

**Suppl. Figure 1.** Knockdown of RIPK1signicantly increases the serum levels of cytokines/chemokines (**A**) and hepatic leukocytes (**B**) in response to  $\alpha$ GalCer treatment. Groups of mice were pretreated with Cont ASO or RIPK1 ASO to silence RIPK1 prior to  $\alpha$ GalCer (4µg/mouse, i.p.). (**A**) Serum cytokine/chemokine levels at 6hr after  $\alpha$ GalCer (n=4-6). \*p<0.05 vs. Cont ASO; (**B**) Total numbers of hepatic leukocytes per liver tissue at 6hr after  $\alpha$ GalCer. \*p<0.05 vs. Cont ASO. \*\*Reduced NKT numbers in both groups reflected an activation-induced cell death of NKT cells in response to  $\alpha$ GalCer as expected.





**Suppl. Figure 2.** RIPK1 knockdown does not sensitize to Fas-mediated liver injury. Groups of Cont ASO and RIPK1 ASO pretreated mice (n=5 per group) were administered i.p with anti-Fas (Jo2, 4μg per mouse). (A) Serum ALT at 6 and 24hr after Jo2; (B) H&E staining of liver sections at 24hr after Jo2.



## **B** Gene expression in liver tissues at 3hr after αGalCer

Gene	Cont ASO+aGalCer 3hr	RIPK1 ASO+aGalCer 3hr
	vs Cont ASO+aGalCer 0h (Fold Change)	vs RIPK1 ASO+aGalCer 0h (Fold Change)
nfkb1 (p105 sub)	5.5	4.5
nfkb2 (p100 sub)	2.9	2.7
Nfkbia (IkBa)	2.4	4.1
Rela (Nfkb p65)	2.5	2.1
Relb	3.1	2.7
Birc3 (cIAP2)	5.2	5.7
ΙΓΝγ	2.3	2.5
Tnf	2.9	3.7
ICAM-1	34.2	29.2
Vcam1	16.0	21.8
IL-4	7.6	9.9
Sod2	2.0	2.0
iNOS	2.3	7.6

## C Gene expression in primary hepatocytes at 3hr after $\alpha$ GalCer

Gene	Cont ASO+aGalCer 3hr vs Cont ASO+aGalCer 0h (Fold Change)	RIPK1 ASO+αGalCer 3hr vs RIPK1 ASO+αGalCer 0h (Fold Change)
nfkb1 (p105 sub)	3.2	3.0
nfkb2 (p100 sub)	1.6	1.5
Nfkbia (IkBa)	6.2	9.8
Rela (Nfkb p65)	2.9	3.2
Birc2 (cIAP1)	10.8	11.0
Birc3 (cIAP2)	28.6	53.7
IFNy	7.2	7.7
Tnf	3.5	7.9
ICAM-1	20.8	47.6
CCL2	32.7	56.6
c-FLIP	3.8	3.1
Sod2	10.0	8.5
iNOS	6.8	31.6

**Suppl. Figure 3.** Knockdown of RIPK1 does not impair the induction of NF-κB downstream genes. (**A**) qPCR analysis of mRNA levels of c-FLIP and cIAP1 in the liver from Cont ASO and RIPK1 ASO treated mice at indicated times after αGalCer treatment. (**B**) mRNA levels in the liver tissues from Cont ASO and RIPK1 ASO treated mice at 3hr after αGalCer treatment were analyzed by mouse NF-κB Signaling Pathway RT<sup>2</sup> Profiler<sup>TM</sup> PCR array kit (QIAGEN). Fold changes at 3hr over time zero were expressed. (**C**) mRNA levels in the primary hepatocytes isolated from Cont ASO and RIPK1 ASO treated mice at 3hr after αGalCer treatment were analyzed by mouse NF-κB Signaling Pathway RT<sup>2</sup> Profiler<sup>TM</sup> PCR array kit (QIAGEN). Fold changes at 3hr over time zero were expressed. (**C**) mRNA

A





**Suppl. Figure 4.** Necostatin-1 (Nec-1) does not prevent  $\alpha$ GalCer-mediated liver injury. Groups of mice were pretreated with inactive Nec-1 or Nec-1 (1.65 mg/kg, i.p.) 15min prior to  $\alpha$ GalCer (4µg per mouse, i.p.). (**A**) Serum ALT at 24hr after  $\alpha$ GalCer (n=5 per group), p>0.05; (**B**) H&E staining of liver sections at 24hr after  $\alpha$ GalCer.