The ubiquitin-proteasome system (UPS) serves as a crucial pathway in turnover and degradation of cellular proteins. The rate of cellular protein breakdown is increased in comparison to non-malignant cells, which sensitizes tumors for any protein changes. Proteasome inhibitor - bortezomib was the first inhibitor registered in reality. However, the studies showed that only a few solid tumors are still sensitive. There are several other strategies that target other proteasome components of UPS. Targeting E1 enzyme as an initiation of UPS serves as a promising anticancer therapy. Malignant cells are assessed for a passed nM of response. 231 dedicated Ub may be suspended. After cellular concentration, propidium 250 is stained. The cellular proportion and the potential Cancer human enzyme inhibitors are present in cells and it is associated with the solid tumors therapy.

**MATERIALS AND METHODS**

A novel E1 small molecule inhibitor, CPL-410-005 was designed. Biochemical assay with the use of purified E1 enzyme to analyze the inhibitor potency was assessed. As a control, in cell proliferation or ubiquitin-like modifications were developed. The biological potency and selectivity of the compound was evaluated in a number of cancer cell-based models by cell viability test. Western blot and flow cytometry monitored the rate of programmed cellular death, inhibited protein response or cell cycle inhibition, respectively.

**RESULTS**

**CPL-410-005 inhibits E1 enzyme with greater potency than MLN7243.**

**CPL-410-005 inhibits proliferation of tumor cells with higher efficiency in comparison to non-malignant cells.**

**CPL-410-005 inhibits proliferation of plethora of tumor cells.**

**CPL-410-005 inhibits cellular polyubiquitination, but not neddylation/somiliation. The polyubiquitination inhibition is pronounced in malignant cells in comparison to normal cells.**

**REFERENCES**


