SUPPLEMENTARY DATA

Metabolism of primary high-grade serous ovarian carcinoma (HGSOC) cells under limited glutamine or glucose availability

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Supplementary Tables

Table S1. Description of the clinical parameters of the study cohort of HGSOC patients (n=45).

Data are shown in percent of the total; age at diagnosis is shown as mean±SD (range).

Variable	Value
Age at diagnosis	64±8.9 (45–79)
Histotype	
- Serous	100%
Tumor grade	
- III	100%
FIGO substage	
- II	3%
- IIA	3%
- IIB	3%
- IIIA	3%
- IIIB	8%
- IIIC	75%
- IV	3%
- IVB	3%
Genetic background	
- Germinal BRCA1	14%
- Germinal BRCA2	8%
- Somatic BRCA1	3%
- Somatic BRCA1 & somatic RAD51D	3%
- Germinal MUTYH heterozygote	3%
- Negative	61%
- Unknown	8%
Neoadjuvant chemotherapy	
- Naïve	61%
- Paclitaxel / CBDCA, three cycles	39%
Postoperative residua	
- None (R0)	59%
- Macroscopic (R2)	41%
Adjuvant chemotherapy	
- Paclitaxel / CBDCA	75%
- CBDCA	6%
- Paclitaxel / CBDCA / Bevacizumab	3%

- Paclitaxel / CBDCA / cDDP / Etoposide	3%
- Docetaxel / CBDCA / Bevacizumab	3%
- Doxorubicin / cDDP	3%
- Doxorubicin / cDDP / Cyclofosfamid	3%
Consolidation therapy	
- PARPi	28%
- Aromatase inhibitors	3%
Postoperative recurrence within three years	59%
- In patients with R0	47%
- In patients with R2	62%

Table S2. Primary antibodies used in immunohistochemical staining, including reaction conditions.

Target	Manufacturer, clone	Dilution	Buffer pH
E-cadherin	Cell Signaling Technology, clone 24E10	1:200	pH 6
N-cadherin	Cell Signaling Technology, clone D4R1H	1:125	pH 6
Vimentin	Abcam, clone EPR3776	1:400	pH 6
Calnexin	Cell Signaling Technology, clone C5C9	1:400	pH 6
CHOP/ GADD153	Proteintech, catalogue No. 15204-1-AP	1:100	pH 9
BiP	Cell Signaling Technology, clone C50B12	1:500	pH 6
PERK	Cell Signaling Technology, clone D11A8	1:100	pH 9
eIF2α	Cell Signaling Technology, catalogue No. #9722	1:200	pH 9
p53	Agilent DAKO, catalogue No. #DO-7	1:200	pH 9

Table S3. List of gene-specific TaqMan probes used in the qRT-PCR analyses.

Gene	Probe
ADPGK	Hs00971680_m1
APAF1	Hs00559441_m1
ASNS	Hs04186194_m1
FABP4	Hs01086177_m1
GAPDH	Hs99999905_m1
GLS1	Hs01014020_m1
GLS2	Hs00998733_m1
HK1	Hs00175976_m1
HK2	Hs00606086_m1
IDO1	Hs00984148_m1
NAT8L	Hs00402258_m1
PSAT1	Hs00253548_m1
SCD	Hs01682761_m1
SLC7A11	Hs00921938_m1
TBP	Hs00427620_m1

Table S4. List of primary antibodies used in Western blotting.

Target	Manufacturer, clone or catalog No.	Dilution
SLC1A5	Merck, cat. No. HPA035240	1:500 in 5% milk
Vinculin	Cell Signaling Technology, clone E1E9V	1:1000 in 5% BSA
xCT	Cell Signaling Technology, clone D2M7A	1:1000 in 5% BSA
SLC25A12	Abcam, clone EPR16294	1:1000 in 5% milk
LDHA	Cell Signaling Technology, clone C4B5	1:1000 in 5% milk
c-Myc	Cell Signaling Technology, clone D84C12	1:1000 in 5% BSA
FASN	Cell Signaling Technology, clone C20G5	1:1000 in 5% milk
HK1	Cell Signaling Technology, clone C35C4	1:1000 in 5% milk
HK2	Cell Signaling Technology, clone C65G5	1:1000 in 5% BSA
SLC25A13	Abcam, clone EPR9969(B)	1:1000 in 5% milk
P-Raptor (S792)	Cell Signaling Technology, clone 2083	1:1000 in 5% BSA
Raptor	Cell Signaling Technology, clone 24C12	1:1000 in 5% BSA
ETC I – V	Abcam, cat. No. 110411	1:500 in 5% milk
MTCO2	Abcam, clone EPR3314	1:2000 in 5% milk
IDH2	Cell Signaling Technology, clone D8E3B	1:1000 in 5% milk
P-Akt (S473)	Cell Signaling Technology, clone 736E11	1:500 in 5% milk
Akt	Cell Signaling Technology, clone 40D4	1:1000 in 5% milk
P-ULK1 (S757)	Cell Signaling Technology, clone 6888	1:1000 in 5% BSA
ULK1	Cell Signaling Technology, clone D8H5	1:1000 in 5% BSA
BiP	Cell Signaling Technology, clone C50B12	1:1000 in 5% milk
P-eIF2α (S51)	Cell Signaling Technology, clone D9G8	1:1000 in 5% BSA
eIF2α	Cell Signaling Technology, clone D7D3	1:1000 in 5% milk
P-AMPK (T172)	Cell Signaling Technology, clone 40H9	1:1000 in 5% BSA
AMPK	Cell Signaling Technology, clone D63G4	1:1000 in 5% BSA
P-PERK (T982)	Abcam, cat. No. 192591	1:500 in 5% BSA

PERK	Cell Signaling Technology, clone D11A8	1:1000 in 5% BSA
VPS34	Santa Cruz Biotechnology, clone F-11	1:500 in 5% milk
LC3B	Novusbio, cat. No. NB100-2220	1:1000 in 5% milk
β-actin	Santa Cruz Biotechnology, clone C4	1:200 in 5% milk

Supplementary figure legends

Fig. S1. Changes in ATP levels and cell counts of tumor cells following incubation with metformin under glucose- and glutamine-deprived conditions. The data shown represent matched measurements of ATP levels by CellTiter-Glo and counting of live cells by the trypan blue exclusion assay. The analyses included six randomly selected isolates of tumor cells cultivated in complete medium (+Q, +G) or medium with depleted glucose (+Q, -G) or glutamine (-Q, +G) and with 10 mM, 2 mM or 0 mM metformin (Metf.). The cells for both assays were plated in parallel at the same time and from the same cell suspensions. The dots represent the means of three measurements from each patient-derived cell isolate and are shown relative to those of the isolates in the complete (control) medium (+Q, +G) without metformin. The bars indicate the SEs.

Fig. S2. Correlations among the mRNA expression data of selected proteins involved in cellular metabolism and correlations of these mRNA expression data with the measured endpoints. Volcano plots are shown for Spearman *rho* and log-transformed *p* values for data from (A) ovarian fibroblasts and (B) tumor cells and (C) for the comparison of the mRNA expression of selected genes between ovarian fibroblasts and tumor cells. Significant correlations ($p < 0.05$) are shown in blue and are listed in the tables shown on the right side of the figure. The data points highlighted in the tables are assigned numbers, which are also highlighted in the corresponding scatterplots. There is no table provided for (C), as there were no significant correlations. The blue line indicates $p = 0.05$.

Fig. S3. Titration of the metformin response of tumor cell isolates by AlamarBlue assay readout. Titration was performed using the tumor cell isolates 22N, 20N, and 09N; metformin (dissolved

in water) was used at concentrations of 0.2, 0.5, 1.0, 2.0, 5.0, and 10.0 mM, with distilled water used as a control. The cells were incubated in complete medium (+Q, +G), in medium with depleted glucose (+Q, -G), or in medium with depleted glutamine (-Q +G). The data are presented as the relative absorbance, with the signal of control metformin-untreated cells cultivated in complete medium set as 1. All measurements were performed in triplicate; the mean values are shown.

Fig. S4. Changes in ATP levels and cell counts of ovarian fibroblasts following incubation with metformin under glucose- and glutamine-deprived conditions. The data shown represent matched measurements of ATP levels by CellTiter-Glo and counting of live cells by the trypan blue exclusion assay. The analyses included three randomly selected isolates of ovarian fibroblasts cultivated in complete medium (+Q, +G) or medium with depleted glucose (+Q, -G) or glutamine (-Q, +G) and with 10 mM, 2 mM or 0 mM metformin (Metf.). The cells for both assays were plated in parallel at the same time and from the same cell suspensions. The dots represent the means of three measurements from each patient-derived cell isolate and are shown relative to those of the isolates in complete (control) medium (+Q, +G) without metformin. Bars indicate the SEs.

Fig. S5. Examples of immunohistochemical staining for epithelial and mesenchymal markers and for markers of ER stress in HGSOC and adjacent ovaries. Representative images of E-cadherin, N-cadherin, vimentin, calnexin, CHOP, PERK, and eIF2α are shown.

Fig. S6. Western blot analysis of BiP, eIF2α, and P-eIF2α (S51). The data are shown for five isolates of nontransformed ovarian fibroblasts (individual patients are labeled with numbers followed by the letter "Z") and seven isolates of HGSOC cells (individual patients are labeled

with numbers followed by the letter "N"); β-actin was used as a loading control. The cells were incubated with DMSO (as a control), salubrinal, copper(II)-phenanthroline complexes C0 and C1, or a mixture of C1 with salubrinal or tunicamycin.

Fig. S7. Changes in P-eIF2α (S51) levels (relative to total eIF2α) following treatment with compounds affecting ER stress. The adherently grown primary cells isolated from the HGSOC tumors (tumor) (A) and surrounding nontransformed ovarian fibroblasts (fibroblasts) (B) were incubated with DMSO (as a control), salubrinal, copper(II)-phenanthroline complexes C0 and C1, a mixture of C1 with salubrinal, or tunicamycin, and the protein expression of BiP was analyzed by Western blotting. The identical color of individual data points indicates data from the same patient, allowing the matching of tumor cells and ovarian fibroblasts from the same patient. The data were normalized to that of β-actin. (C) Heatmap showing the relative levels of P-eIF2α (S51) relative to levels of total eIF2α in individual patients. The data are shown as log2 quantities relative to those of the DMSO control (0; white). Blue indicates decreased expression; red indicates increased expression.

Fig. S8. Western blot analysis of P-PERK (T982). The data are shown for three isolates of nontransformed ovarian fibroblasts (individual patients are labeled with numbers followed by the letter "Z"); β-actin was used as a loading control. The cells were incubated with DMSO (as a control), salubrinal, copper(II)-phenanthroline complexes C0 and C1, or a mixture of C1 with salubrinal or tunicamycin. As shown at the bottom of the figure, we analyzed P-PERK (T982) phosphorylation relative to total PERK (left), PERK expression relative to β-actin (right), and P-PERK (T982) phosphorylation relative to β-actin (bottom). The identical color of individual data points indicates data from the same patient, allowing the matching of tumor cells and ovarian

fibroblasts from the same patient. Note that the loading controls were identical to those used in the fourth batch of blots shown in Fig. S5.

Fig. S9. Changes in P-ULK1 (S757), P-AMPK (T172), and LC3B II/I levels following treatment with compounds that modulate ER stress. Adherently grown primary cells isolated from HGSOC tumors (tumor) (A,C,E) and surrounding nontransformed ovarian fibroblasts (fibroblasts) (B,D,F) were incubated with DMSO (as a control), salubrinal, copper(II)-phenanthroline complexes C0 and C1, a mixture of C1 with salubrinal, or tunicamycin. The levels of P-ULK1 (S757) relative to levels of total ULK1 (A,B), the levels of P-AMPK (T172) relative to levels of total AMPK (C,D), and the LC3B II/I levels (E,F) were analyzed by Western blotting. The identical color of individual data points indicates data from the same patient, allowing the matching of tumor cells and ovarian fibroblasts from the same patient. The expression levels were normalized to those of β-actin.

Fig. S10. Western blot analysis of P-ULK1 (S757), ULK1, P-AMPK (T172), AMPK, and LC3B. The data are shown for five isolates of nontransformed ovarian fibroblasts (individual patients are labeled with numbers followed by the letter "Z") and seven isolates of HGSOC cells (individual patients are labeled with numbers followed by the letter "N"); β-actin was used as a

loading control. The cells were incubated with DMSO (as a control), salubrinal, copper(II)-phenanthroline complexes C0 and C1, or a mixture of C1 with salubrinal or tunicamycin.

Fig. S11. Heatmap showing relative levels of VPS34 relative to those of β-actin in individual patients. The data are shown as log2 quantities relative to the DMSO control (0; white). Blue indicates decreased expression; red indicates increased expression.

Fig. S12. Changes in relative ATP levels following the incubation of tumor cells with erastin and TUDCA under glucose- and glutamine-deprived conditions. The analyses included eight randomly selected isolates of tumor cells cultivated in complete medium (+Q, +G) or medium with depleted glucose (+Q, -G) or glutamine (-Q, +G) and with 5 μM erastin and/or 500 μM TUDCA. Dots represent the means of three measurements of relative ATP levels assessed with CellTiter-Glo from each patient-derived cell isolate and are shown relative to those of the isolates in complete (control) medium (+Q, +G) without erastin and TUDCA. The bars indicate the SEs.

Fig. S13. Changes in relative ATP levels following the incubation of tumor cells with erastin or CB-839 and TUDCA under glucose- and glutamine-deprived conditions. The analyses included six randomly selected isolates of tumor cells cultivated in complete medium (+Q, +G) or medium with depleted glucose (+Q, -G) or glutamine (-Q, +G) and with 5 μM erastin or 1 μM CB-839 and/or 500 μM TUDCA. The dots represent the means of three independent replicates. Each well was assessed for reactive oxygen species (using CM-H_2DCFDA), mitochondrial superoxide (using MitoSOX), and intracellular reduced glutathione (using ThiolTracker), and these measurements were immediately followed by endpoint ATP measurement (with CellTiter-Glo). The data from each patient-derived cell isolate are shown relative to data of the isolates in

complete (control) medium (+Q, +G) without erastin, CB-839, and TUDCA. Bars indicate the SEs.

Fig. S14. Changes in relative ATP levels following the incubation of tumor cells with benzylserine and TUDCA under glutamine-deprived conditions. The analyses included five randomly selected isolates of tumor cells cultivated in complete medium (+Q, +G) or medium with depleted glutamine (-Q, +G) and with 10 mM benzylserine and/or 500 µM TUDCA. The dots represent the means of three independent replicates. The data represent endpoint ATP measurements (with CellTiter-Glo) after 24 h of incubation with the respective compounds. The data from each patient-derived cell isolate are shown relative to data of the isolates in complete (control) medium (+Q, +G) without benzylserine and TUDCA. The bars indicate the SEs.

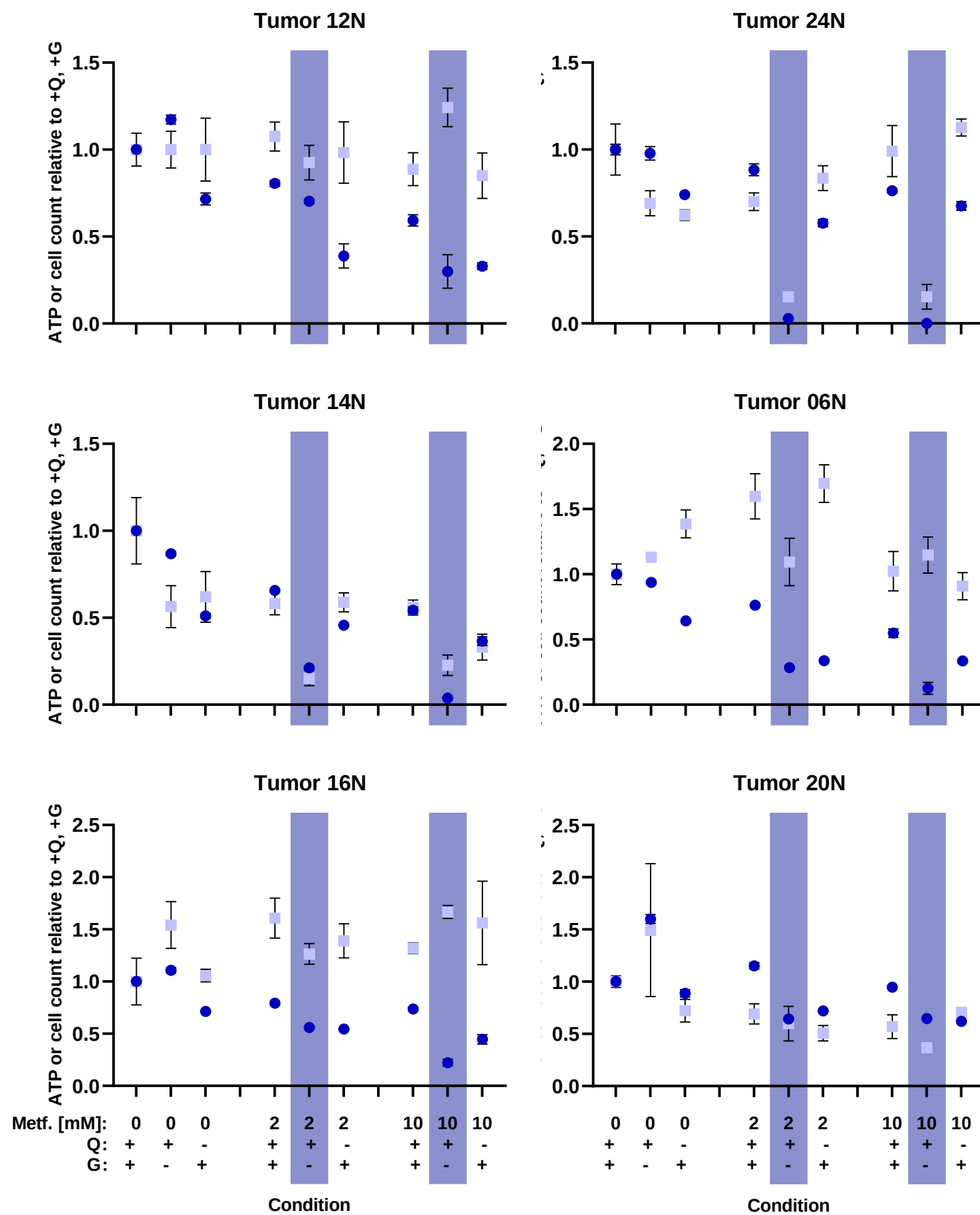
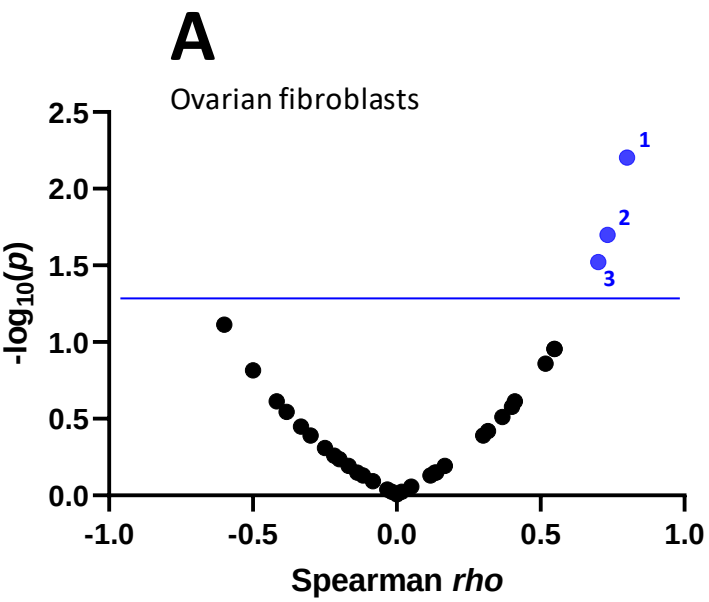
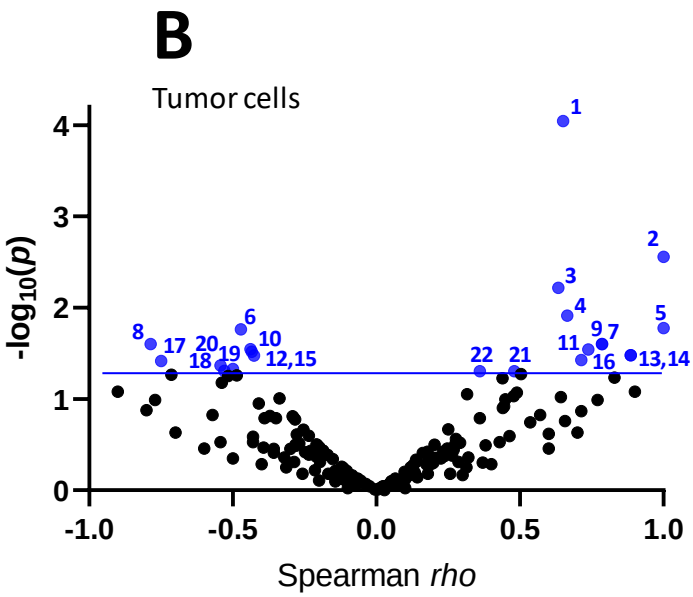

Tumor 12N
Tumor 24N
Tumor 14N
Tumor 06N
Tumor 16N
Tumor 20N
ATP or cell count relative to +Q, +G
Metf. [mM]: 0 0 0 2 2 2 10 10 10
Q: + + - + + - + + -
G: + - + + - + + - +
Condition
ATP relative to +Q, +G
Cell count relative to +Q, +G

Fig. S1



	Variable 1	Variable 2	p	rho
1	*IDO1*	AlamarBlue, absolute, -Q, +G	0.006	0.80
2	*IDO1*	AlamarBlue, absolute, +Q +G	0.020	0.73
3	*HK1*	*HK2*	0.030	0.70



	Variable 1	Variable 2	p	rho
1	*HK1*	*HK2*	0.000	0.65
2	*APAF1*	AlamarBlue, absolute, +Q -G	0.003	1.00
3	*SCD*	*SLC71A11*	0.006	0.63
4	*FABP4*	CellTiter, relative, +Q -G	0.012	0.67
5	*ASNS*	AlamarBlue, absolute, +Q +G	0.017	1.00
6	*HK2*	CellTiter, relative, +Q -G	0.017	-0.47
7	*ASNS*	*GLS1*	0.025	0.79
8	*PSAT1*	*HK2*	0.025	-0.79
9	*PSAT1*	*SCD*	0.025	0.79
10	*HK2*	CellTiter, absolute, +Q -G	0.028	-0.44
11	*APAF1*	*IDO1*	0.029	0.74
12	*HK1*	CellTiter, relative, +Q -G	0.030	-0.43
13	*TBP*	CellTiter, absolute, +Q +G	0.033	0.89
14	*APAF1*	AlamarBlue, relative, +Q -G	0.033	0.89
15	*HK2*	CellTiter, absolute, -Q +G	0.034	-0.43
16	*HK1*	*APAF1*	0.037	0.71
17	*ADPGK*	*GLS1*	0.038	-0.75
18	*SCD*	CellTiter, absolute, -Q +G	0.043	-0.54
19	*HK2*	*FABP4*	0.047	-0.50
20	*SCD*	CellTiter, absolute, +Q +G	0.049	-0.53
21	*HK1*	*SCD*	0.050	0.48
22	*HK1*	*SLC71A11*	0.050	0.36

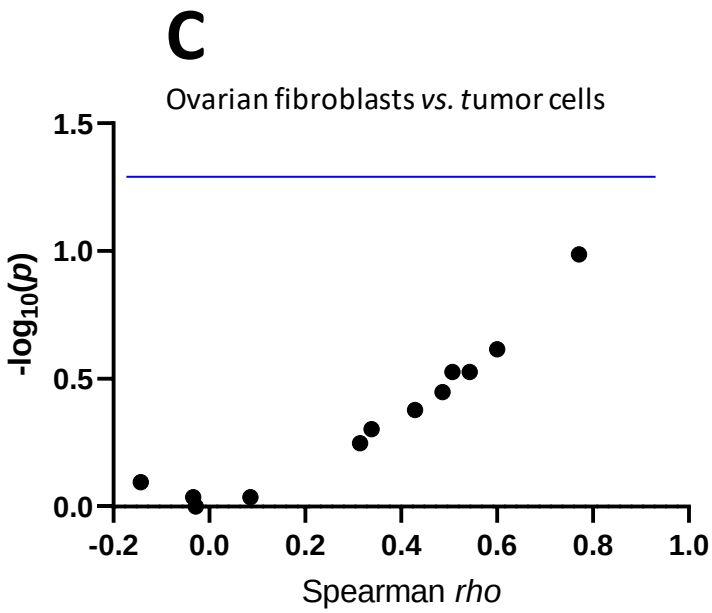


Fig. S2

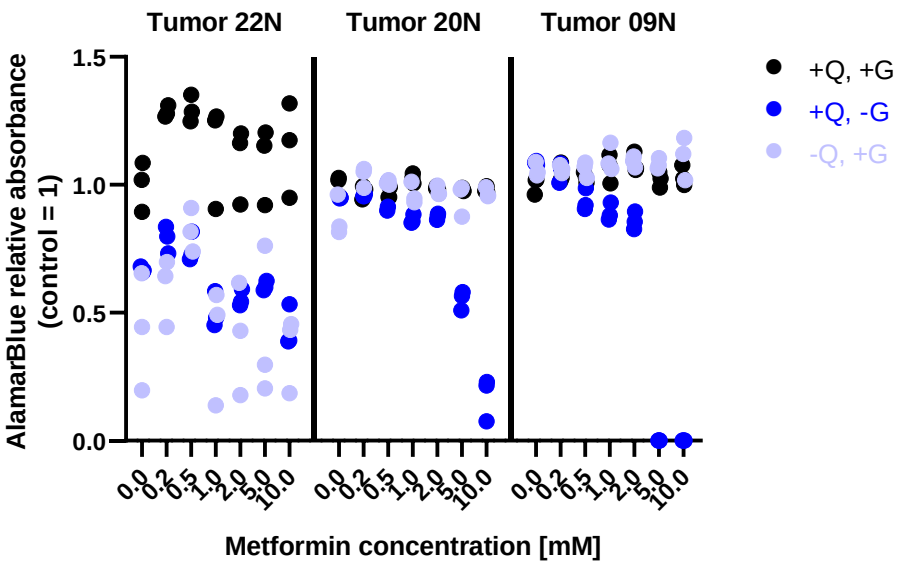

Tumor 22N
Tumor 20N
Tumor 09N
AlamarBlue relative absorbance (control = 1)
1.5
1.0
0.5
0.0
0.0
0.2
0.5
1.0
2.0
5.0
10.0
Metformin concentration [mM]
+Q, +G
+Q, -G
-Q, +G

Fig. S3

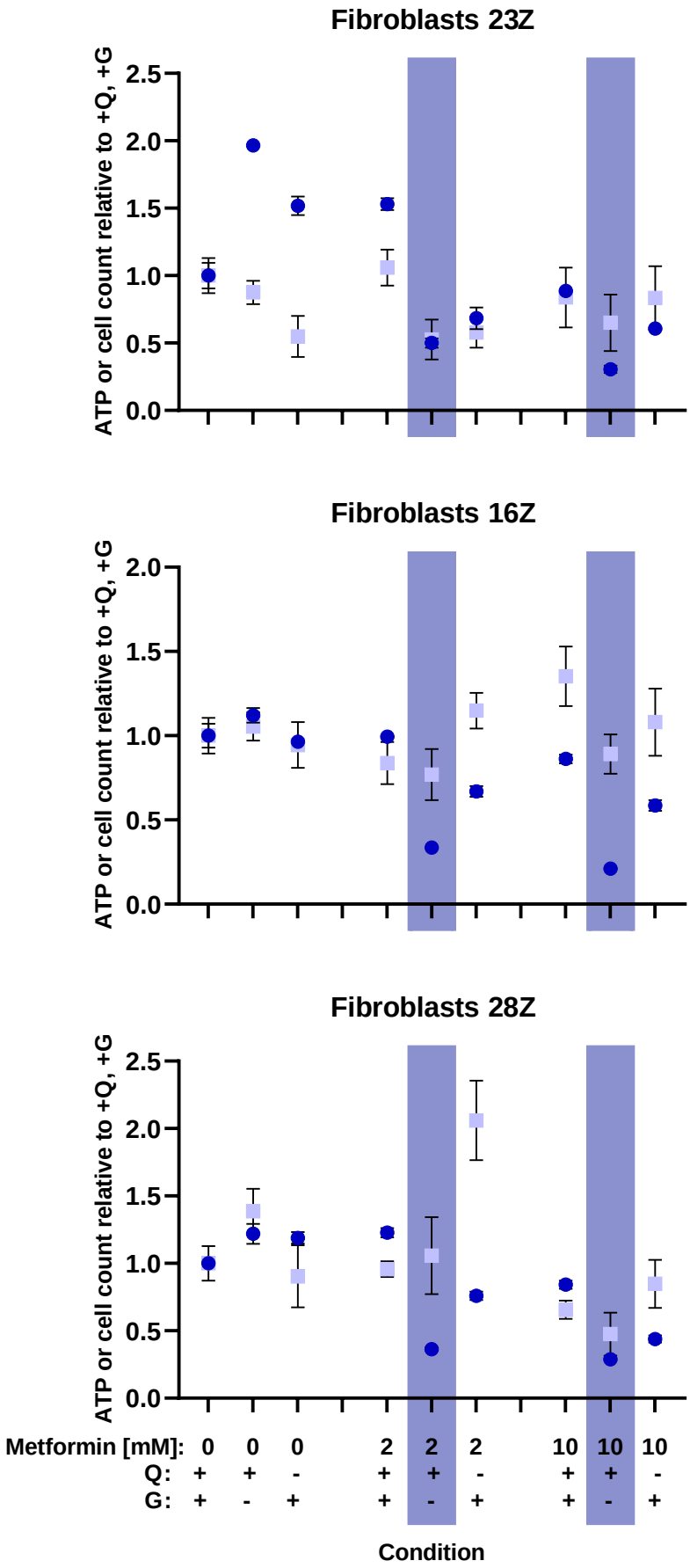

Fibroblasts 23Z
Fibroblasts 16Z
Fibroblasts 28Z
ATP or cell count relative to +Q, +G
2.5
2.0
1.5
1.0
0.5
0.0
Metformin [mM]: 0 0 0 2 2 2 10 10 10
Q: + + - + + - + + -
G: + - + + - + + - +
Condition
ATP relative to +Q, +G
Cell count relative to +Q, +G

Fig. S4

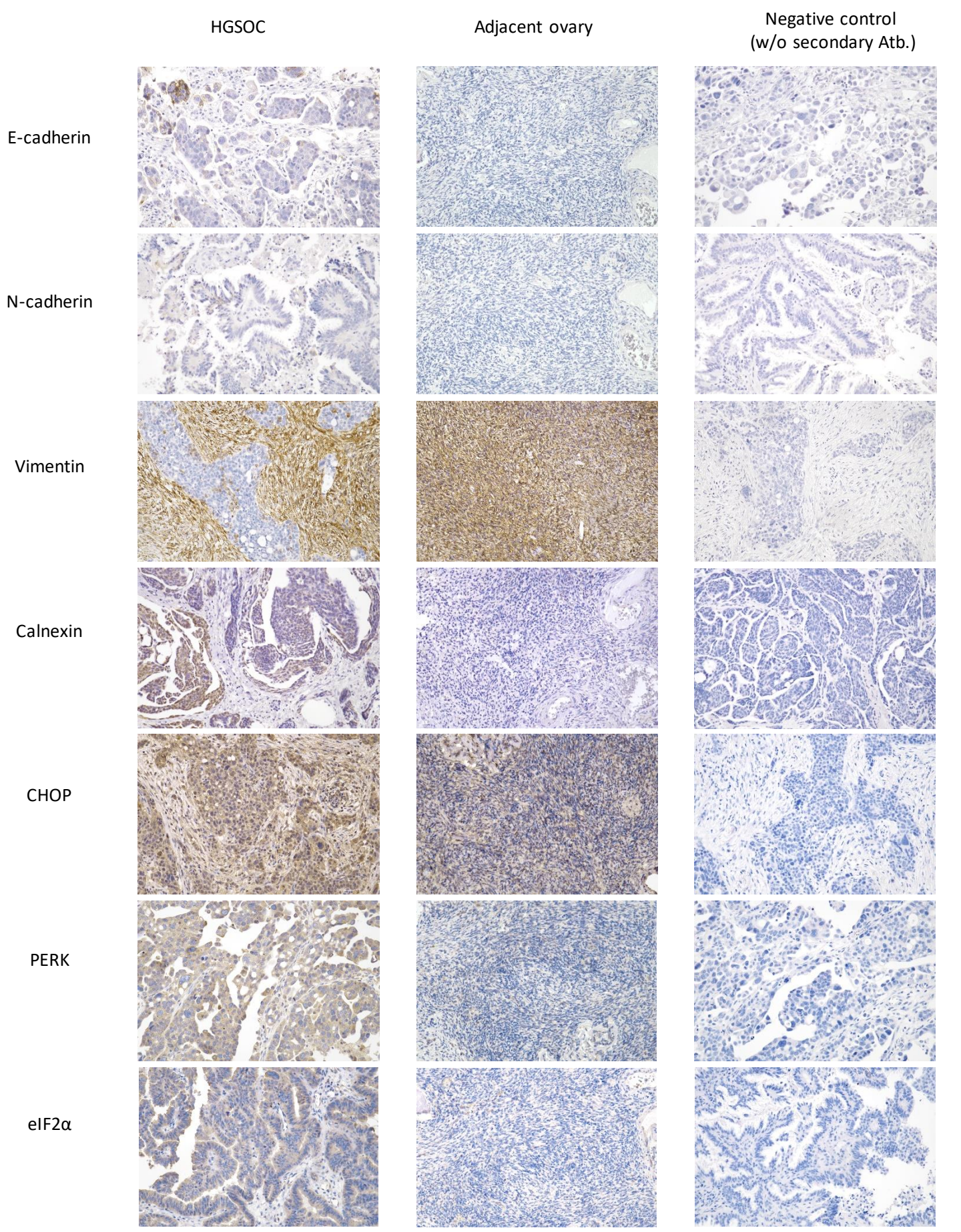

HGSOC
Adjacent ovary
Negative control
(w/o secondary Atb.)
E-cadherin
N-cadherin
Vimentin
Calnexin
CHOP
PERK
eIF2α

Fig. S5

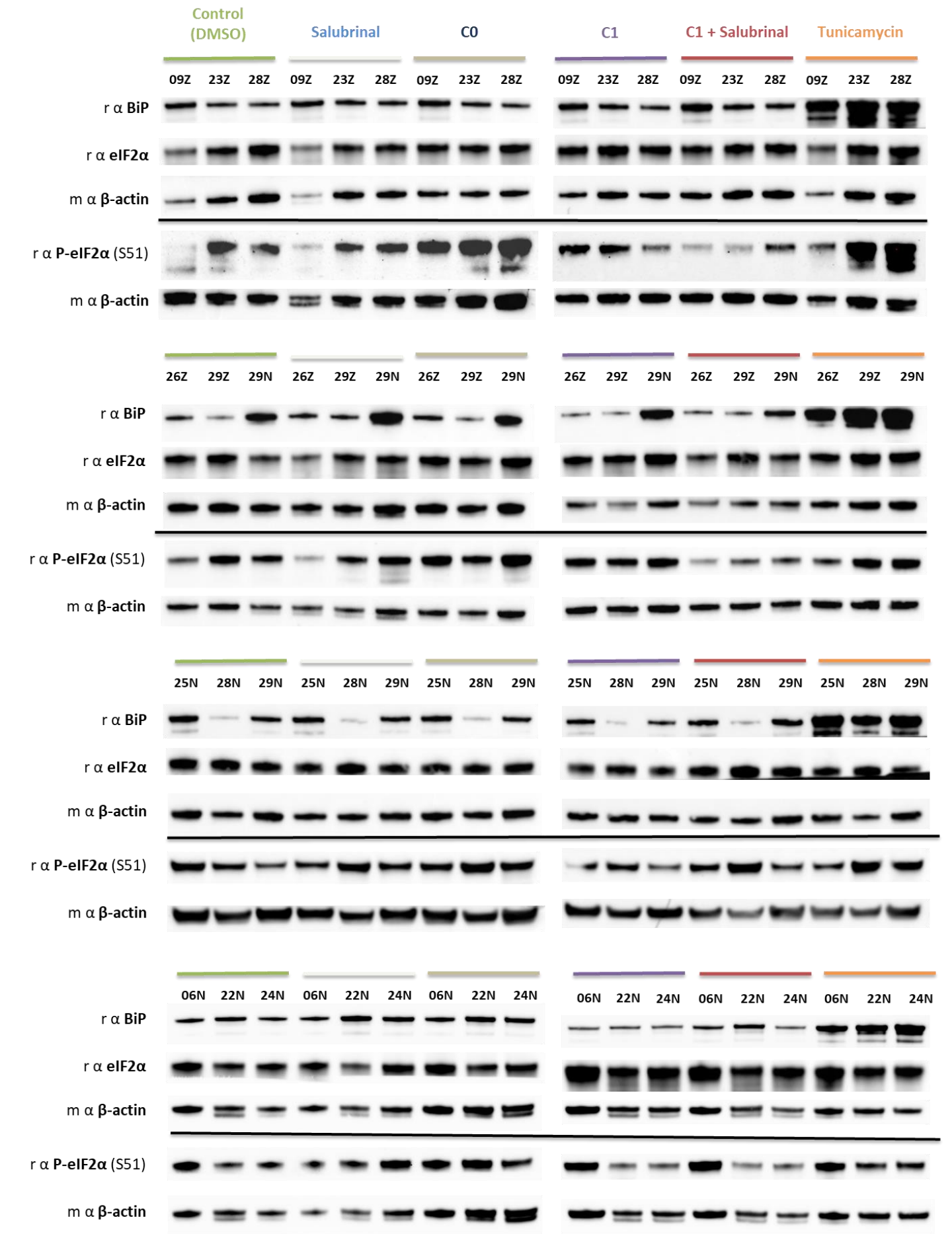

Control (DMSO)
Salubrinal
C0
C1
C1 + Salubrinal
Tunicamycin
09Z 23Z 28Z 09Z 23Z 28Z 09Z 23Z 28Z 09Z 23Z 28Z 09Z 23Z 28Z 09Z 23Z 28Z
r α BiP
r α eIF2α
m α β-actin
r α P-eIF2α (S51)
m α β-actin
26Z 29Z 29N 26Z 29Z 29N 26Z 29Z 29N 26Z 29Z 29N 26Z 29Z 29N 26Z 29Z 29N
r α BiP
r α eIF2α
m α β-actin
r α P-eIF2α (S51)
m α β-actin
25N 28N 29N 25N 28N 29N 25N 28N 29N 25N 28N 29N 25N 28N 29N 25N 28N 29N
r α BiP
r α eIF2α
m α β-actin
r α P-eIF2α (S51)
m α β-actin
06N 22N 24N 06N 22N 24N 06N 22N 24N 06N 22N 24N 06N 22N 24N 06N 22N 24N
r α BiP
r α eIF2α
m α β-actin
r α P-eIF2α (S51)
m α β-actin

Fig. S6

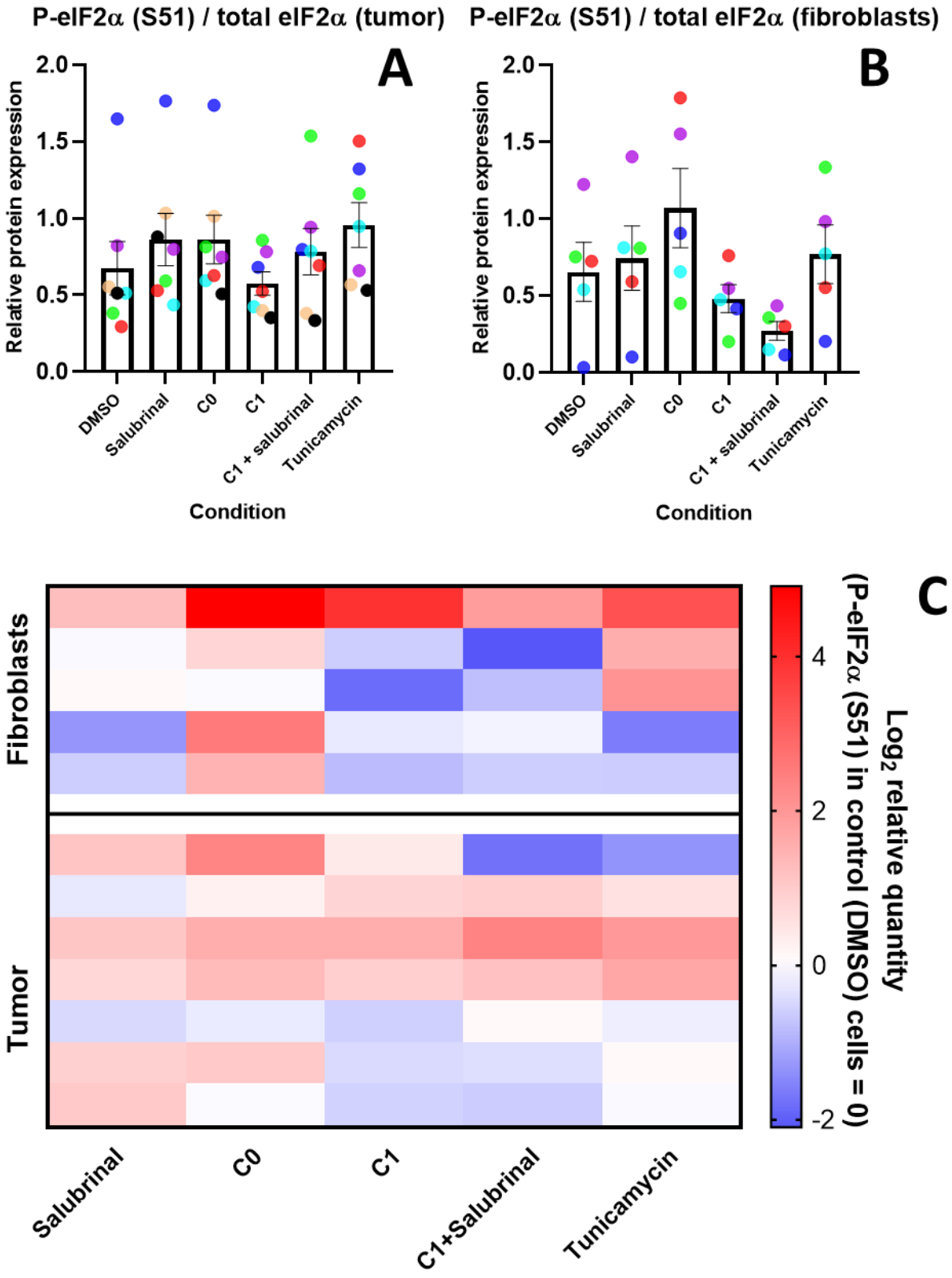
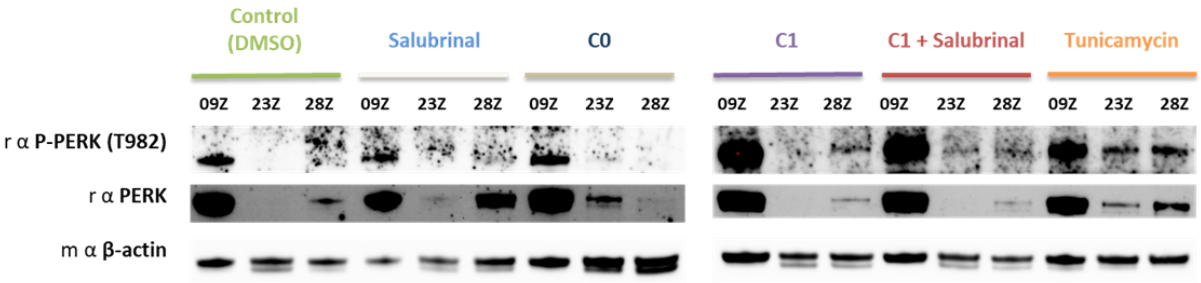
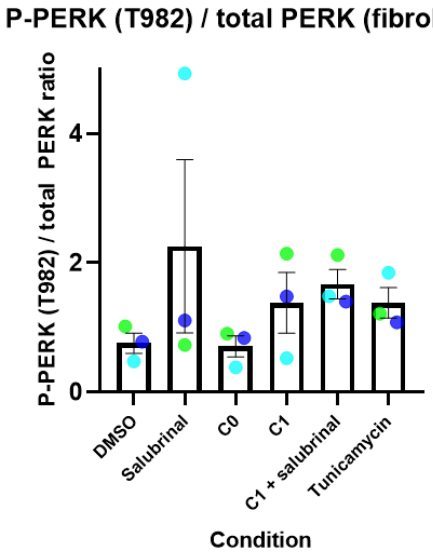
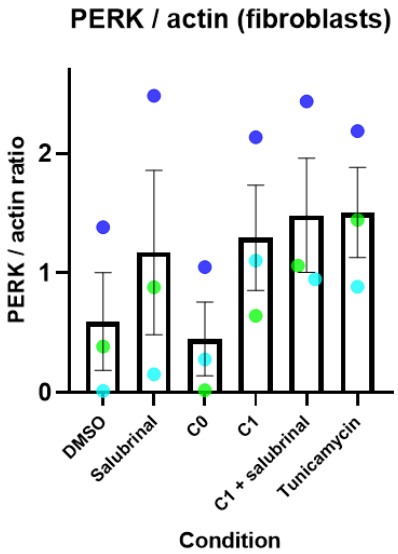

P-eIF2α (S51) / total eIF2α (tumor)
A
Relative protein expression
2.0
1.5
1.0
0.5
0.0
DMSO
Salubrinal
C0
C1
C1 + salubrinal
Tunicamycin
Condition
P-eIF2α (S51) / total eIF2α (fibroblasts)
B
Relative protein expression
2.0
1.5
1.0
0.5
0.0
DMSO
Salubrinal
C0
C1
C1 + salubrinal
Tunicamycin
Condition
C
Fibroblasts
Tumor
Salubrinal
C0
C1
C1+Salubrinal
Tunicamycin
Log2 relative quantity
(P-eIF2α (S51) in control (DMSO) cells = 0)
4
2
0
-2

Fig. S7


Control (DMSO)
Salubrinal
C0
C1
C1 + Salubrinal
Tunicamycin
09Z 23Z 28Z 09Z 23Z 28Z 09Z 23Z 28Z 09Z 23Z 28Z 09Z 23Z 28Z 09Z 23Z 28Z
r α P-PERK (T982)
r α PERK
m α β-actin


P-PERK (T982) / total PERK (fibroblasts)
P-PERK (T982) / total PERK ratio
0
2
4
DMSO
Salubrinal
C0
C1
C1 + salubrinal
Tunicamycin
Condition


PERK / actin (fibroblasts)
PERK / actin ratio
0
1
2
DMSO
Salubrinal
C0
C1
C1 + salubrinal
Tunicamycin
Condition

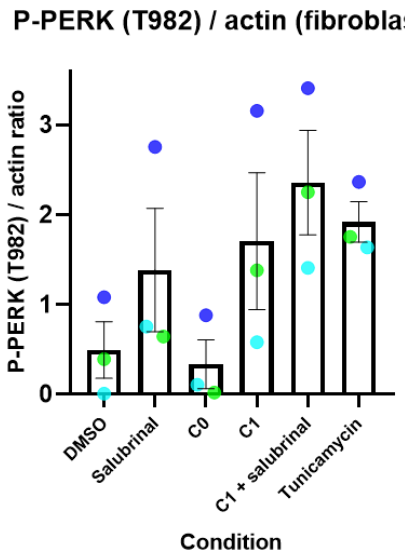

P-PERK (T982) / actin (fibroblasts)
P-PERK (T982) / actin ratio
0
1
2
3
DMSO
Salubrinal
C0
C1
C1 + salubrinal
Tunicamycin
Condition

Fig. S8

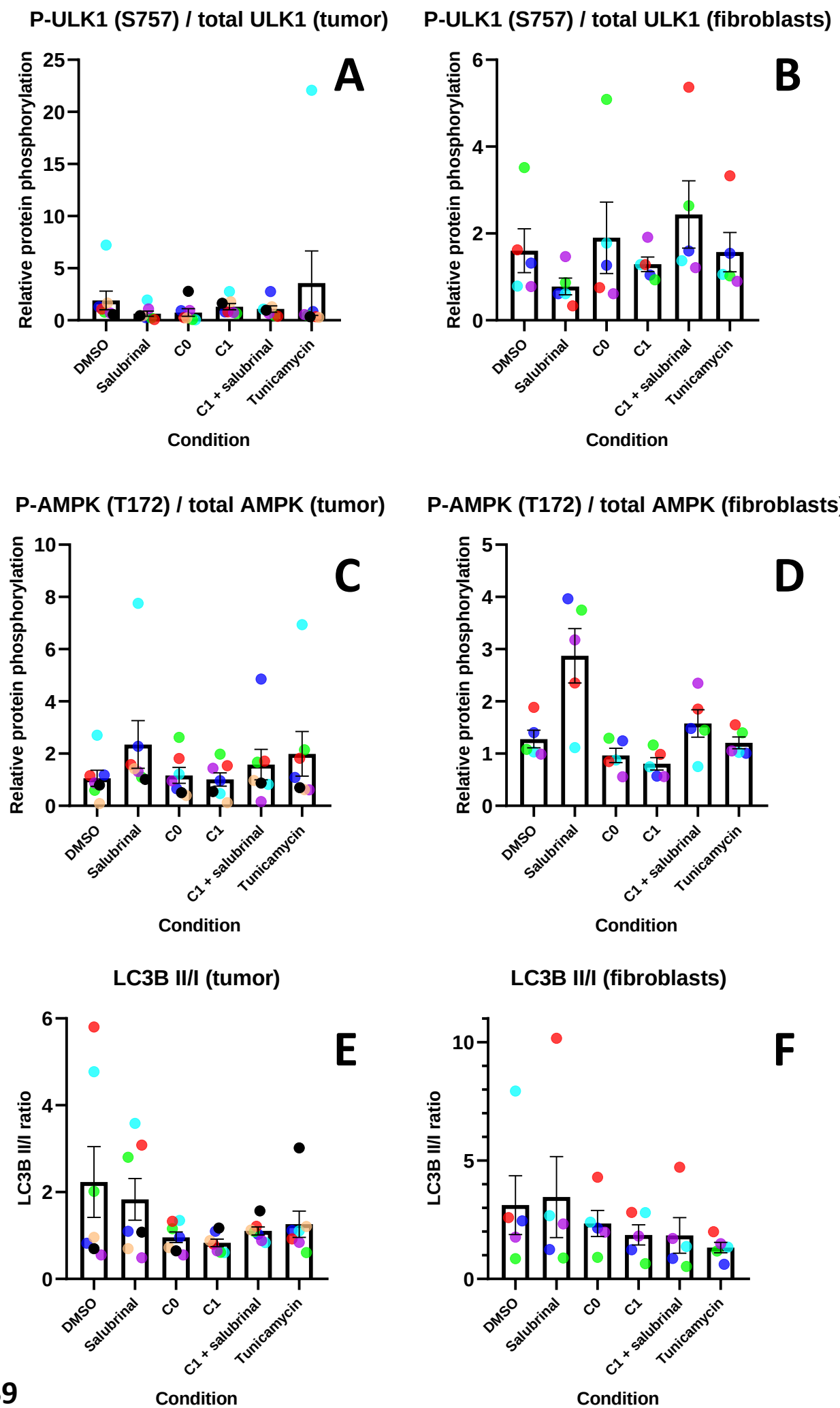

P-ULK1 (S757) / total ULK1 (tumor)
A
Relative protein phosphorylation
25
20
15
10
5
0
DMSO
Salubrinal
C0
C1
C1 + salubrinal
Tunicamycin
Condition
P-ULK1 (S757) / total ULK1 (fibroblasts)
B
Relative protein phosphorylation
6
4
2
0
DMSO
Salubrinal
C0
C1
C1 + salubrinal
Tunicamycin
Condition
P-AMPK (T172) / total AMPK (tumor)
C
Relative protein phosphorylation
10
8
6
4
2
0
DMSO
Salubrinal
C0
C1
C1 + salubrinal
Tunicamycin
Condition
P-AMPK (T172) / total AMPK (fibroblasts)
D
Relative protein phosphorylation
5
4
3
2
1
0
DMSO
Salubrinal
C0
C1
C1 + salubrinal
Tunicamycin
Condition
LC3B II/I (tumor)
E
LC3B II/I ratio
6
4
2
0
DMSO
Salubrinal
C0
C1
C1 + salubrinal
Tunicamycin
Condition
LC3B II/I (fibroblasts)
F
LC3B II/I ratio
10
5
0
DMSO
Salubrinal
C0
C1
C1 + salubrinal
Tunicamycin
Condition

Fig. S9

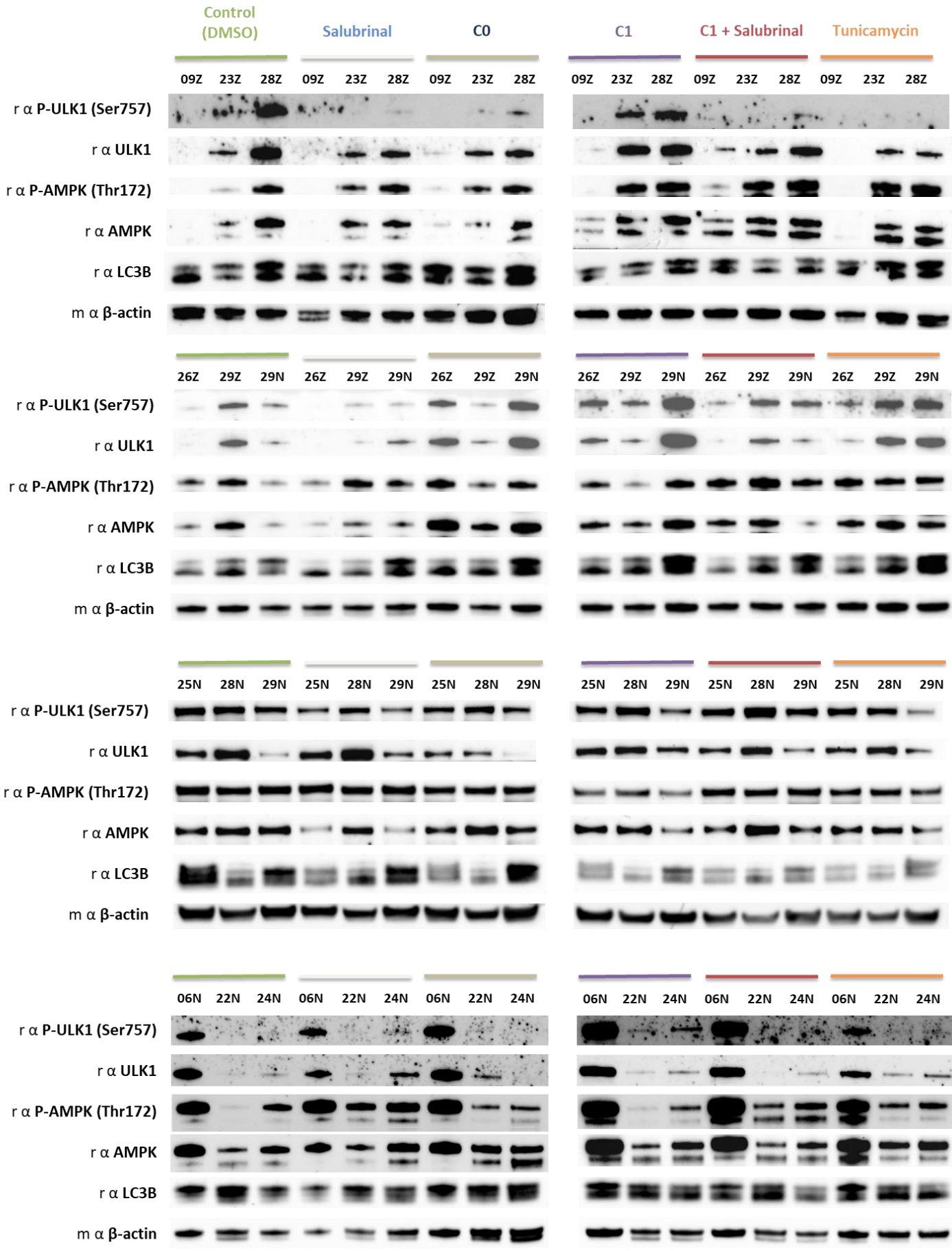

Control (DMSO)
Salubrinal
C0
C1
C1 + Salubrinal
Tunicamycin
09Z 23Z 28Z 09Z 23Z 28Z 09Z 23Z 28Z 09Z 23Z 28Z 09Z 23Z 28Z
r α P-ULK1 (Ser757)
r α ULK1
r α P-AMPK (Thr172)
r α AMPK
r α LC3B
m α β-actin
26Z 29Z 29N 26Z 29Z 29N 26Z 29Z 29N 26Z 29Z 29N 26Z 29Z 29N
r α P-ULK1 (Ser757)
r α ULK1
r α P-AMPK (Thr172)
r α AMPK
r α LC3B
m α β-actin
25N 28N 29N 25N 28N 29N 25N 28N 29N 25N 28N 29N 25N 28N 29N
r α P-ULK1 (Ser757)
r α ULK1
r α P-AMPK (Thr172)
r α AMPK
r α LC3B
m α β-actin
06N 22N 24N 06N 22N 24N 06N 22N 24N 06N 22N 24N 06N 22N 24N
r α P-ULK1 (Ser757)
r α ULK1
r α P-AMPK (Thr172)
r α AMPK
r α LC3B
m α β-actin

Fig. S10

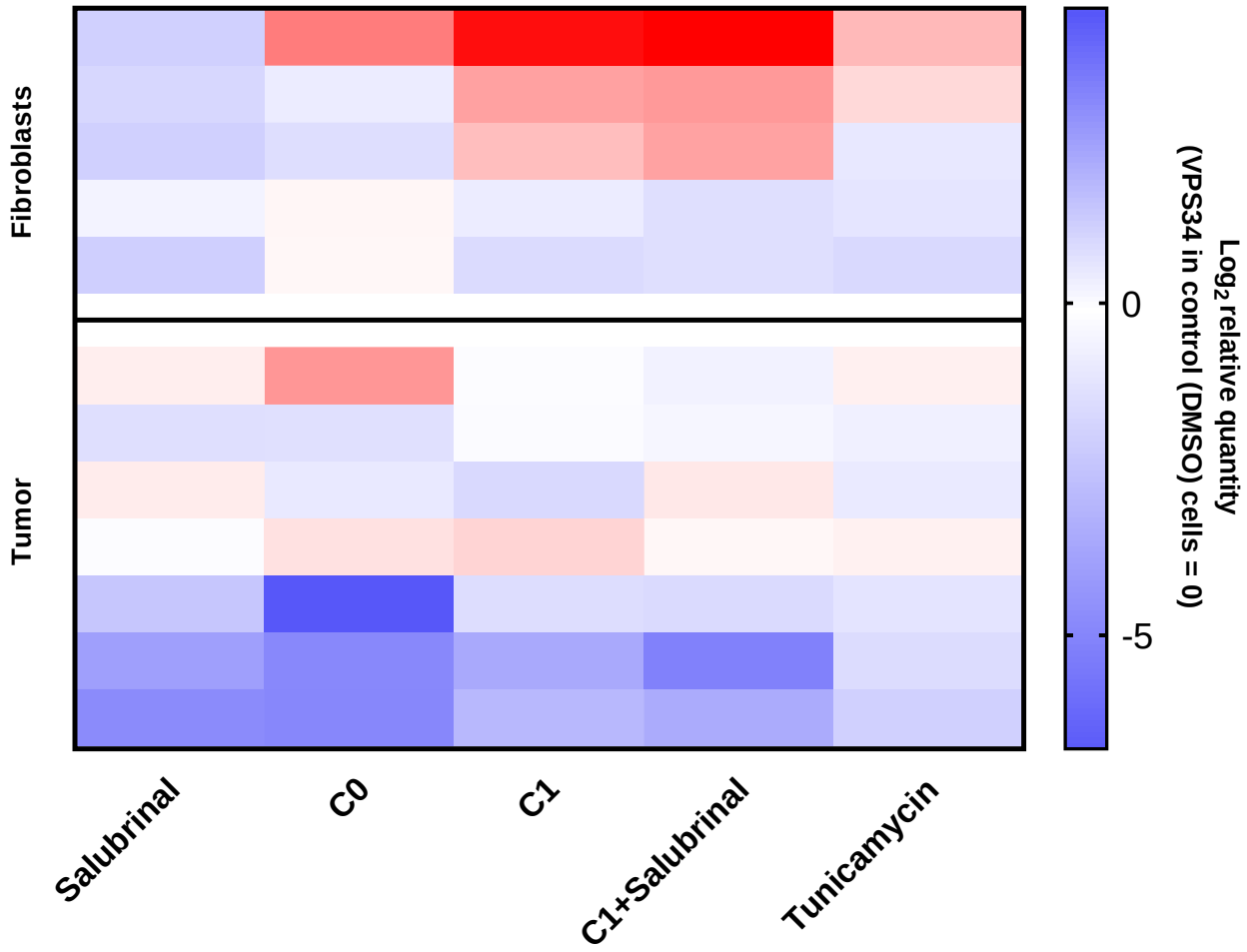

Fibroblasts
Tumor
Salubrinal
C0
C1
C1+Salubrinal
Tunicamycin
0
-5
Log2 relative quantity
(VPS34 in control (DMSO) cells = 0)

Fig. S11

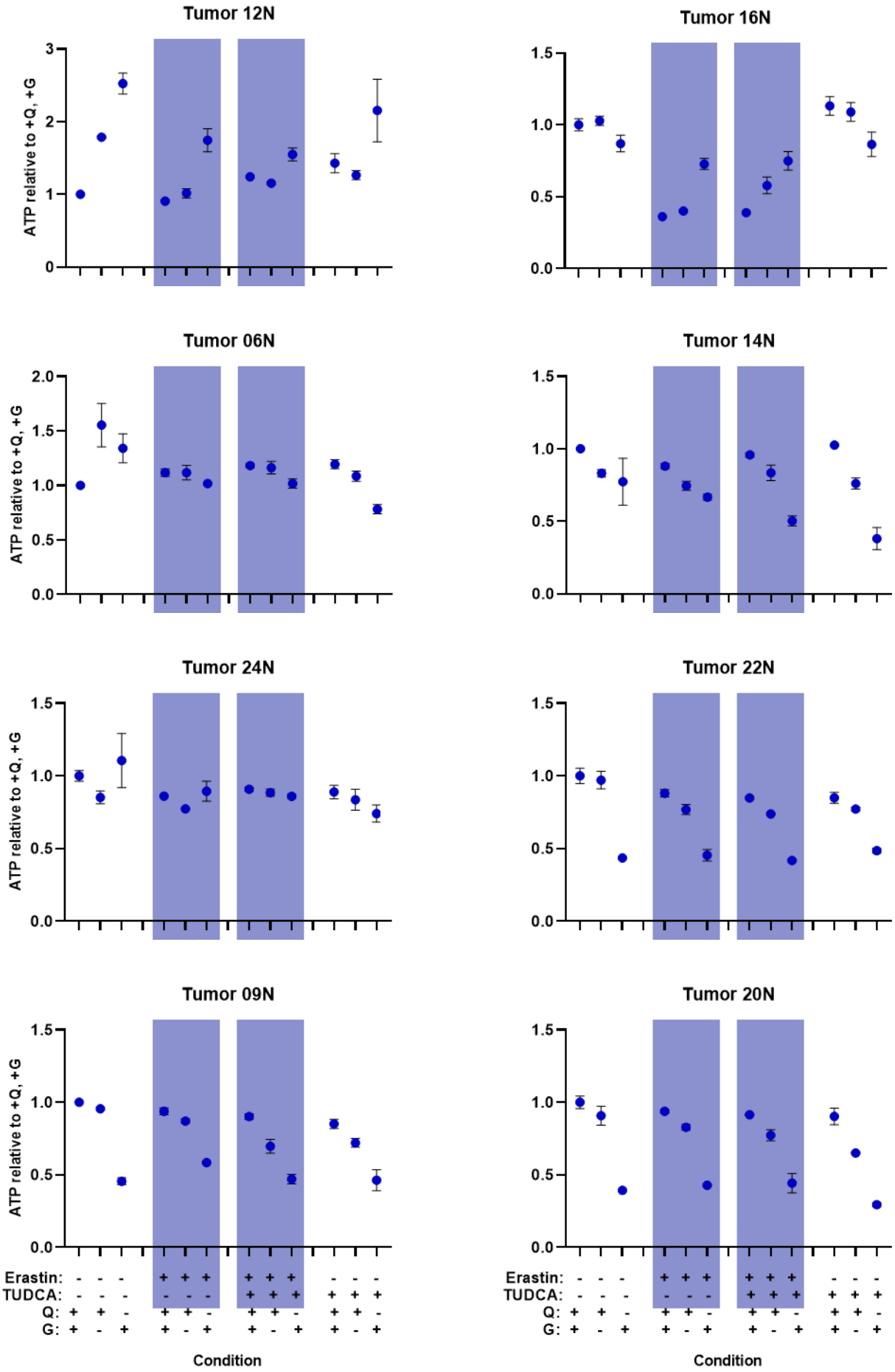

Tumor 12N
Tumor 16N
Tumor 06N
Tumor 14N
Tumor 24N
Tumor 22N
Tumor 09N
Tumor 20N
ATP relative to +Q, +G
Erastin:
TUDCA:
Q:
G:
Condition

Fig. S12

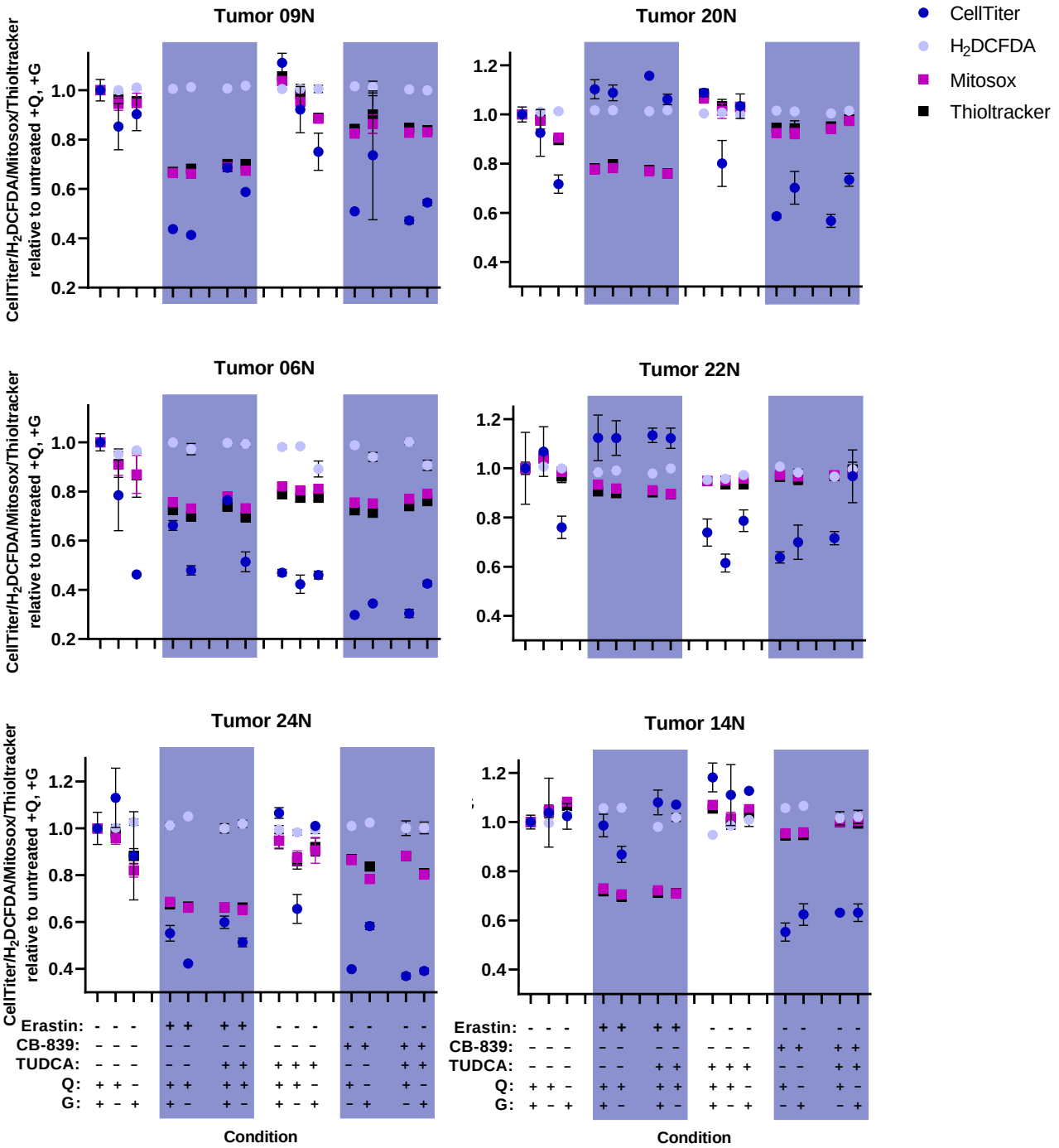

Tumor 09N
Tumor 20N
Tumor 06N
Tumor 22N
Tumor 24N
Tumor 14N
CellTiter
H2DCFDA
Mitosox
Thioltracker
CellTiter/H2DCFDA/Mitosox/Thioltracker relative to untreated +Q, +G
Erastin:
CB-839:
TUDCA:
Q:
G:
Condition

Fig. S13

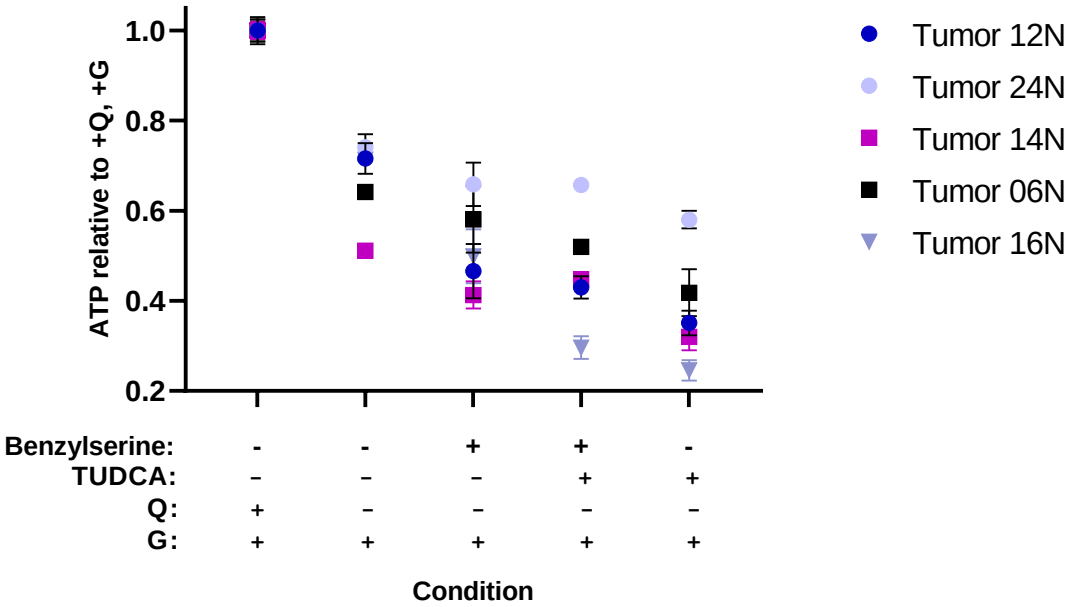

ATP relative to +Q, +G
1.0
0.8
0.6
0.4
0.2
Benzylserine: - - + + -
TUDCA: – – – + +
Q: + – – – –
G: + + + + +
Condition
Tumor 12N
Tumor 24N
Tumor 14N
Tumor 06N
Tumor 16N

Fig. S14