

S1 Table. Top 30 degree nodes in the HCV network. We report the list of the up-regulated (in red) and down-regulated (in green) genes, and the values for average shortest path length, betweenness centrality, closeness centrality, and degree.

Genes	Avg. Shortest Path Length	Betweenness Centrality	Closeness Centrality	Degree
CUL3	2.220269	0.082578	0.450396	238
FN1	2.19918	0.08896	0.454715	195
KIAA0101	2.314587	0.049322	0.432043	175
EEF1A1	2.200937	0.048319	0.454352	169
COP5	2.322789	0.03982	0.430517	153
CAND1	2.364382	0.02612	0.422944	137
YWHAZ	2.262449	0.034463	0.441999	135
FBXO6	2.367897	0.051798	0.422316	132
EGFR	2.347393	0.050513	0.426004	124
RPA2	2.360281	0.023919	0.423678	108
PCNA	2.35618	0.026809	0.424416	105
ITGA4	2.418278	0.017328	0.413517	104
RPA1	2.421793	0.015475	0.412917	99
CUL2	2.421793	0.015302	0.412917	99
YWHAE	2.35208	0.026612	0.425156	95
HNRNPC	2.388987	0.015527	0.418588	94
ICT1	2.783831	0.019037	0.359217	93
POLR2E	2.515524	0.00979	0.397531	93
GAPDH	2.338606	0.018651	0.427605	92
VCAM1	2.489162	0.009337	0.401742	91
YWHAH	2.429994	0.015034	0.411524	88
RAN	2.449326	0.011179	0.408276	88
RPA3	2.472173	0.009155	0.404502	87
EED	2.582308	0.016033	0.38725	86
YWHAQ	2.379028	0.018004	0.42034	79
DNAJA1	2.42355	0.008759	0.412618	79
CUL5	2.566491	0.008132	0.389637	75
POLR2I	2.719977	0.003487	0.36765	73
FYN	2.615114	0.018765	0.382392	72
ATP5B	2.428237	0.013093	0.411821	71

S2 Table. Pathway and molecular function analyses of the HUB genes in the HCV network. We report for each pathway and molecular function name, number of genes, p-values and list of involved genes.

Pathways	Number of genes	P-value	Genes
Mismatch repair	4	3.03E-04	RPA1, RPA2, PCNA, RPA3
Cancer	9	4.59E-04	EGFR, CUL2, JUN, RAC1, SMAD4, SMAD2, STAT1, STAT3, FN1
Neurotrophin signaling pathway	6	6.95E-04	YWHAZ, JUN, RAC1, YWHAB, YWHAQ, YWHAE
Adherens junction	5	9.88E-04	EGFR, FYN, RAC1, SMAD4, SMAD2
DNA replication	4	1.16E-03	RPA1, RPA2, PCNA, RPA3
Function			
RNA polymerase activity	4	7.54E-05	POLR2E, RPA1, RPA2, POLR2I
ubiquitin protein ligase binding	3	7.66E-03	CUL5, CUL3, CUL2
MAP/ERK kinase kinase activity	1	2.72E-02	EGFR

S3 Table. Top 30 degree nodes of the HCV-related cirrhosis network. We report for each gene the values for average shortest path length, betweenness centrality, closeness centrality and degree.

Genes	Avg. Shortest Path Length	Betweenness Centrality	Closeness Centrality	Degree
FN1	2.137518	0.109989	0.467832	195
YWHAZ	2.245416	0.043271	0.445352	141
MDM2	2.330748	0.054989	0.429047	135
COPS5	2.29055	0.047699	0.436576	127
ACTB	2.25952	0.035951	0.442572	126
FBXO6	2.370945	0.052309	0.421773	121
MYC	2.341326	0.043382	0.427108	109
ITGA4	2.354725	0.027465	0.424678	107
HSP90AB1	2.261636	0.022017	0.442158	105
YWHAB	2.430889	0.030047	0.411372	95
CAND1	2.440056	0.023655	0.409827	94
YWHAQ	2.338505	0.018853	0.427624	93
TUBA1A	2.356135	0.020696	0.424424	92
VCAM1	2.444288	0.011617	0.409117	90
YWHAE	2.368124	0.018286	0.422275	88
FYN	2.461918	0.026137	0.406187	88
CUL2	2.45275	0.021857	0.407706	86
GAPDH	2.327221	0.014744	0.429697	83
RPA1	2.480254	0.02393	0.403185	83
RAC1	2.488717	0.028028	0.401814	82
PCNA	2.381523	0.024509	0.419899	79
XPO1	2.45275	0.013865	0.407706	75
RAN	2.380113	0.011322	0.420148	74
DDX3X	2.375176	0.011382	0.421021	73
JUN	2.421721	0.024682	0.41293	73
LCK	2.509873	0.021212	0.398427	72
HSPB1	2.38646	0.01775	0.419031	71
SMAD2	2.503526	0.02234	0.399437	70
CSNK1A1	2.469676	0.009932	0.404911	68
VIM	2.375882	0.016485	0.420896	67

S4 Table. Pathway and molecular functions analysis of the HUB genes in the HCV-related cirrhosis network. We report for each pathway and molecular function name, number of genes, p-values and the list of involved genes

Pathways	Number of genes	P-value	Genes
Cell cycle	9	6.83E-07	YWHAZ, YWHAB, YWHAQ, SMAD4, PCNA, MDM2, SMAD2, YWHAE, MYC
Pathogenic infection	7	1.10E-06	ACTG1, ACTB, YWHAZ, FYN, YWHAQ, TUBA1A, ITGB1
Adherens junction	7	6.56E-06	ACTG1, ACTB, FYN, RAC1, SMAD4, SMAD2, IQGAP1
Pathways in cancer	11	1.95E-05	HSP90AB1, CUL2, JUN, RAC1, SMAD4, MDM2, SMAD2, STAT1, ITGB1, MYC, FN1
Leukocyte transendothelial migration	6	7.54E-04	VCAM1, ACTG1, ACTB, RAC1, ITGA4, ITGB1
Viral myocarditis	5	9.34E-04	ACTG1, ACTB, CAV1, FYN, RAC1
Function			
DNA regulatory region binding	3	1.77E-02	JUN, SMAD2, MYC
E-box binding	1	3.45E-02	MYC
Non-membrane spanning protein tyrosine kinase activity	2	2.26E-02	FYN, LCK
Promoter binding	1	2.72E-02	EGFR
Phosphoserine binding	2	9.94E-04	YWHAB, YWHAE

S5 Table. Top 30 degree nodes in the HCC with HCV-related cirrhosis network. We report the list of the genes, and the values for average shortest path length, betweenness centrality, closeness centrality and degree.

Gene Ids	Avg. Shortest Path Length	Betweenness Centrality	Closeness Centrality	Degree
SUMO2	1.935613	0.157188	0.516632	421
SUMO1	2.087179	0.075808	0.479115	269
FN1	2.129915	0.060845	0.469502	209
KIAA0101	2.241595	0.027991	0.446111	205
COPS5	2.181197	0.037149	0.458464	194
MDM2	2.158405	0.033852	0.463305	177
YWHAZ	2.132764	0.027914	0.468875	170
CAND1	2.230769	0.02352	0.448276	162
FBXO6	2.308262	0.035402	0.433226	147
RPA1	2.237037	0.019153	0.44702	142
HSP90AB1	2.150997	0.020266	0.464901	139
PCNA	2.194302	0.020286	0.455726	139
CDK1	2.19886	0.018056	0.454781	135
HNRNPA1	2.221083	0.009007	0.450231	133
HSPD1	2.211966	0.01087	0.452087	125
CUL2	2.354416	0.013214	0.424734	123
PRKDC	2.186895	0.015348	0.457269	121
RAN	2.262108	0.008157	0.442065	117
AURKA	2.333903	0.012394	0.428467	113
YWHAB	2.307692	0.017809	0.433333	111
CTNNB1	2.248433	0.024576	0.444754	110
UBR5	2.386325	0.009354	0.419054	108
XPO1	2.316809	0.008067	0.431628	105
PABPC1	2.239316	0.010786	0.446565	102
NPM1	2.215385	0.012282	0.451389	99
HNRNPC	2.247293	0.004146	0.44498	98
CSNK1A1	2.376068	0.008253	0.420863	98
YWHAQ	2.292308	0.008742	0.436242	96
CCT3	2.299715	0.006029	0.434836	95
RANBP2	2.331624	0.011077	0.428886	93

S6 Table. Pathway and molecular functions analysis of the HUB genes in the HCC with HCV-related cirrhosis network. We report for each pathway and molecular function name, number of genes, p-values and list of involved genes.

Pathways	Number of genes	P-Value	Genes
acetylation	29	5.75E-16	HSP90AB1, XPO1, XRCC6, NEDD8, SF3B3, YBX1, POLR2A, SF3B1,
isopeptide bond	12	3.31E-11	EGFR, SUMO2, TUBB, CUL5, IKBKG, UBC, PCNA, TP53, NEDD8, CUL1,
phosphoprotein	35	9.94E-10	HSP90AB1, XPO1, XRCC6, KIAA0101, YBX1, SRC, POLR2A, SF3B1, CUL5,
host-virus interaction	10	5.55E-09	XPO1, CUL5, FYN, DDB1, RPLP0, IKBKG, TP53, HSPD1, YWHAЕ, SRC
Glycyl lysine isopeptide (Lys-Gly) (interchain ubl conjugation	9	6.93E-09	EGFR, TUBB, IKBKG, UBC, PCNA, TP53, CUL1, YBX1, CALM1
	12	2.05E-08	EGFR, SUMO2, TUBB, CUL5, DDB1, IKBKG, UBC, PCNA, TP53, CUL1,
Cytoplasm	23	7.52E-08	HSP90AB1, XPO1, VHL, DDB1, YWHAB, TP53, ILF3, SIRT7, YWHAЕ,
mutagenesis site	16	7.79E-06	EGFR, XPO1, VHL, DDB1, TP53, KIAA0101, NEDD8, SIRT7, YBX1,
methylation	7	1.00E-05	TUBB, TP53, ILF3, PABPC1, NCL, HNRNPU, CALM1
nucleus	22	2.82E-05	XPO1, VHL, DDB1, XRCC6, KIAA0101, TP53, NEDD8, ILF3, SIRT7,
Cell cycle	7	7.16E-05	YWHAB, YWHAQ, PCNA, TP53, YWHAЕ, MYC, CUL1
Interaction with phosphoserine on	3	8.91E-05	YWHAB, YWHAQ, YWHAЕ
Glycyl lysine isopeptide (Gly-Lys) (interchain	3	2.32E-04	SUMO2, UBC, NEDD8
Pathogenic Escherichia coli infection	5	3.13E-04	TUBB, FYN, YWHAQ, TUBA1A, NCL
nucleotide-binding	12	4.82E-04	EGFR, HSP90AB1, IKBKE, TUBB, FYN, XRCC6, RUVBL2, HSPA5,
ubl conjugation pathway	7	5.96E-04	SUMO2, CUL5, VHL, DDB1, UBD, NEDD8, CUL1
hsa04722:Neurotrophin signaling pathway	6	6.95E-04	YWHAB, YWHAQ, TP53, SHC1, YWHAЕ, CALM1
mrna splicing	5	9.11E-04	SF3B1, PABPC1, HNRNPU, SF3B3, YBX1
Telomeres, Telomerase, Cellular Aging, and	4	0.001199	EGFR, XRCC6, TP53, POLR2A
atp-binding	10	0.001331	EGFR, HSP90AB1, IKBKE, FYN, XRCC6, RUVBL2, HSPA5, HSPD1,

ATP	5	0.001428	EGFR, FYN, HSPD1, HNRNPU, SRC
RNA binding	3	0.00154	RPLP0, UBC, NCL
Spliceosome	4	0.001977	SF3B1, PABPC1, HNRNPU, SF3B3
mrna processing	5	0.002034	SF3B1, PABPC1, HNRNPU, SF3B3, YBX1
Oocyte meiosis	5	0.003682	YWHAB, YWHAQ, YWHAЕ, CUL1, CALM1
dna-binding	11	0.004067	RPL6, DDB1, XRCC6, PCNA, TP53, ILF3, NCL, MYC, HNRNPU, YBX1,
tyrosine-specific protein kinase	3	0.004477	EGFR, FYN, SRC
autophosphorylation	3	0.004662	EGFR, FYN, SRC

Functions

Protein binding	3.34E-07	31	HSP90AB1, XPO1, YWHAZ, COPS5, PRKDC, AURKA, CCT3, CTNNB1, CUL2, SUMO2, SUMO1, SMAD2, AURKA, CUL4B
Ubiquitin protein ligase binding	3.34E-07	6	CUL2, SUMO2, SUMO1, SMAD2, AURKA, CUL4B
Enzyme binding	1.42E-05	10	CUL2, SUMO2, SUMO1, YWHAB, MDM2, SMAD2, AURKA, CUL4B, RPA1, PCNA, SMAD2, HSPD1, HNRNPA1, CTNNB1
Structure-specific DNA binding	1.53E-05	6	RPA1, PCNA, SMAD2, HSPD1, HNRNPA1, CTNNB1
Transcription factor binding	2.18E-04	8	YWHAZ, COPS5, RAN, NPM1, YWHAB, PRKDC, SMAD2, CTNNB1
Unfolded protein binding	2.08E-03	4	HSP90AB1, NPM1, HSPD1, CCT3
Single-stranded DNA binding	3.42E-03	3	RPA1, HSPD1, HNRNPA1
I-SMAD binding	3.42E-03	2	SMAD2, CTNNB1
Transcription activator activity	3.42E-03	6	COPS5, RAN, NPM1, CAND1, SMAD2, CTNNB1
R-SMAD binding	3.61E-03	2	SMAD2, CTNNB1
Chromatin binding	5.71E-03	4	RPA1, RAN, SMAD2, CTNNB1
Chromatin binding	5.71E-03	4	RPA1, RAN, SMAD2, CTNNB1

S7 Table. Top 30 degree nodes in the HepG2 network. We report for each gene, the values for average shortest path length, betweenness centrality, closeness centrality and degree.

Genes	Avg. Shortest Path Length	Betweenness Centrality	Closeness Centrality	Degree
AURKA	2.534137	0.101047	0.394612	45
PCNA	2.425703	0.125077	0.412252	39
ACTB	2.305221	0.254464	0.433798	35
AURKB	2.586345	0.070503	0.386646	35
CDC20	2.718876	0.033512	0.367799	27
CSNK2A1	2.60241	0.084551	0.384259	25
UBD	2.598394	0.124572	0.384853	23
ZWINT	2.742972	0.042547	0.364568	21
CCNB1	2.791165	0.017372	0.358273	21
MCM6	2.678715	0.023469	0.373313	20
H2AFX	2.558233	0.059787	0.390895	19
SRC	2.658635	0.064603	0.376133	19
MCM3	2.742972	0.018468	0.364568	19
CHEK1	2.807229	0.020556	0.356223	18
UBE2C	2.819277	0.024567	0.354701	18
MAD2L1	2.923695	0.038116	0.342033	18
CENPA	2.722892	0.031222	0.367257	17
SFN	2.751004	0.063396	0.363504	17
RFC4	2.919679	0.011052	0.342503	17
CCNA2	2.919679	0.006355	0.342503	17
HNRNPA1	2.666667	0.040918	0.375	16
CKAP5	2.855422	0.007451	0.350211	16
BIRC5	2.863454	0.009078	0.349229	16
SERPING1	3.506024	0.028728	0.285223	16
CDC25C	2.835341	0.011002	0.352691	15
HLA-B	2.899598	0.048343	0.344875	15
KIF2C	3.02008	0.001272	0.331117	15
MCM4	2.967871	0.005485	0.336942	14
SPC24	2.987952	0.012456	0.334677	13
INCENP	3.008032	0.004193	0.332443	13

S8 Table. Pathway and molecular functions analysis of the HUB genes in the HepG2 network. We report for each pathway and molecular function name, number of genes, p-values and list of involved genes

Pathways	Number of genes	P- Value	Genes
Cell cycle	11	1.58E-11	CCNB1, MAD2L1, PCNA, CHEK1, CDC20, SFN, MCM3, CDC25C, MCM4, CCNA2, MCM6
DNA replication	5	1.16E-05	RFC4, PCNA, MCM3, MCM4, MCM6
Oocyte meiosis	5	9.34E-04	CCNB1, MAD2L1, CDC20, AURKA, CDC25C
Progesterone-mediated oocyte maturation	4	0.004985	CCNB1, MAD2L1, CDC25C, CCNA2
How Progesterone Initiates the Oocyte Maturation	3	0.007749	CCNB1, CDC25C, SRC
p53 signaling pathway	3	0.031419	CCNB1, CHEK1, SFN
Adherence junction	3	0.039471	ACTB, CSNK2A1, SRC
Functions			
Protein binding	5.52E-07	30	PCNA, SRC, CENPA, AURKB, ACTB, AURKA, CDC20, CCNB1, UBD, CHEK1, SFN, HNRNPA1, RFC4, CSNK2A1, UBE2C, H2AFX, HLA-B, CDC25C, CKAP5, ZWINT, CCNA2, INCENP, MCM3, SERPING1, MCM4, BIRC5, KIF2C, MCM6, SPC24, MAD2L1
ATP binding	4.73E-04	12	RFC4, CSNK2A1, SRC, UBE2C, CHEK1, MCM3, MCM4, KIF2C, MCM6, AURKB, ACTB, AURKA
Nucleotide binding	1.76E-03	13	RFC4, CSNK2A1, SRC, UBE2C, AURKB, ACTB, AURKA, CHEK1, MCM3, MCM4, KIF2C, MCM6, HNRNPA1
Single-stranded DNA binding	1.76E-03	3	MCM4, MCM6, HNRNPA1
Structure-specific DNA binding	1.82E-03	4	PCNA, MCM4, MCM6, HNRNPA1
Protein kinase activity	6.83E-03	6	CCNB1, CSNK2A1, SRC, CHEK1, AURKB, AURKA
Protein complex binding	1.04E-02	4	CCNB1, PCNA, SRC, UBD
Enzyme binding	1.04E-02	6	CDC20, CCNB1, H2AFX, BIRC5, ACTB, AURKA

Phosphotransferase activity, alcohol group as acceptor	1.29E-02	6	CCNB1, CSNK2A1, SRC, CHEK1, AURKB, AURKA
DNA polymerase processivity factor activity	1.29E-02	1	PCNA
DNA helicase activity	1.59E-02	2	MCM4, MCM6
Kinase activity	1.59E-02	6	CCNB1, CSNK2A1, SRC, CHEK1, AURKB, AURKA
DNA insertion or deletion binding	2.07E-02	1	PCNA
Protein kinase C inhibitor activity	2.07E-02	1	SFN
protein kinase binding	2.37E-02	3	CCNB1, ACTB, AURKA
MutLalpha complex binding	2.76E-02	1	PCNA
Cobalt ion binding	2.76E-02	1	BIRC5
Transferase activity, transferring phosphorus-containing groups	2.76E-02	6	CCNB1, CSNK2A1, SRC, CHEK1, AURKB, AURKA
Kinase binding	3.20E-02	3	CCNB1, ACTB, AURKA
Microtubule binding	3.20E-02	2	BIRC5, KIF2C
Mismatch repair complex binding	3.22E-02	1	PCNA

S9 Table. Top 30 degree nodes in the HepG2 1st order network. We report for each gene the values for average shortest path length, betweenness centrality, closeness centrality and degree.

Names	Avg. Shortest Path Length	Betweenness centrality	Closeness centrality	Degree
UBC	1.25276583	0.48018962	0.798234	4915
SUMO2	1.86432084	0.01499912	0.536388	1274
NRF1	1.90027658	0.02017872	0.526239	1100
APP	1.9016595	0.02283228	0.525857	961
CUL3	1.92393977	0.00691475	0.519767	950
ELAVL1	1.91994468	0.01468349	0.520848	927
SUMO1	1.93054702	0.00777348	0.517988	859
TP53	1.93039336	0.00781566	0.518029	829
HSP90AA1	1.92178857	0.00745078	0.520349	823
FN1	1.93484942	0.01164406	0.516836	798
CDK2	1.95282729	0.00402974	0.512078	741
EEF1A1	1.95574677	0.00374308	0.511314	733
ESR1	1.95190535	0.00468021	0.51232	727
YWHAZ	1.94698832	0.00468332	0.513614	721
KIAA0101	1.98217578	0.00269152	0.504496	692
CUL1	1.9738783	0.00289177	0.506617	687
MDM2	1.96511985	0.00356405	0.508875	658
GRB2	1.96097111	0.00748759	0.509951	647
COPS5	1.97449293	0.00354007	0.506459	646
CSNK2A1	1.96588814	0.00675211	0.508676	645
UBD	1.99861709	0.00961494	0.500346	644

HSPA5	1.95267363	0.00282914	0.512118	642
HSPA8	1.95789797	0.00293833	0.510752	617
NEDD8	1.98417333	0.00347169	0.503988	614
SRC	1.97080516	0.00820955	0.507407	606
ACTB	1.96204671	0.00587068	0.509672	594
CAND1	2.01275353	0.00226339	0.496832	587
MYC	1.98862938	0.00362258	0.502859	580
TUBB	1.96757837	0.0019447	0.508239	574
SIRT7	2.08113092	0.00212305	0.480508	571

S10 Table. The 84 interacting hub genes from the Venn diagram of Fig 6 with symbols and acronyms.

Gene Symbols	Gene Name	Gene Symbols	Gene Name
ACTB	actin, beta	ITGA4	integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)
ATP5B	ATP Synthase, H ⁺ Transporting, Mitochondrial F1 Complex, Beta Polypeptide	JUN	Jun Proto-Oncogene
AURKA	aurora kinase A	KIAA0101	PCNA- associated factor of 15KDa (PAF)
AURKB	aurora kinase B	KIF2C	kinesin family member 2C
BIRC5	baculoviral IAP repeat-containing 5	LCK	lymphocyte-specific protein tyrosine kinase
CAND1	cullin-associated and neddylation-dissociated 1	MAD2L1	MAD2 mitotic arrest deficient-like 1 (yeast)
CCNA2	cyclin A2	MCM3	minichromosome maintenance complex component 3
CCNB1	cyclin B1	MCM4	minichromosome maintenance complex component 4
CCT3	chaperonin containing TCP1, subunit 3 (gamma)	MCM6	minichromosome maintenance complex component 6
CDC20	cell division cycle 20 homolog (S. cerevisiae)	MDM2	Mdm2 p53 binding protein homolog (mouse)
CDC25C	cell division cycle 25 homolog C (S. pombe)	MYC	v-MYC avian myelocytomatosis viral oncogene homolog (Transcription Factor P64)
CDK1	cell division cycle 2, G1 to S and G2 to M	NPM1	nucleophosmin 1 (nucleolar phosphoprotein B23, numatrin)
CENPA	centromere protein A	PABPC1	poly(A) binding protein, cytoplasmic 1
CHEK1	checkpoint kinase 1	PCNA	proliferating cell nuclear antigen

CKAP5	cytoskeleton associated protein 5	POLR2E	polymerase (RNA) II (DNA directed) polypeptide E, 25kDa
COPS5	COP9 constitutive photomorphogenic homolog subunit 5	POLR2I	polymerase (RNA) II (DNA directed) polypeptide I
CSNK1A1	casein kinase 1, alpha 1	PRKDC	protein kinase, DNA-activated, catalytic polypeptide
CSNK2A1	casein kinase 2, alpha 1 polypeptide pseudogene; casein kinase 2, alpha 1 polypeptide	RAC1	ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)
CTNNB1	catenin (cadherin-associated protein), beta 1, 88kDa	RAN	RAN, member RAS oncogene family
CUL2	cullin-2	RANBP2	RAN binding protein 2
CUL3	cullin-3	RFC4	replication factor C (activator 1) 4, 37kDa
CUL5	cullin-5	RPA1	Replication protein A1
DDX3X	DEAD (Asp-Glu-Ala-Asp) box helicase 3, X-linked	RPA2	Replication protein A2
DNAJA1	DnaJ (Hsp40) homolog, subfamily A, member 1	RPA3	Replication protein A3
EED	embryonic ectoderm development (WD Protein Associating With Integrin Cytoplasmic Tails 1)	SERPING1	serpin peptidase inhibitor, clade G (C1 inhibitor), member 1
EEF1A1	eukaryotic translation elongation factor 1 alpha 1	SFN	Stratifin
EGFR	Epidermal growth factor receptor	SMAD2	SMAD family member 2 (Mothers Against DPP Homolog 2 (Drosophila))
FBXO6	F-box protein 6	SPC24	Spindle Pole Body Component 24
FN1	fibronectin 1	SRC	v-src sarcoma (Schmidt-Ruppin A-2) viral oncogene homolog (avian)

FYN	Oncogene Related To SRC, FGR, YES(OKT3-Induced Calcium Influx Regulator)	SUMO1	small ubiquitin-like modifier 1
GAPDH	glyceraldehyde-3-phosphate dehydrogenase	SUMO2	small ubiquitin-like modifier 2
H2AFX	H2A histone family, member X	TUBA1A	tubulin, alpha 1a
HLA-B	major histocompatibility complex, class I, C; major histocompatibility complex, class I, B	UBD	Ubiquitin D
HNRNPA1	heterogeneous nuclear ribonucleoprotein A1-like 3	UBE2C	ubiquitin-conjugating enzyme E2C
HNRNPC	heterogeneous nuclear ribonucleoprotein C (C1/C2)	UBR5	ubiquitin protein ligase E3 component n-recognin 5
HNRNPM	heterogeneous nuclear ribonucleoprotein M	VCAM1	vascular cell adhesion molecule 1
HSP90AB1	heat shock protein 90kDa alpha (cytosolic), class B member 1	VIM	vimentin (Epididymis Luminal Protein)
HSPB1	heat shock 27kDa protein 1	XPO1	exportin 1 (CRM1 homolog, yeast)
HSPD1	heat shock 60kDa protein 1 (chaperonin) pseudogene 5; heat shock 60kDa protein 1 (chaperonin) pseudogene 6; heat shock 60kDa protein 1 (chaperonin) pseudogene 1; heat shock 60kDa protein 1 (chaperonin) pseudogene 4; heat shock 60kDa protein 1 (chaperonin)	YWHAB	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, beta polypeptide
ICT1	immature colon carcinoma transcript 1	YWHAE	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon
INCENP	inner centromere protein antigens 135/155kDa	YWHAQ	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, theta polypeptide
ZWINT	ZW10 interactor	YWHAZ	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta polypeptide

S11 Table. Recurrence table of the 84 interacting hub nodes from the Venn diagram of figure 1 for HCV, HCV related cirrhosis, HCC with HCV related cirrhosis and HepG2 networks.

Names	Number of genes	Genes
HCC with HCV related Cirrhosis, HCV, HCV Cirrhosis, HepG2	1	PCNA
HCC with HCV related Cirrhosis, HCV, HCV Cirrhosis	10	COPS5, CAND1, YWHAQ, FBXO6, RPA1, RAN, FN1, CUL2, YWHAB, YWHAZ
HCC with HCV related Cirrhosis, HepG2	2	HNRNPA1, AURKA
HCC with HCV related Cirrhosis, HCV Cirrhosis	4	HSP90AB1, XPO1, MDM2, CSNK1A1
HCC with HCV related Cirrhosis, HCV	1	KIAA0101
HCV related Cirrhosis, HepG2	1	ACTB
HCV, HCV related Cirrhosis	5	VCAM1, GAPDH, FYN, YWHAE, ITGA4
HCC with HCV related Cirrhosis	12	HSPD1, CDK1, CCT3, UBR5, PABPC1, SUMO2, SUMO1, NPM1, CTNNB1, HNRNPC, RANBP2, PRKDC
HepG2	26	CENPA, AURKB, CSNK2A1, MCM3, MCM6, CHEK1, SFN, SERPING1, MCM4, CDC20, KIF2C, BIRC5, ZWINT, CCNB1, CKAP5, SPC24, UBD, INCENP, UBE2C, SRC, MAD2L1, H2AFX, HLA-B, RFC4, CCNA2, CDC25C
HCV related cirrhosis	9	HSPB1, RAC1, LCK, SMAD2, MYC, JUN, TUBA1A, VIM, DDX3X
HCV	13	ICT1, RPA2, CUL3, CUL5, EED, DNAJA1, HNRNPM, ATP5B, POLR2I, EGFR, POLR2E, EEF1A1, RPA3

S12 Table. Functional and Molecular properties of the 26 HUB nodes specific for HepG2 as shown in the figure 6. **IDR** = Intrinsically Disordered Region(s), where + = amount of intrinsically disordered region(s) < 15% but not zero; ++ = 15% > IDR < 50%; +++ = IDR > 50%. **INT** = Number of interactions with molecular partners (from BioGrid). **SEQ** = Sequence length (number of amino acids).

Gene name in Gene Cards	Protein code in UniProtKB/Swiss-Prot	Protein name	Biological Function	IDR	INT	SEQ
ZWINT	095229-ZWINT human	Zw10- interactor	Part of kinetochore complex at pro-metaphase involved in cell division control at chromosome level.	+	55	277
CCNB1	P14635-human	G2/mitotic-specific-cyclin B1	Histone kinase activity and control of cell cycle at G2/M (mitosis) transition in cytoplasm (cytoskeleton) and nucleus.	++	89	433
CKAP5	Q14008 human	Cytoskeleton associated protein 5	Control of mitotic nuclear division by establishing and maintaining of microtubule cytoskeleton polarity.	+++	39	2032
SPC24	Q8NBT2-SPC24 human	Kinetochore protein Spc24	Kinetochore complex component for chromosome segregation.	+++	31	197
COPS5	Q92905-CSN5 human	COP9 signalosome complex subunit 5	Part of COP9 nuclear signalosome complex involved in various cellular and developmental processes	+	792	334

CAND1	Q86VP6 human	Cullin-associated NEDD8-dissociated protein 1	Factor of (SKP1-CUL1-F-box protein) E3 ubiquitine ligase complex in cell differentiation control of RNA polymerase II by ubiquitination in nucleus and cytoplasm.	+	682	1229
YWHAQ	P63104-1433Z human	14-3-3 protein theta	Regulation of a large spectrum of general and specialized signaling in metabolism, protein trafficking, signal transduction, apoptosis, cell cycle regulation in zeta/delta complex	+	393	245
FBXO6	Q9NRD1-FBX6 human	F-box only protein 6	Part of FBOX proteins (protein 6) associated degradation for misfolded luminal proteins in ER	+	621	293
SRC	P12931-SRC human	Proto-oncogene tyrosine-protein kinase Src	Non receptor protein kinase controls gene transcription, immune response, cell adhesion, cell cycle progression, apoptosis, migration and transformation.	++	272	536
MAD2L1	Q13257-MD2L1 human	Mitotic spindle assembly check point protein MAD2A	Component of the spindle-assembly check point that controls the proper alignment of chromosomes in anaphase.	+	48	205

H2AFX	P16104-H2AX human	Histone H2AX	Involved in nucleosome complex wrapping and compacting DNA into chromatin and limiting DNA reading, but also in DNA repair, DNA replication and chromosomal stability at level of G1 and S-phase.	+	209	143
HLA-B	P01889-1B07 human	HLA class I histocompatibility antigen, B-7 alpha chain	Involved in the presentation of foreign antigens to the immune system	++	63	362
UBD	O15205-UBD human	Ubiquitin D	Ubiquitin like protein leading to degradation by 26S proteasome. Among other functions mediates mitotic non-disjunction and chromosome instability by abbreviating mitotic phase and impairing kinetochore localization.	+++	667	165
INCENP	Q9NQ57-INCENP human	Inner centromere protein	Component of the chromosomal passenger complex (CPC), a key regulator of mitosis at centromere in ensuring correct chromosome alignment and segregation required for chromatin-induced microtubule	+++	17	918

			stabilization and spindle assembly.			
UBE2C	O00762-UBEC2C human	Ubiquitin-conjugating enzyme E2C.	Accepts ubiquitin from E1 complex and catalyzes its covalent attachment to proteins.	++	59	179
RFC4	P35249-RFC4 human	Replication factor C subunit 4	Involved into elongation of primed DNA templates by DNA polymerase delta and epsilon in a complex requiring PCNA, RFC2, RFC3, RFC4 and RFC5	+	68	363
CCNA2	P20248-CCNA2 human	Cyclin A2	Control of the gene cycle at G1/S (start) and G2/M (mitosis) transitions in complex with CDK1 and CDK2 and is able to interact with human cytomegalovirus protein UL32	++	89	432
CDC25C	P30307-MPIP3 human	M-phase inducer phosphatase 3	Key role in the regulation of cell division also suppressing p53 induced growth arrest.	+++	36	473
HSPB1	P04792-HSPB1 human	Heat shock protein beta-1	Induced by stress and environmental changes. It is involved in stress resistance and actin organization also interacting with microtubules.	+++	114	205

RAC1	P63000-RCA1 human	Ras-related C3 botulinum toxin substrate 1	GTPase of ras superfamily of GTP-binding protein that controls cell growth, cytoskeletal reorganization, activation of protein kinases associated to plasma membrane.	+	134	192
LCK	P06239-LCK human	Tyrosine-protein kinase LCK.	Non-receptor tyr-prot kinase with a role in the selection and maturation of developing T-cells in thymus and in function of mature T-cells also associated to CD4 and CD8 surface receptors	++	85	509
SMAD2	Q15796-SMAD2 human	Mothers against decapentaplegic homolog 2	It is a signal transducer (receptor regulated SMAD) and transcriptional modulator that mediates multiple signaling pathways also mediate the signal of transforming growth factor (TGF)beta and regulates multiple cellular processes such as proliferation, apoptosis, and differentiation binding TRE in the promoter region of many genes regulated by TGF-beta.	+++	259	467

S13 Table. List of up-expressed genes found in HCC with HCV-related cirrhosis and HepG2 (A) and of genes involved in circadian rhythm (B) that can be targets for miR-372.

A)

HCC with HCV-related cirrhosis	HepG2
AAK1	ABR
ADAM9	ADORA2B
AEBP2	ASF1B
AGGF1	BLVRA
AHR	C1orf135
AKAP11	C9orf58
ANGEL2	CDC25A
ANKRD13C	CDCA7
ANKRD29	CDCA8
ANKRD44	CDT1
ANKRD50	CLSTN1
ANKRD9	DCDC2
APBB2	DPYSL2
ARHGAP12	E2F2
ARHGAP18	FAM57A
ARID4B	FANCD2
ASF1A	FBLN1
ASH1L	FOXRED2
ATAD2	GPR44
ATG12	HEPACAM
ATP11A	ITGA2
ATP6V1D	KIF11
ATP8B1	KIF23
ATXN1	KIF3C
B3GNT5	KPNA2
BAMBI	M6PRBP1
BCAP29	MCM10
BCL10	MCM3
BCL2L11	MCM4
BCLAF1	MCM6
BLVRA	NBL1
BLZF1	NCAPD2
BMPR1A	OTX1

BPNT1	PAQR4
BRWD1	PBK
BTN3A3	PFN2
BTN3A3	PHYHIPL
C10orf118	PLAGL2
C15orf40	PLEKHB2
C1orf63	SFT2D1
C1QTNF3	SLC2A3
C5orf28	SLC2A6
CALD1	TNFRSF21
CAPRIN1	VAV3
CASP8	
CCL5	
CCNG2	
CCNT2	
CD109	
CD44	
CD47	
CDC23	
CDKN2B	
CENPL	
CEP57	
CEP68	
CFLAR	
CHD9	
CHM	
CHMP4C	
CLCC1	
CLINT1	
CLIP4	
CLOCK	
CNOT6	
COG5	
COL4A2	
COMMD2	
COPA	
CREB1	
CREB3L2	
CRIM1	
CRIP1	

CYB5B
DBF4
DCDC2
DDHD1
DDX18
DHX40
DIP2A
DIP2B
DMTF1
DNAJA2
DNM1L
DPY30
DPY30
DYRK2
E2F3
ECT2
EEA1
EGLN1
EIF2AK4
ELK3
ENAH
ERAP1
ERAP2
ERBB2IP
FAM102B
FAM134A
FAM73A
FANCD2
FBXO11
FBXO31
FBXO45
FBXO6
FCF1
FCHO2
FNBP1
FPGT
FZD6
GATAD1
GCLM
GDAP1

GK5
GMFB
GNPTAB
GNS
GOLGA8A
GORASP2
GPLD1
GTPBP10
GTPBP4
HEG1
HERPUD2
HIF1A
HN1
HOOK3
HOXA3
HP1BP3
IFIT5
INPP5F
INTS6
INTS7
IPO9
IRAK1
IRF9
ITGA2
ITPR2
JAZF1
JMY
KBTBD6
KCTD18
KCTD20
KIF11
KLF9
KLHL12
KLHL20
KLHL24
KLHL28
KLHL8
KPNA2
KPNA3
LAMA3

LAMC1
LAMP2
LAMP3
LARS
LEF1
LPGAT1
LYRM4
LYSMD3
LYST
MAFF
MAP3K1
MAP3K2
MAPK1IP1L
MAPK9
MASTL
MBD2
MBNL3
MCM3
MCM4
MCM6
MED17
MED23
MGAT4A
MGEA5
MIB1
MIER3
MKLN1
MKRN1
MPP7
MRS2
MS4A7
MTMR12
MYO5A
NFATC2IP
NFYB
NIN
NMT2
NR2C2
NRCAM
NRIP1

NSL1
NUFIP2
NUP35
NUP43
NUPL1
OLA1
OSBPL8
OSTM1
PAN3
PBK
PCDH17
PCGF5
PHC3
PHF20
PHF20L1
PHF6
PHYHIPL
PIK3R3
PLXNA1
POLE3
POLK
PTGER4
PTGFRN
PTK2
PTPLAD1
PURB
QKI
RAB10
RAB11A
RAB11FIP1
RAB23
RAB30
RAB7L1
RAB8B
RAD23B
RAP2C
RB1
RB1CC1
RBBP5
RBBP7

RBM12B
RIT1
RNASEL
RNF141
RNF38
RNF6
ROCK2
RPL28
RPS6KA3
RRAGD
RRP15
RSAD2
RSBN1
RSF1
RSL1D1
RYBP
SAC3D1
SACS
SAMD9L
SCRN3
SGK3
SGTB
SHANK2
SHCBP1
SLC30A10
SLC35F5
SLC7A11
SLK
SMAD2
SMAD5
SMNDC1
SNRPE
SNTB2
SOCS5
SOX4
SPATS2
SPOPL
SQSTM1
SRFBP1
SRPK1

STC1
STK4
SUZ12
SUZ12
SWAP70
SYNJ2
TACC1
TANC1
TBX3
TET3
THEM4
TIMM17A
TIMM50
TMED5
TMEM64
TMF1
TMPO
TNFRSF21
TNKS2
TNRC6A
TOPORS
TRIM33
TRPS1
TSNAX
TTC33
TTL
UBE2B
UBE2Q1
UBE2Q2
UBE2W
UBR3
UBR5
UEVLD
UHRF1BP1
UNK
UNKL
UPF3A
UQCRC1
USP24
USP3

USP42
UXS1
VASH2
VPS13C
VPS26A
VPS35
WAC
WDR26
WEE1
WNK3
XPR1
YOD1
YTHDF3
YWHAZ
ZBED3
ZBTB11
ZBTB33
ZBTB41
ZDHHC17
ZFP36L2
ZFP90
ZKSCAN1
ZMAT3
ZNF12
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B)

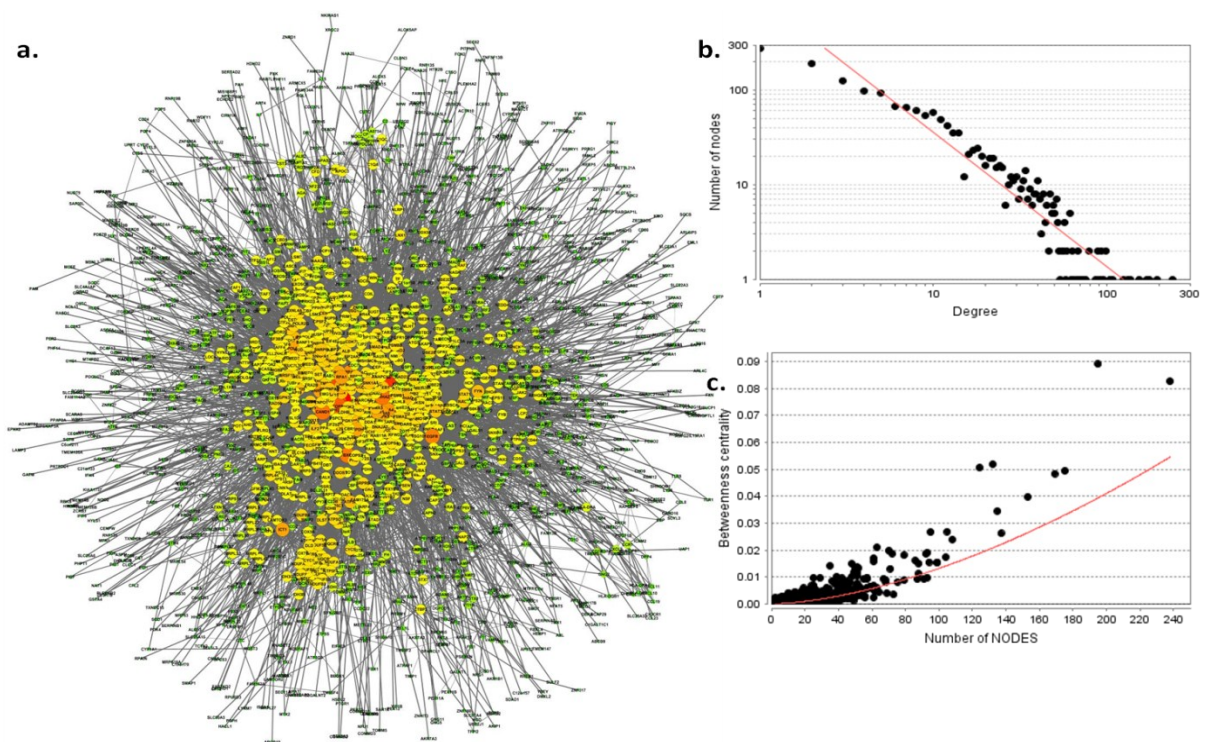
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FBXL3
NPAS2
PER2
SERPINE1

S14 Table. Genes found functionally related to HULC by GeneDecks Partner Hunter analysis. In red the genes in common with the HepG2 1st order network (MDM2, MYC, and CDK1).

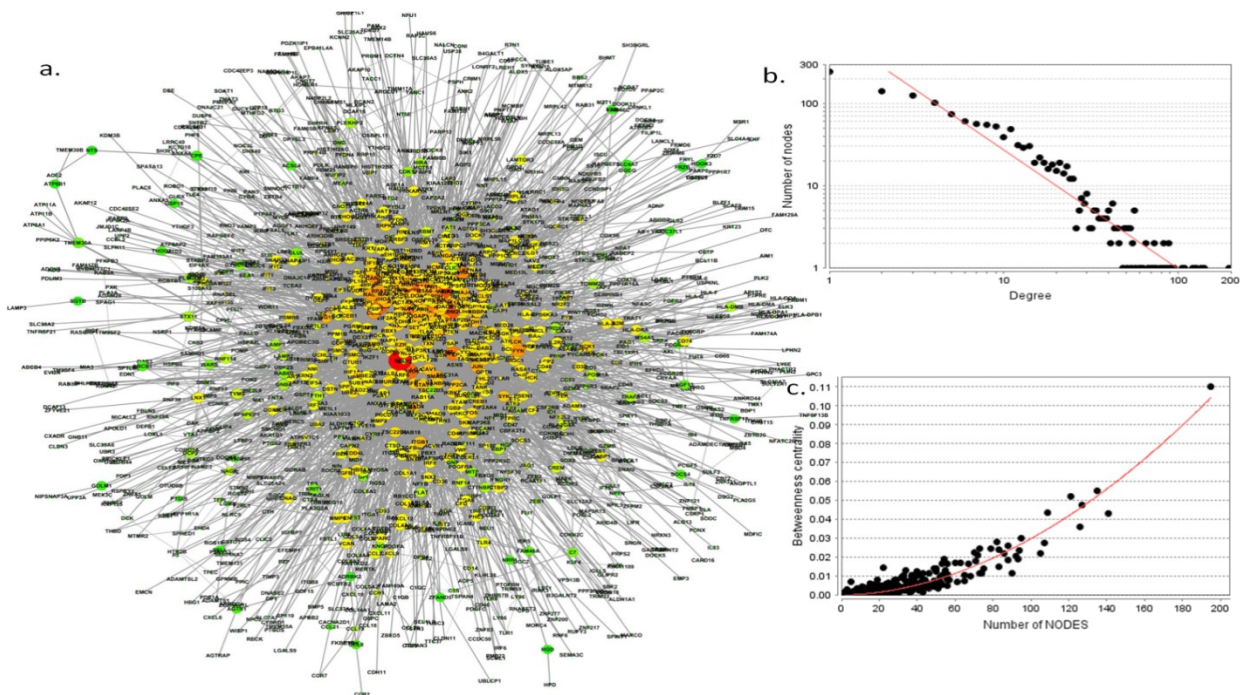
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6	ERBB3	1
7	HLA-A	1
8	GSTM1	1
9	FGL1	1
10	KRT8	1
11	SEPP1	1
12	GSTP1	1
13	RHOA	1
14	GDF15	1
15	GHRL	1
16	ITGA5	1
17	ASGR2	1
18	SLC2A2	1
19	HLF	1
20	PHF20	1
21	RHOC	1
22	RHOD	1
23	FGF2	1
24	HNF1B	1
25	CEACAM6	1
26	GSTT1	1
27	ASPH	1
28	APOD	1
29	SPINT1	1
30	FGF3	1
31	XBP1	1
32	FGFR1	1
33	MDK	1
34	FGFR4	1
35	KRT14	1
36	ITGA1	1
37	CAPN2	1
38	YBX3	1

39 MDM2	1
40 KLF6	1
41 E2F1	1
42 MTUS1	1
43 SLC25A47	1
44 F9	1
45 FGF1	1
46 CEACAM1	1
47 GSTA2	1
48 BRCA2	1
49 IL32	1
50 SLC17A5	1
51 KRAS	1
52 MKI67	1
53 CCR1	1
54 FGFR2	1
55 SPP1	1
56 PPARA	1
57 SCARB1	1
58 ARG1	1
59 HCCAT5	1
60 MYC	1
61 KRT1	1
62 PPIG	1
63 PKM	1
64 SP1	1
65 IL1RAPL2	1
66 BIRC5	1
67 ILK	1
68 THRB	1
69 AHR	1
70 IL15	1
71 PINX1	1
72 BID	1
73 CEACAM7	1
74 CCL21	1
75 AHSG	1
76 FAS	1
77 H19	1
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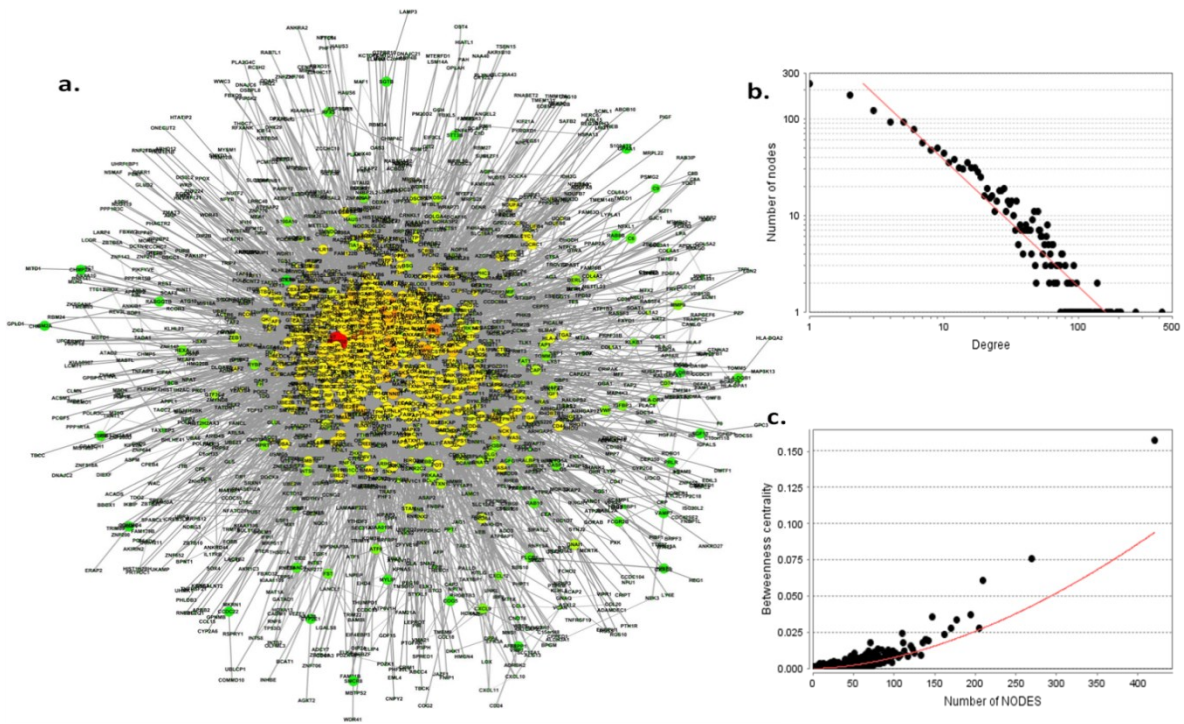
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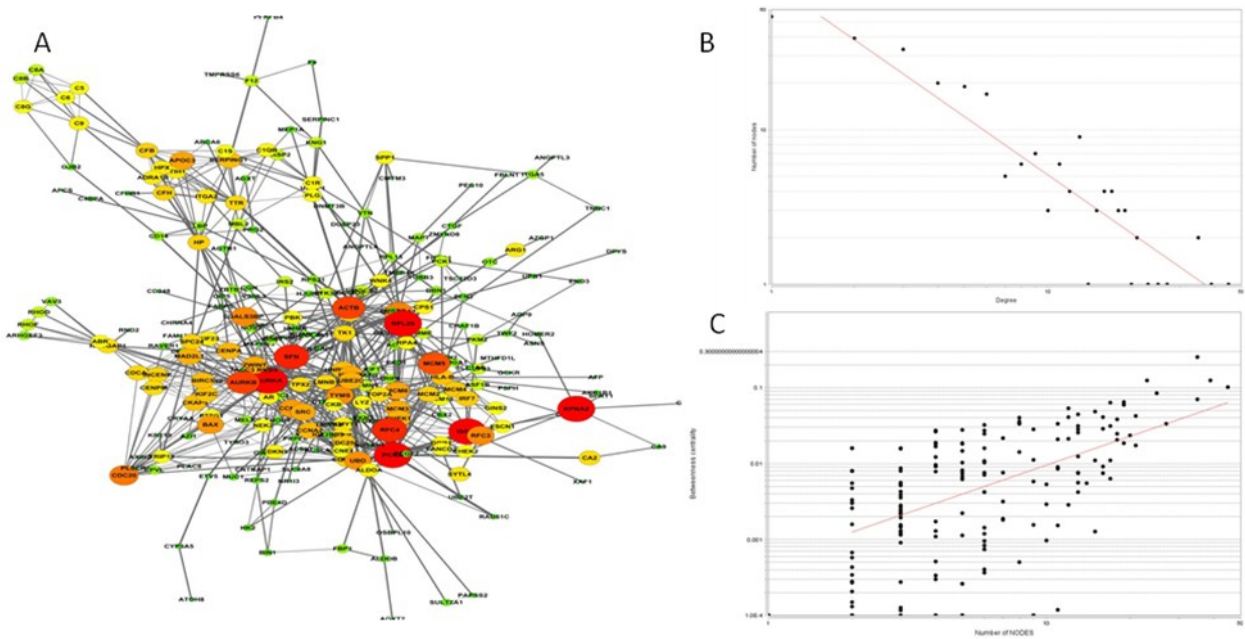
S1 Fig. a) HCV network. Red color shows the high degree of a node while yellow and green an intermediate and low degree, respectively. b) Degree distribution and c) Betweenness distribution.



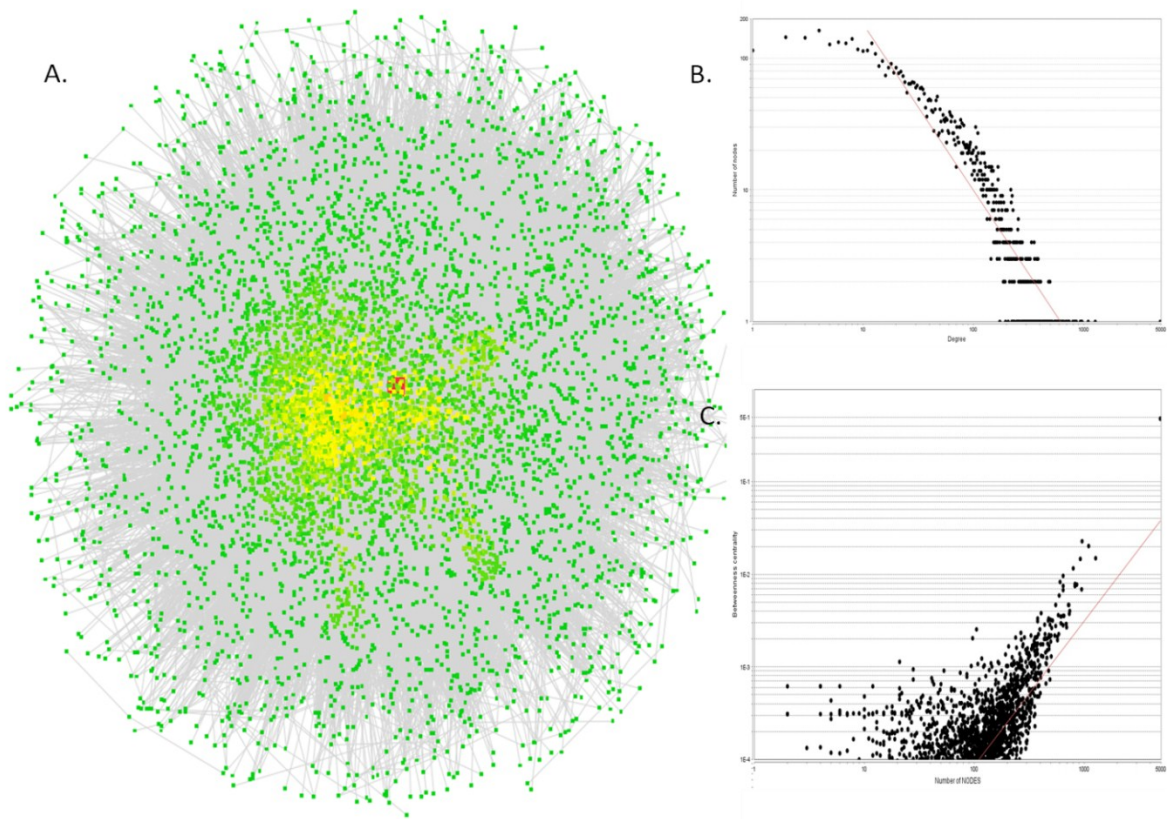
S2 Fig. a) HCV-related cirrhosis network. Red color shows the high degree of a node while yellow and green an intermediate and low degree, respectively. b) Degree distribution and c) Betweenness distribution.



S3 Fig. a) HCC with HCV-related cirrhosis network. Red color shows the high degree of a node while yellow and green an intermediate and low degree, respectively. b) Degree distribution and c) Betweenness distribution.



S4 Fig. A) HepG2 network. The red color shows high degree nodes while yellow and green colors an intermediate and low degree, respectively. B) Degree distribution and C) Betweenness distribution.



S5 Fig. A) HepG2 first order network. Red color shows the high degree nodes while yellow and green intermediate and low degree, respectively. B) Degree distribution and C) Betweenness distribution.