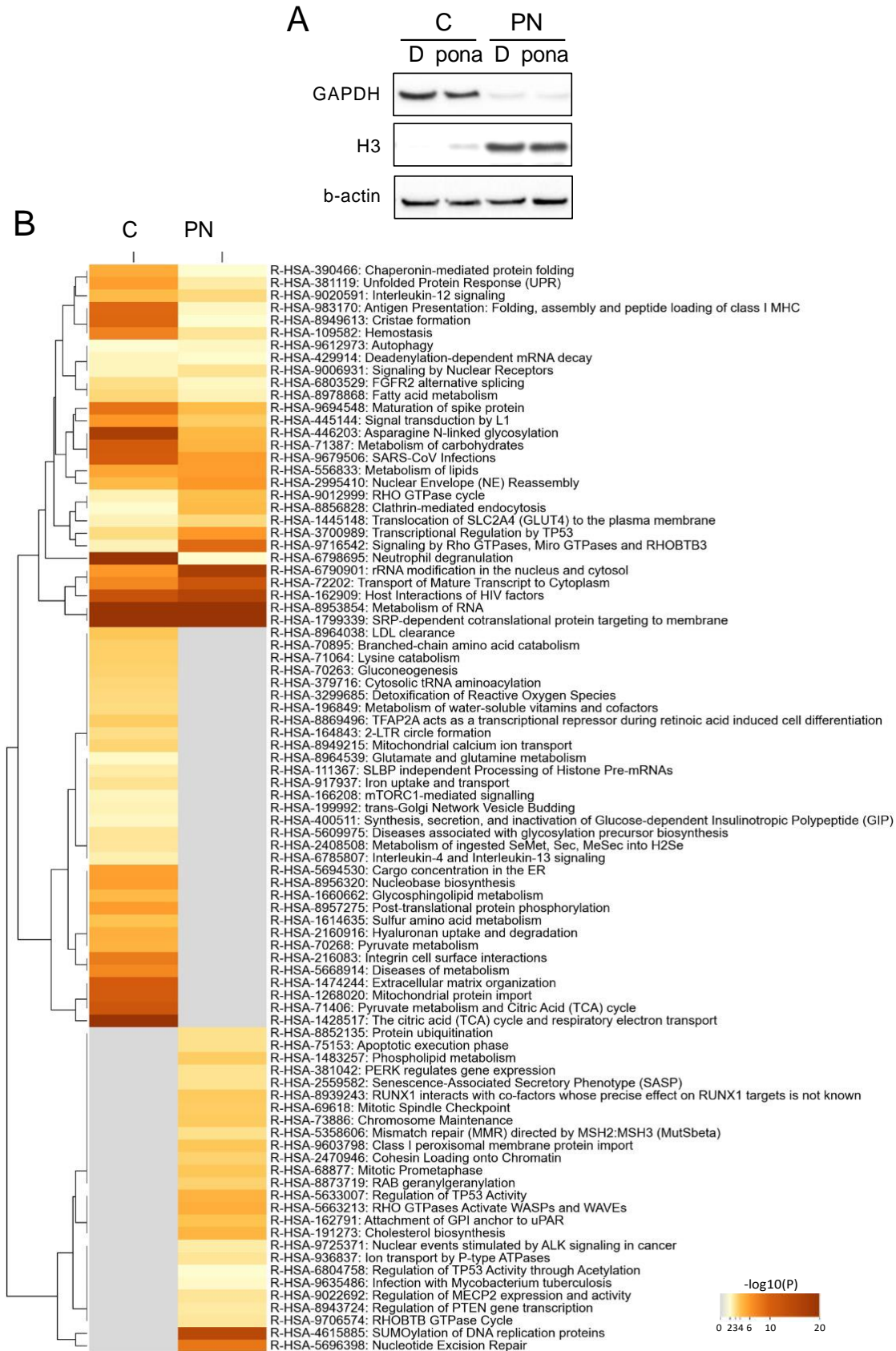


## Supplementary Table S1

**Table S1.** List of acronyms

ABCD	ATP binding cassette transporter D
ACS	acetyl-CoA synthetase
ALL	Acute lymphocytic leukemia
BBB	blood brain barrier
BCFA	branched chain fatty acid
C fraction	cellular fraction
CACAT	Solute Carrier Family 25 Member 20, SLC25A20
CML	chronic myelogenous leukaemia
CPT1	carnitine palmitoyltransferase 1
CPT2	carnitine palmitoyltransferase 2
DMSO	dimethyl sulfoxide
EE	early endosome
EGFR	epidermal growth factor receptor
ER	endoplasmic reticulum
FAO	fatty acid beta-oxidation
GAPDH	glyceraldehyde 3-phosphate dehydrogenase
GBM	glioblastoma
GM1	monosialic ganglioside 1
GM2	monosialic ganglioside 2
GM3	monosialic ganglioside 3
GSC	glioblastoma
H3	histone H3
LCFA	long chain fatty acid
LDL	low-density lipoprotein
LDLR	low-density lipoprotein receptor
LE	late endosome
LY	lysosome
MCFA	medium chain fatty acid
OXPPOS	oxidative phosphorylation
P	peroxisome
PDGFR	platelet derived growth factor receptor
PN fraction	peri/nuclear fraction
PONA	ponatinib
RANO	ranolazine
RTK	receptor tyrosine kinase
SFA	short chain fatty acid
SM4	sulfatide, sulfated galactocerebroside
TCA	tricarboxylic acid
THIO	thioridazine
TKI	tyrosine kinase inhibitor
UPR	unfolded protein response
VLFA	very-long chain fatty acid



# Supplementary Figure S1 continued

C

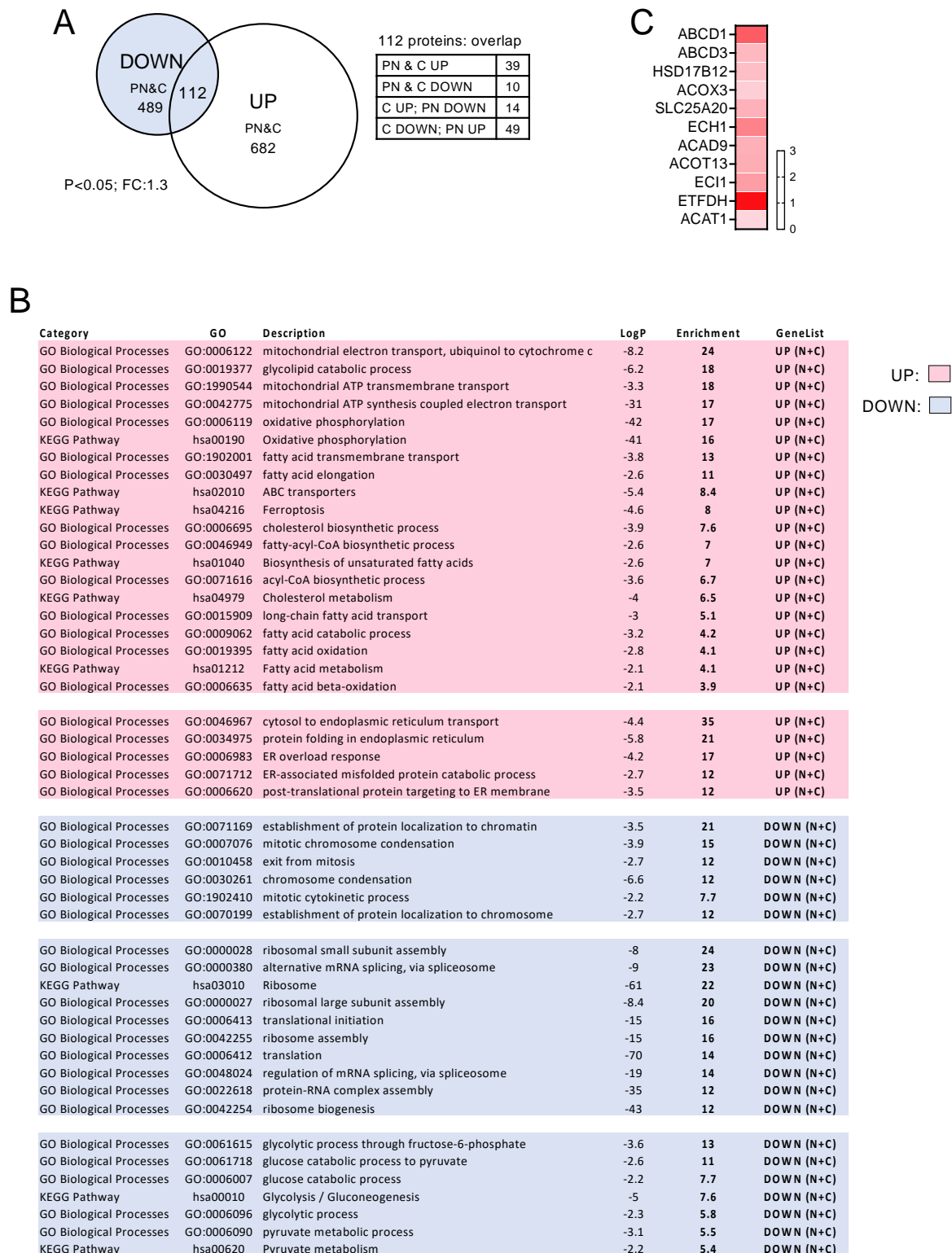
GO	Description	LogP	Enrichm.
R-HSA-390466	Chaperonin-mediated protein folding	-51	48
R-HSA-390466	Chaperonin-mediated protein folding	-21	4
R-HSA-381119	Unfolded Protein Response (UPR)	-58	5
R-HSA-381119	Unfolded Protein Response (UPR)	-27	46
R-HSA-6790901	rRNA modification in the nucleus and cytosol	-61	66
R-HSA-6790901	rRNA modification in the nucleus and cytosol	-17	20
R-HSA-1799339	SRP-dependent cotranslational protein targeting to membrane	-76	22
R-HSA-1799339	SRP-dependent cotranslational protein targeting to membrane	-35	22
R-HSA-381042	PERK regulates gene expression	-3	9
R-HSA-69618	Mitotic Spindle Checkpoint	-37	51
R-HSA-73886	Chromosome Maintenance	-38	46
R-HSA-68877	Mitotic Prometaphase	-39	39
R-HSA-75153	Apoptotic execution phase	-31	69
R-HSA-1268020	Mitochondrial protein import	-11	91
R-HSA-70268	Pyruvate metabolism	-48	82
R-HSA-1428517	The citric acid (TCA) cycle and respiratory electron transport	-49	12
R-HSA-71406	Pyruvate metabolism and Citric Acid (TCA) cycle	-12	11
R-HSA-1660662	Glycosphingolipid metabolism	-45	63
R-HSA-1483257	Phospholipid metabolism	-37	37
R-HSA-191273	Cholesterol biosynthesis	-47	14
R-HSA-9603798	Class I peroxisomal membrane protein import	-38	14

C:   
PN: 

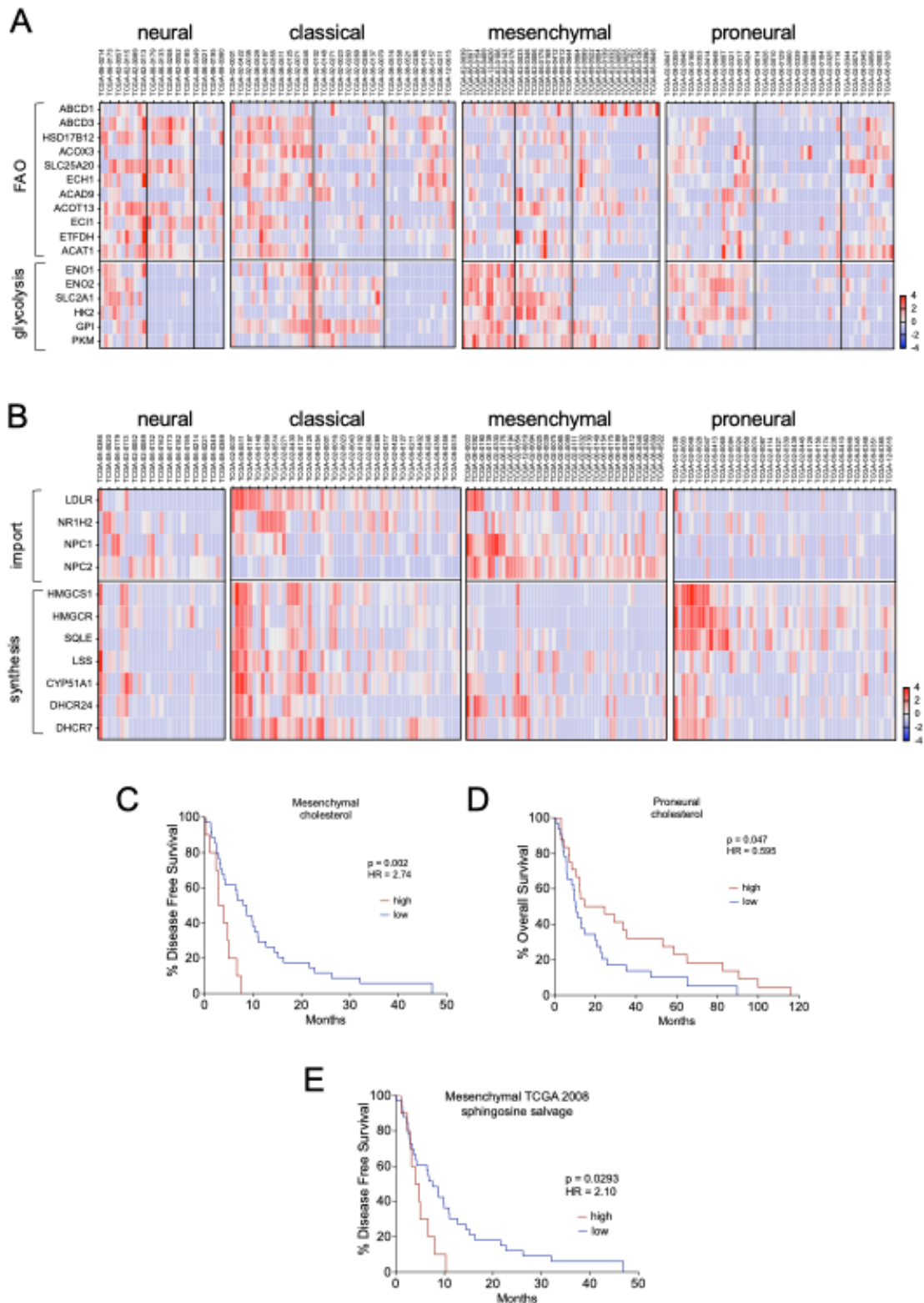
D

	GO	Description	LogP	Enrichment/localisation
GO Biological Processes	GO:0006457	protein folding	-24	74 C
GO Biological Processes	GO:0050658	RNA transport	-91	49 C
GO Biological Processes	GO:0022900	electron transport chain	-27	87 C
WikiPathways	WP368	Mitochondrial long chain fatty acid beta-oxidation	-3	86 C
KEGG Pathway	hsa04216	Ferroptosis	-64	79 C
KEGG	ko00620	Pyruvate metabolism	-5	75 C
WikiPathways	WP143	Fatty acid beta-oxidation	-45	75 C
Reactome	R-HSA-159223	Mitochondrial biogenesis	-82	61 C
Reactome	R-HSA-77289	Mitochondrial Fatty Acid Beta-Oxidation	-25	49 C
KEGG Pathway	hsa01212	Fatty acid metabolism	-2	38 C
GO Biological Processes	GO:0015908	fatty acid transport	-26	34 C
GO BP	GO:0061732	mitochondrial acetyl-CoA biosynthetic process from pyruv	-56	29 C
GO Biological Processes	GO:0009062	fatty acid catabolic process	-22	29 C
KEGG	hsa_M00307	Pyruvate oxidation, pyruvate => acetyl-CoA	-37	22 C
GO BP	GO:0042776	mitochondrial ATP synthesis coupled proton transport	-92	17 C
KEGG Pathway	hsa03008	Ribosome biogenesis in eukaryotes	-10	93 PN
GO Biological Processes	GO:0050658	RNA transport	-89	71 PN
GO Biological Processes	GO:0007052	mitotic spindle organization	-59	65 PN
GO Biological Processes	GO:0007091	metaphase/anaphase transition of mitotic cell cycle	-28	58 PN
GO Biological Processes	GO:0061077	chaperone-mediated protein folding	-27	56 PN
GO Biological Processes	GO:0035337	fatty-acyl-CoA metabolic process	-38	95 PN
KEGG Pathway	hsa01040	Biosynthesis of unsaturated fatty acids	-24	94 PN
WikiPathways	WP4718	Cholesterol metabolism with Bloch and Kandutsch-Russe	-43	92 PN
GO Biological Processes	GO:0035336	long-chain fatty-acyl-CoA metabolic process	-23	87 PN
KEGG Pathway	ko00062	Fatty acid elongation	-23	87 PN
GO Biological Processes	GO:0000038	very long-chain fatty acid metabolic process	-29	85 PN
GO Biological Processes	GO:1901568	fatty acid derivative metabolic process	-41	68 PN

**Supplementary Figure S1.** Subcellular proteome analysis of ponatinib treated T98G neurosphere cells. (a) Western-blot of cytoplasmic (C) and peri/nuclear (PN) fractions purified from T98-CSC cell lysates. Histone H3 (H3) and GAPDH were used as markers for the nuclear and cytoplasmic enriched fraction. Beta-actin served as loading control; (b) Heatmap of Reactome pathways enriched in the C and PN fractions; (c) Enrichment score of relevant Reactome pathways enriched in the C and PN fractions (d) Enrichment score of relevant gene ontology terms in the C and PN fractions.



**Supplementary Figure S2.** Pathway enrichment by ponatinib in T98G neurosphere cells. (a) Venn diagram representing the overlap of ponatinib induced up- and down-regulated proteomes identified in cytoplasmic (C) and peri/nuclear (PN) fractions; (b) Enrichment score of relevant ponatinib induced up- and down-regulated gene ontology terms in the C and PN fractions. (c) FAO related proteins upregulated in T98G neurosphere cells in response to ponatinib.



**Supplementary Figure S3.** Metabolic pathway analysis in GBM patients. (a,b) Expression of the indicated genes in the indicated tumour subtypes extracted from the TCGA 2008 patient cohort [4]; (c-d) Disease free and overall survival of patients from the indicated TCGA 2008 patient cohorts [4] expressing the ponatinib regulated cholesterol regulators LDLR, NPC1, NPC2, SQLE, LSS, CYP51A1, DHCR14B, DHCR24 and DHCR7. (e) Disease free survival of patients from the TCGA 2008 patient ‘mesenchymal’ cohort [4] expressing the genes indicated in Figure 7B.