

Transepithelial transport of [¹⁴C]trabectedin (0.22 μ M) in MDCK-II cells either nontransduced (A) or transduced with human ABCC2 (B), mouse Abcc2 (C) or human ABCC3 (D) cDNA, in the presence of elacridar (5 μ M). At t = 0 h, [¹⁴C]trabectedin was applied in one compartment (apical or basolateral), and the percentage of radioactivity translocated to the opposite compartment at t = 2 and 4 h was measured by scintillation counting (n = 3). Translocation from the basolateral to the apical compartment (B to A); translocation from the apical to the basolateral compartment (A to B). Data represent means \pm S.D. r represents the relative transport ratio (*i.e.*, the apically directed translocation divided by the basolaterally directed transport in MDCK-II parental cells, in both ABCC2- and Abcc2-transduced cells the translocation of trabectedin in the apical direction was higher than in the basolateral direction. The net basolaterally directed transport of trabectedin was modestly but significantly increased in ABCC3-transduced cells compared to that in parental cells (Figure 1). *In vitro*, trabectedin is thus fairly efficiently transported by ABCC2/Abcc2 but only modestly by ABCC3.

Supplemental data 2



Levels of ALAT (A), ASAT (B), Alk. Phos. (C) and total (free and conjugated) bilirubin (D) in plasma of wild-type, Cyp3a^{-/-}, Abcb1a/1b/Abcc2^{-/-}, Cyp3a/Abcb1a/1b/Abcc2^{-/-} after i.v. administration of 100 μ g/kg trabectedin. Values represent means \pm SD. n = 6-9 male mice for each strain. Significance is represented as comparison to wild-type. Note break in y-axes of the ALAT and ASAT levels.



Levels of ALAT (A), ASAT (B), Alk. Phos. (C) and total (free and conjugated) bilirubin (D) in plasma of wild-type, Abcb1a/1b^{-/-}, Abcc2^{-/-}, Abcb1a/1b/Abcc2^{-/-}, Abcc3^{-/-} and Abcc2/Abcc3^{-/-} mice after i.v. administration of 100 µg/kg trabectedin. Values represent means \pm SD. n = 6-11 male mice for each strain. Significance is represented as comparison to wild-type. Note break in y-axes of the ALAT and ASAT levels.