**Abstract:**

Acute lymphoblastic leukaemia is the most common cancer in children. Unfortunately, it has been difficult to replicate the excellent survival rates found in children with those that experience relapse – a marker of which is glucocorticoid resistance. Proposed therapies to treat relapse are currently not sufficiently cost-effective enough, so novel treatments are required. HDAC enzymes and the PI3K/mTOR pathway have been implicated in glucocorticoid resistance acquisition and as CUDC-907 is an inhibitor of both HDACs and the PI3K/mTOR pathway, cytotoxic synergy might be achieved upon combination treatment with dexamethasone.

MTT and MTS assays were both utilised to determine the IC50 of CUDC-907, confirm dexamethasone resistance, and identify any cytotoxic synergy between the two drugs at varying concentrations. After 24-hour incubation at selected concentrations, in-solution digestion, STAGE tip purification, and high pH reverse phase fractionation were performed. Data from LC-MS experiments were analysed and protein correlation with Dexamethasone/ CUDC-907 sensitivity was determined with the FOR-ALL software.

Cell-viability assays determined that the IC50 of CUDC-907 was 0.05μM and confirmed dexamethasone resistance. MTS assays revealed significant (p<0.01) glucocorticoid resistance reduction in cells treated with a combination of CUDC-907: Dexamethasone (0.05 μM:10 μM). Finally, proteomic experiments suggested 3 proteins that likely mediated glucocorticoid resistance upheaval: SSRP1, PARP1, and LRMP. These proteins are associated with chromatin remodelling (PARP1; SSRP1), and microtubular polymerisation (LRMP), and may all be involved in CUDC-907 mediated sensitisation of Hal-01 cells to dexamethasone. Exploiting these pathways could improve the survival rates of patients with relapsed ALL.