

Supplemental data for “Virus Genotype-Dependent Transcriptional Alterations in Lipid Metabolism and Inflammation Pathways in the Hepatitis C Virus-infected Liver”

d'Avigdor W.M.H.*^{1,2}, Budzinska M.A.*^{1,2,3}, Lee M.¹, Lam R.¹, Kench J.², Stapelberg M.^{1,2}, McLennan S.V.², Farrell G.⁴, George J.⁵, McCaughan G.W.^{1,2,6}, Tu T.^{#1,7,8,10}, and Shackel N.A. #^{1,2,8,9}

* Authors contributed equally to this study; # Authors contributed equally to this study

¹Liver Injury and Cancer Laboratory, Centenary Institute of Cancer Medicine and Cell Biology, Sydney, NSW, Australia

²Sydney Medical School, University of Sydney, Sydney, NSW, Australia

³Gastroenterology and Liver Research Laboratory, Ingham Institute, Liverpool, NSW, Australia

⁴Australian National University, Canberra, ACT, Australia

⁵Storr Liver Centre, Westmead Institute for Medical Research, University of Sydney and Westmead Hospital, Westmead, NSW 2145, Australia

⁶A.W. Morrow Gastroenterology and Liver Centre, Royal Prince Alfred Hospital, Sydney, NSW, Australia

⁷Department of Infectious Diseases, Molecular Virology, Heidelberg University Hospital, Heidelberg, Germany

⁸South-Western Sydney Clinical School, University of New South Wales, Liverpool, NSW, Australia

⁹Department of Gastroenterology and Hepatology, Liverpool Hospital, Liverpool, NSW, Australia

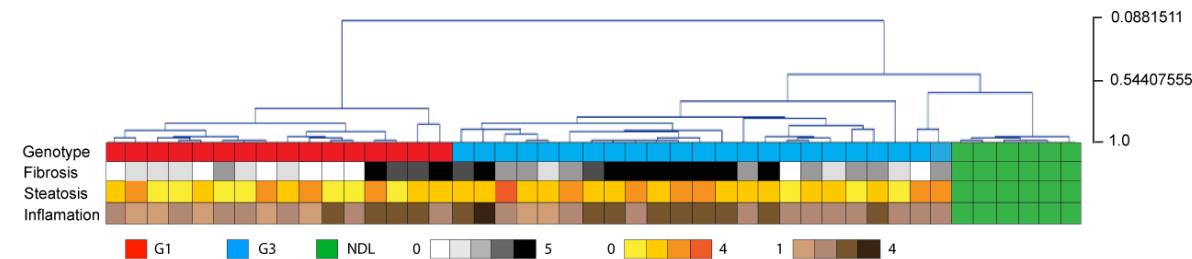
¹⁰German Center for Infection Research (DZIF), Heidelberg Partner Site, Heidelberg, Germany

Correspondence

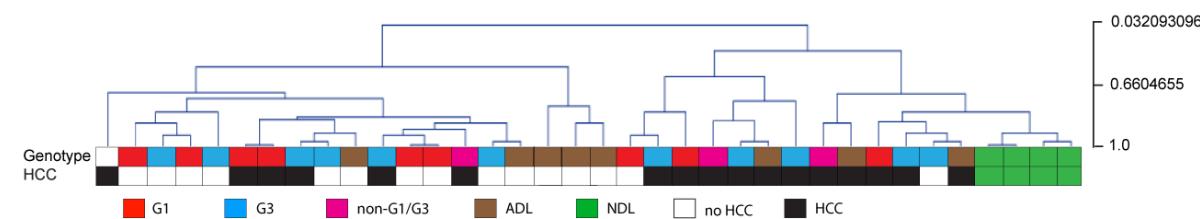
Nicholas Shackel, Gastroenterology and Liver Research Group, Ingham Institute, University of New South Wales, via PO Box 3151 (Westfields Liverpool), Liverpool NSW 2170, Australia; Email: n.shackel@unsw.edu.au

Supplementary Figure 1

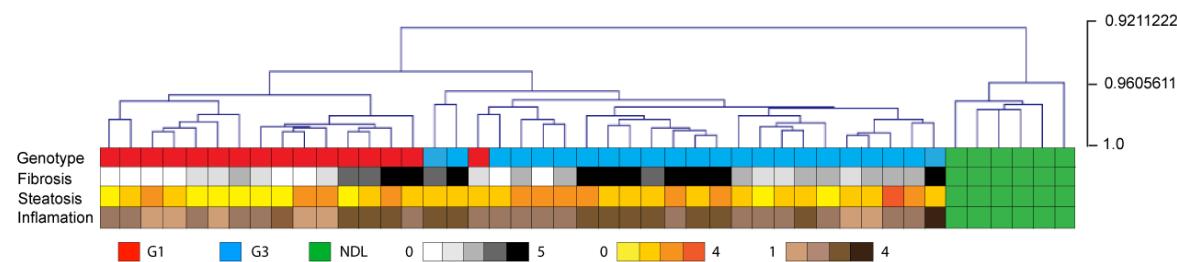
A Non-negative matrix factorisation



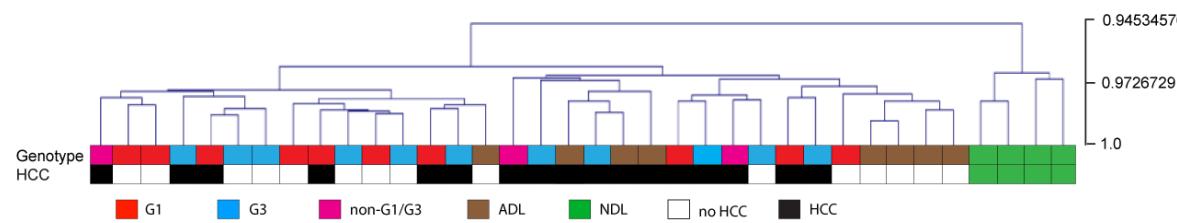
B



C Hierarchical Clustering

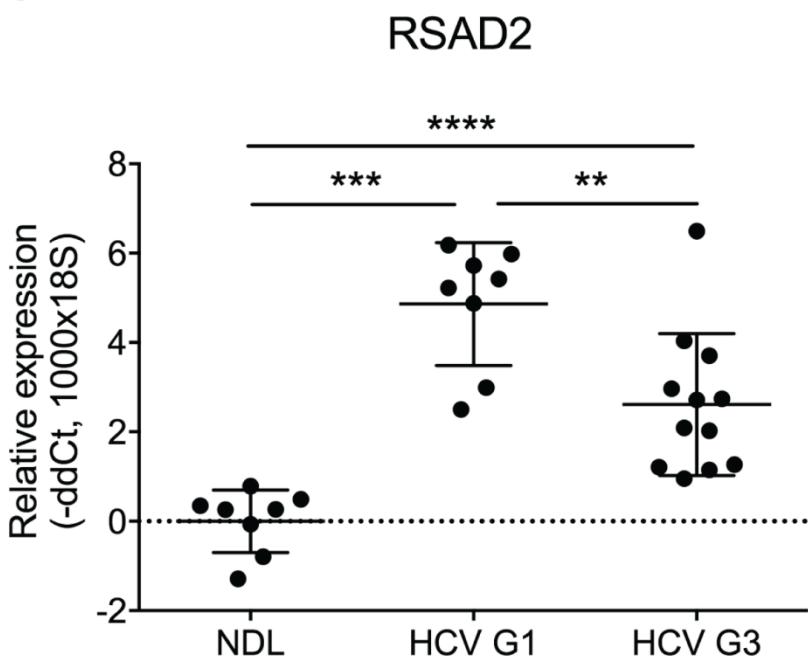


D

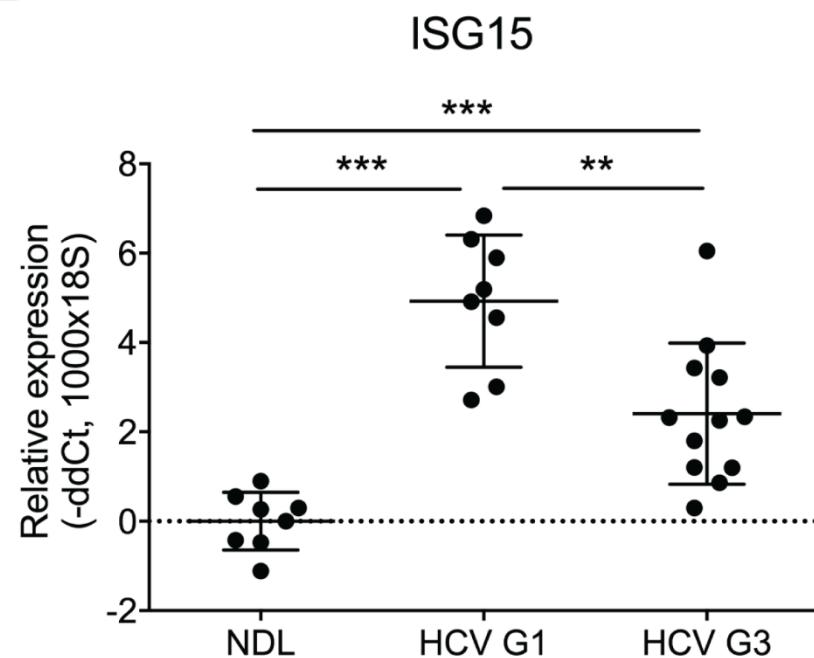


Supplementary Figure 2

A

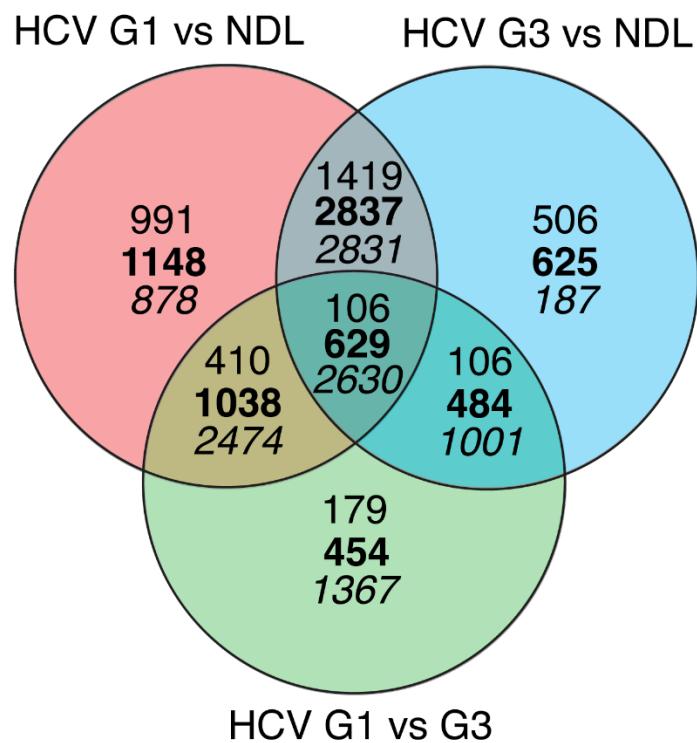


B

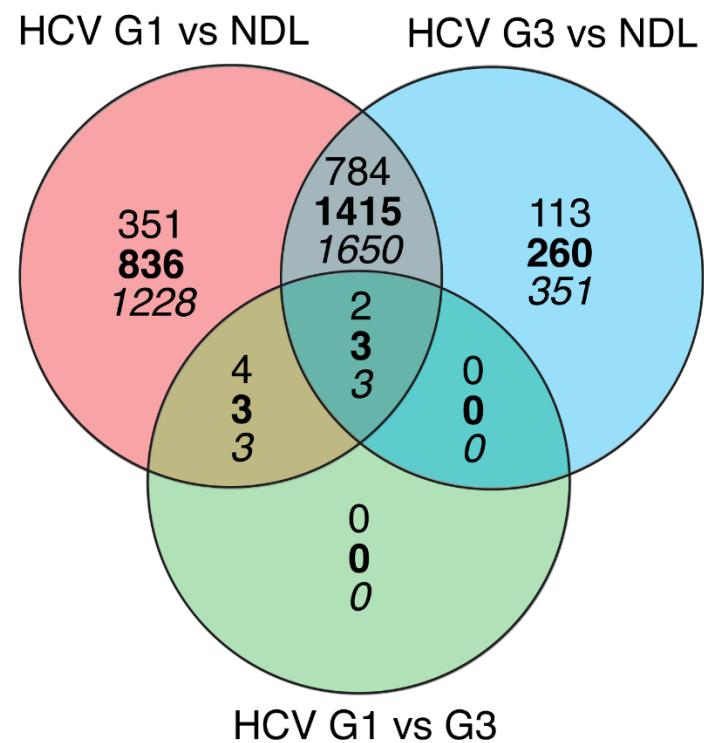


Supplementary Figure 3

A Progressive Liver Injury



B Advanced Liver Injury



Normal > 2-fold

Bold > 1.5-fold

Italics No cut-off

Supplementary Figure legends

Supplementary Figure 1 – Unsupervised analysis of liver genes expression in HCV liver injury

Non-negative matrix factorisation (A-B) and hierarchical clustering (C-D) of the whole liver gene expression profiles of HCV-induced progressive liver injury (A, C) and advanced liver injury (B, D). In progressive liver injury (A, C) 3 groups shows distinct separation: patients infected with HCV Genotype 1 (red); genotype 3 (blue) and non-diseased liver (green). This separation is not observed in advanced liver injury (B, D).

Supplementary Figure 2 – ISGs are upregulated in HCV-infected tissues

Taqman qRT-PCR validation of interferon stimulated genes RSAD2 and ISG15 in progressive HCV-induced liver disease comparing genotype 1 (HCV G1, n=8), genotype 3 (HCV G3, n=12), and non-diseased liver (NDL, n=8); Mann-Whitney *U*-test; ** $p<0.01$, *** $p<0.001$, **** $p<0.0001$.

Supplementary Figure 3 - Overlap of differentially expressed genes between non-diseased livers (NDL) and livers from patients infected with HCV genotype 1 (HCV G1) or genotype 3 (HCV G3)

Venn diagrams show the overlap of differentially expressed liver genes in HCV-induced progressive (A) and advanced (B) liver injury. Numbers refer to genes thresholded with a fold change of >2 (normal font), of >1.5 (bold), and with no threshold (italics).

Supplementary Tables

Supplementary Table 1 – Top 100 up- and down-regulated genes in progressive HCV liver injury (HCV genotype 3 vs genotype 1).

Increased expression in HCV genotype 3				Decreased expression in HCV genotype 3		
Rank	Gene symbol	Fold Change	p-value*	Gene symbol	Fold Change	p-value*
1	STMN2	4.61	0.031	CROP	-14.68	<0.001
2	MMP7	4.22	<0.001	ASCL1	-14.36	0.042
3	ACTG2	4.01	0.478	C1orf63	-14.08	<0.001
4	AKR1B10	3.95	0.379	PILRB	-13.75	<0.001
5	CLOCK	3.85	<0.001	AFAR3	-13.40	<0.001
6	SPINK1	3.68	0.164	AHSA2	-11.36	<0.001
7	HLA-DQB2	3.67	0.017	RAPH1	-11.31	<0.001
8	IGJ	3.53	<0.001	CDK5RAP3	-10.32	<0.001
9	SAA2	3.45	0.053	DNAH1	-10.25	<0.001
10	C15orf48	3.42	<0.001	GSDML	-9.23	<0.001
11	RBM43	3.37	<0.001	FAM99A	-9.00	<0.001
12	CLDN11	3.30	<0.001	NKTR	-8.59	<0.001
13	SCGB3A1	3.24	0.006	CAPN12	-8.13	<0.001
14	SAA1	3.20	0.070	LOC440354	-8.11	<0.001
15	CTSG	3.20	<0.001	WDR33	-8.07	<0.001
16	COL1A1	3.12	<0.001	HAPLN4	-7.87	<0.001
17	SPP1	3.11	0.012	RBM33	-7.76	<0.001
18	ITM2A	3.05	<0.001	LOC440993	-7.68	<0.001
19	MYH11	3.05	0.026	PLA2G4B	-7.36	<0.001
20	THY1	2.97	<0.001	ATHL1	-7.28	<0.001
21	TMEM119	2.93	<0.001	PRPF4B	-7.25	<0.001
22	CD24	2.91	0.012	LOC285908	-6.85	<0.001
23	CLDN10	2.87	<0.001	PNN	-6.82	<0.001
24	FCER1A	2.86	<0.001	LOC387601	-6.74	<0.001
25	MOXD1	2.82	0.012	NSUN5C	-6.71	<0.001
26	LYZ	2.81	0.007	CHRD	-6.54	<0.001
27	CTSC	2.81	<0.001	C6orf111	-6.39	<0.001
28	FABP4	2.80	<0.001	LOC149134	-6.37	<0.001
29	ENTPD1	2.80	<0.001	LRCH4	-6.33	<0.001
30	S100A11	2.76	<0.001	LRP5L	-6.31	<0.001
31	HLA-DPB1	2.73	<0.001	SCNN1D	-6.21	<0.001
32	NTS	2.73	<0.001	SMG1	-6.18	<0.001
33	CTHRC1	2.73	<0.001	C20orf59	-6.16	<0.001
34	TIMD4	2.71	<0.001	AFG3L1	-6.16	<0.001
35	LCN2	2.69	<0.001	HEMK1	-6.01	<0.001
36	CXCR3	2.68	<0.001	NPHP3	-5.87	<0.001
37	SPON1	2.68	0.012	MAPK8IP3	-5.67	<0.001
38	CD248	2.66	<0.001	LOC440503	-5.60	<0.001
39	GPC4	2.64	<0.001	WBSCR14	-5.54	<0.001

89	PLA2G7	2.35	<0.001	NFKBIZ	-3.96	<0.001
90	CCL4L1	2.34	<0.001	MGC33556	-3.93	<0.001
91	AIF1	2.33	<0.001	SFRS14	-3.93	<0.001
92	RNASE1	2.32	<0.001	XAF1	-3.92	<0.001
93	IGFBP6	2.32	<0.001	DDX17	-3.87	<0.001
94	CLDN10	2.32	<0.001	INDOL1	-3.87	<0.001
95	HSPB8	2.32	<0.001	C17orf55	-3.85	<0.001
96	EGR1	2.32	0.053	TDRD6	-3.84	<0.001
97	SYT13	2.32	0.031	MT1E	-3.82	<0.001
98	CST7	2.31	<0.001	SLC25A27	-3.82	<0.001
99	FBLN1	2.31	0.007	JOSD3	-3.75	<0.001
100	NQO1	2.31	0.012	FAM76B	-3.74	<0.001

* FDR adjusted p-value (Benjamini-Hochberg)