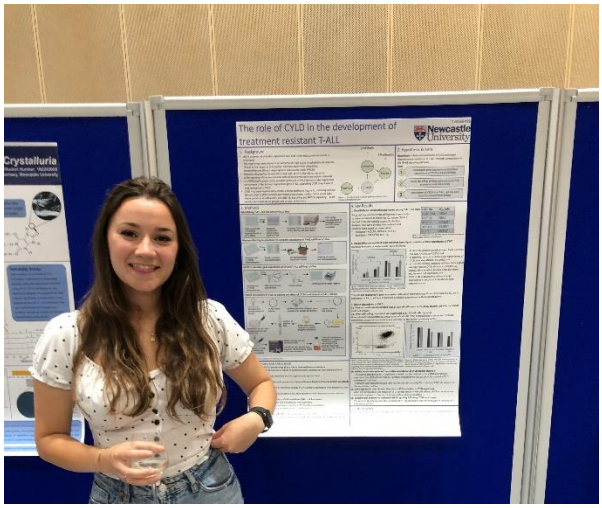

Hannah Elkatkat - bursary awarded 2021, Newcastle Medical School.

With the help from BDIAP, I undertook an intercalated Master of Research in Cancer. The course consisted of one taught semester and one semester to undertake a research project. My taught modules included Applied Immunobiology of Human Disease, Cancer Studies, Research Skills and Principles for the Biosciences, and Transplantation Science, which I particularly enjoyed. Though the lectures were very different to ones I have encountered, with more focus on recent advances, I found them to be engaging and interesting.

My research topic was paediatric treatment resistant T cell acute lymphoblastic leukaemia (T-ALL) undertaken at the Wolfson Childhood Cancer Centre at Newcastle University, under the supervision and guidance from Dr Frederik van Delf and Dr Alistair Poll. Despite having no lab experience, I was keen to do a lab-based project; I wanted to learn new skills and I was excited at the prospect of generating my own data. The research focussed on a tumour suppressor gene, *CYLD*, and its role in the survival of T-ALL cells through dysregulation of apoptosis and the NF-kB signalling pathway. We hypothesised that loss of *CYLD* promotes chemotherapy resistance in T-ALL through disruption of the NF-κB signalling pathway. The aims were to explore the role of *CYLD* in T-ALL cell lines and its effect on Dexamethasone resistance through investigating CYLD gene and protein abundance in T-ALL cell lines, studying the effect of Dexamethasone on *CYLD* expression and cell survival, and to knockdown *CYLD* in a T-ALL cell line and study the effects.

I first established the sensitivity of different T-ALL cell lines to Dexamethasone using cell viability assays. Then, we correlated this to CYLD protein abundance and gene expression data (under basal conditions and following dexamethasone treatment) obtained by western blotting and quantitative-PCR, respectively. The main bulk of the work consisted of the development of a short-hairpin RNA (shRNA) knockdown of CYLD in a T-ALL cell line. The aim was then to study the downstream effects of CYLD knockdown, although this was limited by project time constraints. However, we did find a correlation between Dexamethasone sensitivity and CYLD protein abundance (cell lines with higher basal protein abundance of CYLD were more resistant to Dexamethasone). This was consistent with a role for the tumour suppressor gene in Dexamethasone resistance, however, needs more in-depth investigation to validate the data and potentially reveal a mechanism. *CYLD* knockdown cell line is now isolated and frozen down ready for further downstream experiments by the lab group.

During the project I learnt a variety of lab techniques including the culturing of cell lines, cell viability assays, western blotting, RNA extraction, cDNA extraction, qPCR, as well as a range of techniques for the shRNA knockdown including bacterial transformation and flow cytometry. It was a fantastic opportunity and widened my understanding the role research can play in a clinical career, and whilst I found it challenging at times, I am exceedingly grateful for the experience! I would certainly consider coming back to research in the future and I am excited to hear from the rest of the lab group what the future investigations using the knockdown cell line reveal.