

**Table S7. List of proteomic structural hotspots of HepaRG proteins, comparison with PHH and HepG2 cells.**

Family or system	N	Protein Identifiers	Fold change (LOG10) of copy numbers in HepaRG or HepG2 cells vs. PHH
<b>Extracellular matrix</b>			
Integrin and integrin-associated	10	ILK, ILKAP, ITGA1, ITGA2#, ITGA3*#, ITGA5*, ITGA6, ITGAV, ITGB1, ITGB5	
Collagen and collagen-associated	9	COL18A1, COL4A3BP, COL7A1*#, COL8A1*#, COLGALT1, PLOD1, PLOD2, PLOD3, PLOLCE*#	
Fibronectin, laminin, proteoglycan	7	FN1, GPC1, GPC6, HSPG2, LAMB1, LAMC1, SDC1	
Proteinase-associated	16	ADAM9, ADAM15*#, SERPINA1, SERPINA3, SERPINB1, SERPINB2*, SERPINB6, SERPINB8*, SERPINB9, SERPINC1, SERPINE1, SERPINE2*, SERPINF2, SERPING1*, SERPINH1, TIMP1*	
<b>Membrane receptors</b>			
Immune and cytokines	5	FAS, FCGRT, IL17RA, TLR2*, TLR3*	
Hormones and Growth factors	5	EGFR, GPR5C, IGF2R, M6PR, MET	
Cell-cell adhesion and communication	4	ANTXR2, CXADR, EPHB4, PTPRF	
(micro)nutrient	3	ASGR1, LSR, TFRC	
<b>Membrane and canalicular transporters</b>			
ABC	4	ABCB1, ABCC1#, ABCC2, ABCC3	
SLC	7	SLC16A1, SLC16A7*, SLC22A18*, SLC29A1, SLC22A6*#, SLCO2B1, SLCO1B1*	
<b>Tight junctions</b>			
MAGUK and protein kinase	4	CASK, PRKCI, ZO-1, ZO-2	
Occludin, Claudin and Immunoglobulin	3	CLDN1, F11R (JAM), OCLN	
Ezrin/radixin/moesin	3	EPB41, EZR, RDX	
Morphogenesis	5	CGN*, CTNNB1*, MLLT4*, SPTBN1, TJAP1	
<b>Polarisation</b>			
Rho, PAR3, lin-7, LAP, and MAGUK	6	CDC42, DLG1*, LIN7A, LIN7C, PARD3, SCRIB	
<b>Cytoskeleton</b>			
Actin-associated	11	ACTB, ACTG1, ACTN1, ACTN4, ACTR2*, ACTR3, ACTR10, CFL1, CFL2, VASP, VCL	
Myosin and tropomyosin	11	MYH9, MYH10, MYL1*, MYL6, MYL12A, MYL12B, MYLK, MYO19, MYO1E, TPM3, TPM4	
Tubulin-associated	15	TBCA, TBCB, TBCE, TPPP*, TUBA1A*#, TUBA1B*, TUBA1C, TUBA4A, TUBB, TUBB2A, TUBB3, TUBB4, TUBB6, TUBG, TUBGCP2	
Other	1	KIF2A	
<b>Trafficking</b>			
Rho and Rho-associated	27	ARAP1, ARHGAP1, ARHGAP12*#, ARHGAP17, ARHGAP18, ARHGAP35, ARHGAP44*#, ARHGAP5, ARHGDIA, ARHGEF1, ARHGEF10L, ARHGEF12*, ARHGEF18, ARHGEF2, ARHGEF5*, ARHGEF7, FARP1, RAC1, RAC2*, RHOA*, RHOB, RHOC, RHOG, RHOT2, ROCK1, ROCK2, SRGAP1*#	
Rab and Rab-associated	62	CHM, ERC1, GDI1, GDI2, RAB10, RAB11B, RAB11FIP5*#, RAB12, RAB13, RAB14, RAB18, RAB1A, RAB1B, RAB21, RAB22A, RAB23, RAB24, RAB27A, RAB27B*, RAB29, RAB2A, RAB2B, RAB30, RAB32, RAB35, RAB3A, RAB3GAP1*, RAB3GAP2, RAB43, RAB4A, RAB4B, RAB5A, RAB5B, RAB5C*, RAB6A*, RAB6B*#, RAB6C*#, RAB7A, RAB8A, RAB8B, RAB9A, RABAC1, RABEP1, RABEP2, RABEPK, RABGAP1, RABGAP1L*, RABL3, RILP, RIN1*, TBC1D1*, TBC1D15, TBC1D17, TBC1D2, TBC1D22A*, TBC1D23, TBC1D2B*, TBC1D31*#, TBC1D4, TBC1D5, TBC1D8B, TBC1D9B	
Ras and Ras-associated	21	DAB2IP, G3BP1, G3BP2, HRAS, IQGAP1, IQGAP2, IQGAP3, NRAS, PDE6D*, RALA, RALB, RAP1A, RAP1B, RAP2C, RASA1, RIN1*, RRAGA, RRAGC, RRAS, RRAS2, RSU1	
Clathrins	5	CLINT1*, CLTB, CLTC, CLTCL1, PICALM	
SNAREs	5	BNIP1, SNAPIN, USE1, VTI1A, VTI1B	
Coatomeer-associated	8	COPA, COPB1, COPB2, COPE, COPG1, COPG2, COPZ1, COPZ2*	
Others	3	GOLT1B, SFT2D2, SFT2D3	
<b>Degradation machineries</b>			
Ubiquitin-proteasome system	77	ADRM1, BAG2, BAG3, BAG5, BAG6, CACUL1*, CAND1, CUL1, CUL2, CUL3, CUL4A, CUL4B, CUL5, DDI2, DNAJB2, ECM29, PAAF1, PSMA1, PSMA2, PSMA3, PSMA4, PSMA5, PSMA6, PSMA7, PSMB1, PSMB10, PSMB2, PSMB3, PSMB4, PSMB5, PSMB6, PSMB7, PSMB8, PSMB9, PSMB10, PSMB11, PSMB12, PSMB13, PSMB14, PSMB15, PSMB16, PSMB17, PSMB18, PSMB19, PSMB20, PSMB21, PSMB22, PSMB23, PSMB24, PSMB25, PSMB26, PSMB27, PSMB28, PSMB29, PSMB30, PSMB31, PSMB32, PSMB33, PSMB34, PSMB35, PSMB36, PSMB37, PSMB38, PSMB39, PSMB40, PSMB41, PSMB42, PSMB43, PSMB44, PSMB45, PSMB46, PSMB47, PSMB48, PSMB49, PSMB50, PSMB51, PSMB52, PSMB53, PSMB54, PSMB55, PSMB56, PSMB57, PSMB58, PSMB59, PSMB60, PSMB61, PSMB62, PSMB63, PSMB64, PSMB65, PSMB66, PSMB67, PSMB68, PSMB69, PSMB70, PSMB71, PSMB72, PSMB73, PSMB74, PSMB75, PSMB76, PSMB77, PSMB78, PSMB79, PSMB80, PSMB81, PSMB82, PSMB83, PSMB84, PSMB85, PSMB86, PSMB87, PSMB88, PSMB89, PSMB90, PSMB91, PSMB92, PSMB93, PSMB94, PSMB95, PSMB96, PSMB97, PSMB98, PSMB99, PSMB100, 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PSMB989, PSMB990, PSMB991, PSMB992, PSMB993, PSMB994, PSMB995, PSMB996, PSMB997, PSMB998, PSMB999, PSMB1000	
Cathepsins	8	CTSB, CTSD, CTSF*, CTSH, CTSL, CTSO*, CTSS*, CTSZ*	
Calpains (CAPNs)	3	CAPN1, CAPN2, CAPNS1	
COP9 signalosome complex	8	COPS2, COPS3, COPS4, COPS5, COPS6, COPS7A, COPS7B, COPS8	

The comparison of protein abundances (copy number per cell) was made using the HepaRG, primary human hepatocyte (PHH), and HepG2 proteomics datasets. Only the proteins commonly quantified in at least two of the three systems were considered for this comparison. For a given family or system, the mean fold change of copy numbers of proteins commonly quantified in the three systems is shown in red (HepaRG vs. PHH) and green (HepG2 vs. PHH). \*indicates proteins that are not present in the HepG2 proteomics dataset. # indicates proteins that are not present or for which quantitative values are not available in the PHH proteomics dataset. See supplemental Information for detailed annotations of proteins.