Elective report – George Tang

I spent seven weeks at the School of Optometry in The Hong Kong Polytechnic University where I performed research into the development of myopia using a mouse retina model. I wanted to gain experience in a physiology lab, as all of my previous lab placements had been in pathology labs where very different experimental techniques are used. I chose this research group because I wanted to experience ophthalmology research as well as practise confocal microscopy. I was aware that research often involves international collaboration and decided that I wanted to do a lab project in a country that had a similar level of resources and staffing so that I would be able to see whether the procedures differ from those of the UK.

I had previously completed a year 5 student selected placement (SSP) in ophthalmology and used a confocal microscope extensively in my year 4 student selected component (SSC). I had used a Leica Sp5 confocal during my SSC and the lab I visited for my elective had a ZEISS LSM 800 and I was keen to try both of them. I liked the idea of ophthalmology as it has close links to many medical specialties including endocrinology and diabetes, cardiovascular medicine and gastroenterology (e.g. with inflammatory bowel disease patients). I also felt that a retinal system would be easier to understand compared to one that involved the brain or central visual processing as there are only a few major cell types in the retina.

The original plan had been for me to test the action of neuroprotective compounds on mouse models of glaucoma and diabetic retinopathy, but there were delays in preparing the retinas, so my project was changed to mainly be on myopia instead. I found glaucoma interesting as our understanding of the pathophysiology of the disease is limited and therapy tends to involve eye drops and/or surgery that aims to reduce the intraocular pressure, even in patients with normal-tension glaucoma. The research lab focuses on the roles of gap junctions in mediating intercellular communication, especially between retinal ganglion cells and amacrine cells. The lab has used small molecule inhibitors of gap junctions, such as 18-β-glycyrrhetinic acid, and observed that death of ganglion cells causes the spread of neurotoxic molecules to other ganglion cells through gap junctions which can be blocked using these inhibitors. This secondary ganglion cell death is something that can hopefully be prevented with the development of more selective gap junction inhibitors.

My supervisor had previously used rabbit and chicken models to study the retina but had now switched to mouse models as transgenic mice had been created using cre-loxP systems. This has allowed lab groups to perform research that has more relevance to human disease. As mice are dichromats with only green and blue cones, it is possible to use red lights while performing experiments to allow people working in the lab to visualise the equipment and tissues with minimal risk of causing bleaching desensitisation in the cones. This has allowed the lab to induce dark adaptation in the retinas and record signals in ganglion cells following exposure of the photoreceptor cells to light stimuli.

I started off by watching and learning about techniques including patch clamps, single cell injections and multielectrode arrays. I found this interesting because some of these physiology experiments were taught in detail in the Medical and Veterinary Sciences Tripos, Part IA Homeostasis course, but I had not previously had an opportunity to see

how the techniques had developed since the experiments of Hodgkin and Huxley in Cambridge and how they are applied to current electrophysiology research. I was then taught to use the confocal microscope so that I could take images of the retinal neurons and Muller cells following the injections. I used this time to gain a greater understanding of the mechanisms by which confocal microscopy works and had a lot more time to test different settings on the microscope to get a better quality of image. I found that the software used to control this confocal microscope was very different to the one used for the Leica confocal microscope in the Department of Medicine at Cambridge and has shown me the importance of gaining a better understanding of the underlying mechanisms by which this technology works.

As well as the experimental techniques, I learned how to edit the images using ImageJ and perform statistical analysis using OriginLab software. This has allowed me to gain a greater understanding of data analysis and designing figures for manuscripts. I enjoyed this part of the project as data analysis has a role in all types of research and is a skill that I am very likely to need in the future. I have also been able to continue the image processing and data analysis since returning to the UK from my elective and will continue to work on this data.

This elective helped me to gain a better understanding of how research groups work in a different country and I learned new laboratory techniques, so I feel that it has met my expectations. As my elective was purely in research rather than clinical work, a lot of the work was more routine and there was no single event that was particularly memorable, but the working style seemed to be quite different to what I was used to. The lab members would often work from 9am until beyond midnight 6 or 7 days a week and did not seem to have time for other activities. My supervisor did not expect me to work these hours, but I felt that there was still perhaps an expectation that I would generate and analyse data very quickly and be prepared to present my findings on the same day, or perhaps the day after, performing the experiments. From my experiences in the UK, my supervisors had been less hands-on, and I therefore had time to be working on multiple projects over a longer period of time, which is my preferred way of working. Nevertheless, the pressure on principal investigators to generate and publish data quickly in order to get grants to fund their future research is present everywhere.

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