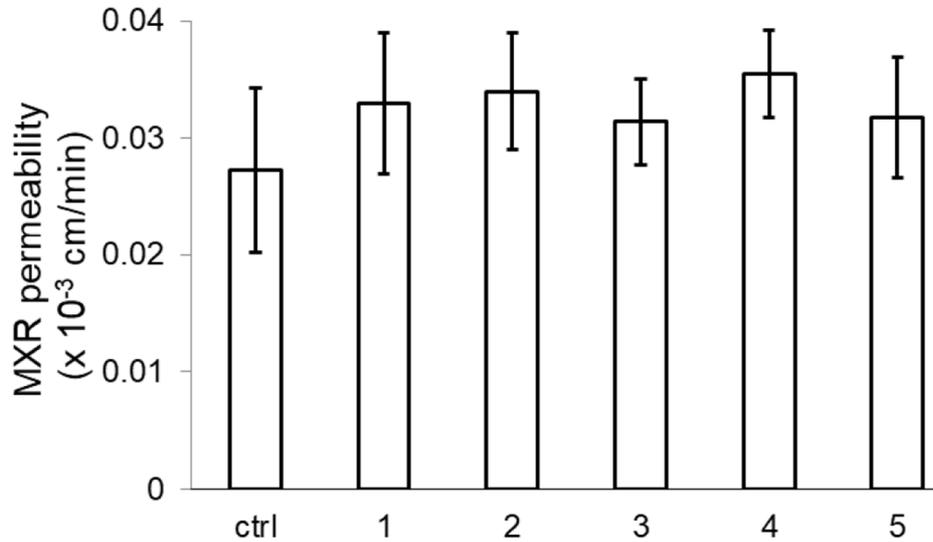


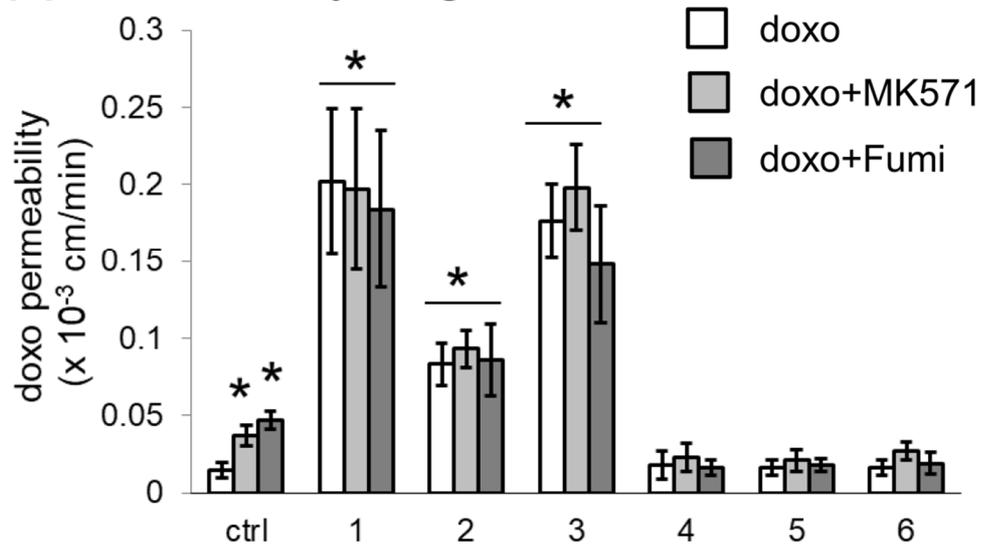
Supplementary Figure 1



Supplementary Figure 1. Effects of Pgp ligands on mitoxantrone permeability across BBB

hCMEC/D3 cells were grown in the upper insert of Transwell devices for 7 days, then medium was replaced with fresh medium (ctrl) or with medium containing 1 nM of compounds **1-6** for 24 h. 10 μ M mitoxantrone (MXR) was added in the last 3 h. The amount of mitoxantrone in the medium of the lower chamber was measured spectrofluorimetrically, in duplicates. Data are presented as means \pm SD (n = 3).

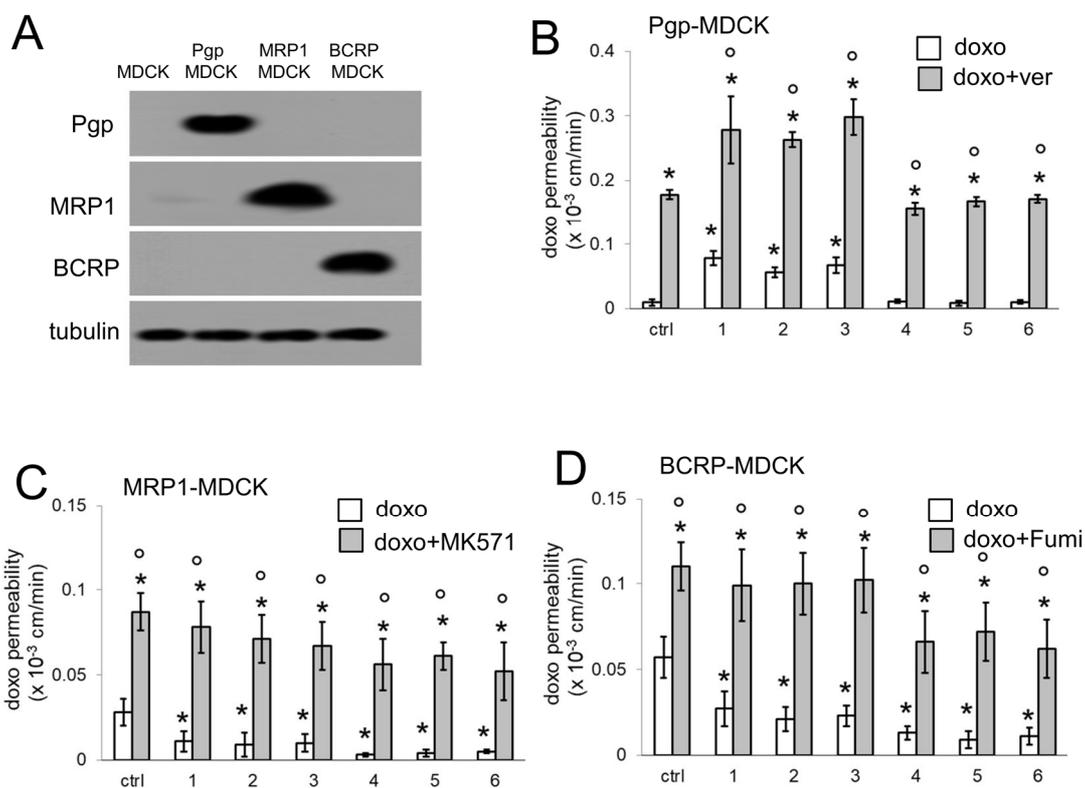
Supplementary Figure 2



Supplementary Figure 2. Effects of MRP1 and BCRP inhibitors on doxorubicin transport across BBB

hCMEC/D3 cells were grown in the upper insert of Transwell devices for 7 days, then medium was replaced with fresh medium (ctrl) or with medium containing 1 nM of compounds 1-6 for 24 h. 5 μ M doxorubicin (doxo) was added during the last 3 h, in the presence of 25 μ M MK571, an inhibitor of MRP1, or 5 μ M fumitremorgin C (Fumi), an inhibitor of BCRP. The amount of doxorubicin in the medium of the lower chamber was measured spectrofluorimetrically, in duplicates. Data are presented as means \pm SD (n = 3). Versus doxo: * p < 0.01.

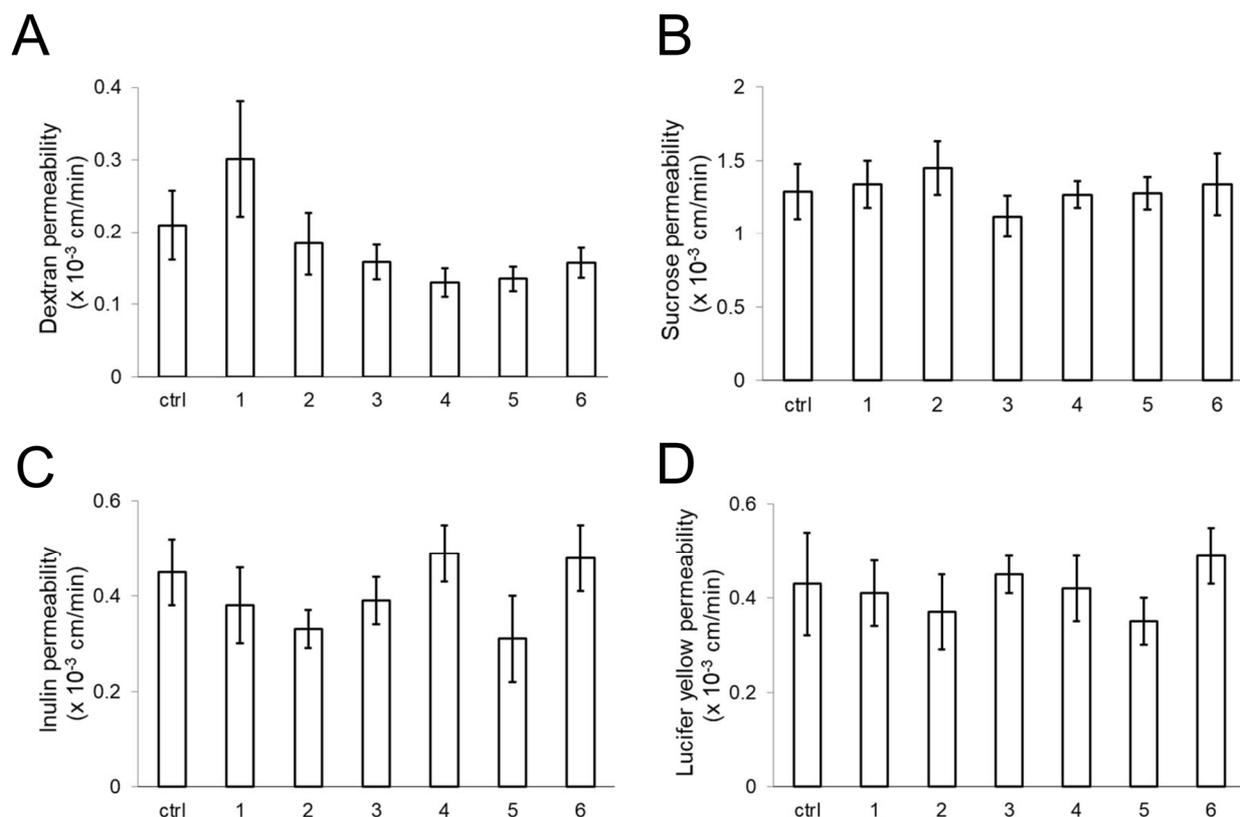
Supplementary Figure 3



Supplementary Figure 3. Effects of Pgp ligands on doxorubicin transport on Pgp-MDCK, MRP1-MDCK and BCRP-MDCK cells

A. MDCK, Pgp-MDCK, MRP1-MDCK, BCRP-MDCK were lysed and immunoblotted with the indicated antibodies. β -tubulin level was used as control of equal protein loading. The figure is representative of one out of three experiments with similar results. **B-D.** Pgp-MDCK (panel B), MRP1-MDCK (panel C), BCRP-MDCK (panel D) were grown in the upper insert of Transwell devices for 7 days, then medium was replaced with fresh medium (ctrl) or with medium containing 1 nM of compounds 1-6 for 24 h. 5 μ M doxorubicin (doxo) was added during the last 3 h. When indicated, 50 μ M verapamil (ver), an inhibitor of Pgp, 25 μ M MK571, an inhibitor of MRP1, or 5 μ M fumitremorgin C (Fumi), an inhibitor of BCRP were added. The amount of doxorubicin in the medium of the lower chamber was measured spectrofluorimetrically, in duplicates. Data are presented as means \pm SD (n = 3). Versus doxo: * p < 0.05; doxo+ver/doxo+MK571/doxo+Fumi vs doxo:° p < 0.001.

Supplementary Figure 4



Supplementary Figure 4. Effects of Pgp ligands on dextran, sucrose, inulin and lucifer yellow permeability across BBB

hCMEC/D3 cells were grown in the upper insert of Transwell devices for 7 days, then medium was replaced with fresh medium (ctrl) or with medium containing 1 nM of compounds **1-6** for 24 h. 2 μ M dextran-FITC (panel **A**), 2 μ Ci/ml [14 C]-sucrose (panel **B**), 2 μ Ci/ml [14 C]-inulin (panel **C**), 100 μ M lucifer yellow (panel **D**) were added in the last 3 h. The amount of each compound in the medium of the lower chamber was measured spectrofluorimetrically (for dextran-FITC and luciferin yellow) or by liquid scintillation (for [14 C]-sucrose and [14 C]-inulin), in duplicates. Data are presented as means \pm SD (n = 3).

Supplementary Table 1. Phenotypic characterization of cells from patient number 1, 2, 3 by immunofluorescence analysis

	NS	NS	NS	AC	AC	AC
Marker	CV17	010627	Nov3	CV17	010627	Nov3
Nestin	++	+	+	+	-	-
CD133	+	+	+	-	-	-
Musashi	+	+	+	-	-	-
SOX2	+	+	+	-	-	-
EGFR	+/-	+	+	+	-	-
p53	+	+	+	-	-	-
GFAP	-	-	-	+	+	+
GalC	+	-	-	+	+/-	++