Title

Evaluation of Organic Anion Transporter 1A2-knockin Mice as a Model of Human Blood-Brain Barrier

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Journal Title

Drug Metabolism and Disposition

Supplementary Figure and Table Legends

Supplemental Table 1. Analytical conditions for quantification of drugs and compounds

Supplementary Figure 1. Information of OATP1A2 Substrates

(a) Screening of OATP1A2 substrates with *Xenopus laevis* oocytes. Uptake of cibenzoline, pindolol, ranitidine, sulpiride, and varenicline into oocytes injected with water or OATP1A2 cRNA for 2 hours were measured. “Water” and “1A2” represent oocytes injected with water and OATP1A2 cRNA, respectively. (b) Chemical structures of sulpiride, amisulpride, and sultopride.

Supplementary Figure 2. Human OATP1A2 Topology and Location of Peptides Employed in QTAP

Illustration of human OATP1A2 topology. The peptides employed in QTAP were

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highlighted in red.

Supplementary Figure 3. Uptake of Zolmitriptan by OATP1A2-expressing Cells

The uptake of triptans (zolmitriptan, 0.3 μM; sumatriptan, 1 μM; naratriptan, 1 μM; rizatriptan, 1 μM; almotriptan, 1 μM) by OATP1A2-transiently expressing HEK293T cells was examined. Each bar represents the mean ± S.E., n=3. Statistically significant differences between empty vector and the transporter expressing cells: **, $P < 0.01$. EV and 1A2 indicate empty vector and OATP1A2, respectively.

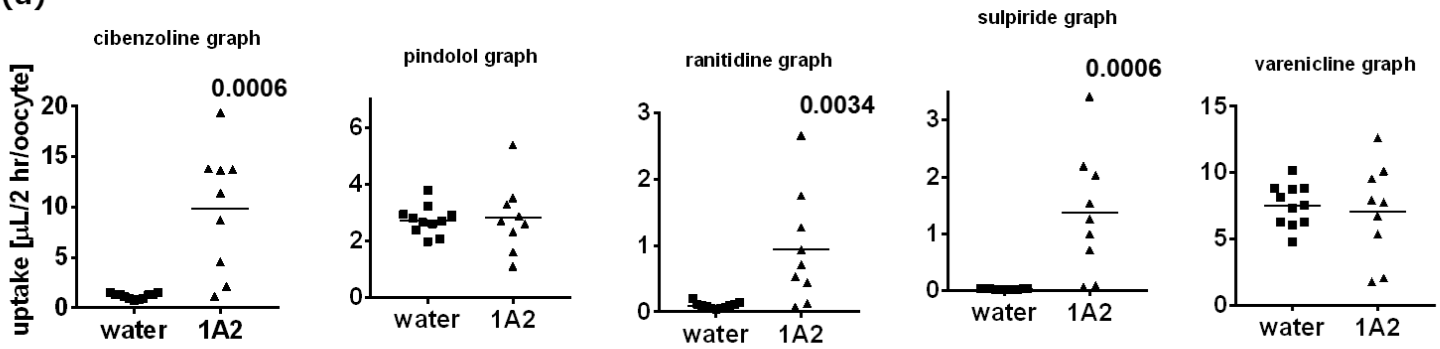
Supplemental Table 1 Analytical conditions for quantification of drugs and compounds

LC-MS/MS conditions were listed below. An AB Sciex QTRAP 5500 mass spectrometer (Applied Biosystems, Foster City, CA) equipped with a Prominence LC system (Shimadzu, Kyoto, Japan) was employed and operated in electrospray ionization mode. The flow rate was 0.4 mL/min.

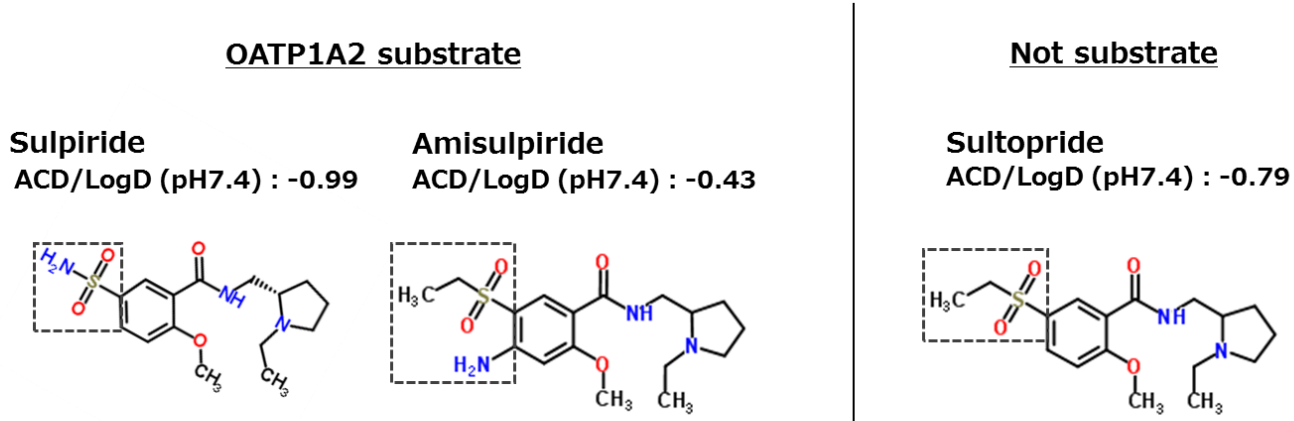
Compounds	Column	Mobile Phase		Gradient condition	Mass-to-charge	Ion mode
		A	B	(B conc. %)		
sulpiride	Atlantis T3 (3 μm, 2.1 mm × 50 mm Waters, Tokyo, Japan)	0.1% formic acid	acetonitrile		342.1→112.1	pos
amisulpride				0 min; 3%	370.2→241.8	
cimetidine				0.5 min; 3%	253.1→159.2	
ranitidine				2.4 min; 90%	315.1→176.2	
cibenzoline				3.9 min; 90%	262.9→115.0	
sultopride				3.91 min; 3%	355.1→112.0	
diazepam					285.2→193.0	
zolmitriptan				0 min; 3%	288.1→58.0	
sumatriptan				0.5 min; 3%	296.2→157.1	
naratriptan				2.4 min; 90%	335.7→98.1	
almotriptan				2.8 min; 90%	335.8→58.1	
rizatriptan				2.81 min; 3%	296.7→58.0	
pitavastatin				0 min; 20% 0.5 min; 20% 2.5 min; 80% 2.6 min;20% 2.5 min; 20%	422.0→290.1	

Supplementary Figure 1.

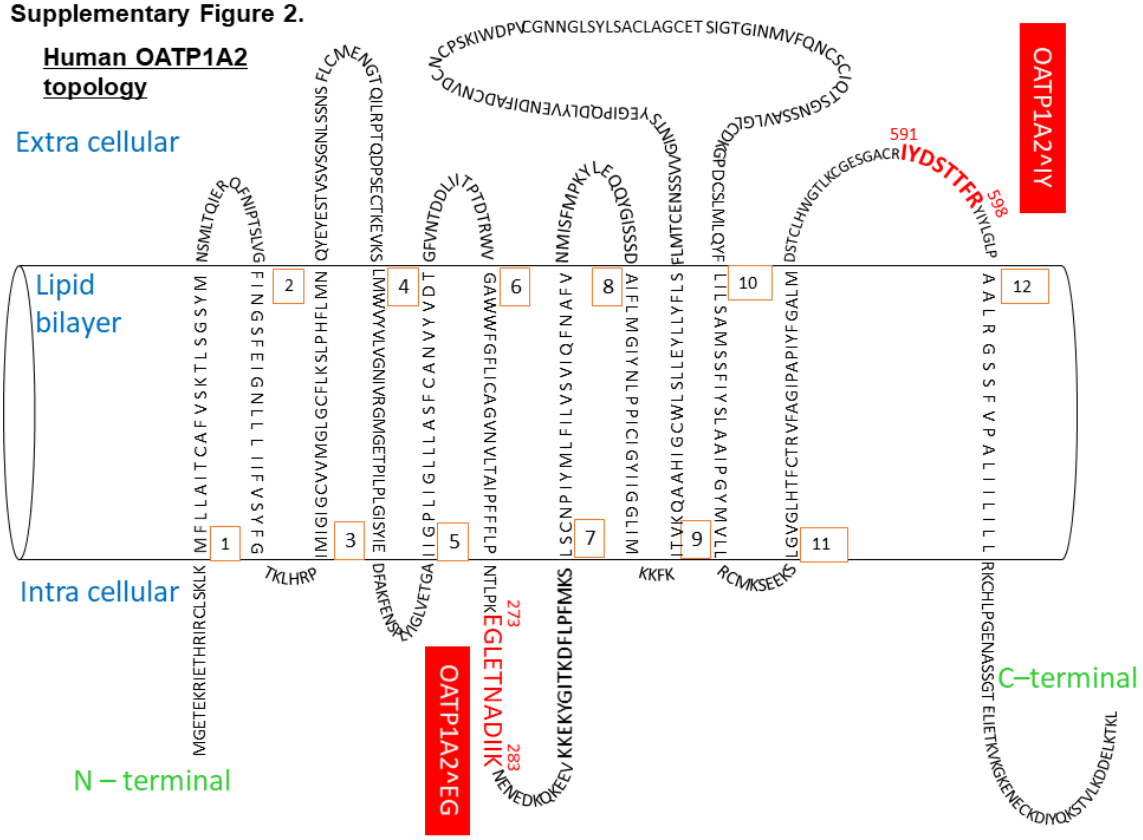
(a)



(b)



Supplementary Figure 2.



Supplementary Figure 3.