Supplementary Materials

Synthetic route of di-2,2'-pyridineketone hydrazone dithiocarbamate S-propionic acid podophyllotoxin ester (Ptox^{Dpt})

The details for Ptox^{Dpt} preparation as described in section of Materials and methods

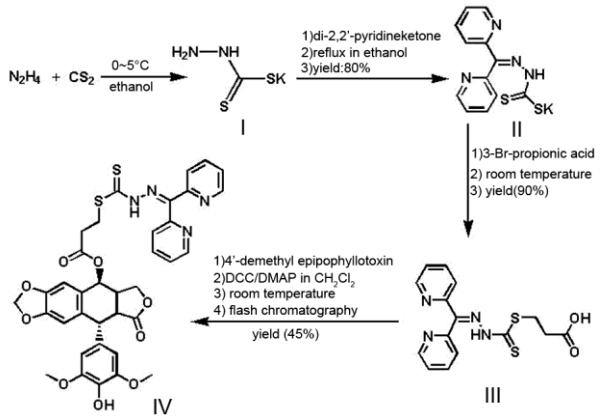

Fig. S1: synthetic route of Ptox^{Dpt}, the condition as indicated in the scheme. The data of NMR and HRMS are shown in Methods and Materials section

Conformation comparison of etoposide with Ptox^{Pdt} in catalytic center of DNA Topoisomerase II

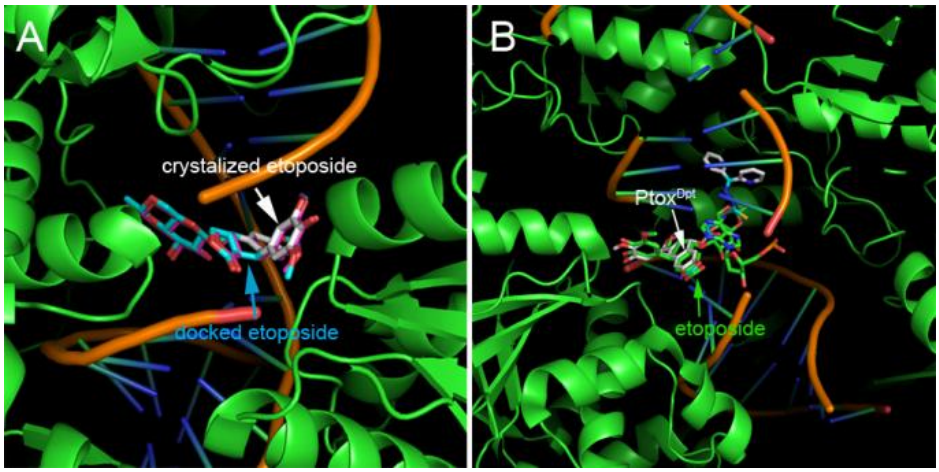

Fig. S2: Molecular simulation of etoposide and Ptox^{Pdt}. (A) Comparison of docked etoposide with crystalized etoposide in DNA-topoisomerase complex; (B) Comparison of docked etoposide with docked Ptox^{Pdt} in DNA-topoisomerase complex.

Comparison of etoposide with Ptox^{Pdt} in growth inhibition against indicated cell lines

The protocol used was similar to that in section of Materials and methods, 4.4 Cytotoxicity assay (MTT assay).

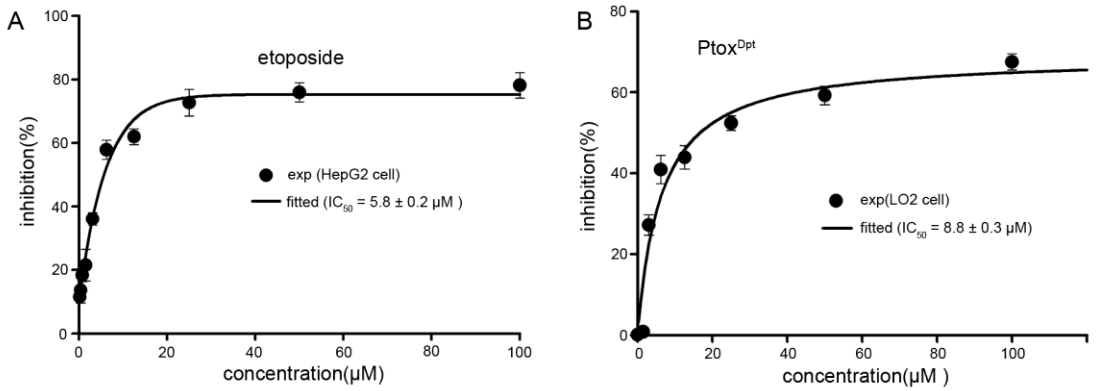

Fig. S3: Proliferation inhibition of etoposide against HepG2(A), and $Ptox^{Dpt}$ against normal human hepatic cell line LO2 cell (B).

$Ptox^{Pdt}$ induced ROS during the time period

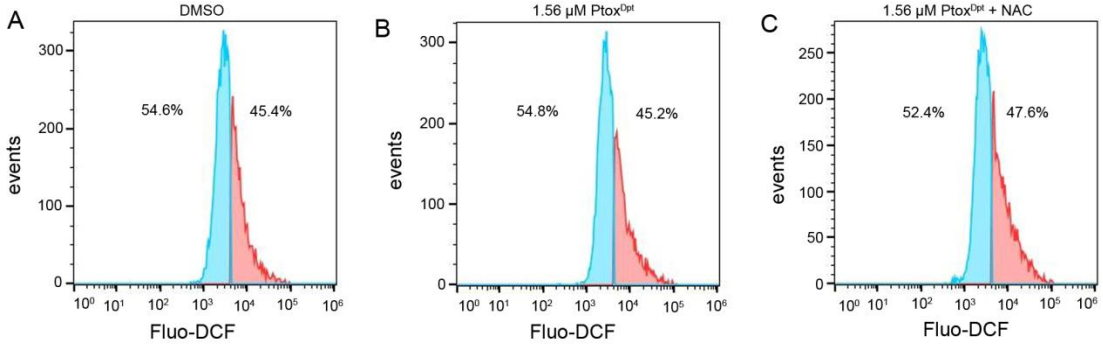

Fig. S4: ROS production induced by $Ptox^{Dpt}$ after 24 h during EMT reversal: (A) DMSO; (B) 1.56 μM $Ptox^{Dpt}$; (C) 1.56 μM $Ptox^{Dpt}$ + 3 mM NAC.