

SUPPORTING INFORMATION

The antiviral enzyme viperin inhibits cholesterol biosynthesis

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Running title: *Viperin inhibits cholesterol biosynthesis*

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Table S1. List of the top 100 proteins identified as candidates for the interactome of viperin. The data are sorted by SAINT score and then by fold enrichment over empty vector control. The percentage of the protein sequence covered and the number of unique peptides identified from each protein in the proteomics analysis are also given. Cholesterol biosynthetic enzymes are highlighted.

The full set of mass spectrometry proteomics data has been deposited to the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifier PXD023999.

UniProt ID	Gene	Description	Enrichment (Fold change)	SAINT score	Percentage coverage	Number of unique peptides
Q8WXG1	RSAD2	Radical S-adenosyl methionine domain-containing protein 2	417.64	1	85.6	40
P48449	LSS	Lanosterol synthase	32.96	1	59.01	35
Q14534	SQLE	Squalene monooxygenase	24.78	1	53.5	23
Q6ZRQ5	MMS22L	Protein MMS22-like	24.27	1	23.4	27
Q6NUQ4	TMEM214	Transmembrane protein 214	23.21	1	45.3	26
Q9UHG3	PCYOX1	Prenylcysteine oxidase 1	22.95	1	46.3	17
O95470	SGPL1	Sphingosine-1-phosphate lyase 1	21.32	1	50	23
P07099	EPHX1	Epoxide hydrolase 1	20.01	1	49.7	23
O94830	DDHD2	Phospholipase DDHD2	19.62	1	54.8	29
Q9H497	TOR3A	Torsin-3A	18.37	1	59.2	18
Q9H6V9	LDAH	Isoform 2 of Lipid droplet-associated hydrolase	17.77	1	52.3	18
Q96AD5	PNPLA2	Patatin-like phospholipase domain-containing protein 2	15.76	1	42.06	14
P23786	CPT2	Carnitine O-palmitoyltransferase 2, mitochondrial	15.49	1	56.8	31
Q15738	NSDHL	Sterol-4-alpha-carboxylate 3-dehydrogenase, decarboxylating	14.93	1	67.3	19
Q9H3N1	TMX1	Thioredoxin-related transmembrane protein 1	14.11	1	40	14
Q9HDC9	APMAP	Adipocyte plasma membrane-associated protein	13.62	1	54.8	20
Q96HA7	TONSL	Tonsoku-like protein	13.55	1	33.2	29
Q96BW9	TAMM41	CDP-diacylglycerol--glycerol-3-phosphate 3-phosphatidyltransferase, mitochondrial	13.46	1	52.5	15
O15270	SPTLC2	Serine palmitoyltransferase 2	13.46	1	33.8	15
Q32NB8	PGS1	Isoform 3 of Phosphatidate cytidyltransferase, mitochondrial	13.44	1	33.3	13
Q86UE4	MTDH	Protein LYRIC	13.33	1	55.8	34

Q8WTS1	ABHD5	1-acylglycerol-3-phosphate O-acyltransferase ABHD5	13.14	1	58.2	11
Q8NBM8	PCYOX1L	Prenylcysteine oxidase-like	12.95	1	31.4	14
O43156	TTI1	TELO2-interacting protein 1 homolog	12.36	1	24.0	19
Q13505	MTX1	Metaxin-1	12.15	1	26.0	11
Q8N128	FAM177A1	Isoform 2 of Protein FAM177A1	12.14	1	44.1	10
O15228	GNPAT	Dihydroxyacetone phosphate acyltransferase	12.06	1	60.7	36
Q8IZ81	ELMOD2	ELMO domain-containing protein 2	11.5	1	32.8	11
Q8NBX0	SCCPDH	Saccharopine dehydrogenase-like oxidoreductase	10.5	1	39.9	11
Q16850	CYP51A1	lanosterol 14-alpha demethylase	10.18	1	27.2	11
Q9UH92	MLX	MAX-like protein X	10.17	1	43.3	2
P33121	ACSL1	Long-chain-fatty-acid--CoA ligase 1	10.02	1	50.1	31
Q9BSY9	DESI2	Desumoylating isopeptidase 2	9.85	1	62.9	6
P56937	HSD17B7	3-keto-steroid reductase	9.84	1	32.6	10
P42345	MTOR	Serine/threonine-protein kinase mTOR	9.76	1	41.7	83
O15269	SPTLC1	Serine palmitoyltransferase 1	9.53	1	29.2	12
Q9HBH5	RDH14	Retinol dehydrogenase 14	9.52	1	36.3	10
Q9BV23	ABHD6	Monoacylglycerol lipase ABHD6	9.2	1	27.3	9
Q99487	PAFAH2	Platelet-activating factor acetylhydrolase 2, cytoplasmic	9.2	1	39.3	12
Q96KC8	DNAJC1	DnaJ homolog subfamily C member 1	9.2	1	27.3	12
Q96E22	NUS1	Dehydrodolichyl diphosphate synthase complex subunit nus1	8.87	1	46.1	10
Q8TC12	RDH11	Retinol dehydrogenase 11	8.65	1	40.3	12
Q8NBQ5	HSD17B11	Estradiol 17-beta-dehydrogenase 11	8.65	1	42.3	12
P50336	PPOX	Protoporphyrinogen oxidase	8.61	1	39.8	14
Q9UIA9	XPO7	Exportin-7	8.12	1	42.3	36
P21964	COMT	Catechol O-methyltransferase	8.04	1	51.7	10
Q9UI26	IPO11	Isoform 2 of Importin-11	7.69	1	36.3	28
P51648	ALDH3A2	Aldehyde dehydrogenase family 3 member A2	6.9	1	32.9	13
Q9NW68	BSDC1	BSD domain-containing protein 1	6.89	1	37.9	13

P40855	PEX19	Peroxisomal biogenesis factor 19	6.87	1	75.6	16
P47712	PLA2G4A	Cytosolic phospholipase A2	6.62	1	43.5	26
O43681	ASNA1	ATPase ASNA1	6	1	61.2	16
Q9BXW9	FANCD2	Isoform 1 of Fanconi anemia group D2 protein	5.91	1	44.8	50
O60313	OPA1	Isoform 2 of Dynamin-like 120 kDa protein, mitochondrial	5.88	1	59.5	60
Q13724	MOGS	Mannosyl-oligosaccharide glucosidase	5.83	1	38.4	24
O76071	CIAO1	Probable cytosolic iron-sulfur protein assembly protein Ciao1	5.66	1	57.8	14
Q9Y4R8	TELO2	Telomere length regulation protein TEL2 homolog	4.86	1	48.5	32
Q96T76	MMS19	Isoform 5 of MMS19 nucleotide excision repair protein homolog	4.61	1	63.7	50
P40939	HADHA	Trifunctional enzyme subunit alpha, mitochondrial	3.97	1	59.0	35
Q6NXR4	TTI2	TELO2-interacting protein 2	8.86	0.99	27.8	11
Q86SQ9	DHDDS	Isoform 2 of Dehydrodolichyl diphosphate synthase complex subunit DHDDS	8.53	0.99	36.2	10
Q99653	CHP1	Calcineurin B homologous protein 1	8.53	0.99	67.2	10
Q92575	UBXN4	UBX domain-containing protein 4	8.21	0.99	25.0	7
P50897	PPT1	Palmitoyl-protein thioesterase 1	7.71	0.99	45.1	9
Q13190	STX5	Syntaxin-5	7.11	0.99	40.0	12
Q53GQ0	HSD17B12	Very-long-chain 3-oxoacyl-CoA reductase	6.68	0.99	32.7	9
P00387	CYB5R3	Isoform 3 of NADH-cytochrome b5 reductase 3	5.42	0.99	36.8	10
O95573	ACSL3	Long-chain-fatty-acid--CoA ligase 3	4.77	0.99	42.9	20
P55084	HADHB	Trifunctional enzyme subunit beta, mitochondrial	4.1	0.99	63.5	26
Q99807	COQ7	5-demethoxyubiquinone hydroxylase, mitochondrial	7.56	0.98	31.3	6
Q9H1E5	TMX4	Thioredoxin-related transmembrane protein 4	7.55	0.98	28.1	8
Q9BRX8	FAM213A	Redox-regulatory protein FAM213A	7.55	0.98	35.8	8

Q6PIU2	NCEH1	Isoform 2 of Neutral cholesterol ester hydrolase 1	7.22	0.98	25.7	9
Q9HAP2	MLXIP	MLX-interacting protein	5.92	0.98	21.9	11
P43378	PTPN9	Tyrosine-protein phosphatase non-receptor type 9	5.71	0.98	26.3	13
O75155	CAND2	Cullin-associated NEDD8-dissociated protein 2	5.03	0.98	23.0	16
Q86U38	NOP9	Nucleolar protein 9	3.63	0.98	43.7	21
Q9H1A3	METTL9	Methyltransferase-like protein 9	7.22	0.97	31.8	8
P37268	FDFT1	Squalene synthase	5.45	0.97	40.0	14
Q9Y2Z9	COQ6	Ubiquinone biosynthesis monooxygenase COQ6, mitochondrial	6.9	0.96	26.3	9
Q6PI48	DARS2	Aspartate--tRNA ligase, mitochondrial	3.93	0.96	43.9	21
Q96AG4	LRRC59	Leucine-rich repeat-containing protein 59	3.77	0.96	47.9	13
Q8WVC6	DCAKD	Dephospho-CoA kinase domain-containing protein	7.23	0.95	35.1	7
Q3SXM5	HSDL1	Inactive hydroxysteroid dehydrogenase-like protein 1	6.25	0.95	32.4	9
O14656	TOR1A	Torsin-1A	4.51	0.95	42.2	13
O75915	ARL6IP5	PRA1 family protein 3	6.25	0.94	20.2	4
Q9Y673	ALG5	Dolichyl-phosphate beta-glucosyltransferase	5.92	0.94	17.6	5
Q6UX53	METTL7B	Methyltransferase-like protein 7B	5.59	0.94	27.5	6
O75691	UTP20	Small subunit processome component 20 homolog	5.31	0.94	9.6	24
Q13637	RAB32	Ras-related protein Rab-32	3.94	0.93	40.0	8
A6NDU8	C5ORF51	UPF0600 protein C5orf51	3.49	0.93	37.8	10
Q99541	PLIN2	Perilipin-2	3.37	0.93	63.6	21
P02649	APOE	Apolipoprotein E	6.91	0.92	35.3	10
P53701	HCCS	Cytochrome c-type heme lyase	5.26	0.92	37.3	8
P01111	NRAS	GTPase NRas	4.72	0.92	58.2	8
A1L0T0	ILVBL	Acetolactate synthase-like protein	5.59	0.91	24.5	8
Q2TAA5	ALG11	GDP-Man:Man(3)GlcNAc(2)-PP-Dol alpha-1,2-mannosyltransferase	5.26	0.91	23.6	7
Q96CS3	FAF2	FAS-associated factor 2	3.85	0.91	38.4	12
Q68D91	MBLAC2	Metallo-beta-lactamase domain-containing protein 2	6.89	0.9	28.3	7
Q9NP73	ALG13	Putative bifunctional UDP-N-acetylglucosamine	5.58	0.9	44.8	1

		transferase and deubiquitinase				
P04843	RPN1	Dolichyl-diphosphooligosaccharide-protein glycosyltransferase subunit 1	4.45	0.9	26.7	13
P05023	ATP1A1	Sodium/potassium-transporting ATPase subunit alpha-1	4.33	0.9	17.2	12

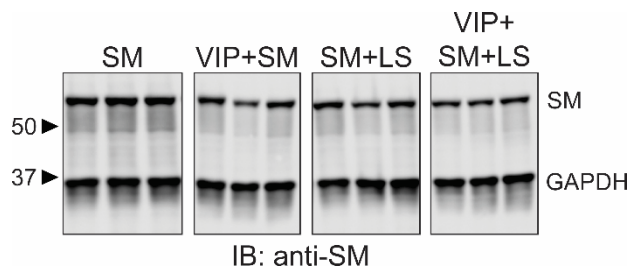


Figure S1. Representative western blots used in quantification of relative SM concentrations for SM activity assays. Each lane is one biological replicate. 'SM only' cells were co-transfected with empty vector as a control.

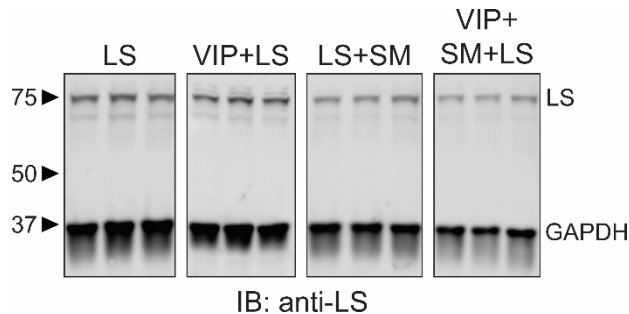


Figure S2. Representative western blots used in quantification of relative LS concentrations for LS activity assays. Each lane is one biological replicate. 'LS only' cells were co-transfected with empty vector as a control.

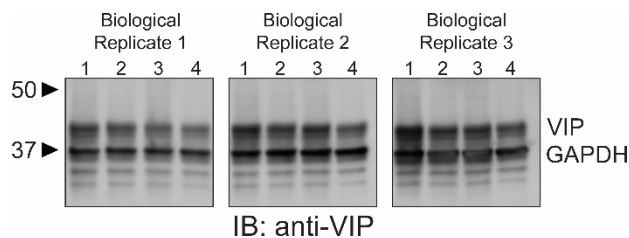


Figure S3. Western blots used in quantification of VIP concentrations for radical-SAM assays. 1: VIP; 2: VIP+LS; 3: VIP+SM; 4: VIP+LS+SM. Each panel is a single biological replicate.