

Figure S1

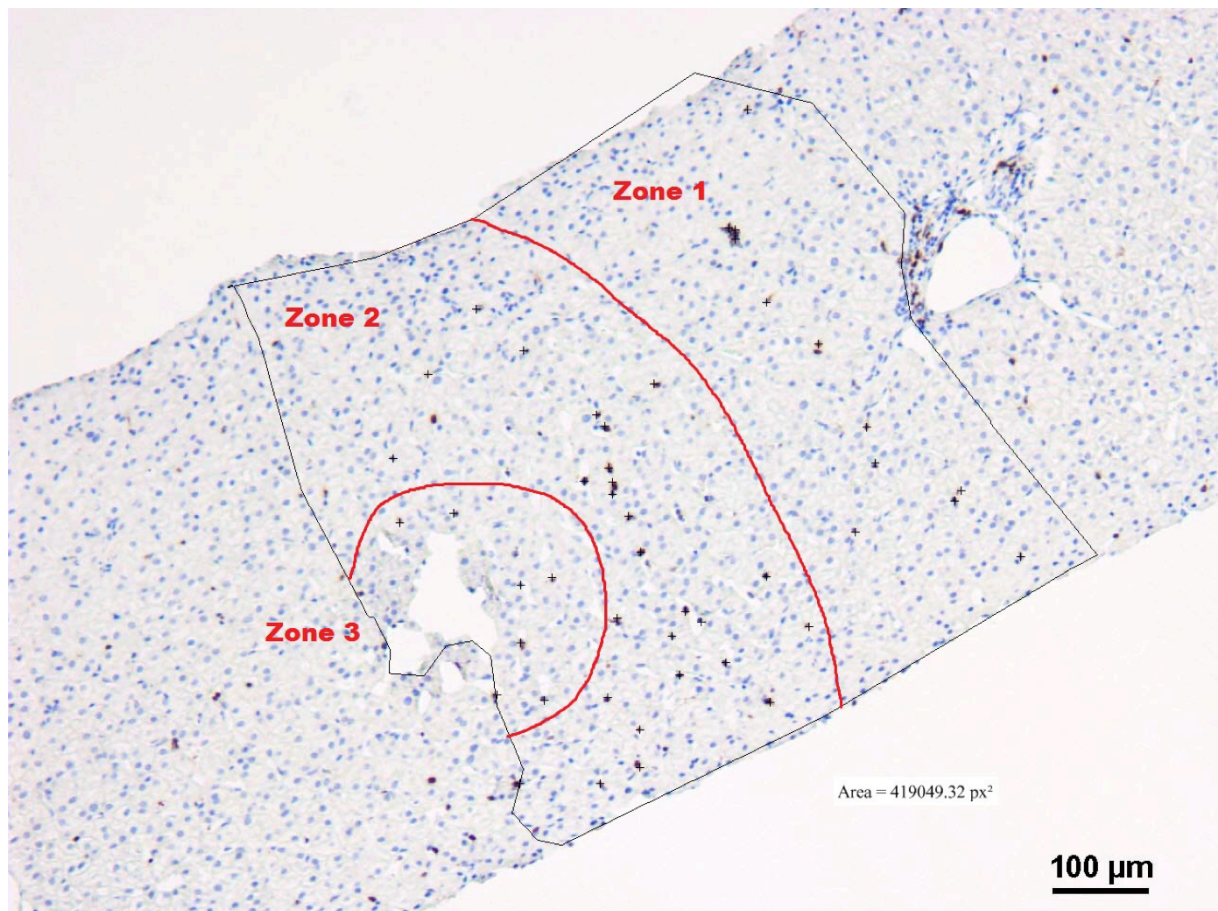


Figure S2

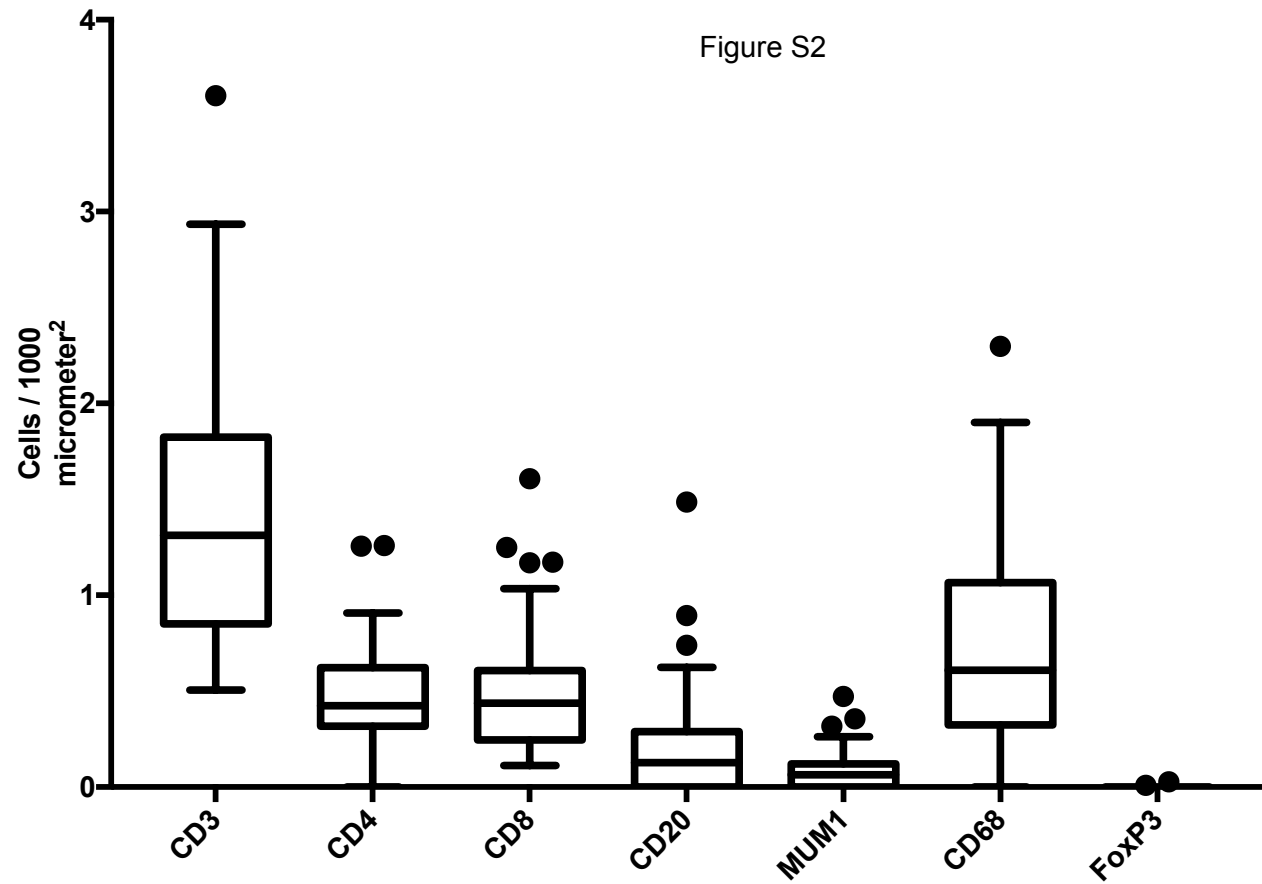
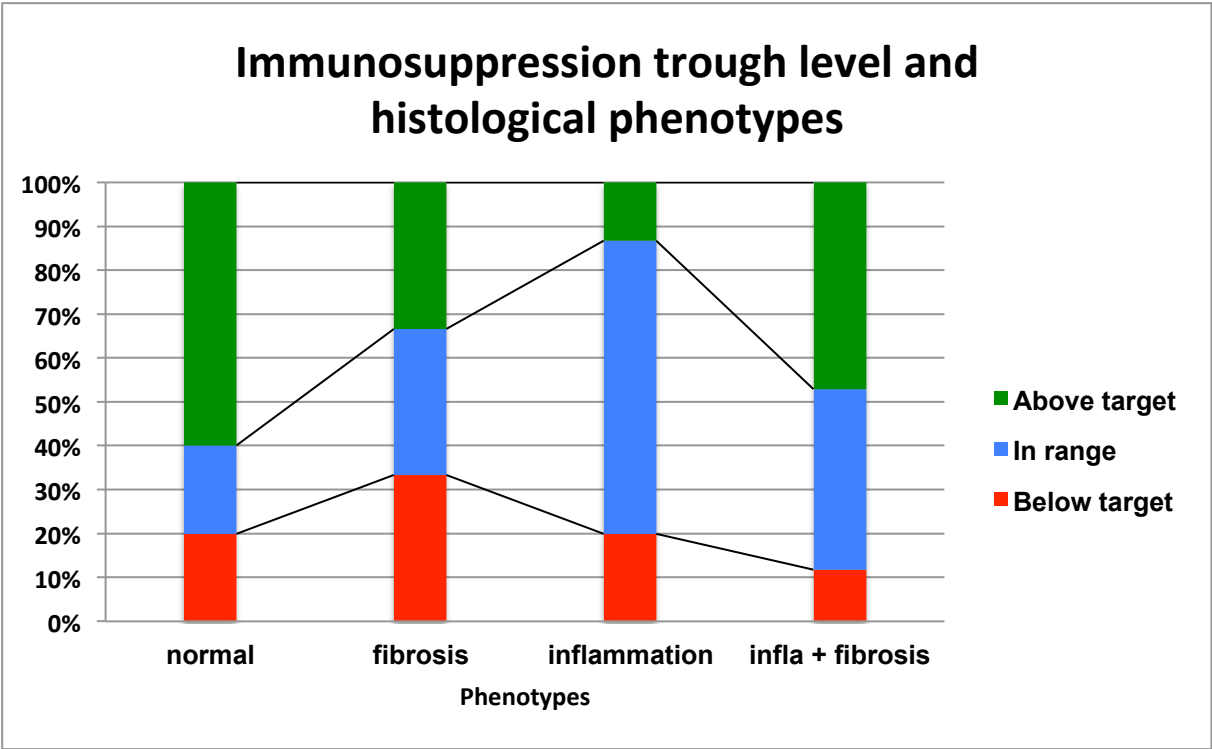


Figure S3



A

Figure S4

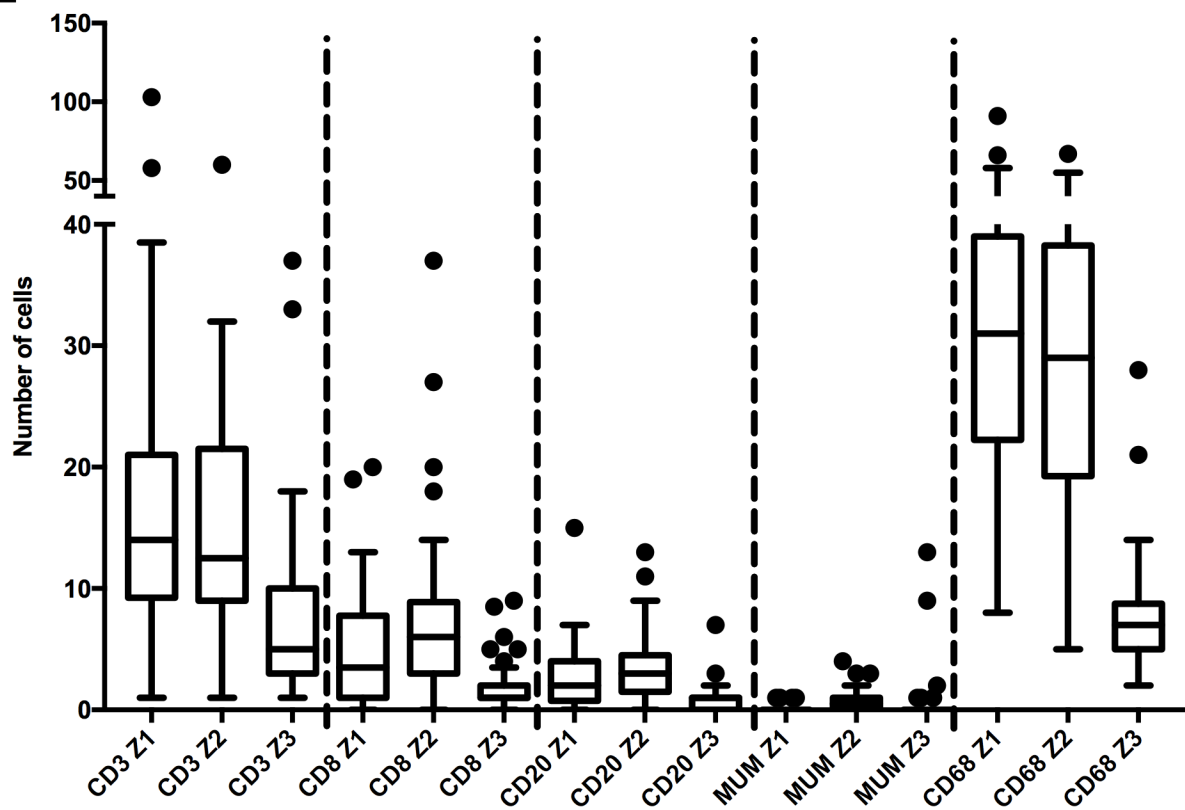
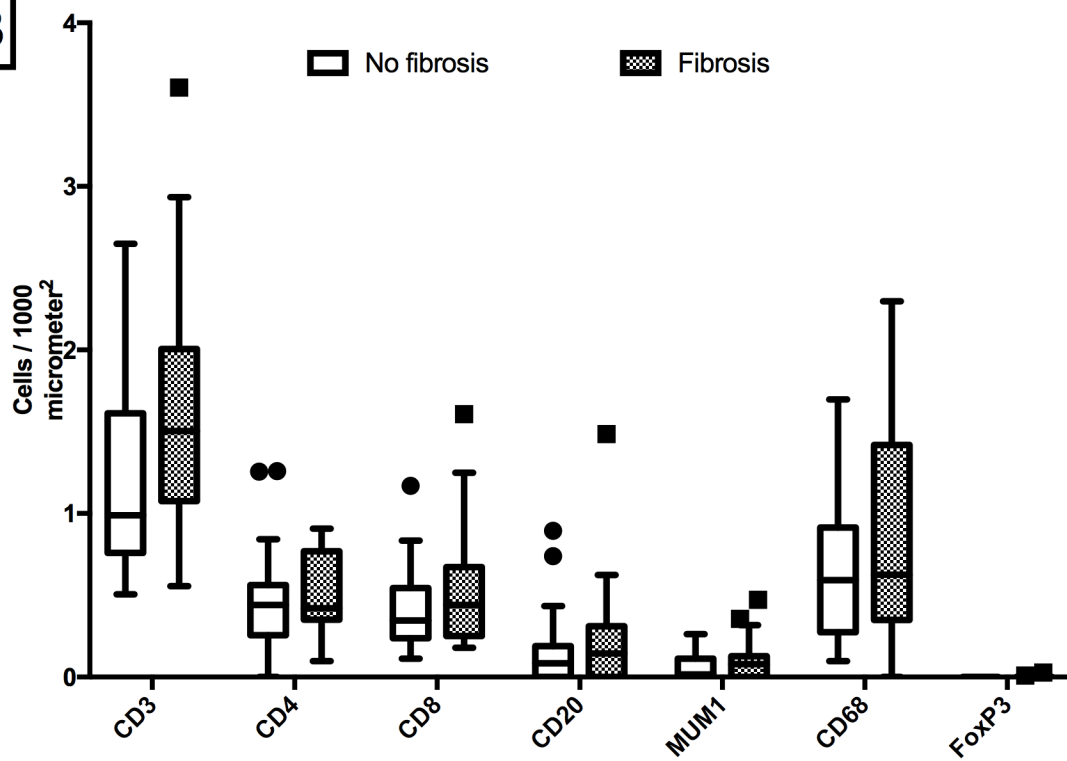
**B**

Figure S1. Illustration of liver lobule.

Lobules pictures. Lobular zone were defined as follows: zone 1, juxting portal venule, zone 2 between zone 1 and 3 and zone 3, surrounding centrolobular vein.

Zone 1, 2 and 3 are separated using the red line. Surface of the lobule is reported in μm^2 .

Figure S2: Overall characteristics of portal infiltrate

Aggregate data from all portal tracts. Y axis: cellular density in the portal tract expressed as cells / 1000 μm^2 . X axis: cellular subtypes.

Figure S3: Immunosuppression trough level and histological phenotypes.

Representation of patients with different histological phenotypes and calcineurin inhibitor trough levels at biopsy. There was no significant difference between groups. Above target: trough levels in excess of target trough. In range: in target range. Below target: trough level below target trough.

Figure S4: Lobular infiltrate in PB and portal infiltrate in biopsies with fibrosis only.

Panel A: overall lobular infiltrate. Panel B: portal infiltrate in case of fibrosis. $*=p<0.05$.

$**=p<0.01$.

SDC1

Immunohistochemistry methods

High temperature antigen retrieval was applied. Reactivity to primary antibodies was identified using the Ultravision detection system and DAB as the chromogen substrate (Thermo Fisher Scientific) for the following antibodies: CD3 (Novocastra mouse monoclonal, clone 17C2; dilution 1:20), CD4 (Dako mouse monoclonal, clone Ber-H2; prediluted) and CD8 (Dako mouse monoclonal and rabbit monoclonal, 1:25) for T lymphocytes; CD20 (CellMarque mouse monoclonal, clone 1G12; dilution 1:20) and MUM1 (BioCare Medical mouse monoclonal, clone 6E3; 1:100 dilution) for B lymphocytes and plasma cells; CD68 (Dako mouse monoclonal, clone PG-M1; 1:50 dilution) for macrophages, and FoxP3 (Abcam mouse monoclonal, clone 236A/E7; 1:400 dilution) for regulatory T-cells.

Laboratory tests for auto-antibodies at time of pLB:

ANCA: indirect immunofluorescence on fixed neutrophils (with ethanol) slide. Positive titre >20.

ANA: indirect immunofluorescence on a Hep-2 slide. Positive titre >80

Anti smooth muscle (anti-actin): 2000 to 12/2014 indirect immunofluorescence on rat smooth muscle cell slide. After 12/2014, mouse smooth muscle slide. Positive titre >40

Anti-mitochondrial: 2000 to 12/2014 indirect immunofluorescence on rat smooth muscle cell slide. After 12/2014, mouse smooth muscle slide. Then, confirmation with immunodot (Kit liver 4 Ag dot, AlphaDia, Belgium) and Elisa M2 (substrate: M2 subunit from pyruvate-deshydrogenase (PDC-E2) complex, 2-oxodeshydrogenase acid ramified chains (BCOADC-E2) and 2-oxoglutarate-deshydrogenase (OGDC-E2) Kit quantaLite M2 (Inova). Positive titre >20

Anti-liver-kidney-microsome (LKM): 2000 to 12/2014 indirect immunofluorescence on rat smooth muscle cell slide. After 12/2014, mouse smooth muscle slide. Then confirmation with immunodot (Kit liver 4Ag dot, AlphaDia, Belgium). Positive titre >20

Anti-Soluble Liver Antigen (SLA): immunodot (Kit liver 4 Ag dot, AlphaDia, Belgium). Positive titre:

Table S1

Preformed DSA		De novo DSA		C1q binding DSA	
	N		N		N
DQ	5	DQ	24	DQ	12
DR	4	DR	8	DP	0
DP	0	DP	0	DR	1
A	1	A	2	A	3
B	3	B	0	B	1
C	0	C	0	C	0
DQ7	3	DQ7	12	DQ2	8
DQ6	1	DQ9	3	DQ6	1
DQ8	1	DQ2	10	DQ7	6
DR4	3	DQ8	5	DQ8	3
DR7	1	DQ6	3	DR4	1
A24	1	DQ5	3	DR53	1
B51	2	DQ4	1	A29	1
B39	1	DR53	1	A2	2
B56	1	DR51	1	B38	1
B44	1	DR17	1		
		DR4	4	MFI C1q binding DSA class I	730.5 (IQR 587.5-952.5)
		DR7	1	MFI C1q binding DSA class II	23381 (IQR 12500-45261)
MFI preformed DSA class I	6507 (IQR 3484-14050)	DR13	1		
MFI preformed DSA class II	1576.5 (IQR 1247-2475.5)	A32	1		
		A2	1		
		MFI de novo DSA class I	1767 (IQR 1309-2225)		
		MFI de novo DSA class II	17556 (IQR 2004-23232)		

Table S1: Description of preformed, de novo and C1q binding DSA. Grey box indicates number of different DSA class. Patients may have multiple DSA, explaining the total number variation. C1q binding DSA were previously tested using a LSA. DSA with a high MFI were detected as C1q binding DSA. DSA: donor specific antibody. LSA: Luminex Single-Antigen

Table S2

	No fibrosis N(%)	Fibrosis N(%)	P value
No inflammation	5 (25)	6 (25)	p= 1
Inflammation	15 (75)	18 (75)	
	20	24	
	No portal fibrosis N(%)	Portal Fibrosis N(%)	
No inflammation	8 (30)	3 (18)	p= 0.48
Inflammation	19 (70)	14 (82)	
	27	17	
	No CLF N(%)	CLF N(%)	
No inflammation	6 (21)	5 (31)	p= 0.49
Inflammation	22 (79)	11 (69)	
	28	16	

Table S2: Associations between inflammation and fibrosis, portal fibrosis and centrolobular fibrosis. CLF: centrolobular fibrosis.