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Supplemental Information

**ATP-binding cassette transporters restrict
drug delivery and efficacy against brain tumors
even when blood-brain barrier integrity is lost**

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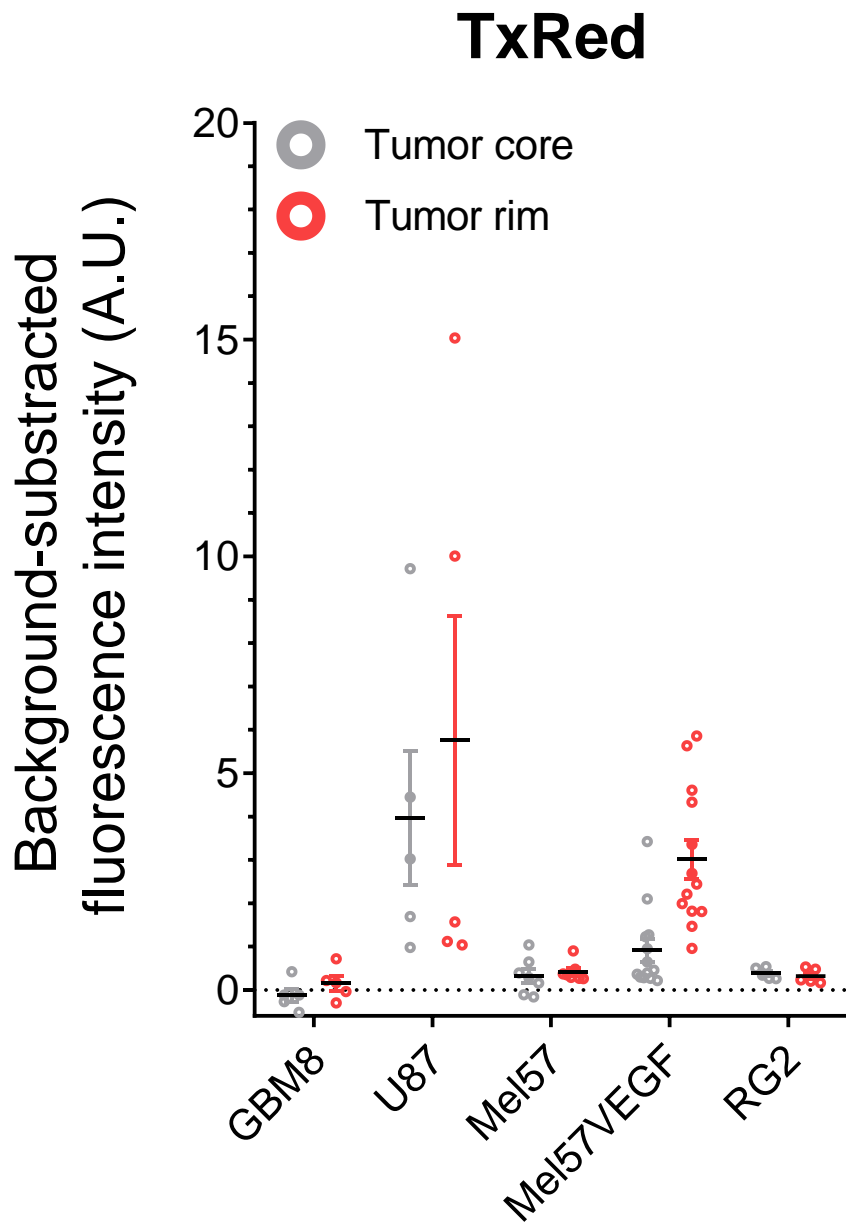


Figure S1, related to Figure 1. Quantification of TexasRed extravasation in intracranial tumor models. The TexasRed (TxRed) fluorescence intensity (arbitrary units, A.U.) in tumor core and tumor rim (100 μm from tumor edge) of different intracranial tumor mouse models was quantified and corrected for autofluorescence in contralateral healthy brain regions (background). GBM8 displayed no TexasRed leakiness, while a marginal level of fluorescence was observed in RG2 and Mel57 tumors. U87 and Mel57VEGF tumors displayed a profound leakiness with ring enhancement, as apparent by the higher intensity in tumor rim versus tumor core. $n = 5-13$.

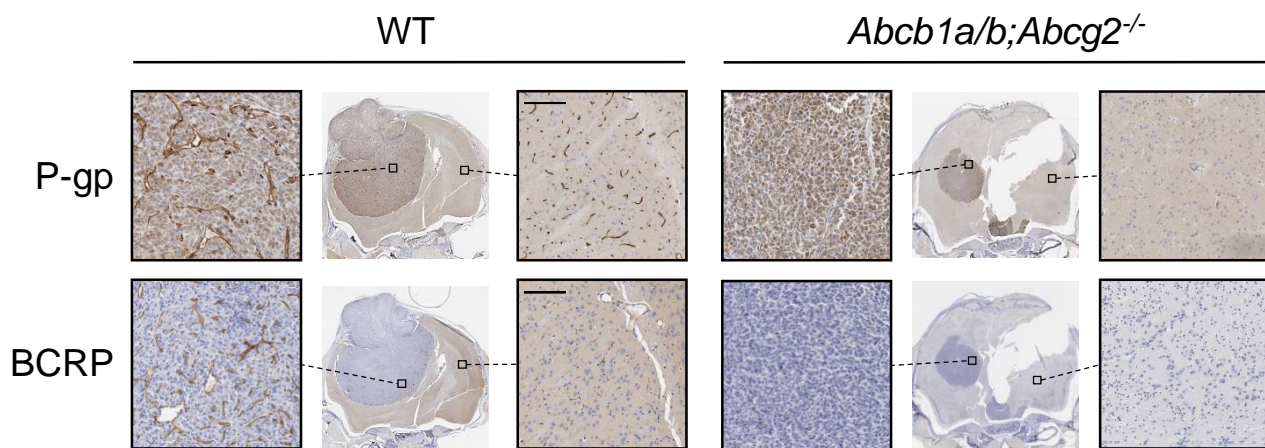


Figure S2, related to Figure 1. Validation of ABC transporter immunohistochemistry staining. Immunohistochemical staining of P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP) in U87 tumor regions and healthy brain tissue of wild-type (WT) and *Abcb1a/b;Abcg2*^{-/-} mice. Scale bar, 100 μm.

RG2

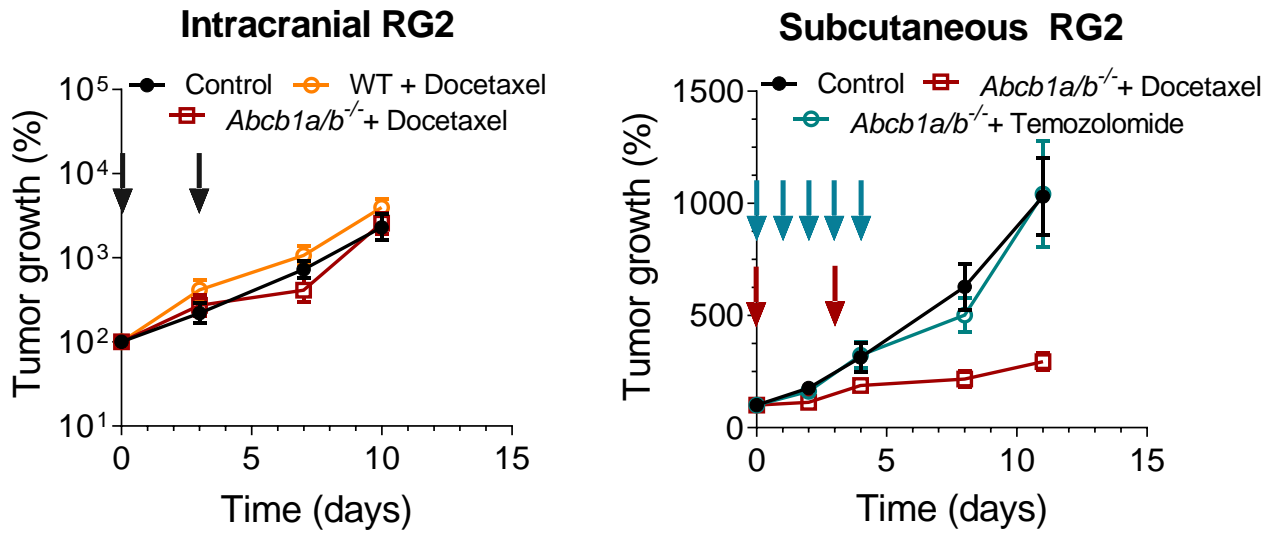
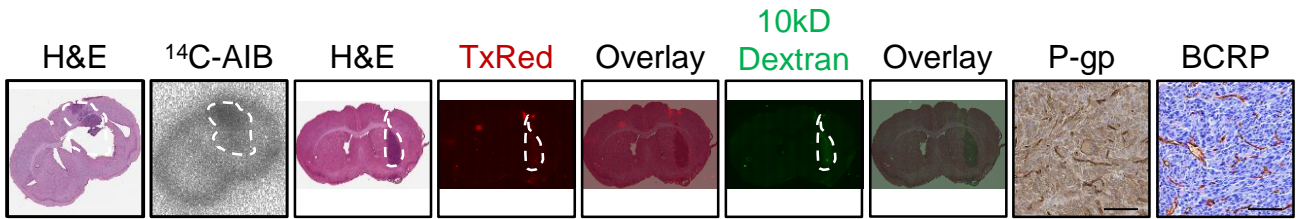


Figure S3, related to Figure 4. Studies using the RG2 model. The rat-derived glioma model RG2 shows evidence for mild to moderate leakiness by using fluorescent dyes (Texas Red; TxRed), 10KD-Dextran-Fluorescein and ¹⁴C-aminoisobutyrate (AIB). RG2 tumors vessels stained positive for P-gp and BCRP. Intracranial RG2 did not respond to docetaxel (30 mg/kg *q3dx2*), even in *Abcb1a/b*^{-/-} KO mice, but subcutaneous tumors did respond. Note that these subcutaneous lesions did not respond to temozolomide given 100 mg/kg *qdx5*. Scale bar, 100 μm.

Marker	U87		GBM8		Mel-57		Mel-57-VEGF	
	Allele 1	Allele 2	Allele 1	Allele 2	Allele 1	Allele 2	Allele 1	Allele 2
Amelogenin	X		X		X		X	
CSF1PO	10	11	11	13	11		11	
D21S11	28	32.2	29	30	28		28	
D5S818	11	12	12	13	12		12	
D7S820	8	9	8	10	10	13	10	13
D13S317	8	11	12		11	13	11	13
D16S539	12		11	12	11		11	
TH01	9.3		9.3		9		9	
TPOX	8		8		12		12	
vWA	15	17	18	19	14	17	14	17

Table S1, related to Experimental Procedures. Overview of STR markers as analyzed by the GenePrint 10 System.