

Supplemental Table S1. Proteins Associated with Autophagosomes**Proteins that are associated with autophagosomes in only GLR cells**

| GENE NAME | Protein | FUNCTION |
|-----------|---|--------------------------------|
| STX7* | Syntaxin 7 | Membrane trafficking/fusion |
| STX12 | Syntaxin 12 | Membrane trafficking |
| NSF | N-ethylmaleimide-sensitive factor | Membrane trafficking |
| RAB5B* | Ras-related protein Rab-5B | Membrane trafficking |
| ANXA2* | Annexin A2 | Membrane trafficking |
| CAV1* | Caveolin 1 | Membrane trafficking/signaling |
| CAV2* | Caveolin 2 | Membrane trafficking/signaling |
| GNB2 | G Protein Subunit Beta 2 | Signal transduction |
| RGSL2 | Regulator of G-protein signaling like 2 | Signal transduction |
| IGHG1 | Ig gamma-1 | Innate immunity |
| ATRNL1 | Attractin-like protein 1 | Innate immunity |
| PIGN | phosphatidylinositol glycan, class N | Glycolipid |
| ZNF662 | ZNF662 protein | Transcriptional regulation |
| GNS | N-acetylglucosamine-6-sulfatase | Lysosomal enzyme |
| ARG1 | Arginase-1 | Urea cycle |
| NS3 (1b) | HCV non-structural protein 3 | HCV nonstructural protein |
| NS4B (1b) | HCV non-structural protein 4B | HCV nonstructural protein |
| NS5A (1b) | HCV non-structural protein 5A | HCV nonstructural protein |
| NS5B (1b) | HCV non-structural protein 5B | HCV nonstructural protein |

Proteins that are associated with autophagosomes in both GLR and Huh7-GFP-LC3 cells

| GENE | NAME | FUNCTION |
|---------|--|----------------------|
| ATL3 | Atlastin-3 | Membrane fusion |
| RAB5A* | Ras-related protein Rab-5A | Membrane trafficking |
| RAB1B* | Ras-related protein Rab-1B | Membrane trafficking |
| SCARB2* | Scavenger receptor class B member 2 | Membrane trafficking |
| ERC1 | Rab6-interacting protein 1 | Membrane trafficking |
| LRP4 | Low density lipoprotein receptor-related protein 4 | Membrane trafficking |
| LMAN2 | Vesicular integral-membrane protein VIP36 | Membrane trafficking |
| MAN1A1 | Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA | Membrane trafficking |
| TFRC* | Transferrin receptor | Membrane trafficking |
| YIPF5 | Protein YIPF5 | Membrane trafficking |
| SEC23B | Protein transport protein Sec23B | Membrane trafficking |

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| SCAMP3 | Secretory carrier-associated membrane protein 3 | Membrane trafficking |
| PLIN3* | Perilipin-3 | Membrane trafficking |
| ERGIC1 | Endoplasmic reticulum-Golgi intermediate compartment protein 1 | Membrane trafficking |
| SLC3A2 | 4F2 cell-surface antigen heavy chain | Transport |
| M6PR | Cation-dependent mannose-6-phosphate receptor | Transport |
| TM9SF4 | Transmembrane 9 superfamily protein member 4 | Transport/cell adhesion |
| ATP1A1 | ATPase Na+/K+ Transporting Subunit Alpha 1 | Ion channel transport |
| ATP5A1 | ATP synthase subunit alpha, mitochondrial | Ion channel transport |
| ATP5B | ATP synthase subunit beta | Ion channel transport |
| LAMP1* | Lysosome-associated membrane glycoprotein 1 | Autophagic cell death/apoptosis/transport |
| POR | NADPH--cytochrome P450 reductase | Electron transfer |
| CANX* | Calnexin | Receptor-mediated endocytosis/chaperone |
| CPD | Carboxypeptidase D | Protein processing |
| CTSD | Cathepsin D | Protein degradation |
| N4BP1 | NEED4-binding protein 1 | Ubiquitination |
| ITPR3 | ITPR3 protein | Secretion of intracellular calcium |
| ATP2A2 | Sarcoplasmic/endoplasmic reticulum calcium ATPase 2 | Secretion/transport |
| SPTBN1 | Spectrin, beta, non-erythrocytic 1 | Secretion |
| ERP44 | Endoplasmic reticulum resident protein 44 | Stress response |
| P4HB | Protein disulfide-isomerase | ER stress/apoptotic signaling |
| SCARB1* | Scavenger receptor class B member 1 | Signal transduction |
| CALR | Calreticulin | Chaperon |
| PTPRK | Receptor-type tyrosine-protein phosphatase kappa | Signal transduction |
| OGDHL | Oxoglutarate dehydrogenase-like | Signal transduction |
| WUGSC:H_LUCA16.1 | GTP-binding regulatory protein Gi alpha-2 chain | Signal transduction |
| NCSTN | Nicastrin | Signal transduction |
| DUSP14 | Dual specificity protein phosphatase 14 | Signal transduction |
| NOMO3 | Nodal modulator 3 | Signal transduction |
| ANPEP | Aminopeptidase N | Signal transduction |

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|--------|--|---|
| GNB1 | Guanine nucleotide binding protein (G protein), beta polypeptide 1 | Signal transduction |
| BCAM | Basal cell adhesion molecule | Cell adhesion/signal transduction |
| ICAM1 | Intercellular adhesion molecule 1 | Cell adhesion/signal transduction |
| ITGA2 | Integrin alpha-2 | Cell adhesion/signal transduction |
| DSC1 | Desmocollin 1 | Cell adhesion |
| SENP2 | Sentrin-specific protease 2 | mRNA transport/protein transport/signaling |
| PPIB | Peptidyl-prolyl cis-trans isomerase B | Protein folding |
| PDIA3 | Protein disulfide-isomerase A3 | Protein folding/apoptosis/signal transduction |
| PDIA4 | Protein disulfide-isomerase A4 | Protein folding/secretion/ER stress |
| TRA1 | Tumor rejection antigen (Gp96) 1 | Protein folding/stress response |
| NR5A2 | Nuclear receptor subfamily 5 group A member 2 | Transcriptional regulation |
| ZNF648 | Zinc finger protein 648 | Transcriptional regulation |
| NUP188 | Nucleoporin NUP188 | Nuclear pore complex |
| ZNF563 | Zinc finger protein 563 | Transcriptional regulation |
| KDR | Vascular endothelial growth factor receptor 2 | Angiogenesis/cell proliferation/apoptosis |
| HKR3 | HKR3 protein | Metal ion binding |
| GANAB | Neutral alpha-glucosidase AB | N-glycan metabolism |
| LMNA | Lamin A/C | DNA transcription/repair |

Proteins that are associated with autophagosomes in only Huh7-GFP-LC3 cells

| GENE | NAME | FUNCTION |
|----------|---|---------------------------|
| HSPD1 | Mitochondrial heat shock 60kD protein 1 variant 1 | Protein folding |
| PDIA6 | Protein disulfide-isomerase A6 | Protein folding/apoptosis |
| CCT6A | T-complex protein 1 subunit zeta | Protein folding |
| TOR1B | Torsin-1B | Protein folding |
| RPN1 | Ribophorin I | Glycosylation |
| RPN2 | Ribophorin 2 | Glycosylation |
| PCYOX1 | Prenylcysteine oxidase 1 | Protein catabolic process |
| SURF4 | Surfeit 4 | Membrane trafficking |
| SLC2A1 | Solute carrier family 2, facilitated glucose transporter member 1 | Transport |
| SLC25A13 | Calcium-binding mitochondrial carrier protein Aralar2 | Transport |
| VDAC2 | Voltage-dependent anion-selective channel protein 2 | Transport |
| ATP1B3 | Sodium/potassium-transporting ATPase subunit beta-3 | Ion transport/transport |
| ITGB1 | Integrin beta | Cell adhesion |

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|-----------|--|------------------------------------|
| RALA | Ras-related protein Ral-A | Exocytosis/cell cycle |
| PON2 | Serum paraoxonase/arylesterase 2 | Oxidative stress response |
| HSP90AA1 | Heat shock protein HSP 90-beta | Stress response |
| EGFR | Epidermal growth factor receptor | Signal transduction |
| YWHAB | Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, beta | Signal transduction |
| CAT | Catalase | Signal transduction |
| RAP1B | Ras-related protein Rap-1b | Signal transduction |
| COPS2 | COP9 signalosome complex subunit 2 | Ubiquitination/signal transduction |
| UBC | Polyubiquitin-C | Ubiquitination/signal transduction |
| BSG | Basign | Immunity |
| ALCAM | CD166 | Immunity |
| ANXA1 | Annexin A1 | Immunity |
| HLA-DRB1 | MHC class II antigen | Immunity |
| S100A9 | S100 calcium binding protein A9 | Immunity |
| LYZ | Lysozyme C | Immunity |
| POLK | Polymerase kappa isoform 1 | DNA repair |
| HIST1H4A | Histone H4 | Transcription regulation |
| HIST1H2BC | Histone H2B | Transcription regulation |
| H2AFY | Histone H2A | Transcription regulation |
| HIST1H3A | Histone H3 | Transcription regulation |
| ZNF276 | Zinc finger protein 276 | Transcription regulation |
| SCNM1 | Sodium channel modifier 1 | mRNA processing |
| PCF11 | Pre-mRNA cleavage complex 2 protein Pcf11 | mRNA processing |
| PES1 | Pescadillo homolog 1 | rRNA processing |
| NCEH1 | Neutral cholesterol ester hydrolase 1 | Lipid metabolism |
| FDFT1 | Squalene synthetase | Cholesterol metabolism |
| PRKCSH | Glucosidase 2 subunit beta | N-glycan metabolism |
| SACM1L | Phosphatidylinositide phosphatase SAC1 | Hydrolase |
| IFT80 | Intraflagellar transport 80 homolog | Motile and sensory cilia |
| TMEM | transmembrane protein 2 | Development |
| C8orf73 | Maestro heat-like repeat-containing protein family member 6 | Unknown |
| ILVBL | Acetylactate synthase-like protein | Unknown |

Asterisks (*) denote proteins that had previously been reported to be important for HCV replication. The proteins and their references are: STX7 (1), RAB5B (2, 3), ANXA2 (4, 5), CAV1 (6),

CAV2 (4, 7), RAB1B (8), RAB5A (9, 10), SCARB2 (11), TFRC (12), PLIN3 (13), LAMP1 (14, 15), CANX (16), and SCARB1 (17, 18).

References

1. Mannova P, Fang R, Wang H, Deng B, McIntosh MW, Hanash SM, Beretta L. 2006. Modification of host lipid raft proteome upon hepatitis C virus replication. *Mol Cell Proteomics* 5:2319-25.
2. Stone M, Jia S, Heo WD, Meyer T, Konan KV. 2007. Participation of rab5, an early endosome protein, in hepatitis C virus RNA replication machinery. *J Virol* 81:4551-63.
3. Su WC, Chao TC, Huang YL, Weng SC, Jeng KS, Lai MM. 2011. Rab5 and class III phosphoinositide 3-kinase Vps34 are involved in hepatitis C virus NS4B-induced autophagy. *J Virol* 85:10561-71.
4. Saxena V, Lai CK, Chao TC, Jeng KS, Lai MM. 2012. Annexin A2 is involved in the formation of hepatitis C virus replication complex on the lipid raft. *J Virol* 86:4139-50.
5. Backes P, Quinkert D, Reiss S, Binder M, Zayas M, Rescher U, Gerke V, Bartenschlager R, Lohmann V. 2010. Role of annexin A2 in the production of infectious hepatitis C virus particles. *J Virol* 84:5775-89.
6. Mahdy MM, El-Ekiaby NM, Hashish RM, Salah RA, Hanafi RS, Azzazy HM, Abdelaziz AI. 2016. miR-29a Promotes Lipid Droplet and Triglyceride Formation in HCV Infection by Inducing Expression of SREBP-1c and CAV1. *J Clin Transl Hepatol* 4:293-299.
7. Shi ST, Lee KJ, Aizaki H, Hwang SB, Lai MM. 2003. Hepatitis C virus RNA replication occurs on a detergent-resistant membrane that cofractionates with caveolin-2. *J Virol* 77:4160-8.
8. Nevo-Yassaf I, Yaffe Y, Asher M, Ravid O, Eizenberg S, Henis YI, Nahmias Y, Hirschberg K, Sklan EH. 2012. Role for TBC1D20 and Rab1 in hepatitis C virus replication via interaction with lipid droplet-bound nonstructural protein 5A. *J Virol* 86:6491-502.
9. Coller KE, Berger KL, Heaton NS, Cooper JD, Yoon R, Randall G. 2009. RNA interference and single particle tracking analysis of hepatitis C virus endocytosis. *PLoS Pathog* 5:e1000702.
10. Berger KL, Cooper JD, Heaton NS, Yoon R, Oakland TE, Jordan TX, Mateu G, Grakoui A, Randall G. 2009. Roles for endocytic trafficking and phosphatidylinositol 4-kinase III alpha in hepatitis C virus replication. *Proc Natl Acad Sci U S A* 106:7577-82.
11. Grove J, Huby T, Stamatakis Z, Vanwolleghem T, Meuleman P, Farquhar M, Schwarz A, Moreau M, Owen JS, Leroux-Roels G, Balfe P, McKeating JA. 2007. Scavenger receptor BI and BII expression levels modulate hepatitis C virus infectivity. *J Virol* 81:3162-9.
12. Martin DN, Uprichard SL. 2013. Identification of transferrin receptor 1 as a hepatitis C virus entry factor. *Proc Natl Acad Sci U S A* 110:10777-82.
13. Ferguson D, Zhang J, Davis MA, Helsley RN, Vedin LL, Lee RG, Crooke RM, Graham MJ, Allende DS, Parini P, Brown JM. 2017. The lipid droplet-associated protein perilipin 3 facilitates hepatitis C virus-driven hepatic steatosis. *J Lipid Res* 58:420-432.
14. Wang L, Tian Y, Ou JH. 2015. HCV induces the expression of Rubicon and UVRAG to temporally regulate the maturation of autophagosomes and viral replication. *PLoS Pathog* 11:e1004764.
15. Chan ST, Lee J, Narula M, Ou JJ. 2016. Suppression of Host Innate Immune Response by Hepatitis C Virus via Induction of Autophagic Degradation of TRAF6. *J Virol* 90:10928-10935.

16. Triyatni M, Berger EA, Saunier B. 2016. Assembly and release of infectious hepatitis C virus involving unusual organization of the secretory pathway. *World J Hepatol* 8:796-814.
17. Scarselli E, Ansuini H, Cerino R, Roccasecca RM, Acali S, Filocamo G, Traboni C, Nicosia A, Cortese R, Vitelli A. 2002. The human scavenger receptor class B type I is a novel candidate receptor for the hepatitis C virus. *EMBO J* 21:5017-25.
18. Bartosch B, Vitelli A, Granier C, Goujon C, Dubuisson J, Pascale S, Scarselli E, Cortese R, Nicosia A, Cosset FL. 2003. Cell entry of hepatitis C virus requires a set of co-receptors that include the CD81 tetraspanin and the SR-B1 scavenger receptor. *J Biol Chem* 278:41624-30.