

**P034** Drug binding motif conjugated to Tat peptide traffics the delivery of doxorubicin in human leukaemia cells

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Multidrug resistance (MDR) is a clinical phenomenon by which cancers develop resistance to many commonly used chemotherapeutic drugs. Increased efflux of drug by membrane proteins such as P-glycoprotein (P-gp) plays a key role in MDR by removing drugs from cytoplasm, thus lowering the intracellular drug concentration below therapeutic levels. In this study, a hybrid peptide (DBM-Tat) constructed from cell penetrating peptide Tat and drug binding motif (DBM) was synthesized. Then the DBM-Tat monomer was dimerized through C-terminal cysteine to form (DBM-Tat)<sub>2</sub>. The uptake and localization of non-covalently peptide bound anti-cancer drug doxorubicin (Dox) were studied in human leukaemia K562 cell line and its drug resistant subline KD30. Enhanced drug uptake was observed in both cell lines when Dox was bound to DBM-Tat and (DBM-Tat)<sub>2</sub>. Uptake kinetics of Dox was altered in the presence of both peptides in KD30 cells. DBM-Tat and (DBM-Tat)<sub>2</sub> bound Dox appears to be more localized in perinuclear area probably certain cytoplasmic organelles of KD30 cells, compared to free Dox. (DBM-Tat)<sub>2</sub> has higher efficiency than DBM-Tat in affecting cellular uptake.