

Expanded View Figures

Figure EV1. Generation and characterization of Slc10a1^{S267F} mutant mice.

A Schematic diagram for the generation of Slc10a1^{S267F} mutant mice.
 B Genotyping of Slc10a1^{S267F} mutant mice. Genomic DNA was extracted from mouse tails, and the specific region covering the mutation was amplified by PCR.

C Identification of *Slc10a1*^{S267F} homozygous mice by Sanger sequencing analysis.

Source data are available online for this figure.

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Figure EV2. Generation and characterization of Sema7a^{R145W} mutant mice.

A Schematic diagram for the generation of Sema7a^{R145W} mutant mice.
 B Genotyping Sema7a^{R145W} mutant mice. Genomic DNA was extracted from mouse tails, and the specific region was amplified by PCR.
 C Identification of Sema7a^{R145W} homozygous mice by Sanger sequencing analysis.

Source data are available online for this figure.



Figure EV3.

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Figure EV3. A Sema7a^{R145W} homozygous mutation causes the elevated serum ALT, AST, and TBA levels and remarkable hydropic degeneration in mouse livers.

- A–C Serum ALT, AST, and TBA in Sema7a^{R14SW} WT (n = 6, two male/four female), heterozygous (n = 10, six male/four female) and homozygous mice (n = 12, seven male/five female). Data are shown as means \pm SD.
- D Representative images of H&E staining, Sirius Red staining, and IHC analysis of CK19 expression in WT, Sema7a^{R145W} heterozygous and homozygous mice. The Sema7a^{R145W} homozygous mutation caused significant liver injury with elevated levels of serum ALT, AST, and TBA and striking hydropic degeneration in hepatocytes. Scale bar, 50 μm.

Data information: The data were analyzed by the Mann–Whitney U-test. Source data are available online for this figure.

Α	1	 Heterozygote 					 Homozygote 								
	#1	#2	#3	#4	#1	#2	#3	#4	#5	# 1	#2	#3	#4	#5	_
84KD		-		-	-		-		-	-		-	-	-	p-PKCɛ (Ser729)
1.00 ± 0.34			2.26 ± 0.44*					3.03 ± 0.57*#				_ (0000120)			
90KD	-	-	-	-	-	-	-	-	-		-	-	-	-	ΡΚϹε
		1.00 :	± 0.07	7	i	0.9	2 ± 0).16		1	0.8	37 ± 0).10		
78KD	-	-	-	-	-	-	-	-	-	-	-	-	-	1	p-PKCo
		1.00 :	± 0.32	2	i	1.8	0 ± 0	.35*		<u>i</u>	1.8	9 ± 0	.50*		(poz <i>oo)</i>
78KD	1	-	-	-	-	-	-	-	-		-	-	-	-	ΡΚCδ
		1.00 :	± 0.1 1			1.0	0 ± 0	0.05		-	1.0)7 ± ().05		
36KD	-		-		-	-							i.		Gapdh
			Wh	ole	lys	ate	s fro	om I	live	r tis	sue	s			_
в Prin	nary	mo	use	hep	oato	ocy	tes		с	Tr	ans	fect	ted	Нер	G2 cells
		W	TI	10	1		_		Plasi	nids		WT	R14	8W	
84	KD				p- (S	PK er72	Cε 9)		8	4KI	D		-		ο-ΡΚCε (Ser729)
00	חאי				_	<i>(</i>)			•	01/1			_		
90KD				ΡΚΟε				90KD			-	-		KCE	
78KD					p-PKCδ (pS299)				78KD			p			-ΡΚCδ (pS299)
] \r]		•,					1000000			(00200)
78K[ΡΚϹδ				78KD			P			РКСδ
36	KD	-			Gapdh				36KD						Gapdh
	ates				W	Whole cell lysates									

Figure EV4.

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Figure EV4. The Sema7a^{R145W} mutation increases PKC δ/ϵ phosphorylation in hepatocytes.

- A The levels of hepatic PKC8/e phosphorylation were significantly higher in $Sema7a^{R145W}$ homozygous mice than in heterozygous mice and WT mice. Wild type, wild-type mice, n = 4; Heterozygote, $Sema7a^{R145W}$ heterozygous mice, n = 5; homozygote, $Sema7a^{R145W}$ homozygous mice, n = 5. *P < 0.05 versus the Heterozygous mutant mice. The data were analyzed by the independent-samples Student's t-test and the Mann–Whitney U-test.
- B, C Furthermore, Sema7a^{R145W} (human R148W) homozygous mutation increased PKCδ/ε phosphorylation in Sema7a^{R145W} mouse primary hepatocytes (B) and human HepG2 cells following transfection with SEMA7A_R148W construct (C).

Source data are available online for this figure.