Sam Chamberlain-Keen Pathology Studentship Report

I set out to investigate the potential of CD47 as a therapeutic target for treatment of marginal zone lymphomas (MZL). CD47 is a plasma membrane molecule and its interaction with SIRPα on macrophages prevents phagocytosis. It has been found that overexpression in various cancers such as ovarian cancer, hepatocellular carcinoma and mantle-cell lymphoma is associated with poor prognosis. Anti-CD47 monoclonal antibody (mAb) therapy has been shown to increase phagocytosis of cancer cells and inhibition of tumour growth in solid tumour mouse xenograft models (such as ovarian cancer; colon cancer; breast cancer; glioblastoma). In combination with rituximab, anti-CD47 mAb results in elimination of NHL in mouse xenograft models. However, CD47 expression is not well documented in MZL and so measuring CD47 expression may reveal CD47 to be a new therapeutic target in MZL.

Method and results

Using single immunohistochemistry, I stained for CD47 on samples of a range of non-Hodgkin lymphomas (mainly MZL) and solid tumours. I am currently analysing samples by scanning slides with the Hamamatsu Nanozoomer and then application of QuPath software. I am categorising samples by percentage of positive cells into negative samples (<1%), weak-expressing samples (1-50%) or strong-expressing samples (>50%). I will further analyse samples for percentage of cells with expression intensities 1, 2 and 3. However, I am still currently developing the intensity threshold values for this.

I encountered a ‘hiccup’ during the analysis stage: I discovered very weak and patchy CD47 expression in some of my slides, which I reported to my supervisor. Long delays between cutting sections and staining can decrease IHC reaction intensity, leading to the ‘blush’ that I observed. Due to the age of some of the slides I was using, I will have to re-cut and stain samples for more accurate results.

At this stage, I can say that there is overexpression of CD47 in some, but not all, cases of MZL and this expression is heterogeneous within samples.

Experience and take-aways

The studentship has provided me the opportunity to become involved with hands-on research and this has been a hugely valuable experience. I have been trained in the whole process from cutting sections to analysing samples (though I am yet to take my microtome examination) and it has been amazing to be able to translate what I have learnt from reading research papers on CD47 to my project. Obviously there have been challenges during the process: the blushing present in some samples; difficulty in adapting the QuPath software to my samples for more accurate cell detection; designing and presenting a poster on my research project at the Rani-Rawji Studentship Seminar, which was awarded 1st prize.

There is plenty of work left to do, but I am looking forward to completing my project over the coming months and writing a paper on my findings.