well as future experiments, I gained an insight into experimental design, while analysing my results made me better at computational work and data analysis.

As so far I only had very limited experience in laboratory research, I found this studentship incredibly useful for preparing me for a career in science. Besides providing me with the required experience and teaching me valuable skills, it also made me more confident in my decision to pursue a PhD and a career in academic research, and helped me develop further both as a person and a student in a supportive and exciting environment.