LB-100, a protein phosphatase 2A inhibitor, suppresses ABCB1 protein level and increases doxorubicin efficacy in multidrug resistant glioblastoma and non-small cell lung carcinoma cells

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This study investigates the potential of LB-100, a small molecule inhibitor of protein phosphatase 2A, in combination with doxorubicin (DOX) to overcome multidrug resistance (MDR) in cancer cells and improve treatment efficacy. We examined ABCB1 protein expression and drug resistance genes' expression in MDR glioblastoma and non-small cell lung carcinoma (NSCLC) cells after treatment with LB-100, as well as LB-100 sensitizing effect on DOX. LB-100 reduces ABCB1 levels and alters transcriptional dynamics of genes associated with treatment response in MDR glioblastoma and NSCLC cells. LB-100 effectively enhances the accumulation of DOX and its cytotoxicity in MDR cancer cells, especially when administered in a subsequent treatment. Rhodamine 123 accumulation assay showed that LB-100 does not affect ABCB1 activity, while SWISSAdme analysis indicated that LB-100 is not an ABCB1 substrate. Our results suggest that LB-100 sensitizes MDR cancer cells by altering ABCB1 expression. The combination of LB-100 with anticancer drugs is a promising strategy to overcome drug resistance in cancer therapy.