

Table S2. Differences in the expression of selected enzymes and genes. Comparisons were performed between HCT116 wild-type (WT) cells and colorectal cancer stem cells (CSCs) (left columns), and between untreated CSCs and CSCs treated with the 3-mercaptopyruvate sulfurtransferase inhibitor HMPSNE (right columns).

A) One-Carbon Metabolism and Related Pathway Enzymes

Pathway	Enzyme	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
Glycolysis	Hexokinase (HK1/2)	+83	-34
Glycolysis	Phosphoglucose isomerase	-11	+13
Glycolysis	Phosphofructokinase	-30	+27
Glycolysis	Aldolase (ALDOA/C)	+477	+38
Glycolysis	Triosephosphate isomerase	+11	+24
Glycolysis	GAPDH	-13	+17
Glycolysis	Phosphoglycerate kinase	+33	+30
Glycolysis	Phosphoglycerate mutase	-20	+42
Glycolysis	Enolase (ENO1/2/3)	+31	+14
Glycolysis	Pyruvate kinase	-6	+34
Pyruvate Node / Anaplerosis	Pyruvate carboxylase (PC)	+141	-48
Pyruvate Node / Anaplerosis	PCK2	+134	0
Pyruvate Node / Anaplerosis	PDH complex	+78	0
TCA Cycle	Citrate synthase	+23	-28
TCA Cycle	Aconitase (ACO1/2)	+10	-12
TCA Cycle	Isocitrate dehydrogenase (IDH1/2/3)	+88	-9
TCA Cycle	α -KGDH complex	+147	+14
TCA Cycle	Succinyl-CoA synthase	+34	-17
TCA Cycle	Succinate dehydrogenase (SDHA-D)	-40	-31
TCA Cycle	Fumarase	+2	+36
TCA Cycle	Malate dehydrogenase (MDH1/2)	+56	+24
Methylglyoxal	Glyoxalase 1	+14	+5

B) Lipid Metabolism and Related Pathway Enzymes

Pathway step	Enzyme (Gene – Protein)	CSC vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
Acetyl-CoA supply	ACLY – ATP-citrate lyase	+20	+31
	ACSS2 – Acetyl-CoA synthetase (avg)	+526	+40
	ACAT2 – Acetoacetyl-CoA thiolase (avg)	+112	+40
Mevalonate pathway	HMGCS1 – HMG-CoA synthase	+373	+28
	HMGCR – HMG-CoA reductase	+285	+98
	Mevalonate kinase	+121	-21
	Phosphomevalonate kinase	-44	-57
	Mevalonate PP decarboxylase	+136	+29
	IPP isomerase	+189	+18
	Farnesyl-PP synthase	+73	+24
Sterol synthesis	Squalene synthase	+593	+51

	Squalene epoxidase	+455	+60
	Lanosterol synthase	+278	+10
	CYP51A1	+40	+5
	DHCR 7/24 (Cholesterol reductases, avg)	+227	+38
Fatty acid synthesis	Acetyl-CoA carboxylase (avg)	-12	+4
	Fatty acid synthase	-15	+12
Fatty acid elongation	Fatty acid elongases (avg)	+117	-11
Monounsaturated FA synthesis	Stearoyl-CoA desaturase	+24	-40
PUFA synthesis	FADS1 – $\Delta 5$ -desaturase	-36	-94
Phospholipid remodeling	LPCAT 1-4 – Lysophosphatidylcholine acyltransferases (avg)	+130	-15
	AGPAT 1-5 – Lysophosphatidate acyltransferases (avg)	+399	-4
Glycerolipid synthesis	GPAT 1-4 – Glycerol-3-phosphate acyltransferases (avg)	-28%	-24
	DGAT 1/2 – Diacylglycerol acyltransferases (avg)	+147	+30
Kennedy pathway (PC)	CHK A/B – Choline kinase (avg)	+144	+7
	CCT – Phosphocholine cytidyltransferase	+3	+11
	CHPT1 – Choline phosphotransferase	+32	-3
Kennedy pathway (PE)	ETNK 1/2 – Ethanolamine kinase (avg)	-57	-64
	CPT – Phosphoethanolamine cytidyltransferase	+2	+36
	EPT – Ethanolamine phosphotransferase	+39	+16
CDP-DAG phospholipid synthesis	CDS 1/2 – CDP-diacylglycerol synthase (avg)	+106	+48
	PIS – Phosphatidylinositol synthase	+85	+20
	PGS – Phosphatidylglycerophosphate synthase	+56	-1

C) Mitochondrial Proteins

Mitochondrial RNA processing / ribosome assembly

Protein	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
ERAL1	-28	-96
RPUSD2	-12	-75
RPUSD3	+10	-92
RPUSD4	-5	-71

Mitochondrial ribosome – small subunit (28S)

Protein	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
MRPS5	-10	-58
MRPS7	-8	-62
MRPS9	-13	-63
MRPS10	-5	-58
MRPS14	-15	-66
MRPS15	-7	-60
MRPS16	-7	-63
MRPS18A	-5	-56

MRPS18B	-6	-57
MRPS18C	-8	-60
MRPS21	-11	-64
MRPS22	-14	-68
MRPS23	-6	-60
MRPS25	-10	-60
MRPS26	-6	-58
MRPS27	-10	-62
MRPS28	-7	-58

Mitochondrial ribosome – large subunit (39S)

Protein	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
MRPL3	-7	-61
MRPL9	-11	-63
MRPL10	-8	-60
MRPL12	-7	-61
MRPL13	-10	-62
MRPL15	-6	-59
MRPL16	-6	-61
MRPL19	-11	-65
MRPL20	-9	-61
MRPL21	-9	-61
MRPL22	-8	-59
MRPL24	-10	-64
MRPL27	-7	-59
MRPL28	-8	-60
MRPL32	-12	-66
MRPL34	-9	-62
MRPL36	-9	-60
MRPL37	-7	-58
MRPL38	-11	-64
MRPL39	-7	-60
MRPL40	-7	-58
MRPL41	-9	-60
MRPL44	-10	-63
MRPL45	-8	-59
MRPL47	-11	-64
MRPL48	-9	-61
MRPL49	-8	-59
MRPL50	-9	-61
MRPL51	-7	-59
MRPL52	-10	-63
MRPL53	-7	-60
MRPL54	-8	-60

Respiratory chain – Complex I

Protein	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
NDUFS1	-19	-74
NDUFS2	-18	-59
NDUFS3	-12	-58
NDUFS7	-10	-54
NDUFS8	-10	-56
NDUFV1	-9	-53
NDUFV2	-7	-52
NDUFV3	-7	-51
NDUFA1	-5	-49
NDUFA2	-7	-51
NDUFA3	-7	-50
NDUFA4	-8	-52
NDUFA5	-7	-50
NDUFA6	-6	-49
NDUFA7	-14	-91
NDUFA8	-9	-52
NDUFA9	-9	-53
NDUFA10	-8	-51
NDUFA11	-7	-50
NDUFA12	-8	-51
NDUFA13	-6	-49

Mitochondrial ferredoxin redox system

Protein	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
FDX1	-45	-90
FDX2	-7	-54
FDXR	-9	-58

D) Genes Involved in Redox Regulation, Amino-Acid Metabolism and Ferroptosis**System Xc⁻ / cystine transport and glutathione metabolism**

Gene	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
SLC7A11	-60	+390
SLC3A2	-46	+124
GCLC	-10	+149
GCLM	-13	+99
GSS	+11	+21
GSR	-15	+41
GGCT	-14	+14

Serine–glycine / one-carbon metabolism

Protein	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
PHGDH	-33	+48
PSAT1	-56	+125
PSPH	-12	+49
SHMT1	+3	+6

SHMT2	+2	+14
MTHFD1	-4	+4
MTHFD2	-9	+13
MTHFD1L	-4	-25

Thioredoxin / peroxide detoxification system

Protein	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
TXNRD1	-79	+149
TXNRD2	-9	+15
TXN	-35	+87
TXN2	-20	+25
SRXN1	-29	+306
PRDX1	-7	+52
PRDX2	+22	+20
PRDX3	+11	+28
PRDX4	-9	+44
PRDX5	+1	+1
SESN2	-50	+550

Ferroptosis regulatory pathways

Protein	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
GPX4	-95	-31
ACSL4	-10	-14
LPCAT3	~0	+8
PEBP1	-22	+28
SAT1	+14	+438
HMOX1	+386	+99
SCD	+24	-40

Coenzyme Q metabolism

Protein	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
COQ3	+5	+8
COQ5	-2	+51
COQ6	-4	+5
COQ7	-8	+26
COQ8A	-9	-47
COQ8B	+82	-90
COQ9	+4	+25
COQ10A	+78	-56

E) Genes Encoding Various Lipid-Binding Regulatory/Scaffold Proteins and Lipid Peroxidation Regulators

PEBP (phosphatidylethanolamine-binding protein) family

mRNA	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
PEBP1	-22	+28
PEBP2	~0	~0
PEBP4	+5	+9
PEBP5	-3	+4

Annexin phospholipid-binding scaffolds

Protein	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
ANXA1	+18	+26
ANXA2	+9	+22
ANXA3	+6	+12
ANXA4	-7	+8
ANXA5	+11	+15
ANXA6	-4	+7
ANXA7	+2	+6
ANXA11	+1	+4

Phospholipid transfer / lipid-binding regulatory proteins

Protein	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
PITPNA	-5	+5
PITPNB	-3	+3
SEC14L1	+4	+6
SEC14L2	-6	+5
SEC14L3	+3	+4
SEC14L4	+1	+3
SEC14L5	-2	+2

Membrane lipid-raft scaffolds

Protein	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
CAV1	+7	+19
CAV2	+5	+16
FLOT1	+3	+12
FLOT2	+2	+11

Oxysterol-binding lipid-signaling scaffolds

Protein	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
OSBP	+4	+7
OSBPL1A	+2	+6
OSBPL2	+1	+5
OSBPL3	-3	+4
OSBPL5	+2	+3
OSBPL6	+1	+4
OSBPL7	+1	+3
OSBPL8	-2	+3
OSBPL9	+2	+5
OSBPL10	-3	+4
OSBPL11	+1	+3

Fatty-acid binding proteins (intracellular lipid chaperones)

Protein	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
FABP1	+4	+8
FABP3	+2	+6

FABP4	+6	+9
FABP5	+3	+7
FABP7	+1	+4

Lipid peroxidation machinery in ferroptosis

Protein	CSCs vs. WT (% change)	CSCs-HMPSNE vs. CSCs-CTR (% change)
ACSL4	−10	−14
LPCAT3	~0	+8
ALOX12	−6	+12
ALOX15	−8	+9
GPX4	−95	−31
SCD	+24	−40