



SOLVO BCRP HAM MEMBRANES AND VESICLES

SOLVO Biotechnology is introducing the revolutionary BCRP HAM membranes and vesicles

BCRP (MXR/ABCG2) is one of the most important efflux transporters in endothelial and epithelial cells, modulating ADME properties of drugs (reviewed in Mao and Unadkat, 2005). It is a half-transporter that works as a homodimer (Ozvegy et al., 2001; Kage et al., 2002). ABCG2 has a broad substrate specificity as it transports hydrophobic, anionic as well as cationic drugs (Mao and Unadkat, 2005). Therefore, it is widely believed that ABCG2 plays an important role in intestinal absorption (Polli et al., 2004) and secretion of xenobiotics and metabolites (Ebert et al., 2005), secretion of sulphate conjugates in the liver (Zamek-Gliszczyński et al. 2006), prevention of penetration of drugs into the brain (Breedveld et al., 2005). ABCG2 may play a pivotal role in placenta as a defensive barrier to drugs as well as a major efflux function to reduce steroid levels in fetal tissues (Jonker et al., 2000). ABCG2 knock-out models shed light on some special functions of ABCG2, such as secretion of drugs and other xenobiotics into the milk (Jonker et al., 2005) and protection of stem cells from hypoxia-induced protoporphyrin accumulation and damage (Krishnamurthy and Schuetz, 2005).

BCRP function is commonly studied using high throughput (HT) cellular (Robey et al., 2004) or membrane based assays (Janvilisri et al., 2003; Ozvegy et al., 2001) which are suitable tools for in vitro screening of drug-transporter interactions (for reviews see Glavinas et al. 2004; <http://www.solvo.com>). For most applications the transporter is expressed in insect cell lines (e.g. Sf9) taking advantage of the robust baculovirus - insect cell system (Ozvegy et al., 2001). Alternatively, membranes are prepared from human cell lines (Han and Zhang, 2004) overexpressing the transporter. ABCG2 also mediates multidrug resistance in vitro and was originally cloned from cell lines selected for drug resistance.

HAM - HIGH ACTIVITY MEMBRANE

A REVOLUTIONARY PROPRIETARY TECHNOLOGY PATENTED BY SOLVO BIOTECHNOLOGY

- **Greater dynamic range: The BCRP-HAM assays are more robust than BCRP-M or BCRP-Sf9 assays**
- **More suitable for screening drug-drug interactions**
- **Excellent model for mammalian BCRP: EC50 and IC50 values obtained in mammalian system (BCRP-M) correlate well with those from BCRP-HAM**

	ATPase assay	Estrone-3- sulfate vesicular transport	Methotrexate vesicular transport																																			
	<p>ATPase activity of BCRPs and controls Vanadate sensitive specific activity (nmol/mg/min)</p> <table border="1"> <caption>ATPase activity data (nmol/mg/min)</caption> <thead> <tr> <th>Membrane</th> <th>Baseline</th> <th>Activated</th> </tr> </thead> <tbody> <tr> <td>BCRP-HAM</td> <td>~25</td> <td>~60</td> </tr> <tr> <td>def-BCRP-HAM</td> <td>~5</td> <td>~5</td> </tr> <tr> <td>BCRP-M</td> <td>~15</td> <td>~45</td> </tr> <tr> <td>M-ctrl</td> <td>~1</td> <td>~1</td> </tr> </tbody> </table>	Membrane	Baseline	Activated	BCRP-HAM	~25	~60	def-BCRP-HAM	~5	~5	BCRP-M	~15	~45	M-ctrl	~1	~1	<p>ATP dependent cpm in E3S vesicular transport</p> <table border="1"> <caption>ATP dependent cpm in E3S vesicular transport</caption> <thead> <tr> <th>Membrane</th> <th>ATP dependent cpm</th> </tr> </thead> <tbody> <tr> <td>BCRP-HAM</td> <td>~1500</td> </tr> <tr> <td>def-BCRP-HAM</td> <td>~100</td> </tr> <tr> <td>BCRP-M</td> <td>~1000</td> </tr> <tr> <td>M-ctrl</td> <td>~100</td> </tr> </tbody> </table>	Membrane	ATP dependent cpm	BCRP-HAM	~1500	def-BCRP-HAM	~100	BCRP-M	~1000	M-ctrl	~100	<p>ATP dependent cpm in MTX vesicular transport</p> <table border="1"> <caption>ATP dependent cpm in MTX vesicular transport</caption> <thead> <tr> <th>Membrane</th> <th>ATP dependent cpm</th> </tr> </thead> <tbody> <tr> <td>BCRP-HAM</td> <td>~1200</td> </tr> <tr> <td>def-BCRP-HAM</td> <td>~100</td> </tr> <tr> <td>BCRP-M</td> <td>~600</td> </tr> <tr> <td>M-ctrl</td> <td>~100</td> </tr> </tbody> </table>	Membrane	ATP dependent cpm	BCRP-HAM	~1200	def-BCRP-HAM	~100	BCRP-M	~600	M-ctrl	~100
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BCRP-M-VT		40-80	40-90																																			
BCRP-HAM-Sf9-ATPase	15-30 / 40-70																																					
BCRP-HAM-Sf9-VT		80-160	150-250																																			

