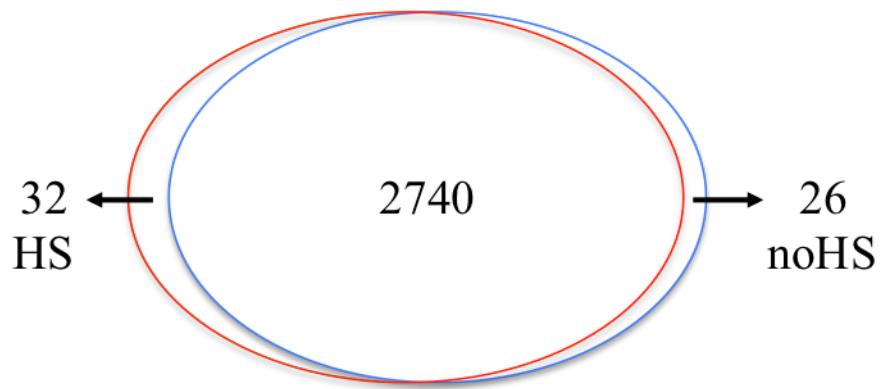
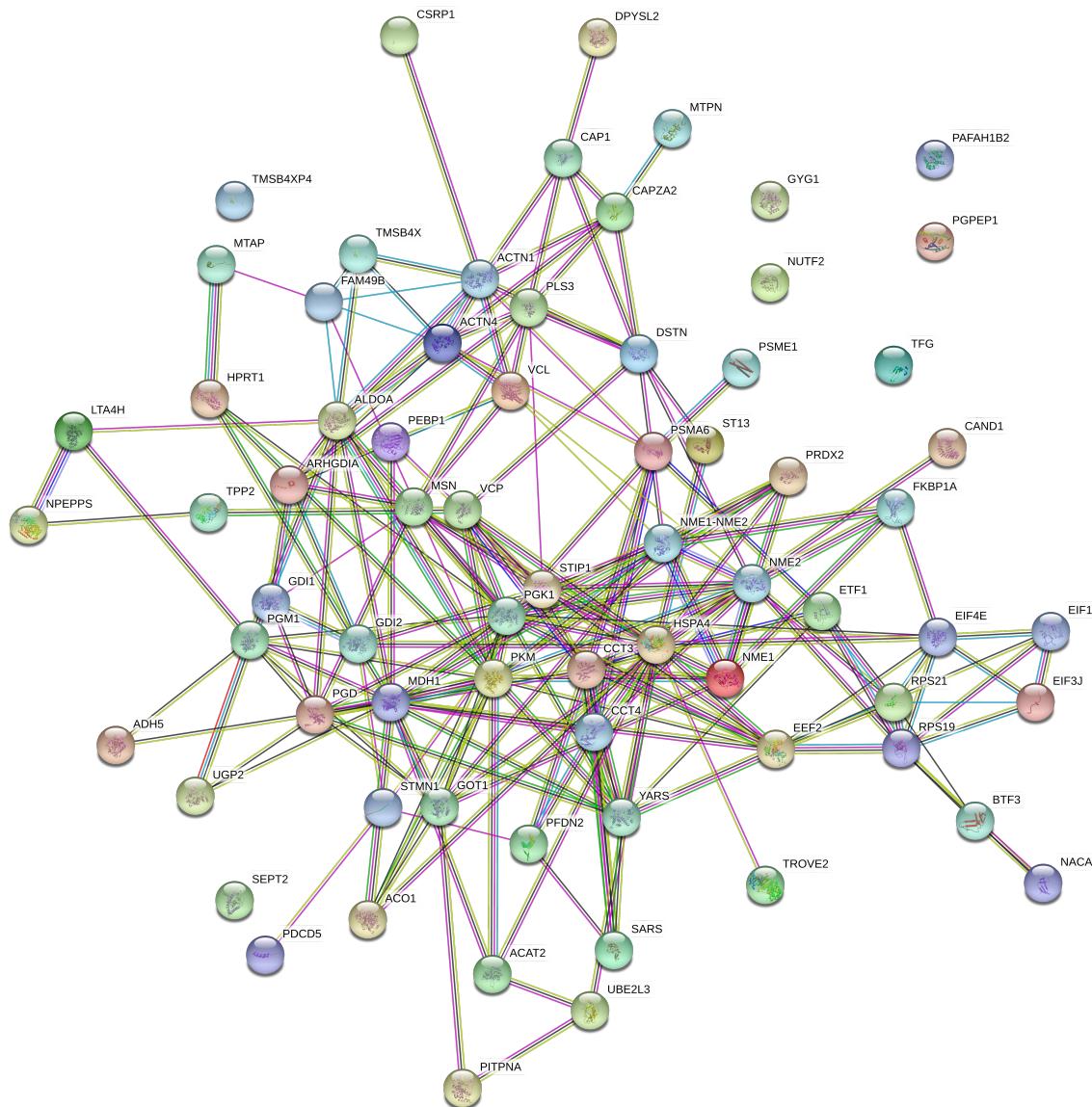


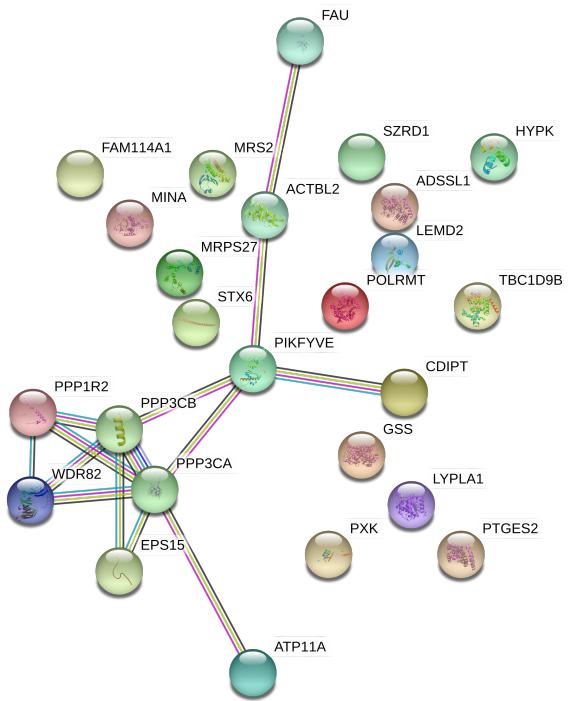
## Supplementary figures



**Supplementary Figure 1.** Venn-diagram illustrating the number of proteins that overlap between HS and no-HS samples and proteins exclusively identified in HS stimulated samples (HS) and unstimulated (noHS) samples.



**Supplementary Figure 2.** Protein-protein interaction network from down-regulated proteins by HS in the lysate TRIMEL. STRING analysis did not find the proteins ST13P4 and ST13P5 (Gene IDs: 145165; 144106), which are not depicted. Line color indicate the type of interaction evidence. Known interactions: cyan, from curated databases; pink, experimentally determined. Predicted interactions: green, gene neighborhood; red, gene fusions; blue, gene co-occurrence. Others: yellow, textmining; black, co-expression; purple, protein homology. Interaction confidence score, 0.4 (medium).



**Supplementary Figure 3.** Protein-protein interaction network of proteins exclusively expressed in no-HS conditioned melanoma-derived lysates samples. STRING analysis did not find the protein PPP1R2P3 (Gene ID: 153743), which is not depicted. Line color indicate the type of interaction evidence. Known interactions: cyan, from curated databases; pink, experimentally determined. Predicted interactions: green, gene neighborhood; red, gene fusions; blue, gene co-occurrence. Others: yellow, textminig; black, co-expression; purple, protein homology. Interaction confidence score, 0.4 (medium).

## Supplementary tables

**Supplementary Table 1. Currently known functions of selected gene-proteins down-regulated by HS. The protein list was filtered by p<0.01 or abs(log2(FC))>1.**

Gen	ID (NCBI)	Full name (NCBI)	Function (Gene Ontology)	Reference
ACAT2	39	<i>Acetyl-CoA acetyltransferase 2</i>	·Acetyl-CoA C-acetyltransferase activity ·Protein binding	[1,2]
ACO1	48	<i>Aconitase 1</i>	·Aconitate hydratase activity ·3 iron, 4 sulfur cluster; 4 iron, 4 sulfur cluster; RNA; iron-responsive element and protein binding	[3-8]
ACTN1	87	<i>Actinin alpha 1</i>	·Ligand-dependent nuclear receptor transcription coactivator and protein homodimerization activity ·Actin filament; double-stranded RNA; integrin; ion channel; protein and vinculin binding	[9-14]
ACTN4	81	<i>Actinin alpha 4</i>	·Ligand-dependent nuclear receptor transcription coactivator and protein homodimerization activity ·RNA; RNA polymerase II regulatory region sequence-specific DNA; actin; actin filament; chromatin DNA; integrin; ion channel; nuclear hormone receptor; nucleoside; protein and retinoic acid receptor binding	[9,12,13,15-19]
ADH5	128	<i>Alcohol dehydrogenase 5 (class III), chi polypeptide</i>	·S-(hydroxymethyl)glutathione dehydrogenase; electron transfer and formaldehyde dehydrogenase activity ·Fatty acid and zinc ion binding	[20,21]
ALDOA	226	<i>Aldolase, fructose-bisphosphate A</i>	·Fructose-bisphosphate aldolase activity ·RNA; actin; cadherin; cytoskeletal protein; fructose; identical protein; protein and tubulin binding	[22-28]
ARHGDI1	396	<i>Rho GDP dissociation inhibitor alpha</i>	·Protein binding	[29]
BTF3	689	<i>Basic transcription factor 3</i>	·RNA and protein binding	[2,15,23]
CAND1	55832	<i>Cullin associated and neddylation dissociated 1</i>	·Protein binding	[30]
CAP1	10487	<i>Cyclase associated actin cytoskeleton regulatory protein 1</i>		
CAPZA2	830	<i>Capping actin protein of muscle Z-line alpha subunit 2</i>		
CCT3	7203	<i>Chaperonin containing TCP1 subunit 3</i>	·RNA; protein and protein binding involved in protein folding	[2,23,31]
CCT4	10575	<i>Chaperonin containing TCP1 subunit 4</i>	·RNA and protein binding	[15,32]
CSRP1	1465	<i>Cysteine and glycine rich protein 1</i>	·RNA and zinc ion binding	[15,33]
DPYSL2	1808	<i>Dihydropyrimidinase like 2</i>	·Dihydropyrimidinase activity ·Identical protein and protein binding	[2,34]
DSTN	11034	<i>Destrin, actin depolymerizing factor</i>	·Actin filament and protein binding	[2,35]
EEF2	1938	<i>Eukaryotic translation elongation factor 2</i>	·RNA; cadherin; protein and protein kinase binding	[15,23,25,36-38]
EIF1	10209	<i>Eukaryotic translation initiation factor 1</i>	·Translation initiation factor activity ·RNA and translation factor activity, RNA binding	[23,39,40]
EIF3J	8669	<i>Eukaryotic translation initiation factor 3 subunit J</i>	·Contributes to translation initiation factor activity ·Protein binding	[41,42]
EIF4E	1977	<i>Eukaryotic translation initiation factor 4E</i>	·Translation initiation factor activity ·RNA 7-methylguanosine cap; RNA; RNA cap; enzyme; eukaryotic initiation factor 4G; protein and repressing transcription factor binding	[23,43-47]

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ETF1	2107	<i>Eukaryotic translation termination factor 1</i>	·Translation release factor and translation termination factor activity ·RNA; protein; ribosome and sequence-specific mRNA binding	[2,15,48-51]
FAM49B	51571	<i>Family with sequence similarity 49 member B</i>	·Protein binding	[2]
FKBP1A	2280	<i>FK506 binding protein 1A</i>	·NOT calcium channel inhibitor; peptidyl-prolyl cis-trans isomerase and signal transducer activity ·FK506; SMAD; activin; ion channel; macrolide; protein; transforming growth factor beta receptor and type I transforming growth factor beta receptor binding	[2,52-59]
GDI1	2664	<i>GDP dissociation inhibitor 1</i>	·GDP-dissociation inhibitor activity ·Protein binding	[30,60,61]
GDI2	2665	<i>GDP dissociation inhibitor 2</i>	·RNA and protein binding	[23,62]
GOT1	2805	<i>Glutamic-oxaloacetic transaminase 1</i>	·L-aspartate:2-oxoglutarate aminotransferase activity	[63,64]
GYG1	2992	<i>Glycogenin 1</i>	·Glycogenin glucosyltransferase activity ·Protein binding	[2,65]
HPRT1	3251	<i>Hypoxanthine phosphoribosyltransferase 1</i>	·Guanine phosphoribosyltransferase; hypoxanthine phosphoribosyltransferase and protein homodimerization activity ·Identical protein; magnesium ion and protein binding	[2,61,66-68]
HSPA4	3308	<i>Heat shock protein family A (Hsp70) member 4</i>	·ATP and protein binding	[2,69]
LTA4H	4048	<i>Leukotriene A4 hydrolase</i>	·Aminopeptidase; epoxide hydrolase; leukotriene-A4 hydrolase; metalloaminopeptidase and peptidase activity ·RNA; protein and zinc ion binding	[15,70-74]
MDH1	4190	<i>Malate dehydrogenase 1</i>	·Malic enzyme activity ·Protein binding	[74,75]
MSN	4478	<i>Moesin</i>	·Cell adhesion molecule; double-stranded RNA; enzyme; protein; protein kinase and receptor binding ·Structural constituent of cytoskeleton	[11,76-82]
MTAP	4507	<i>Methylthioadenosine phosphorylase</i>	·Phosphorylase activity ·Protein binding	[2,83]
MTPN	136319	<i>Myotrophin</i>		
NACA	4666	<i>Nascent polypeptide-associated complex alpha subunit</i>		
NME1/ NME1-NME2/ NME2	4830/ 654364/ 4831	<i>NME/NM23 nucleoside diphosphate kinase 1/ NME1-NME2 readthrough/ NME/NM23 nucleoside diphosphate kinase 2</i>	·Deoxyribonuclease and nucleoside diphosphate kinase activity/-/DNA binding transcription factor and nucleoside diphosphate kinase activity ·ATP; GTP; RNA; identical protein; magnesium ion; protein and ribosomal small subunit binding/-/Protein binding	[2,15,61,84-86]/-[85,87,88]
NPEPPS	9520	<i>Aminopeptidase puromycin sensitive</i>	·Aminopeptidase activity	[89]
NUTF2	10204	<i>Nuclear transport factor 2</i>	·Nucleocytoplasmic transporter activity ·Ran GTPase; identical protein and protein binding	[2,90-92]
PAFAH1B2	5049	<i>Platelet activating factor acetylhydrolase 1b catalytic subunit 2</i>	·Protein binding	[93]
PDCD5	9141	<i>Programmed cell death 5</i>	·Acetyltransferase activator activity ·Beta-tubulin; heparin and protein binding	[94-96]
PEBP1	5037	<i>Phosphatidylethanolamine binding protein 1</i>	·RNA; enzyme; phosphatidylethanolamine; protein and protein kinase binding	[15,95,97]
PFDN2	5202	<i>Prefoldin subunit 2</i>	·Protein; protein binding involved in protein folding and unfolded protein binding	[98-100]
PGD	5226	<i>Phosphogluconate dehydrogenase</i>	·Phosphogluconate dehydrogenase (decarboxylating) activity	[101]

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PGM1	5236	<i>Phosphoglucomutase 1</i>	· Phosphoglucomutase activity · Magnesium ion and protein binding	[74,102,103]
PGK1	5230	<i>Phosphoglycerate kinase 1</i>	· Phosphoglycerate kinase and protein-disulfide reductase activity · Protein binding	[104-106]
PGPEP1	54858	<i>Pyroglutamyl-peptidase I</i>		
PITPNA	5306	<i>Phosphatidylinositol transfer protein alpha</i>	· Phosphatidylcholine transporter and phosphatidylinositol transporter activity · Phosphatidylcholine; phosphatidylglycerol and phosphatidylinositol binding	[107]
PKM	5315	<i>Pyruvate kinase M1/2</i>	· Pyruvate kinase activity · MHC class II protein complex; RNA; cadherin and protein binding	[15,25,108-110]
PLS3	5358	<i>Plastin 3</i>		
PRDX2	7001	<i>Peroxiredoxin 2</i>	· Antioxidant and thioredoxin peroxidase activity · Protein binding	[111-113]
PSMA6	5687	<i>Proteasome subunit alpha 6</i>	· Endopeptidase activity · NF-kappaB; RNA; protein and purine ribonucleoside triphosphate binding	[2,114,115]
PSME1	5720	<i>Proteasome activator subunit 1</i>	· Protein binding	[93]
RPS19	6223	<i>Ribosomal protein S19</i>	· Protein homodimerization activity · RNA; fibroblast growth factor; protein and protein kinase binding · Structural constituent of ribosome	[23,116-120]
RPS21	6227	<i>Ribosomal protein S21</i>	· RNA and protein N-terminus binding	[15,121]
SARS	6301	<i>Seryl-tRNA synthetase</i>	· Protein homodimerization and serine-tRNA ligase activity · RNA; core promoter sequence-specific DNA and protein binding	[122-125]
SEPT2	4735	<i>Septin 2</i>	· Cadherin and protein binding	[25,126]
ST13/ ST13P4/ ST13P5	6767/ 145165/ 144106	<i>ST13, Hsp70 interacting protein/pseudogene 4/ ST13, Hsp70 interacting protein pseudogene 5</i>	· Protein binding · Protein binding, bridging	[127,128]
STIP1	10963	<i>Stress induced phosphoprotein 1</i>	· RNA and protein binding	[15,129]
STMN1	3925	<i>Stathmin 1</i>	· Signal transducer activity · Protein and tubulin binding	[2,130,131]
TFG	10342	<i>TRK-fused gene</i>	· Signal transducer activity · Identical protein and protein binding	[54,132,133]
TMSB4X/ TMSB4XP4	7114/ 7118	<i>Thymosin beta 4, X-linked/pseudogene 4</i>	· RNA; actin monomer; enzyme and protein binding	[15,134-136]
TPP2	7174	<i>Tripeptidyl peptidase 2</i>	· Aminopeptidase and endopeptidase activity · Identical protein and protein binding	[61,89,137,138]
TROVE2	6738	<i>TROVE domain family member 2</i>	· RNA binding	[139]
UBE2L3	7332	<i>Ubiquitin conjugating enzyme E2 L3</i>	· Transcription coactivator; ubiquitin conjugating enzyme; ubiquitin-protein transferase activator and ubiquitin-protein transferase activity · RNA; enzyme; protein and ubiquitin protein ligase binding	[15,140-145]
UGP2	7360	<i>UDP-glucose pyrophosphorylase 2</i>	· UTP:glucose-1-phosphate uridylyltransferase activity · Identical protein and protein binding	[2,146]

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VCL	7414	<i>Vinculin</i>	·Actin; NOT actin; alpha-catenin; beta-catenin; cadherin; dystroglycan; protein and ubiquitin protein ligase binding	[2,25,147-152]
VCP	7415	<i>Valosin containing protein</i>	·ATPase and deubiquitinase activator activity ·BAT3 complex; RNA; identical protein; polyubiquitin modification-dependent protein; protein; protein domain specific; protein phosphatase; ubiquitin protein ligase; ubiquitin-like protein ligase and ubiquitin-specific protease binding	[23,153-164]
YARS	8565	<i>Tyrosyl-tRNA synthetase</i>	·Signal transducer activity ·RNA; interleukin-8 receptor and protein binding	[15,165,166]

Abbreviations: ID, Identification number; NCBI, National Center for Biotechnology Information.

**Supplementary Table 2. Currently known functions of gene-proteins exclusive expressed by non-HS samples.**

Gen	ID (NCBI)	Full name (NCBI)	Function (Gene Ontology)	Reference
ACTBL2	345651	<i>Actin, beta like 2</i>	· Protein binding	[29]
ADSSL1	122622	<i>Adenylosuccinate synthase like 1</i>	· Adenylosuccinate synthase activity · GTP and phosphate ion binding	[167,168]
ATP11A	23250	<i>ATPase phospholipid transporting 11A</i>	· Protein binding	[169]
CDIPT	10423	<i>CDP-diacylglycerol--inositol 3-phosphatidyltransferase</i>	· CDP-diacylglycerol-inositol 3-phosphatidyltransferase activity · Protein binding	[2,170]
EPS15	2060	<i>Epidermal growth factor receptor pathway substrate 15</i>	· Cadherin; polyubiquitin and protein binding	[25,171,172]
FAM114A1	92689	<i>Family with sequence similarity 114 member A1</i>	· Protein binding	[2]
FAU	2197	<i>FAU, ubiquitin like and ribosomal protein S30 fusion</i>	· RNA binding	[23]
GSS	2937	<i>Glutathione synthetase</i>	· Protein homodimerization activity · ATP; glutathione; identical protein; magnesium ion and protein binding	[2,74,173]
HYPK	25764	<i>Huntingtin interacting protein K</i>	· Protein N-terminus and protein binding	[2,174]
LEMD2	221496	<i>LEM domain containing 2</i>	· Protein binding	[175]
LYPLA1	10434	<i>Lysophospholipase I</i>	· Lipase; lysophospholipase and palmitoyl-(protein) hydrolase activity	[176-178]
MINA	84864	<i>Ribosomal oxygenase 2</i>	· Identical protein binding	[2]
MRPS27	23107	<i>Mitochondrial ribosomal protein S27</i>	· Protein binding	[179]
MRS2	57380	<i>MRS2, magnesium transporter</i>	· Magnesium ion transmembrane transporter activity	[180]
PIKFYVE	200576	<i>Phosphoinositide kinase, FYVE-type zinc finger containing</i>	· 1-phosphatidylinositol-4-phosphate 5-kinase activity · Protein binding	[2,181]
POLRMT	5442	<i>RNA polymerase mitochondrial</i>	· DNA-directed 5'-3' RNA polymerase activity · RNA and protein binding	[15,23,182]
PPP1R2/ PPP1R2P3	5504/ 153743	<i>Protein phosphatase 1 regulatory inhibitor subunit 2/ Protein phosphatase 1 regulatory inhibitor subunit 2 pseudogene 3</i>	· Protein serine/threonine phosphatase inhibitor activity · Protein binding/Protein binding	[29,183]/ [2]
PPP3CA/ PPP3CB	5530/ 5532	<i>Protein phosphatase 3 catalytic subunit alpha/ Protein phosphatase 3 catalytic subunit beta</i>	· Calmodulin-dependent protein phosphatase; protein dimerization and protein serine/threonine phosphatase activity/Calmodulin-dependent protein phosphatase; protein dimerization and protein serine/threonine phosphatase activity · Calcium ion; calmodulin; cyclosporin A; drug; enzyme and protein binding/Calcium ion; calmodulin; drug; enzyme; protein and protein phosphatase 2B binding	[2,184-188]/ [185,186,189-191]
PTGES2	80142	<i>Prostaglandin E synthase 2</i>	· Protein binding	[2]
PXK	54899	<i>PX domain containing serine/threonine kinase like</i>	· NOT protein kinase activity · NOT ATP and NOT nucleotide binding	[192]
STX6	10228	<i>Syntaxin 6</i>	· Protein and syntaxin binding	[2,193]

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SZRD1	26099	<i>SUZ RNA binding domain containing 1</i>				
TBC1D9B	23061	<i>TBC1 domain family member 9B</i>	· Protein binding			[194]
WDR82	80335	<i>WD repeat domain 82</i>	· Contributes methyltransferase (specific) · Protein binding	to activity	histone (H3-K4)	[195,196]

Abbreviations: ID, Identification number; NCBI, National Center for Biotechnology Information.

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