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Supplemental Data

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Article Title

Organic anion transporting polypeptides (OATPs)-mediated drug-drug interaction study between rosuvastatin and cyclosporine A in chimeric mice with humanized liver.

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Supplemental Table 1. Pharmacokinetic parameters of rosuvastatin after intravenous (1 mg/kg) administrations of rosuvastatin to male PXB-mice and SCID mice, and effect of oral pre-administration of cyclosporine A on systemic exposure of rosuvastatin in the both mice

Cyclosporine A (mg/kg)	PXB-mice			SCID mice		
	50	10	0 (vehicle)	50	10	0 (vehicle)
$C_{0,iv}$ (ng/mL)	3235 ± 952*	1971 ± 629*	699 ± 426	997 ± 383*	480 ± 258	133 ± 22
$AUC_{0-4h, iv}$ (ng·h/mL)	1743 ± 518*	711 ± 172*	280 ± 169	340 ± 120*	119 ± 40*	26.2 ± 2.8
CL_{tot} (L/h/kg)	0.541 ± 0.162*	1.33 ± 0.27*	3.82 ± 1.56	2.98 ± 0.96*	8.40 ± 2.32*	38.1 ± 4.5
V_d (L/kg)	0.329 ± 0.091*	0.549 ± 0.178*	1.76 ± 0.75	1.14 ± 0.48*	2.45 ± 1.02*	7.66 ± 1.36
$V_{d,ss}$ (L/kg)	0.859 ± 0.426*	1.55 ± 0.73*	5.31 ± 2.25	3.18 ± 2.11*	6.84 ± 2.66	10.0 ± 4.1
$AUCR_{iv}$	6.2	2.5	-	13	4.6	-

Data are presented as mean ± S.D. from three or four animals.

$AUCR_{iv} = AUC_{0-4h, iv}$ with pretreatment of cyclosporine A / $AUC_{0-4h, iv}$ with pretreatment of vehicle (control)

$V_d = \text{Dose}/C_{0,iv}$

* $P < 0.05$, statistically significant compared with control (vehicle) group

Supplemental Table 2. Fraction unbound of cyclosporine A in blood of PXB-mice

CsA Concentration ($\mu\text{mol/L}$)	$f_{u,p}$ (%)	f_p (%)	RB	$f_{u,b}$ (%)
0.20	10.4	89.7	2.14	4.86
2.0	16.8	83.3	1.64	10.3

$f_{u,p}$: fraction unbound in plasma

f_p : fraction bound in plasma

RB: blood to plasma concentration ratio

$f_{u,b}$: fraction unbound in blood

Supplemental Table 3. Blood and tissue concentrations of hydroxy form of cyclosporine A, cyclosporine AM1, in the liver after oral administration of doses of 10 and 50 mg/kg of cyclosporine A in PXB-mice and SCID mice.

	Dose (mg/kg)	Systemic exposure		Liver tissue exposure
		C _{max} ($\mu\text{mol/L}$)	AUC ($\mu\text{mol}\cdot\text{h/L}$)	C _{8h} ^a ($\mu\text{mol/kg}$ issue)
PXB-mice	10	0.150	0.314	2.22
	50	0.340	0.830	7.84
SCID mice	10	0.386	0.771	5.56
	50	1.08	3.02	10.5

Data are presented as mean from three or four animals.

a Corresponding to liver concentrations 4 hours after oral administration of rosuvastatin