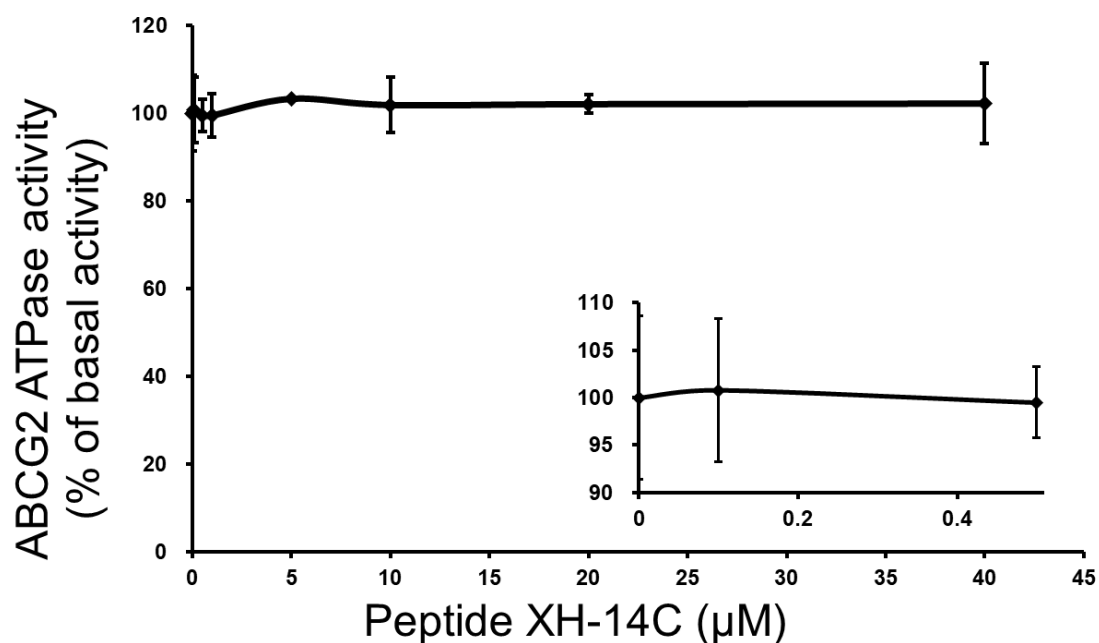
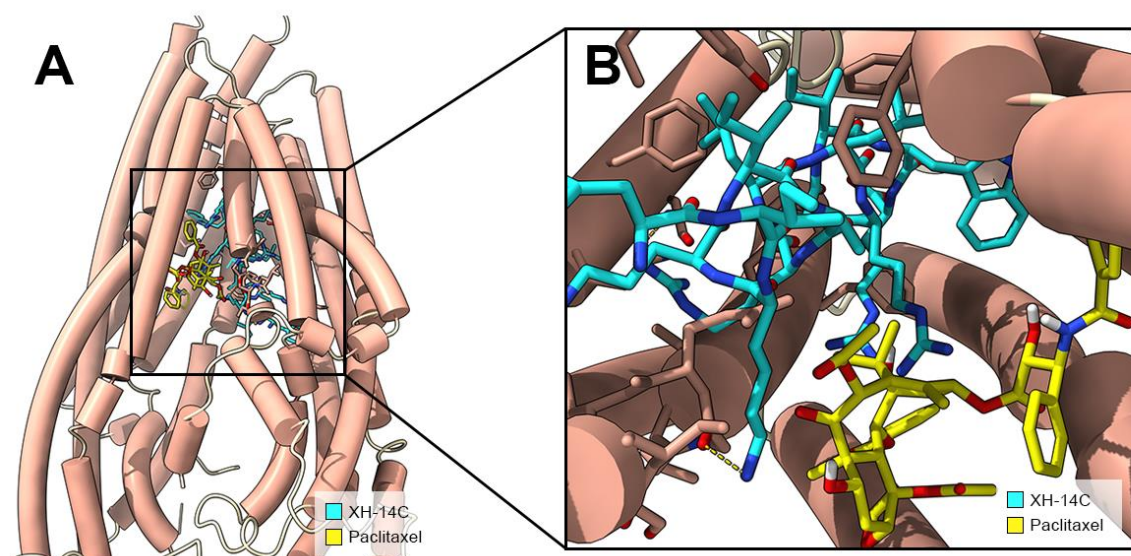


**Figure S1.** Dose-response curve of A) XH-14A, B) XH-14B and C) XH-14C on drug-selected ABCG2-overexpressing cell lines (NCI-H460/MX20) and its parental drug-sensitive cell line (NCI-H460) with gradient concentrations. Each point with error bar represents the mean  $\pm$  SD of the cytotoxicity with different concentrations calculated from at least three independent experiments performed in triplicate.



**Figure S2.** The vanadate sensitive ABCG2 transporter specific ATPase activity does not change by XH-14C. Gradient concentration of XH-14C (0-40  $\mu$ M) as x-axis and ABCG2 ATPase activity represented in percentage of basal activity as y-axis was plotted. The small inner figure plotted the lower concentrations (0-0.5  $\mu$ M) of XH-14C versus ATPase activity. The points with error bar represent the mean  $\pm$  SD calculated from three independent experiments.



**Figure S3.** Docking simulation of XH-14C and paclitaxel with ABCB1. A. Best scoring poses of XH-14C and paclitaxel in the drug binding pocket of ABCB1. XH-14C was depicted as cyan sticks and paclitaxel was depicted as yellow sticks. ABCB1 (4M2T) was depicted as colored tubes. B. Details of the positions of XH-14C and paclitaxel with ABCB1 binding pocket.

**Table S1.** The cytotoxicity of ABCG2 substrates with or without combination of a reversal agent.

Treatment	IC <sub>50</sub> <sup>1</sup> (μM) (RF <sup>2</sup> )	
	NCI-H460	NCI-H460/MX20
Mitoxantrone	0.039 ± 0.005 (1.00)	36.55 ± 4.53 (937)
+ XH-14A (3 μM)	0.055 ± 0.003 (1.41)	34.28 ± 4.13 (879)
+ XH-14B (3 μM)	0.051 ± 0.008 (1.31)	38.49 ± 3.55 (987)
+ XH-14C (3 μM)	0.041 ± 0.006 (1.05)	36.85 ± 3.95 (945)
+ Ko143 (3 μM)	0.043 ± 0.004 (1.10)	0.089 ± 0.0040 <sup>#</sup> (2.28)
Topotecan	0.049 ± 0.006 (1.00)	39.16 ± 4.85 (799)
+ XH-14A (3 μM)	0.062 ± 0.004 (1.27)	34.95 ± 4.21 (713)
+ XH-14B (3 μM)	0.040 ± 0.009 (0.82)	35.96 ± 4.04 (734)
+ XH-14C (3 μM)	0.042 ± 0.005 (0.86)	37.83 ± 3.16 (772)
+ Ko143 (3 μM)	0.037 ± 0.003 (0.76)	0.096 ± 0.0064 <sup>#</sup> (1.96)
Cisplatin	2.76 ± 0.23 (1.00)	3.15 ± 0.47 (1.14)
+ XH-14A (3 μM)	3.17 ± 0.31 (1.15)	3.29 ± 0.26 (1.19)
+ XH-14B (3 μM)	2.82 ± 0.22 (1.02)	2.96 ± 0.31 (1.07)
+ XH-14C (3 μM)	2.77 ± 0.32 (1.00)	3.17 ± 0.33 (1.15)
+ Ko143 (3 μM)	3.47 ± 0.35 (1.26)	3.40 ± 0.46 (1.23)

<sup>1</sup> IC<sub>50</sub> values are calculated from at least three independent experiments performed in triplicate and finally represented as mean ± SD with unit of nM. <sup>2</sup> RF, resistant fold, calculated by the IC<sub>50</sub> in the drug-selected ABCG2-overexpressing cancer cell line NCI-H460/MX20 divided by the IC<sub>50</sub> in the drug-sensitive cancer cell line NCI-H460. <sup>#</sup>, represents  $p < 0.001$ , compared to the value of NCI-H460/MX20 control group.