



SOLVO

BIOTECHNOLOGY

Ko134 – BCRP Specific Inhibitor

SOLVO Biotechnology is introducing Ko134 for ABCG2/BCRP membrane transporter inhibition studies.

Ko134, the tetracyclic fumitremorgin C (FTC) analog, is a highly potent and specific inhibitor of the ABCG2 (BCRP) multidrug transporter protein. Our data show that Ko-134 inhibits BCRP with IC_{50} 0,070 μ M and it inhibits P-gp at IC_{50} > 1 μ M. Contrarily, GF120918 - a model P-gp inhibitor - more potently inhibits P-gp (IC_{50} =0.132) than BCRP (IC_{50} =7.906). Additional data are published by Allen et al, 2002 (1).

	P-gp IC_{50} (μ M)	BCRP IC_{50} (μ M)
Ko134	>1	0.070
GF120918	0.132	7.906

Due to its non-toxic property at its effective concentrations both *in vivo* and *in vitro*, Ko134 is an excellent laboratory reagent.

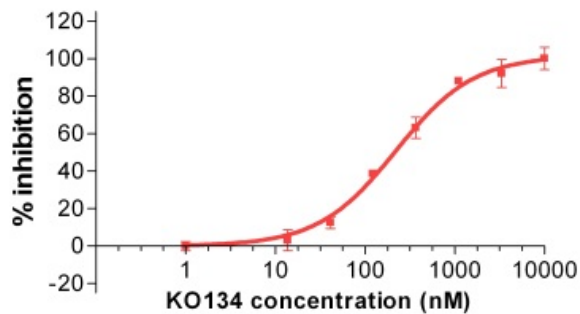


Figure 1 Inhibitory effect of Ko134 on Hoechst 33342 (BCRP substrate) efflux in a fluorescent whole cell based assay.

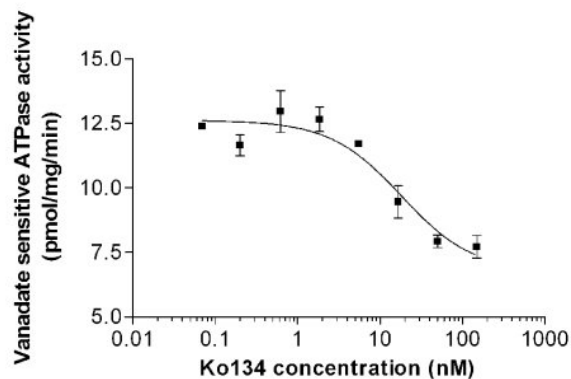


Figure 2 Inhibition of the vanadate sensitive ATPase activity of SB-BCRP-Sf9 preparations by Ko134

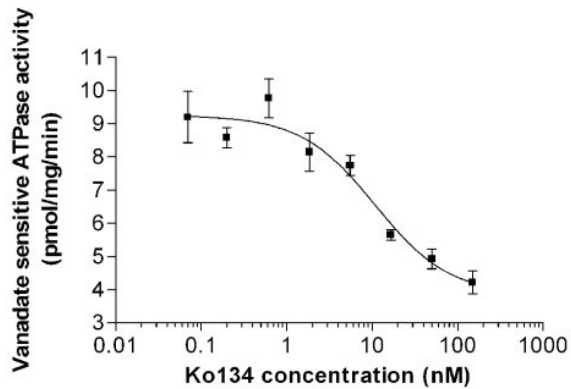


Figure 3 Inhibition of the vanadate sensitive ATPase activity of SB-BCRP-M preparations by Ko134

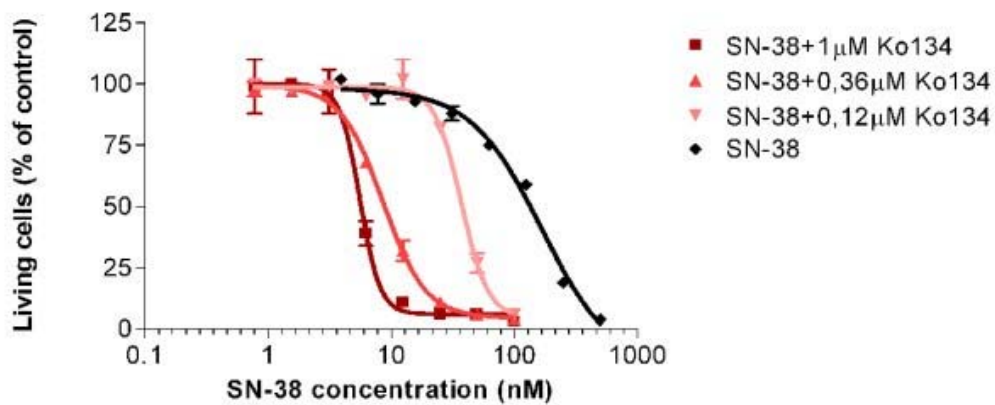


Figure 4 Ko134 enhanced SN-38 (BCRP substrate anticancer agent) cytotoxicity in BCRP expressing P388 cells at various concentrations

Reference:

1. John D. Allen, Arnold van Loevezijn, Jeany M. Lakhai, Martin van der Valk, Olaf van Tellingen, Glen Reid, Jan H. M. Schellens, Gerrit-Jan Koomen, and Alfred H. Schinkel (2002) *Molecular Cancer Therapeutics* Vol. 1, 417- 425
2. Glavinas H., et al., ABCG2 (breast cancer resistance protein/mitoxantrone resistance-associated protein) ATPase assay: a useful tool to detect drug-transporter interactions. *Drug Metab Dispos.* 35(9):1533-42, (2007)
3. Pál A., et al., Cholesterol potentiates ABCG2 activity in a heterologous expression system: improved in vitro model to study function of human ABCG2. *J. Pharmacol Exp. Ther.* 321(3):1085-94, (2007).
4. Van Loevezijn, A., et al., Inhibition of BCRP-mediated drug efflux by fumitremorgin-type indolyl diketopiperazines. *Bioorg. Med. Chem. Lett.* 11, 29-32, (2001)