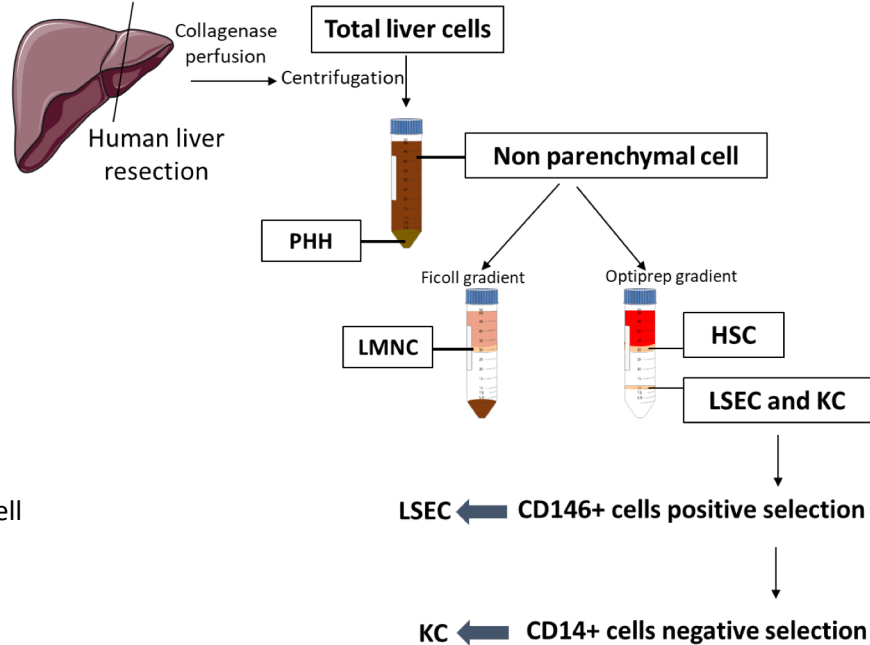


A.

PHH: primary human hepatocyte

LMNC: liver mononuclear cell

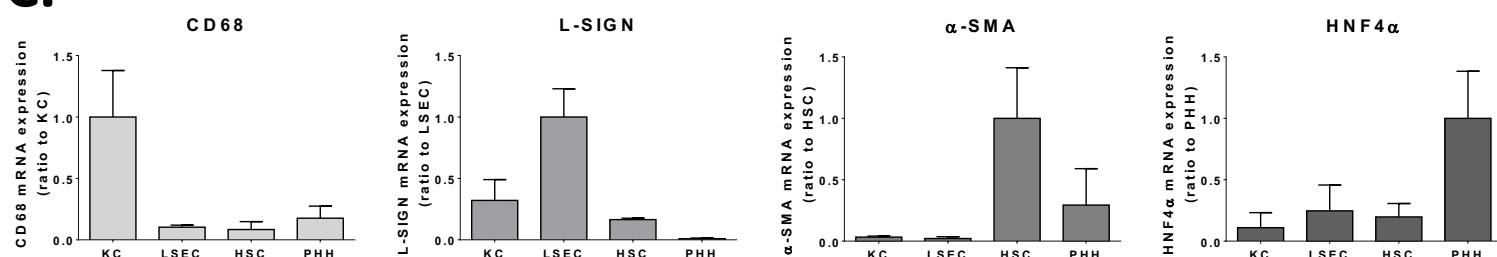
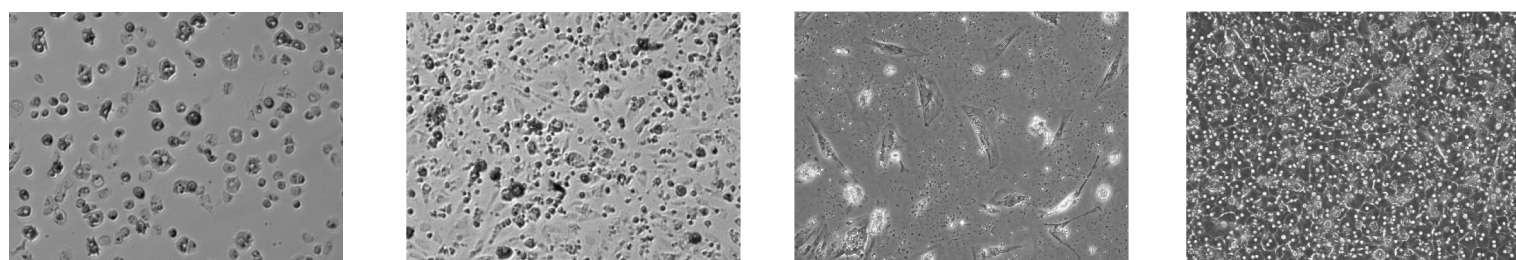
HSC: hepatic stellate cell

LSEC: liver sinusoidal endothelial cell

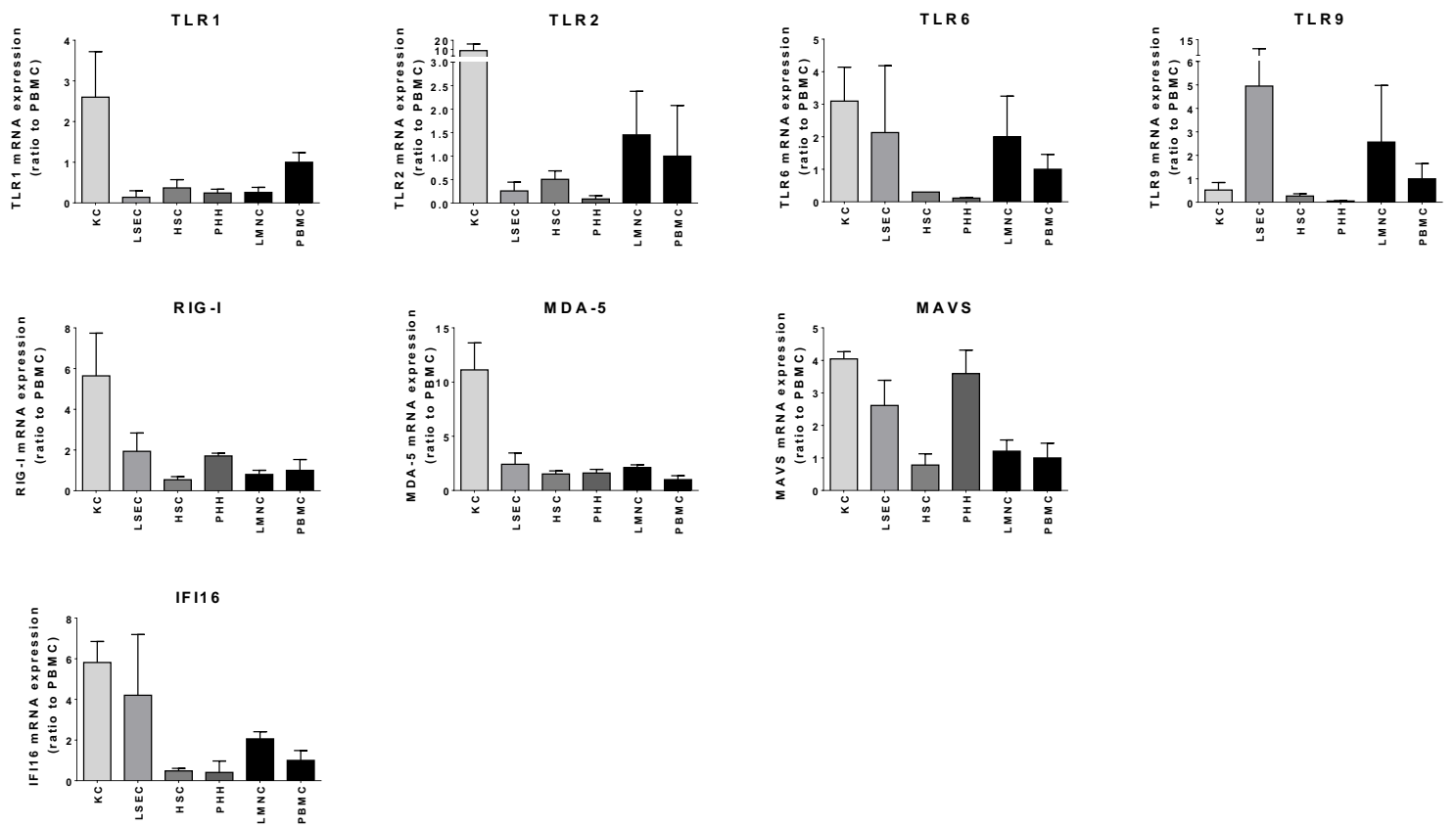
KC: kupffer cell

B.

Cells (million)	Donor 1	Donor 2	Donor 3	Donor 4	Donor 5	Donor 6	Donor 7	Donor 8	Donor 9	Donor 10	Donor 11	Donor 12
PHH	1000	1600	14	300	1280	1500	1429	1000	150	1500	850	80
LMNC	N/A	1710	N/A	N/A	1626	N/A	400	110	36	N/A	N/A	150
HSC	25	40	N/A	N/A	N/A	N/A	N/A	12	10	15	7	20
LSEC	N/A	70	2	53	50	80	N/A	44	2	25	6,5	6
KC	125	95	12	60	90	200	220	28	20	59	15	14
Photos				N/A					N/A			

C.**D.**

Supplementary Figure 1: Isolation method and purity of liver cells. (A) Schematic representation of the experimental procedure to purify PHH, LMNC, HSC, LSEC, and KC from liver resection. (B) Photos of the liver and yield of purified cells for the different donors used (N/A: data not available). (C) PHH, LSEC, HSC and KC were purified from three different donors and cultured for 24h. mRNAs were extracted and expression level of the indicated mRNA were analysed by RT-qPCR. Data are presented as mean \pm standard deviation of three different experiments (three different donors). (D) Representative photos of the different type of purified liver cells.



Supplementary Figure 2: TLR1, TLR2, TLR6, TLR9, RIG-I, MDA-5, and IFI16 mRNA expression in liver primary cells. PHH, LSEC, HSC, KC, LMNC and PBMC were purified from different donors and cultured for 24h. RNAs were extracted and expression level of the indicated mRNA were analysed by RT-qPCR. Data are presented as mean +/- standard deviation of three different experiments (three different donors).

Gene	Full name	Forward	Reverse
RPLP0	ribosomal protein lateral stalk subunit P0	CACCATTGAAATCCTGAGTGATGT	TGACCAGCCCAAAGGAGAAG
GUS	β-glucuronidase	CGTGGTTGGAGAGCTCATTTGGAA	ATTCCCCAGCACTCTCGTCCGT
TLR1	Toll like receptor 1	ACAAGCAGGTTGCTTTGTGTT	GAGGGCCTGGTACCCCTATT
TLR2	Toll like receptor 2	CTCTGGTGCTGACATCCAATGGAA	GGGCTTGAACCAGGAAGACGATAA
TRL3	Toll like receptor 3	AGAAGGTTTTCGGGCCAGCTTT	TGACAGCTCAGGGATGTTGGTATG
TLR4	Toll like receptor 4	CACACCAGAGTTGCTTTCAATGGC	AGAGAGGTCCAGGAAGGTCAAGTT
TLR5	Toll like receptor 5	CCTGACCTTATAGTTGCCAGCTT	TCCGACATCTCCCTGGATGCTAA
TLR6	Toll like receptor 6	ACCCATTCCACAGAACAGCATTCC	TCCTTGGGCCACTGCAAATAAGTC
TLR7	Toll like receptor 7	CCAACTGTTCAGAAGCCTCAAGA	CCAGATATCGCAACTGGAAGGCAT
TLR8	Toll like receptor 8	AGTTTCCTCGTCTCGAGTTGCTTG	AGAGGGTAGGTGGGAAATCCTGTT
TLR9	Toll like receptor 9	AACTGGCTGTTTCTGAAGTCTGTG	AGGTGGGCAAAGTCAGAATCATGG
MyD88	myeloid differentiation primary response 88	AGAAAGAGTTCCTCCAGCATCCTGA	CAAGGCGAGTCCAGAACCAAGATT
TIRAP	TIR domain containing adaptor protein	GCGCAGGCCTTACATAGGAA	CTGGCCAGGAGGATATTCGG
TRIF	TIR-domain-containing adapter-inducing interferon-β	AGAAACCAGCACCAACTACCCA	GGTCTTTGACAGAGCAGGGGTTTT
TRAM	translocation associated membrane protein	TGGGTCTGCATGGACAATCT	GGCCGCATGGGTATAACAGA
RIG-I	retinoic acid inducible gene I	TTCTGATTGCCACCTCAGTTGC	TCCTCTGCCTCTGGTTTGGATCAT
MDA-5	melanoma differentiation-associated protein 5	AGGTCTGGGGCATGGAGAATAACT	TGCCTGAATCACTGCCCATGTT
MAVS	mitochondrial antiviral-signaling protein	TGAACACAGTGGCCCTGAAAGT	ACGGGTTGAGTTGATGGGCAAT
LGP2/DHX58	DExH-box helicase 58	GGCACCCACCATGTCAATG	CCCAGACCTCCCCACAGTT
DDX3	DEAD-box helicase 3	CAGTTCAGGGTGGAGTTCTAGCAA	CTGCCAATGCCATCGTAATCACTC
cGAS	cyclic GMP-AMP synthase	GAAGGCCTGCGCATTCAAACCT	GAGAGAAGGATAGCCGCCATGTTT
IFI16	gamma interferon inducible protein 16	GACCAGCCCTATCAAGAAAGAGGA	TCTGGGAGTTACCTGACATTTGGC
DAI	DNA-dependent activator of IFN-regulatory factors	GGTGAAGGAATGCCAAGCAC	CCTTCAGGATCAGTCCCGC
Ku70	-	GCATGCGTGGATTGTGCTC	TAGTCTCCACTTGCTTCAAGGT
LRRFIP1	LRR binding FLII interacting protein 1	GAGCTCCGCTCTGCATTGGATAAA	CAAGAGTGCCTCCGATTTGCT
MRE11	meiotic recombination 11 homolog	GGGTCTCAAAGAGGAAGAGACAC	GACATTTGCGGAAGGCTGCT
DDX41	DEAD-box helicase 41	GCAGTCTGAGGAGTGAGCTTC	CTACCCCTCAGATCAAGCCG
DHX9	DExH-box helicase 9	AGCAATGCTGCCAGAGACTT	GCGGAGATGCTACCCCAAAA
DHX36	DExH-box helicase 36	AGTGCCATTTAGTTGCGGA	TGTTTTCTTGCCAACCGACT
STING	stimulator of interferon genes	CCATGGGCTGGCATGGTCATATTA	AATATACAGCCGCTGGCTCACT
B-catenin	-	TTGTGCGGCGCCATTTAAG	TCCTCAGACCTTCTCCGTC
AIM2	absent in melanoma 2	TCGGCACAGTGGTTTCTTAGAGG	TCGGGGTTTCACCAGCTTTTCT
NLRP1	NLR family pyrin domain containing 1	CTACGTTGGCCACTTGGGAT	AGGTGAAGGTACGGCTATGC
NLRP3	NLR family pyrin domain containing 3	AAAGGAAGGCCGACACCTTGAT	TGGCTGGTGCTCAGAAGTAAA
NLRC4	NLR family CARD domain containing 4	GAGGTCCCACAACCTCGTCAA	GATTTCCCGCCAAATTCAAC
ASC	apoptosis-associated speck-like protein containing a CARD	CGCGAGGGTCAAAAACGT	TGCTCATCCGTGAGGACCTT
Caspase 1	-	AAAATCTCACTGCTTCGGACATG	GGAACGTGCTGTCAGAGGTCTT
IRF1	interferon regulatory factor 1	TTGTGCCGGACAGCACCAGT	TCCACGTTTGTGGCTGCCACT
IRF3	interferon regulatory factor 3	ACCCAGCCGTGGACCAAGAG	TACCAAGGCCCTGAGGCAC
IRF4	interferon regulatory factor 4	GACCGAAGCTGGAGGGACTA	TGTCACCTGGCAACCATTTTC
IRF5	interferon regulatory factor 5	TGTCAGTGCAAGGTGTTCTGGA	TGTTGGTCTGGCCCTTTTGGAA
IRF7	interferon regulatory factor 7	TGGTCTGGTGAAGCTGGAA	GATGTCGTCATAGAGGCTGTTGG
NOD1	nucleotide-binding oligomerization domain-containing protein 1	AGAGGCTCTGCGGAACCA	TGTGGAGATGCCGTTGGA
NOD2	nucleotide-binding oligomerization domain-containing protein 2	CCCTGCAGCTGGACTACAACCT	AGATGCCTCGGTCTGAGATATTG
RIP2	receptor interacting serine/threonine kinase 2	CGCTGCTCGACAGTGAAAAGA	TCAGGCTCATTGCAAATTCCTC
CARD9	caspase recruitment domain-containing protein 9	TTGAGAACTACCGCAGGAAGCG	GGCTAGGAGCCCTCAGTGTC
Mincle	macrophage inducible Ca ²⁺ -dependent lectin receptor	ACGAGAAAATTTGTGCGCTGA	CTGGGAAGAGGACCTGAGACT
Dectin-1/CLECL7A	C-type lectin domain family 7 member A	TCAGGGGCTCTCAAGAACAA	GAGGAGATGCAGCACACGAT
Dectin-2/CLEC6A	C-type lectin domain family 6 member A	AACACAGGGAGCCTGCATAAT	ATCCCAGCCACAGACCAGAG
Syk	spleen tyrosine kinase	TGAGCCTCACCAAAAACAGG	ACAGCAAAACTGAAATCAATGGGT
SOCS1	suppressor of cytokine signaling protein 1	CACCTCCGCACATTCCGTTT	CAGTAGAATCCGCAGGCGTC
SOCS3	suppressor of cytokine signaling protein 3	CCATTCCGGGAGTTTCTGGAC	TTGGCTTCTTGTGCTTGTGC
PD-1	programmed cell death 1	AAACCCTGGTGGTTGGTGTC	CTCCTATTGTCCCTCGTGCG
PD-L1	programmed cell death ligand 1	CTGAACGCATTTACTGTCACGG	AGACAATTAGTGACGCCAGGT
Tim1	T-cell immunoglobulin and mucin domain 1	ACTGGAGAAAAGCCGACGTG	GGACCTCTGGGTTGGAAATGA
Tim3	T-cell immunoglobulin and mucin domain 3	CTACTGCTGCCGGATCCAAA	GTCCCCTGGTGGTAAGCATC
Gal9	galectin 9	ACAGCCAAGTTGCTTTGGTTT	AAAGGGGACAGCTGGACTCA
Tim4	T-cell immunoglobulin and mucin domain 4	GTCCTGCTGACATCCAAAGAGT	TTGTTTTGTTCTGCTCAGGAACTG
CD68	Cluster of differentiation 68	AGGCTGGCTGTGCTTTTCTC	CTCTGTAACCGTGGGTGTCA
L-SIGN	liver/lymph node-specific ICAM-3-grabbing integrin	GACTGCATTTGAACGCCTGT	TGACGGAGTTGTGCCAGTTC
α-SMA	α-smooth muscle actin	GTGTTGCCCTGAAGAGCAT	GCTGGGACATTGAAAGTCTCA
NTCP	sodium-taurocholate cotransporting polypeptide	TGACCACCTGCTCCACCTTC	GAATGAGAACCAGGACCAGTGAT

Table 1: Primers sequences.

Target protein	Name	Reference	Stimulated Control
TLR1	Polyclonal anti-TLR1 antibody	PA5-11589 (Thermo Fisher)	THP1 + PAM3CSK4
TLR2	Monoclonal anti-TLR2 antibody	#12276 (Cell Signaling)	THP1 + PAM3CSK4
TLR3	Monoclonal anti-TLR3 antibody	#6961 (Cell Signaling)	LMNC + Riboxsol
TLR4	Monoclonal anti-TLR4 antibody	sc-293072 (Santa Cruz)	THP1 + LPS
TLR5	Monoclonal anti-TLR5 antibody	Ab168382(Abcam)	THP1 + LPS
TLR7	Monoclonal anti-TLR7 antibody	#5632 (Cell Signaling)	THP1 + Imiquimod (R837)
TLR8	Monoclonal anti-TLR8 antibody	#11886 (Cell Signaling)	LMNC + ssRNA40/Lyovec
TLR9	Monoclonal anti-TLR9 antibody	#13674 (Cell Signaling)	pDC
RIG-I	Monoclonal I anti-RIG-I antibody	#3743 (Cell Signaling)	HepaRG + Poly(I:C) (LMNC)/Lyovec
MDA-5	Monoclonal anti-MDA5 antibody	#5321 (Cell Signaling)	HepaRG + Poly(I:C) (LMNC)/Lyovec
cGAS	Monoclonal anti-cGAS antibody	#15102 (Cell Signaling)	THP1 + STING
STING	Monoclonal anti-STING antibody	#13647 (Cell Signaling)	THP1 + STING
PD-1	Polyclonal anti-PD1 antibody	PA5-20350 (Thermo Fisher)	THP1 + PAM3CSK4
PD-L1	Polyclonal anti-PDL1 antibody	PA5-28115 (Thermo Fisher)	THP1 + PAM3CSK4
IFI16	Monoclonal anti-IFI16 antibody	Ab169788 (Abcam)	THP1 + Imiquimod (R837)
MyD88	Monoclonal anti-Myd88 antibody	#4283 (Cell Signaling)	THP1 + PAM3CSK4
TRIF	Polyclonal anti-TRIF antibody	#4596 (Cell Signaling)	LMNC + Riboxsol
MAVS	Polyclonal anti-MAVS antibody	#3993 (Cell Signaling)	HepaRG + Poly(I:C) (LMNC)/Lyovec

Table 2: Antibodies and controls used for western blot analysis.

PRR	Ligand	Reference	Concentration
TLR1/2	PAM3CSK4	t1rl-pms	0,5 µg/ml
TLR2/6	FSL-1	t1rl-fsl	1 µg/ml
TLR3	Poly(I:C) (HMW)	t1rl-pic	5 µg/ml
TLR3	Riboxsol	A-00102	5 µg/ml
TLR4	LPS SM	t1rl-smlps	0,5 µg/ml
TLR7	Imiquimod (R837)	t1rl-imq	5 µg/ml
TLR8	ssRNA40/Lyovec	t1rl-lrna40	1 µg/ml
TLR9	ODN 2395	t1rl-2395	5 µM
RIGI/MDA5	Poly(I:C) (LMW)/Lyovec	t1rl-picwlv	0,025 µg/ml
STING	2'3'-cGAMP	t1rl-cga23	5 µg/ml

Table 3: Ligands and concentration used for PRR stimulation.