Supplementary Table: Donor Characteristics

| Patient	Age	Sex	Genotype/ Diagnosis	NI score	Fibrosis score	Viral Load	ALT	Treatment outcome	FNA	Degranulation assay
HCV donors										
G1-01	31	F	1a	4	1	1.3×10^6	78	Failed	Yes	Yes
G1-03	57	F	1a	7	1	1.7×10^6	134	Failed	Yes	Yes
G1-05	45	M	1a NASH	8	5	6.5×10^5	110	Failed	Yes	Yes
G1-06	36	F	1	4	0	1.7×10^6	47	-	Yes	-
G1-08	62	M	1b	5	1	4.0×10^5	147	-	Yes	-
G1-11	42	M	1	4	3	7.0×10^5	47	-	Yes	Yes
G1-12	43	F	1A	3	0	2.3×10^6	26	-	Yes	-
G1-15	58	M	1	6	5	1.2×10^7	47	-	Yes	-
G1-17	52	M	1A	6	1	6.6×10^5	149		Yes	Yes
G1-18	62	F	1	5	2	6.5×10^5	57	Failed	Yes	Yes
G1-19	50	M	1	5	5	3.0×10^7	139	-	Yes	Yes
G1-21	53	M	1	3	0	3.6×10^6	33	-	Yes	-
G1-22	56	M	1	3	6	4.1×10^6	90	-	Yes	-
G1-23	37	F	1a NASH	6	5	24000	318		Yes	Yes
G1-24	53	M	1	3	0	3.6×10^6	33	-	Yes	-
G1-25	65	M	1a	4	5	3.2×10^6	90	-	Yes	-
G1-41	51	M	1 & 3	5	1	3.8×10^6	38	Failed	-	Yes
G1-42	27	M	1b	5	1	6.0×10^6	63	SVR	-	Yes
G3-01	44	M	3	-	-	5.5×10^5	66	SVR	-	Yes
G3-06	42	F	3a	0	4	2.0×10^6	80	SVR	-	Yes
G3-07	56	M	3a	6	6	2.3×10^6	35	SVR	Yes	Yes
G3-08	41	M	3a	2	1	4.4×10^5	87	-	Yes	-
G3-09	36	M	3a	6	2	2.4×10^6	332	SVR	Yes	Yes
G3-10	27	M	3	7	1	3100	29	SVR	Yes	Yes
G3-11	59	M	3	ND	ND	-	51	-	Yes	-
G3-12	49	M	3	3	2	1.6×10^5	174	-	Yes	-
G3-13	54	M	3	6	3	1900	179	-	Yes	-
G3-14	52	M	3	5	5	2.4×10^5	90	-	Yes	Yes
G3-40	58	M	3	4	6	3.1×10^5	53	Failed	-	Yes
G3-41	47	M	3	-	-	4.7×10^6	169	SVR	-	Yes
G3-42	39	M	3	5	2	1.6×10^6	136	SVR	-	Yes
G3-43	53	M	3	ND	ND	3.9×10^5	26	SVR	-	Yes
G3-44	67	F	3	3	1	2.2×10^5	174	SVR	-	Yes
G4-01	29	F	4	ND	ND	6.2×10^5	38	Failed	-	Yes
G5-01	46	F	5	ND	ND	7.6×10^6	52	SVR	-	Yes

Chronic Liver Disease controls

Patient	Age	Sex	Genotype/ Diagnosis	NI score	Fibrosis score	Viral Load	ALT	Treatment outcome	FNA	Degranulation assay
DD03	61	F	Deranged LFTs? Cause	0	0		89		Yes	
DD12	40	F	PBC	0	1		72		Yes	
DD13	49	F	NASH	0	5-6		25		Yes	
DD14	67	F	NASH	1	3-4		81		Yes	
DD15	52	F	Steatosis	0	1		53		Yes	
DD16	40	M	MTX use - NAD	0	0		17		Yes	
DD18	58	F	NASH	6-7	5-6		57		Yes	Yes
DD19	38	M	Steatosis	0	0		55		Yes	Yes
DD20	46	M	ALD HHC	1	1		73		Yes	Yes
DD21	69	M	Granulomat ous hepatitis	ND	ND		39		Yes	
DD22	53	M	ALD	0	0		34		Yes	
DD23	43	M	Steatosis	2	0		96		Yes	Yes
DD24	55	M	ALD HHC	2	5-6		46		Yes	
DD25	29	M	NASH	1	3		122		Yes	Yes
DD28	58	M	ALD HHC	2	5-6		39		Yes	Yes
DD29	55	F	PBC	2	3-4		59		Yes	Yes
DD30	42	F	PBC	2	3-4		179		Yes	Yes
DD32	55	M	HHC	1	4		23		Yes	Yes
DD33	55	M	PSC	2	1		54		Yes	Yes
DD34	51	F	PBC	2	5		151		Yes	
DD35	29	M	Wilsons				31		Yes	
DD36	58	M	Previous MTX /NASH				64		Yes	

ALD- Alcoholic liver disease, HHC- hereditary haemochromatosis, NASH – Non alcoholic steatohepatitis, PBC- Primary biliary cirrhosis, MTX- methotrexate, LFTs – Liver function tests, SVR – Sustained Viraemic Response, PSC- Primary Sclerosing Cholangitis, NAD – no abnormality detected, ND – not done
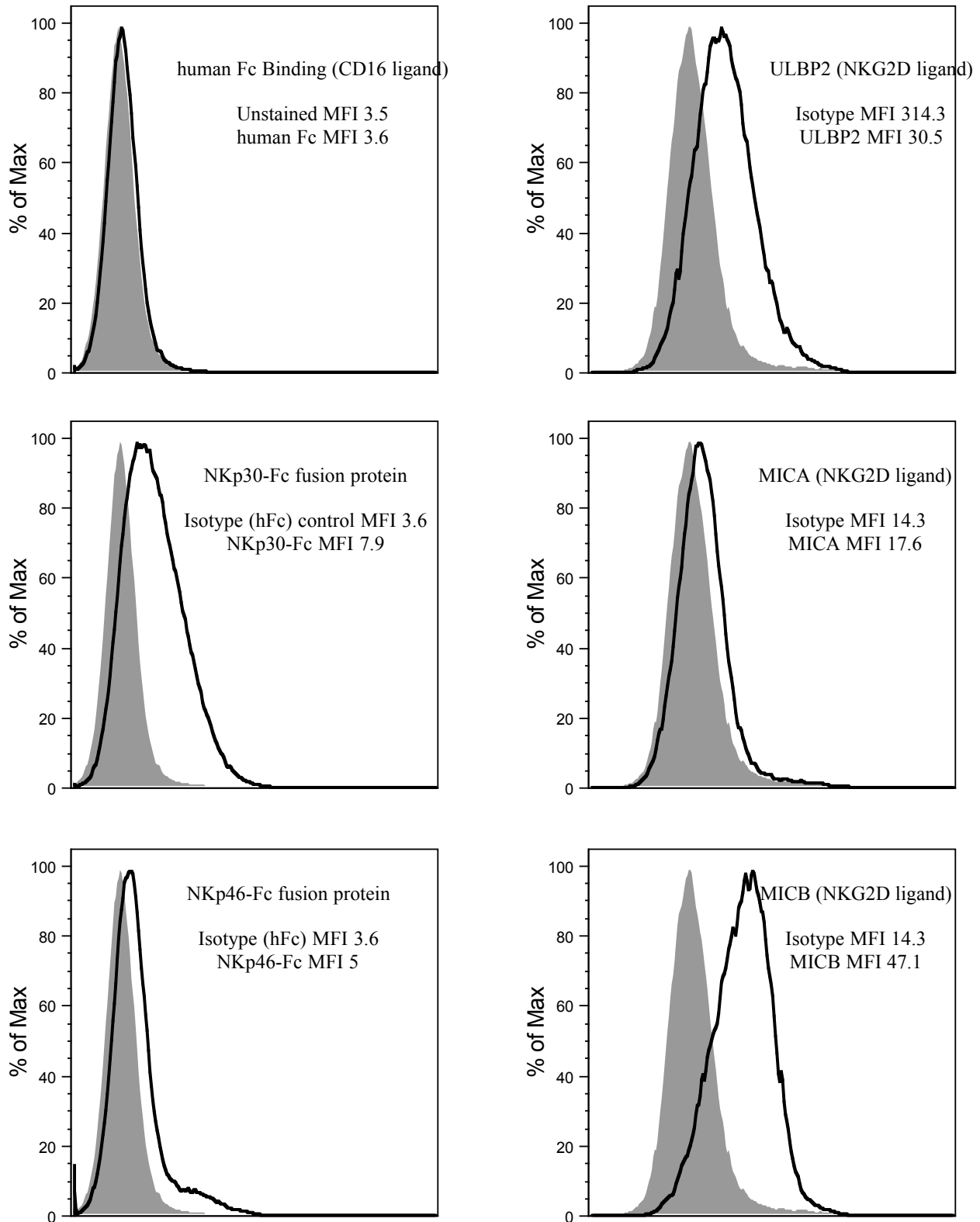
Supplementary figure 1: NK gating strategy

A) Lymphocytes are gated from the forward and side scatter plot. B) Single cells gate. C) Live /dead gate. D) CD56$^+$ CD3, CD14 & CD19$^-$ NK cells.
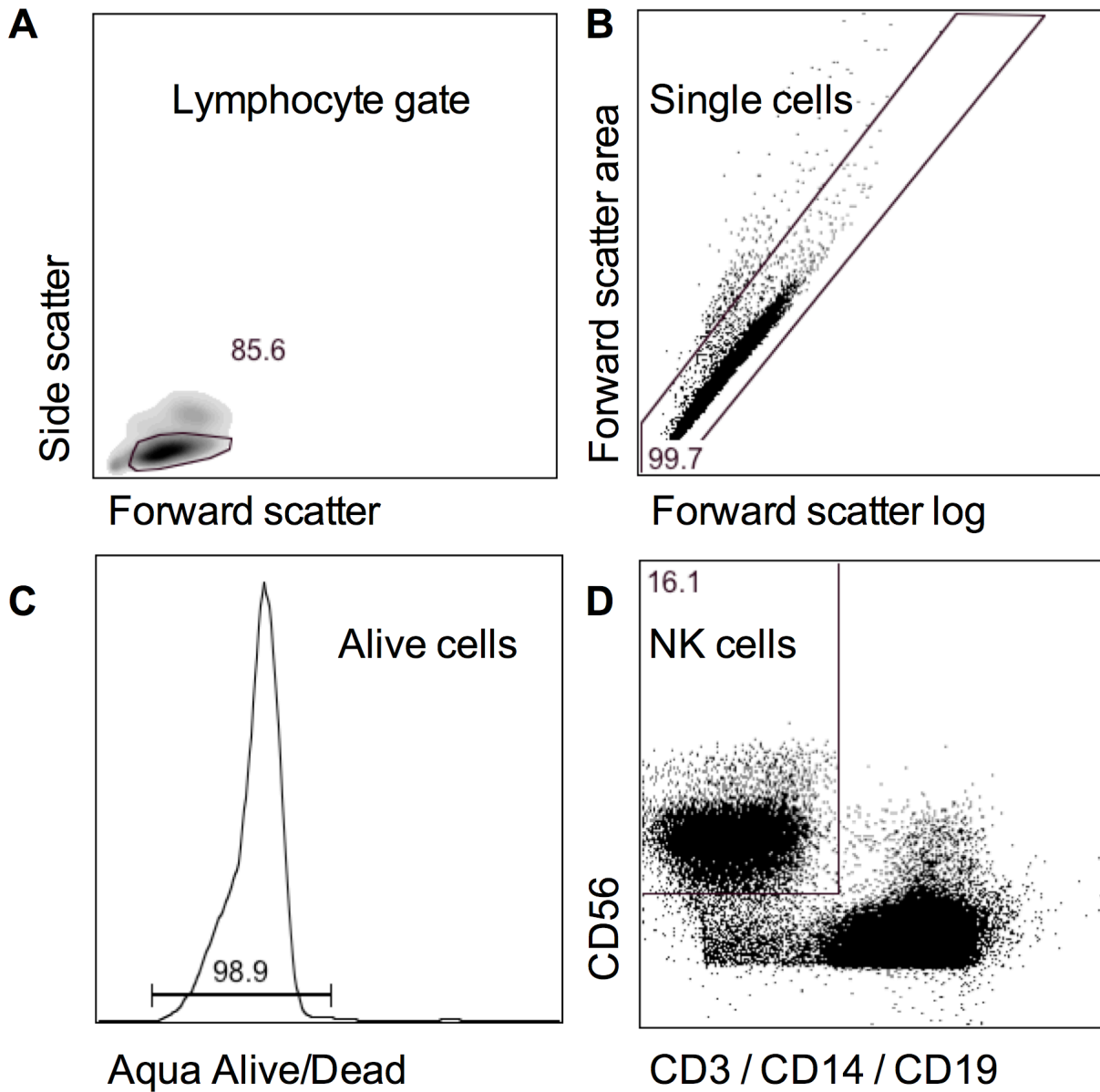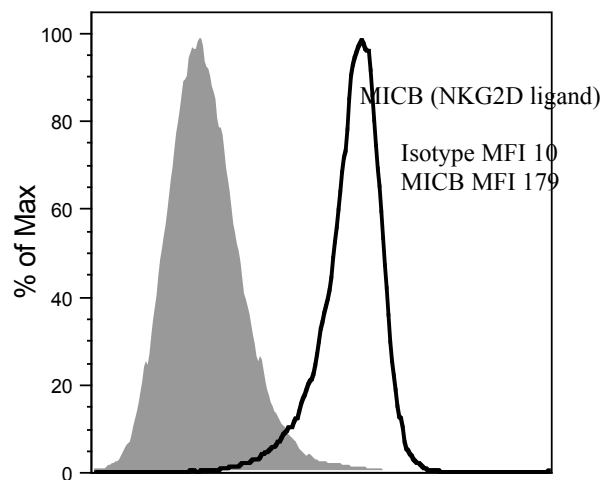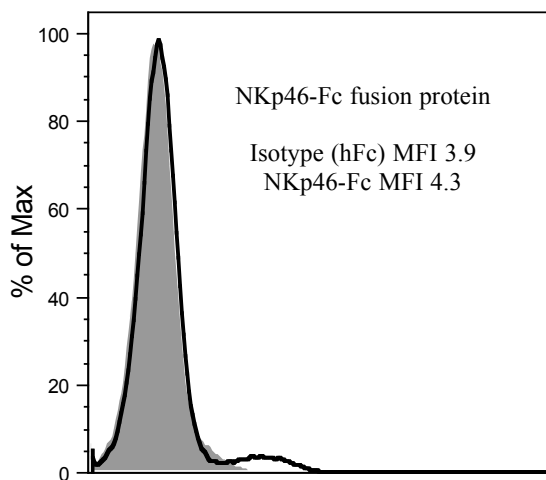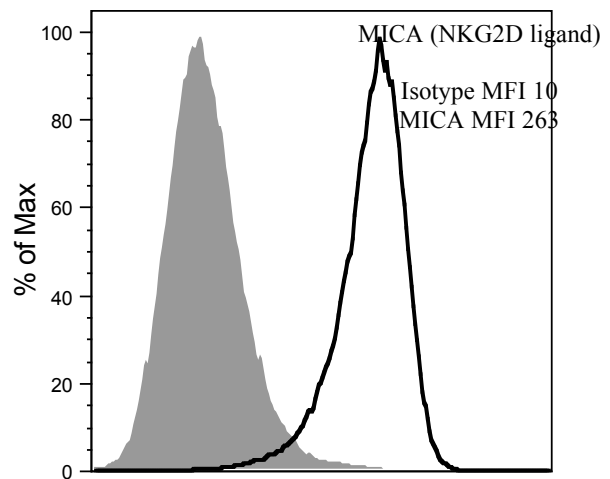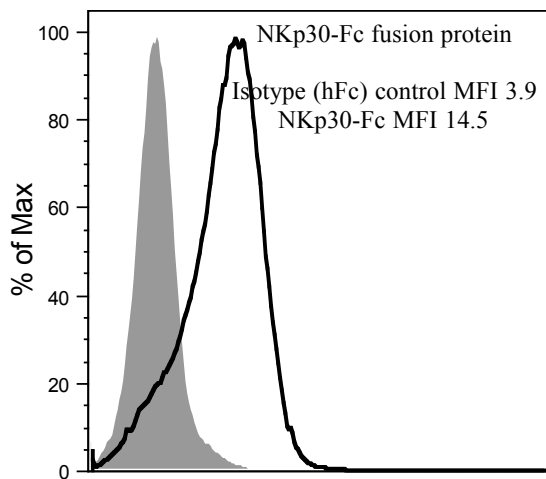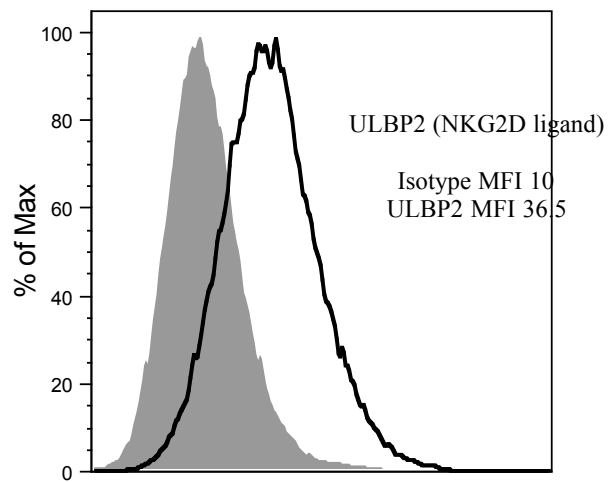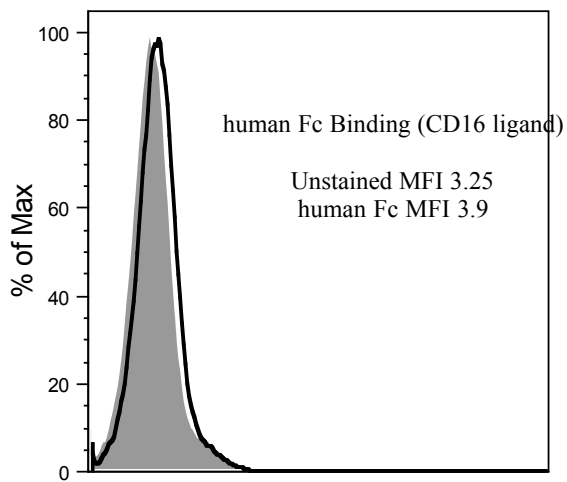
Supplementary figure 2 Expression of NK activating receptor ligands on target cell lines

A) Huh7.5 targets cells Representative FACS histograms demonstrating NKp30-Fc, NKp46-Fc, MICA, MICB and UBLP2 staining (solid grey = isotype control, black line = ligand of interest).


human Fc Binding (CD16 ligand)

Unstained MFI 3.5
human Fc MFI 3.6

ULBP2 (NKG2D ligand)

Isotype MFI 314.3
ULBP2 MFI 30.5

NKp30-Fc fusion protein

Isotype (hFc) control MFI 3.6
NKp30-Fc MFI 7.9

MICA (NKG2D ligand)

Isotype MFI 14.3
MICA MFI 17.6

NKp46-Fc fusion protein

Isotype (hFc) MFI 3.6
NKp46-Fc MFI 5

MICB (NKG2D ligand)

Isotype MFI 14.3
MICB MFI 47.1

B) K562 targets cells Representative FACS histograms demonstrating NKp30-Fc, NKp46-Fc, MICA, MICB and UBLP2 staining (solid grey = isotype control, black line = ligand of interest).

human Fc Binding (CD16 ligand)

Unstained MFI 3.25
human Fc MFI 3.9

ULBP2 (NKG2D ligand)

Isotype MFI 10
ULBP2 MFI 36.5

NKp30-Fc fusion protein

Isotype (hFc) control MFI 3.9
NKp30-Fc MFI 14.5

MICA (NKG2D ligand)

Isotype MFI 10
MICA MFI 263

NKp46-Fc fusion protein

Isotype (hFc) MFI 3.9
NKp46-Fc MFI 4.3

MICB (NKG2D ligand)

Isotype MFI 10
MICB MFI 179

**Supplementary figure 3: Alterations in peripheral blood NK activating receptors on degranulation**. A) Representative FACS plots of CD16 expression on resting NK (left panel) and degranulating NK cells as demonstrated by CD107a externalization (right panel). B) FACS plots demonstrating NKp30 down regulation on degranulating NK cells. C) FACS plots demonstrating NKp46 down regulation on degranulating NK cells. D) FACS plots demonstrating NKG2D down regulation on degranulating NK cells.
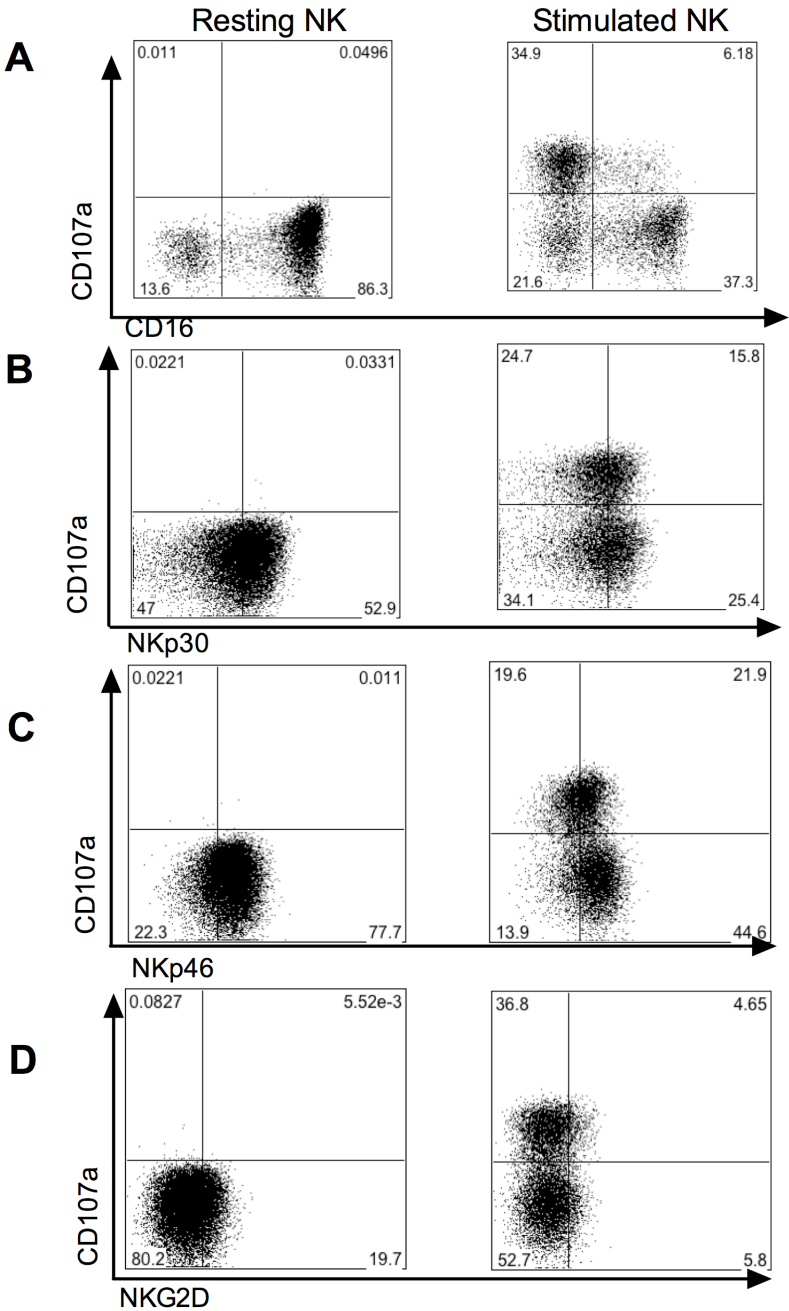
Supplementary figure 4: Intrahepatic NKp46+ cells fall into two clusters. A) Analysis of NKp46+ cells demonstrated that individuals fell into two clusters either >80% or <70%. There was a marked paucity of individuals who fell between these 2 groups. B) Representative FACS plots demonstrating NKp46 expression for FMO (solid gray), FNA (thick line) and peripheral blood NK cells (thin line) of a NKp46-poor subject (left panel) and a NKp46-rich subject (right panel)
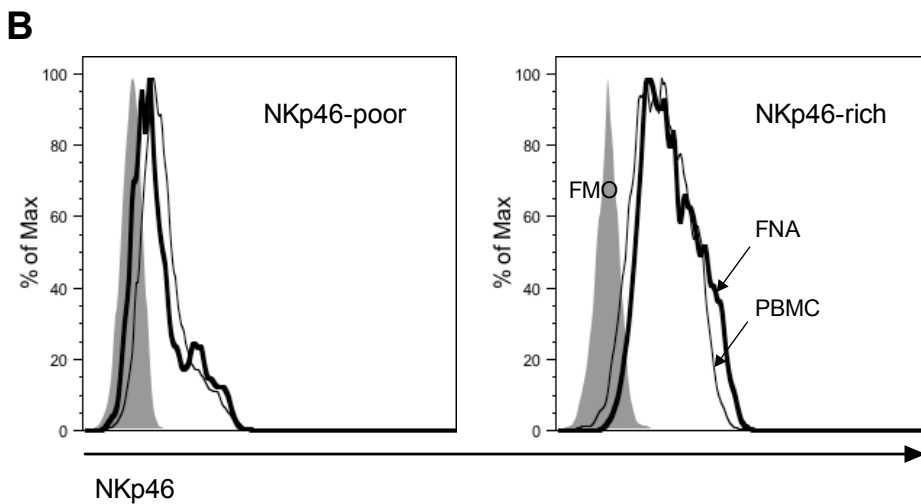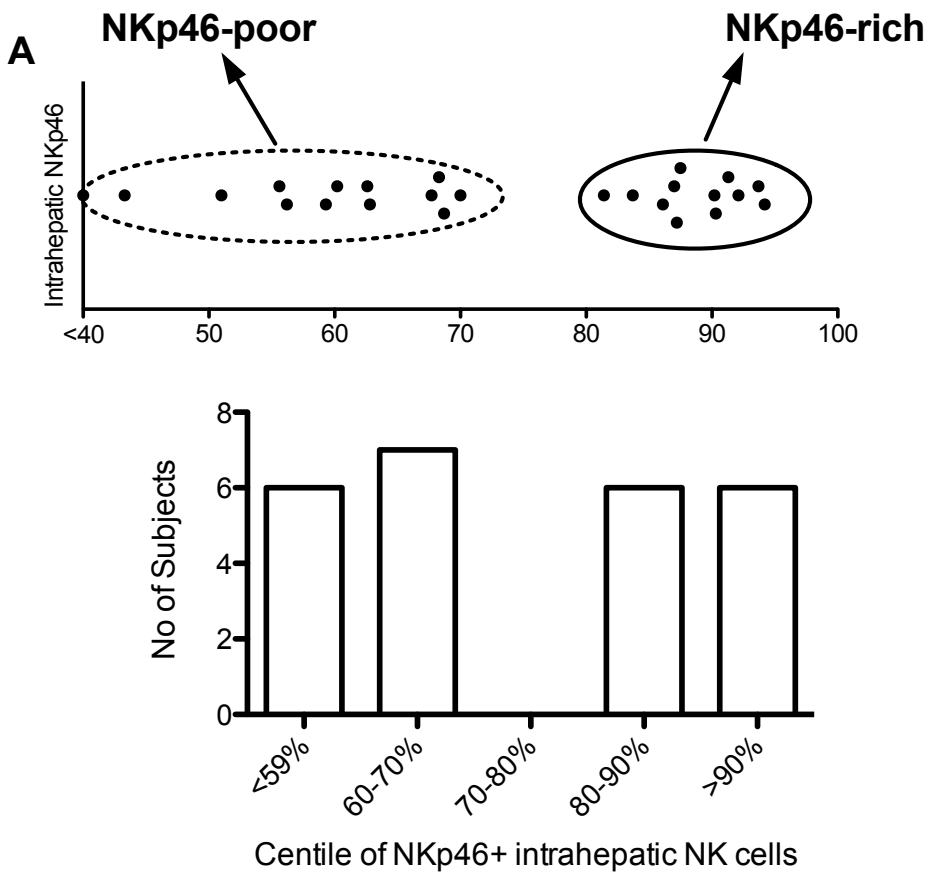
Supplementary figure 5: Functional ratio. Representative pre-treatment peripheral blood FACS plots demonstrating relative increase in CD107a externalisation in response to increasing stimulation from weak stimulation (50 IU/ml IFNα and huh7.5 target cells) and high stimulation (1000 IU/ml and K562 target cells) for an individual with slow viral clearance who failed treatment and a patient with rapid viral clearance who achieved SVR. NK responsiveness = %CD107a+ strong stimulation/ %CD107a+ weak stimulation.
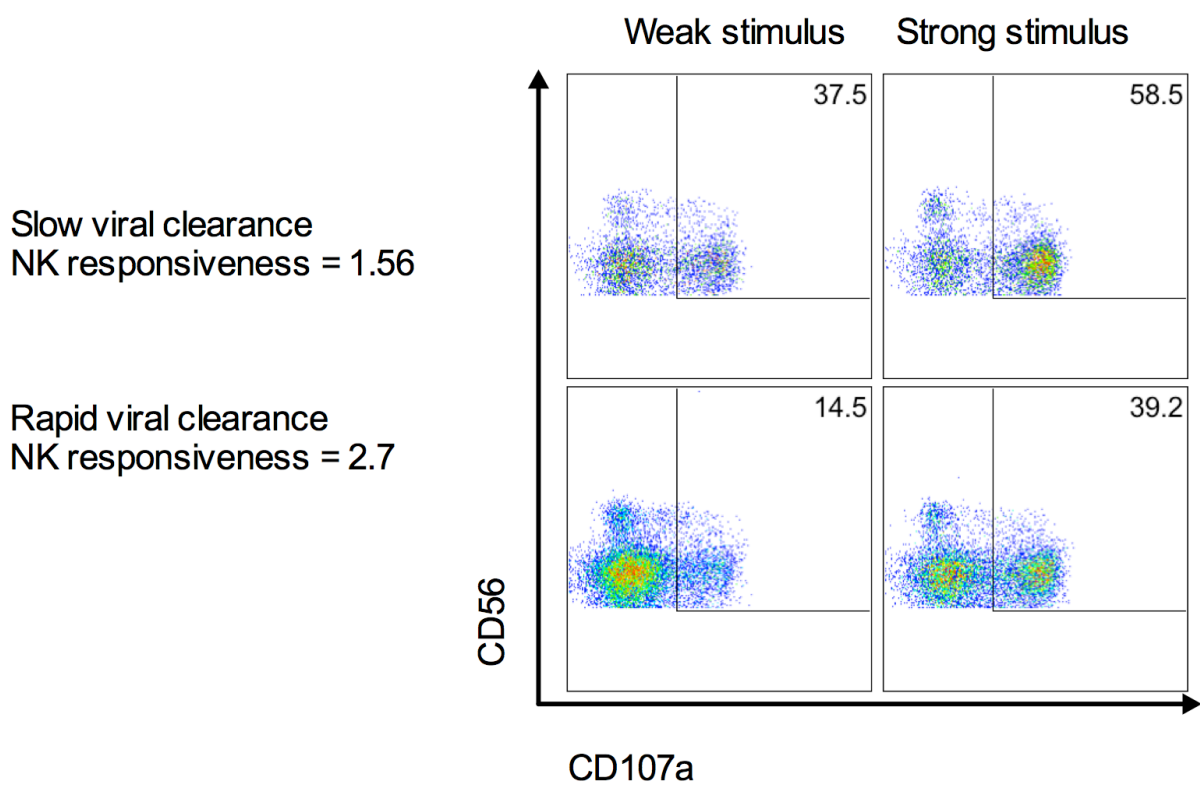
Supplementary Figure 6 A: NKp46 MFI. Representative figures demonstrating NKp46 expression based on MFI. Whilst it was possible to distinguish NKp46^{High} and NKp46^{Low} populations in some subjects (right panel) in 40% of individuals there was a single population of NKp46$^+$ cells (left panel).
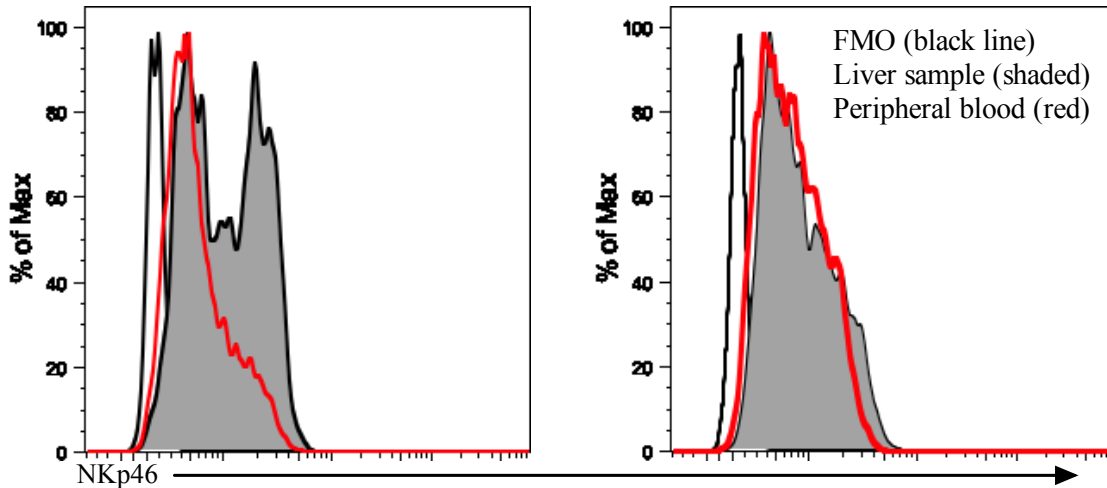
B: NKp46 expression measured by MFI and %NKp46. NKp46 expression measured by MFI correlates strongly with expression measured as % NKp46$^+$