

## Figure 1

Fig.1b One-way ANOVA:  $F=24.93$ ,  $p<0.0001$  (n=3 for primary hPSC #1, 2, primary hPSC and mPSC; n=4 for hPSC#2, IMR90 and MiaPaCa2; n=6 for 8988T, hPSC#1 and control media).

Tukey's multiple comparisons test	p Value		
ctrl media vs. 8988T CM	0.9881	MiaPaCa CM vs. Primary mPSC	0.0012
ctrl media vs. MiaPaCa CM	0.9997	MiaPaCa CM vs. mPSC	0.0002
ctrl media vs. IMR90 CM	0.3703	IMR90 CM vs. Primary hPSC #1	0.5948
ctrl media vs. Primary hPSC #1	0.0044	IMR90 CM vs. Primary hPSC #2	0.9768
ctrl media vs. Primary hPSC #2	0.0497	IMR90 CM vs. hPSC #1	0.0386
ctrl media vs. hPSC #1	< 0.0001	IMR90 CM vs. hPSC #2	0.1544
ctrl media vs. hPSC #2	0.0002	IMR90 CM vs. Primary mPSC	0.4294
ctrl media vs. Primary mPSC	0.0020	IMR90 CM vs. mPSC	0.1437
ctrl media vs. mPSC	0.0003	Primary hPSC #1 vs. Primary hPSC #2	0.9976
8988T CM vs. MiaPaCa CM	0.8622	Primary hPSC #1 vs. hPSC #1	0.9886
8988T CM vs. IMR90 CM	0.8978	Primary hPSC #1 vs. hPSC #2	0.9996
8988T CM vs. Primary hPSC #1	0.0381	Primary hPSC #1 vs. Primary mPSC	> 0.9999
8988T CM vs. Primary hPSC #2	0.2774	Primary hPSC #1 vs. mPSC	0.9973
8988T CM vs. hPSC #1	0.0002	Primary hPSC #2 vs. hPSC #1	0.6227
8988T CM vs. hPSC #2	0.0022	Primary hPSC #2 vs. hPSC #2	0.8711
8988T CM vs. Primary mPSC	0.0190	Primary hPSC #2 vs. Primary mPSC	0.9845
8988T CM vs. mPSC	0.0031	Primary hPSC #2 vs. mPSC	0.8077
MiaPaCa CM vs. IMR90 CM	0.1985	hPSC #1 vs. hPSC #2	> 0.9999
MiaPaCa CM vs. Primary hPSC #1	0.0025	hPSC #1 vs. Primary mPSC	0.9990
MiaPaCa CM vs. Primary hPSC #2	0.0253	hPSC #1 vs. mPSC	> 0.9999
MiaPaCa CM vs. hPSC #1	< 0.0001	hPSC #2 vs. Primary mPSC	> 0.9999
MiaPaCa CM vs. hPSC #2	0.0001	hPSC #2 vs. mPSC	> 0.9999
		Primary mPSC vs. mPSC	0.9998

Fig.1c One-way ANOVA:  $F=15.34$ ,  $p<0.0001$  (n=4)

Tukey's multiple comparisons test	p Value		
Boiled hPSC CM vs. Boiled 8988T CM	0.0011	Boiled 8988T CM vs. 8988T CM	0.1944
Boiled hPSC CM vs. hPSC CM	0.5944	Boiled 8988T CM vs. ctrl media	0.8871
Boiled hPSC CM vs. 8988T CM	0.0908	hPSC CM vs. 8988T CM	0.0055
Boiled hPSC CM vs. ctrl media	0.0064	hPSC CM vs. ctrl media	0.0004
Boiled 8988T CM vs. hPSC CM	< 0.0001	8988T CM vs. ctrl media	0.6378

Fig.1d Unpaired two-tailed T-test (n=3)

Ala	hPSC #1 CM vs 8988T CM	0.0175	Asp	hPSC #1 CM vs 8988T CM	0.0351
	Double CM vs hPSC#1 CM	0.0177		hPSC #1 CM vs 8988T CM	0.0238
	8988T cells + hPSC CM vs 8988T CM	0.0193		hPSC #1 CM vs 8988T CM	0.0423

Fig.1e One-way ANOVA:  $F=11.50$ ,  $p<0.0001$  (n=4)

Tukey's multiple comparisons test	p Value		
1mM NeAAs vs. 1mM Ala	0.9914	1mM NeAAs vs. 1mM Cys	0.0106
1mM NeAAs vs. 1mM Asp	0.0387	1mM NeAAs vs. hPSC CM	0.8053
1mM NeAAs vs. 1mM Gly	0.0004	1mM NeAAs vs. 8988T CM	0.0005
		1mM NeAAs vs. ctrl media	< 0.0001
		1mM Ala vs. 1mM Asp	0.1943

1mM Ala vs. 1mM Gly	0.0029	1mM Gly vs. 1mM Cys	0.8737
1mM Ala vs. 1mM Cys	0.0645	1mM Gly vs. hPSC CM	0.0151
1mM Ala vs. hPSC CM	0.9966	1mM Gly vs. 8988T CM	> 0.9999
1mM Ala vs. 8988T CM	0.0032	1mM Gly vs. ctrl media	0.8823
1mM Ala vs. ctrl media	0.0001	1mM Cys vs. hPSC CM	0.2409
1mM Asp vs. 1mM Gly	0.5602	1mM Cys vs. 8988T CM	0.8894
1mM Asp vs. 1mM Cys	0.9990	1mM Cys vs. ctrl media	0.1831
1mM Asp vs. hPSC CM	0.5392	hPSC CM vs. 8988T CM	0.0165
1mM Asp vs. 8988T CM	0.5849	hPSC CM vs. ctrl media	0.0006
1mM Asp vs. ctrl media	0.0601	8988T CM vs. ctrl media	0.8661

Fig.1f Unpaired two-tailed T-test (n=3)

hPSC#1 CM vs 8988T CM	<0.0001
hPSC#1 CM vs tu8902 CM	<0.0001
8988T CM vs tu8902 CM	0.2346

## Figure2

Fig.2b One-way ANOVA: F=162.8, p<0.0001 (n=3)

Tukey's multiple comparisons test	P Value		
hPSC CM shGFP vs. 8T CM shGFP	< 0.0001	8T CM shGFP vs. hPSC CM shGPT2	< 0.0001
hPSC CM shGFP vs. hPSC CM shGPT1	0.0082	8T CM shGFP vs. 8T CM shGPT2	0.9344
hPSC CM shGFP vs. 8T CM shGPT1	< 0.0001	hPSC CM shGPT1 vs. 8T CM shGPT1	< 0.0001
hPSC CM shGFP vs. hPSC CM shGPT2	0.0014	hPSC CM shGPT1 vs. hPSC CM shGPT2	0.8750
hPSC CM shGFP vs. 8T CM shGPT2	< 0.0001	hPSC CM shGPT1 vs. 8T CM shGPT2	< 0.0001
8T CM shGFP vs. hPSC CM shGPT1	< 0.0001	8T CM shGPT1 vs. hPSC CM shGPT2	< 0.0001
8T CM shGFP vs. 8T CM shGPT1	0.8573	8T CM shGPT1 vs. 8T CM shGPT2	0.3695
		hPSC CM shGPT2 vs. 8T CM shGPT2	< 0.0001

Fig.2c One-way ANOVA: F=13.27, p<0.0001 (n=3)

Tukey's multiple comparisons test	p Value		
shGFP ctrl vs shGFP + 8T CM	0.9997	shGFP + hPSC CM vs shGPT1 1 + 8T CM	< 0.0001
shGFP ctrl vs shGFP + hPSC CM	< 0.0001	shGFP + hPSC CM vs shGPT1 1 + hPSC CM	0.0625
shGFP ctrl vs shGPT1 1 + 8T CM	0.4029	shGFP + hPSC CM vs shGPT1 2 + 8T CM	< 0.0001
shGFP ctrl vs shGPT1 1 + hPSC CM	0.0615	shGFP + hPSC CM vs shGPT2 1 + 8T CM	0.0369
shGFP ctrl vs shGPT1 2 + 8T CM	0.9884	shGFP + hPSC CM vs shGPT2 1 + hPSC CM	0.0711
shGFP ctrl vs shGPT1 2 + hPSC CM	0.1018	shGFP + hPSC CM vs shGPT2 2 + 8T CM	0.0004
shGFP ctrl vs shGPT2 1 + 8T CM	0.9758	shGFP + hPSC CM vs shGPT2 2 + hPSC CM	0.0179
shGFP ctrl vs shGPT2 1 + hPSC CM	0.0540	shGPT1 1 + 8T CM vs shGPT1 1 + hPSC CM	0.0003
shGFP ctrl vs shGPT2 2 + 8T CM	0.9649	shGPT1 1 + 8T CM vs shGPT1 2 + 8T CM	0.9528
shGFP ctrl vs shGPT2 2 + hPSC CM	0.1881	shGPT1 1 + 8T CM vs shGPT1 2 + hPSC CM	0.0005
shGFP + 8T CM vs shGFP + hPSC CM	0.0001	shGPT1 1 + 8T CM vs shGPT2 1 + 8T CM	0.0463
shGFP + 8T CM vs shGPT1 1 + 8T CM	0.1310	shGPT1 1 + 8T CM vs shGPT2 1 + hPSC CM	0.0002
shGFP + 8T CM vs shGPT1 1 + hPSC CM	0.2234	shGPT1 1 + 8T CM vs shGPT2 2 + 8T CM	0.0400
shGFP + 8T CM vs shGPT1 2 + 8T CM	0.7890	shGPT1 1 + 8T CM vs shGPT2 2 + hPSC CM	0.0010
shGFP + 8T CM vs shGPT1 2 + hPSC CM	0.3334	shGPT1 1 + hPSC CM vs shGPT1 2 + 8T CM	0.0057
shGFP + 8T CM vs shGPT2 1 + 8T CM	> 0.9999	shGPT1 1 + hPSC CM vs shGPT1 2 + hPSC CM	> 0.9999
shGFP + 8T CM vs shGPT2 1 + hPSC CM	0.2005		
shGFP + 8T CM vs shGPT2 2 + 8T CM	> 0.9999	shGPT1 1 + hPSC CM vs shGPT2 1 + 8T CM	0.4817
shGFP + 8T CM vs shGPT2 2 + hPSC CM	0.5193	shGPT1 1 + hPSC CM vs shGPT2 1 + hPSC	> 0.9999

CM		shGPT1 2 + hPSC CM vs shGPT2 2 + 8T CM	0.6786
shGPT1 1 + hPSC CM vs shGPT2 2 + 8T CM	0.5236	shGPT1 2 + hPSC CM vs shGPT2 2 + hPSC CM	> 0.9999
shGPT1 1 + hPSC CM vs shGPT2 2 + hPSC CM	> 0.9999	shGPT2 1 + 8T CM vs shGPT2 1 + hPSC CM	0.4446
shGPT1 2 + 8T CM vs shGPT2 1 + hPSC CM	0.0101	shGPT2 1 + 8T CM vs shGPT2 2 + 8T CM	> 0.9999
shGPT1 2 + 8T CM vs shGPT2 1 + 8T CM	0.4781	shGPT2 1 + 8T CM vs shGPT2 2 + hPSC CM	0.8237
shGPT1 2 + 8T CM vs shGPT2 1 + hPSC CM	0.0050	shGPT2 1 + hPSC CM vs shGPT2 2 + 8T CM	0.4854
shGPT1 2 + 8T CM vs shGPT2 2 + 8T CM	0.4375	shGPT2 1 + hPSC CM vs shGPT2 2 + hPSC CM	0.9998
shGPT1 2 + 8T CM vs shGPT2 2 + hPSC CM	0.0212	shGPT2 2 + 8T CM vs shGPT2 2 + hPSC CM	0.8558
shGPT1 2 + hPSC CM vs shGPT2 1 + 8T CM	0.6362		
shGPT1 2 + hPSC CM vs shGPT2 1 + hPSC CM	> 0.9999		

Fig.2d One-way ANOVA:  $F=38.33$ ,  $p<0.0001$  (n=4)

Tukey's multiple comparisons test	P Value		
ctrl media vs. 1mM Ala	< 0.0001	1mM Ala vs. 8988T	0.0003
ctrl media vs. 4mM Ala	< 0.0001	4mM Ala vs. 10mM Ala	> 0.9999
ctrl media vs. 10mM Ala	< 0.0001	4mM Ala vs. 1mM Pyr	0.0046
ctrl media vs. 1mM Pyr	< 0.0001	4mM Ala vs. hPSC #1	0.0069
ctrl media vs. hPSC #1	< 0.0001	4mM Ala vs. 8988T	< 0.0001
ctrl media vs. 8988T	> 0.9999	10mM Ala vs. 1mM Pyr	0.0028
1mM Ala vs. 4mM Ala	0.0023	10mM Ala vs. hPSC #1	0.0041
1mM Ala vs. 10mM Ala	0.0014	10mM Ala vs. 8988T	< 0.0001
1mM Ala vs. 1mM Pyr	> 0.9999	1mM Pyr vs. hPSC #1	> 0.9999
1mM Ala vs. hPSC #1	0.9987	1mM Pyr vs. 8988T	0.0001
		hPSC #1 vs. 8988T	< 0.0001

### Figure3

Fig.3b Two-way ANOVA (n=32 for hPSC; n=38 for 8988T co-culture; n=41 for tu8902 co-culture, n=24 for Mia co-culture)

Source of Variation	% of total variation	P value
Interaction	4.384	0.0023
Row Factor	8.996	< 0.0001
Column Factor	9.493	< 0.0001

Tukey's multiple comparisons test	p Value	autolysosomes	
<b>autophagosomes</b>		hPSC vs. 8988T co-culture	0.0002
hPSC vs. 8988T co-culture	0.6702	hPSC vs. 8902 co-culture	0.0043
hPSC vs. 8902 co-culture	0.2225	hPSC vs. Mia co-culture	< 0.0001
hPSC vs. Mia co-culture	0.6866	8988T co-culture vs. 8902 co-culture	0.7582
8988T co-culture vs. 8902 co-culture	0.8522	8988T co-culture vs. Mia co-culture	0.1368
8988T co-culture vs. Mia co-culture	0.9996	8902 co-culture vs. Mia co-culture	0.0131
8902 co-culture vs. Mia co-culture	0.9319		

Fig.3c Two-way ANOVA (n=65 cells for hPSC CM, n=50 cells for 8988T CM, n=61 cells for 8902 CM, n=62 cells for MiaPaca CM)

Source of Variation	% of total variation	P value
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Interaction	4.384	0.0023		
Row Factor	8.996	< 0.0001		
Column Factor	9.493	< 0.0001		
Tukey's multiple comparisons test	p Value		<b>autolysosomes</b>	
<b>autophagosomes</b>				
hPSC cm vs. 8988T cm	0.6342		hPSC cm vs. 8988T cm	< 0.0001
hPSC cm vs. 8902 cm	0.1158		hPSC cm vs. 8902 cm	< 0.0001
hPSC cm vs. MiaPaca cm	0.5668		hPSC cm vs. MiaPaca cm	< 0.0001
8988T cm vs. 8902 cm	0.8224		8988T cm vs. 8902 cm	0.5164
8988T cm vs. MiaPaca cm	> 0.9999		8988T cm vs. MiaPaca cm	0.6667
8902 cm vs. MiaPaca cm	0.7868		8902 cm vs. MiaPaca cm	0.9938

Fig.3d One-way ANOVA:  $F=13.45$ ,  $p<0.0001$  (n=6 for ATG7 #1, #2; n=5 for ctrl, GFP, 8988T; n=3 for ATG5 #1, #2)

Tukey's multiple comparisons test	p Value	8988T vs. hPSC - ShATG7 #2	0.9998
Ctrl vs. 8988T	0.4329	hPSC - ShGFP vs. hPSC - ShATG5	< 0.0001
Ctrl vs. hPSC - ShGFP	< 0.0001	hPSC - ShGFP vs. hPSC - ShATG5 #2	< 0.0001
Ctrl vs. hPSC - ShATG5	0.9973	hPSC - ShGFP vs. hPSC - ShATG7	< 0.0001
Ctrl vs. hPSC - ShATG5 #2	> 0.9999	hPSC - ShGFP vs. hPSC - ShATG7 #2	0.0001
Ctrl vs. hPSC - ShATG7	0.6639	hPSC - ShATG5 vs. hPSC - ShATG5 #2	0.9998
Ctrl vs. hPSC - ShATG7 #2	0.2169	hPSC - ShATG5 vs. hPSC - ShATG7	0.9814
8988T vs. hPSC - ShGFP	< 0.0001	hPSC - ShATG5 vs. hPSC - ShATG7 #2	0.7322
8988T vs. hPSC - ShATG5	0.8976	hPSC - ShATG5 #2 vs. hPSC - ShATG7	0.8726
8988T vs. hPSC - ShATG5 #2	0.692	hPSC - ShATG5 #2 vs. hPSC - ShATG7 #2	0.4721
8988T vs. hPSC - ShATG7	0.9991	hPSC - ShATG7 vs. hPSC - ShATG7 #2	0.975

Fig.3e One-way ANOVA:  $F=12.13$ ,  $p=0.0078$  (n=3)

Tukey's multiple comparisons test	P Value
hPSC ShGFP cm (vs. 8988T cm) vs. hPSC ShATG5 cm (vs. 8988T cm)	0.0300
hPSC ShGFP cm (vs. 8988T cm) vs. ctrl media	0.0075
hPSC ShATG5 cm (vs. 8988T cm) vs. ctrl media	0.4641

Fig.3f One-way ANOVA:  $F=4.883$ ,  $p=0.0551$  (n=3)

Tukey's multiple comparisons test	p Value
8T ShGFP cell treated w/ hPSC ShGFP cm (vs. treated with 8988T cm) vs. 8T ShGFP cells treated w/ hPSC ShATG5 cm (vs treated with 8988T cm)	0.1856
8T ShGFP cell treated w/ hPSC ShGFP cm (vs. treated with 8988T cm) vs. ctrl media	0.0497
8T ShGFP cells treated w/ hPSC ShATG5 cm (vs treated with 8988T cm) vs. ctrl media	0.5801

**Figure 4****Fig.4a** One-way ANOVA:  $F=25.53$ ,  $p<0.0001$  (n=7)

Tukey's multiple comparisons test	p Value	hpsc cm vs. 10% serum	0.9834
8t cm vs. hpsc cm	< 0.0001	hpsc cm vs. 0% + ala	0.9611
8t cm vs. hpsc Shatg5 cm	0.9999	hpsc Shatg5 cm vs. hpsc ShATG7 cm	0.9955
8t cm vs. hpsc ShATG7 cm	0.9735	hpsc Shatg5 cm vs. 10% serum	< 0.0001
8t cm vs. 10% serum	< 0.0001	hpsc Shatg5 cm vs. 0% + ala	< 0.0001
8t cm vs. 0% + ala	< 0.0001	hpsc ShATG7 cm vs. 10% serum	< 0.0001
hpsc cm vs. hpsc Shatg5 cm	< 0.0001	hpsc ShATG7 cm vs. 0% + ala	< 0.0001
hpsc cm vs. hpsc ShATG7 cm	< 0.0001	10% serum vs. 0% + ala	> 0.9999

**Fig.4b** One-way ANOVA:  $F=9.564$ ,  $p<0.0001$  (n=5 for hPSC alone; n=10 animals for the remaining groups)

Tukey's multiple comparisons test	P Value	8T+hPSC-ShGFP vs. 8T+hPSC-ShATG7	0.0564
8988T vs. 8T+hPSC-ShGFP	< 0.0001	8T+hPSC-ShGFP vs. hPSC shGFP	< 0.0001
8988T vs. 8T+hPSC-ShATG5	0.0226	8T+hPSC-ShATG5 vs. 8T+hPSC-ShATG7	0.9977
8988T vs. 8T+hPSC-ShATG7	0.0494	8T+hPSC-ShATG5 vs. hPSC shGFP	0.0257
8988T vs. hPSC shGFP	0.9833	8T+hPSC-ShATG7 vs. hPSC shGFP	0.0484
8T+hPSC-ShGFP vs. 8T+hPSC-ShATG5	0.1136		

**Fig.4c** Log-rank (Mantel-Cox) test, comparisons by pairs (n=10)

8988T vs. 8988T -shGFP: Chi square=18.38, p-value&lt;0.0001

8988T +hPSC-shGFP vs. 8988T +hPSC-shATG5: Chi square=4.906, p-value=0.0268

8988T +hPSC-shGFP vs. 8988T +hPSC-shATG7: Chi square=5.414, p-value=0.02

8988T +hPSC-shATG5 vs. 8988T +hPSC-shATG7: Chi square=0.5554, p-value=0.4561

**Fig.4d** One-way ANOVA:  $F=9.526$ ,  $p<0.0001$  (n=5 for mPSC alone; n=10 for remaining groups)

Tukey's multiple comparisons test	p Value	shATG7	
iKRAS vs. iKRAS + mPSC-shGFP	< 0.0001	iKRAS + mPSC-shGFP vs. mPSC - ShGFP	0.0007
iKRAS vs. iKRAS + mPSC-shATG5	> 0.9999	iKRAS + mPSC-shATG5 vs. iKRAS + mPSC-shATG7	0.982
iKRAS vs. iKRAS + mPSC-shATG7	0.9675	iKRAS + mPSC-shATG5 vs. mPSC - ShGFP	0.9959
iKRAS vs. mPSC - ShGFP	0.9984	iKRAS + mPSC-shATG7 vs. mPSC - ShGFP	0.9252
iKRAS + mPSC-shGFP vs. iKRAS + mPSC-shATG5	0.0001		
iKRAS + mPSC-shGFP vs. iKRAS + mPSC-	0.0007		

**Fig.4e** Log-rank (Mantel-Cox) test, comparisons by pairs (n=10)

IKRAS-PDAC vs. IKRAS-PDAC+mPSC-shGFP: Chi square=6.255, p-value=0.0124

IKRAS-PDAC+mPSC-shGFP vs. IKRAS-PDAC+mPSC-shATG5: Chi square=5.322, p-value=0.0211

IKRAS-PDAC+mPSC-shGFP vs. IKRAS-PDAC+mPSC-shATG7: Chi square=8.847, p-value=0.0029

IKRAS-PDAC+mPSC-shATG5 vs. IKRAS-PDAC+mPSC-shATG7: Chi square= 0.006147, p-value=0.9375

### Extended Data Figure 1

EFig.1a One-way ANOVA, F=14.71, p<0.0001 (n=5)

Tukey's multiple comparisons test	P Value		
ctrl media vs. 8902 cm	0.9547	8902 cm vs. hPSC cm	0.0011
ctrl media vs. hPSC cm	0.0004	8902 cm vs. hPSC #2 cm	0.0050
ctrl media vs. hPSC #2 cm	0.0018	hPSC cm vs. hPSC #2 cm	0.8709

EFig.1b One-way ANOVA, F=82.15, p<0.0001 (n=3 for MiaPaCa2, hPSC#2, n=4 for ctrl and hPSC#1)

Tukey's multiple comparisons test	p Value		
ctrl vs. MiaPaCa CM	0.0314	MiaPaCa CM vs. hPSC #1 CM	< 0.0001
ctrl vs. hPSC #1 CM	< 0.0001	MiaPaCa CM vs. hPSC #2 CM	< 0.0001
ctrl vs. hPSC #2 CM	< 0.0001	hPSC #1 CM vs. hPSC #2 CM	0.2459

EFig.1c One-way ANOVA, F=7.421, p=0.0239 (n=3)

Tukey's multiple comparisons test	P Value
Ctrl vs. Panc-1	0.9220
Ctrl vs. hPSC#1	0.0293
Panc-1 vs. hPSC#1	0.0466

EFig.1e One-way ANOVA, F=1.910, p=0.1222 (n=3 for MiaPaCa, IMR90, primary hPSC#1, #2; n=6 for 8988T, hPSC#1 and ctrl)

Tukey's multiple comparisons test	P Value		
8988T vs. MiaPaca	0.7590	IMR90 vs. primary hPSC#1	0.9997
8988T vs. IMR90	0.9955	IMR90 vs. primary hPSC#2	0.8772
8988T vs. primary hPSC#1	0.9316	IMR90 vs. hPSC#1	0.9997
8988T vs. primary hPSC#2	0.4219	IMR90 vs. ctrl media	> 0.9999
8988T vs. hPSC#1	0.8721	primary hPSC#1 vs. primary hPSC#2	0.9781
8988T vs. ctrl media	0.9995	primary hPSC#1 vs. hPSC#1	> 0.9999
MiaPaca vs. IMR90	0.5557	primary hPSC#1 vs. ctrl media	0.9891
MiaPaca vs. primary hPSC#1	0.3351	primary hPSC#2 vs. hPSC#1	0.9432
MiaPaca vs. primary hPSC#2	0.0743	primary hPSC#2 vs. ctrl media	0.6247
MiaPaca vs. hPSC#1	0.2124	hPSC#1 vs. ctrl media	0.9797
MiaPaca vs. ctrl media	0.5571		

EFig.1f One-way ANOVA, F=89.58, p<0.0001 (n=3)

Tukey's multiple comparisons test	p Value	8T vs. hPSC #1	< 0.0001
ctrl vs. 8T	0.9529	8T vs. hPSC #2	< 0.0001
ctrl vs. hPSC #1	< 0.0001	hPSC #1 vs. hPSC #2	0.3632
ctrl vs. hPSC #2	< 0.0001		

EFig.1g One-way ANOVA,  $F=33.17$ ,  $p<0.0001$  (n=3)

Tukey's multiple comparisons test	p Value	Tu8902 vs. hPSC #1	0.0041
Ctrl vs. Tu8902	0.3036	Tu8902 vs. hPSC #2	0.0007
Ctrl vs. hPSC #1	0.0005	hPSC #1 vs. hPSC #2	0.4367
Ctrl vs. hPSC #2	0.0001		

EFig.1j One-way ANOVA,  $F=0.2288$ ,  $p=0.8752$  (n=5)

Tukey's multiple comparisons test	p Value	8988T CM vs. 8902 CM	0.8433
Ctrl vs. 8988T CM	0.9798	8988T CM vs. hPSC	0.9618
Ctrl vs. 8902 CM	0.9717	8902 CM vs. hPSC	0.9862
Ctrl vs. hPSC	0.9997		

EFig.1k One-way ANOVA,  $F=16.61$ ,  $p=0.0009$  (n=4)

Tukey's multiple comparisons test	P Value	Boiled hPSC CM vs. hPSC CM	0.9535
ctrl media vs. Boiled hPSC CM	0.0004	Boiled hPSC CM vs. 8902 CM	0.0041
ctrl media vs. Boiled 8902 CM	0.7942	Boiled 8902 CM vs. hPSC CM	0.0009
ctrl media vs. hPSC CM	0.0001	Boiled 8902 CM vs. 8902 CM	> 0.9999
ctrl media vs. 8902 CM	0.7451	hPSC CM vs. 8902 CM	0.0011
Boiled hPSC CM vs. Boiled 8902 CM	0.0035		

EFig.1l One-way ANOVA,  $F=17.19$ ,  $p<0.0001$  (n=4)

Tukey's multiple comparisons test	P Value	hPSC boiled CM vs. hPSC CM	0.9361
ctrl vs. hPSC boiled CM	0.0002	hPSC boiled CM vs. Mia CM	0.0368
ctrl vs. Mia boiled CM	0.4337	Mia boiled CM vs. hPSC CM	0.0009
ctrl vs. hPSC CM	< 0.0001	Mia boiled CM vs. Mia CM	0.7802
ctrl vs. Mia CM	0.0708	hPSC CM vs. Mia CM	0.0084
hPSC boiled CM vs. Mia boiled CM	0.0040		

EFig.1m One-way ANOVA,  $F=15.38$ ,  $p=0.0012$  (n=4)

Tukey's multiple comparisons test	P Value
ctrl vs. 8T F/T	0.2262
ctrl vs. hPSC F/T	0.0011
8T F/T vs. hPSC F/T	0.0133

EFig.1n One-way ANOVA,  $F=17.92$ ,  $p=0.0007$  (n=3)

Tukey's multiple comparisons test	p Value	ctrl vs. hPSC >3KDa	0.0175
ctrl vs. hPSC	0.0007	hPSC vs. hPSC <3KDa	0.8819
ctrl vs. hPSC <3KDa	0.0015	hPSC vs. hPSC >3KDa	0.0996



hPSC <3KDa vs. hPSC >3KDa 0.2701

### Extended Data Figure 2

EFig.2b Unpaired two-tailed T-test, p-values (n=3)

	hPSC CM vs 8988T CM	hPSC CM vs double CM	8988T CM vs double CM
alanine	0.0097	0.0176	0.7665
asparagine	0.0621	0.3931	0.0125
glutamate	0.0024	0.0108	0.4243
proline	0.0013	0.0890	0.0024

EFig.2c One-way ANOVA, F=39.93, p<0.0001 (n=3)

Tukey's multiple comparisons test	P Value	NeAAs 1mM vs. 1mM Asp	0.0002
ctrl vs. NeAAs 1mM	< 0.0001	NeAAs 1mM vs. 1mM Gly	0.0001
ctrl vs. 1mM Ala	< 0.0001	1mM Ala vs. 1mM Asp	0.0059
ctrl vs. 1mM Asp	0.0544	1mM Ala vs. 1mM Gly	0.0024
ctrl vs. 1mM Gly	0.1419	1mM Asp vs. 1mM Gly	0.9670
NeAAs 1mM vs. 1mM Ala	0.1667		

EFig.2e Unpaired two-tailed T-test, p-values (n=3):

hPSC #1 CM vs 8988T CM	0.0001
Double CM vs hPSC#1 CM	<0.0001

EFig.2f Unpaired two-tailed T-test, p-values (n=3)

Ctrl media vs 8988T CM	<0.0001	hPSC#1 CM vs 8988T CM	<0.0001
Ctrl media vs 8902 CM	<0.0001	hPSC#1 CM vs 8902 CM	<0.0001
Ctrl media vs hPSC#1 CM	<0.0001	8988T CM vs 8902 CM	0.0004

EFig.2g Unpaired two-tailed T-test, p-values (n=3):

Ctrl vs hPSC #2 CM	0.0007
Ctrl vs hPSC #1 CM	<0.0001
hPSC #1 vs hPSC #2 CM	0.1176

EFig.2h Unpaired two-tailed T-test, p-values (n=3):

Ctrl vs hPSC #2 CM	0.0004
Ctrl vs hPSC #1 CM	0.0003
hPSC #1 vs hPSC #2 CM	0.0088



## EFig.2j,k two way ANOVA (n=3)

Source of Variation	% of total variation	p value
Interaction	36.94	< 0.0001
Row Factor	17.63	< 0.0001
Column Factor	44.6	< 0.0001

<b>4h</b>		Asp vs. Trp	0.9632	Leu vs. Ser	> 0.9999
Ala vs. Asn	> 0.9999	Asp vs. Tyr	0.845	Leu vs. Lac	0.28
Ala vs. Asp	> 0.9999	Asp vs. Val	0.9224	Lys vs. Met	> 0.9999
Ala vs. Glu	0.7832	Asp vs. Gln	0.8178	Lys vs. Phe	> 0.9999
Ala vs. Pro	> 0.9999	Asp vs. Ser	0.8591	Lys vs. Trp	> 0.9999
Ala vs. Leu	0.7058	Asp vs. Lac	0.9995	Lys vs. Tyr	> 0.9999
Ala vs. Lys	0.8097	Glu vs. Pro	0.9943	Lys vs. Val	> 0.9999
Ala vs. Met	0.7027	Glu vs. Leu	> 0.9999	Lys vs. Gln	> 0.9999
Ala vs. Phe	0.7519	Glu vs. Lys	> 0.9999	Lys vs. Ser	> 0.9999
Ala vs. Trp	0.8178	Glu vs. Met	> 0.9999	Lys vs. Lac	0.3821
Ala vs. Tyr	0.5896	Glu vs. Phe	> 0.9999	Met vs. Phe	> 0.9999
Ala vs. Val	0.7207	Glu vs. Trp	> 0.9999	Met vs. Trp	> 0.9999
Ala vs. Gln	0.5519	Glu vs. Tyr	> 0.9999	Met vs. Tyr	> 0.9999
Ala vs. Ser	0.6105	Glu vs. Val	> 0.9999	Met vs. Val	> 0.9999
Ala vs. Lac	> 0.9999	Glu vs. Gln	> 0.9999	Met vs. Gln	> 0.9999
Asn vs. Asp	> 0.9999	Glu vs. Ser	> 0.9999	Met vs. Ser	> 0.9999
Asn vs. Glu	0.7129	Glu vs. Lac	0.3524	Met vs. Lac	0.2775
Asn vs. Pro	> 0.9999	Pro vs. Leu	0.9866	Phe vs. Trp	> 0.9999
Asn vs. Leu	0.6285	Pro vs. Lys	0.996	Phe vs. Tyr	> 0.9999
Asn vs. Lys	0.7429	Pro vs. Met	0.9862	Phe vs. Val	> 0.9999
Asn vs. Met	0.6252	Pro vs. Phe	0.9917	Phe vs. Gln	> 0.9999
Asn vs. Phe	0.6783	Pro vs. Trp	0.9965	Phe vs. Ser	> 0.9999
Asn vs. Trp	0.7523	Pro vs. Tyr	0.9647	Phe vs. Lac	0.321
Asn vs. Tyr	0.5091	Pro vs. Val	0.9884	Trp vs. Tyr	> 0.9999
Asn vs. Val	0.6444	Pro vs. Gln	0.9541	Trp vs. Val	> 0.9999
Asn vs. Gln	0.472	Pro vs. Ser	0.9697	Trp vs. Gln	> 0.9999
Asn vs. Ser	0.53	Pro vs. Lac	0.9897	Trp vs. Ser	> 0.9999
Asn vs. Lac	> 0.9999	Leu vs. Lys	> 0.9999	Trp vs. Lac	0.3917
Asp vs. Glu	0.9502	Leu vs. Met	> 0.9999	Tyr vs. Val	> 0.9999
Asp vs. Pro	> 0.9999	Leu vs. Phe	> 0.9999	Tyr vs. Gln	> 0.9999
Asp vs. Leu	0.9149	Leu vs. Trp	> 0.9999	Tyr vs. Ser	> 0.9999
Asp vs. Lys	0.9603	Leu vs. Tyr	> 0.9999	Tyr vs. Lac	0.1976
Asp vs. Met	0.9133	Leu vs. Val	> 0.9999	Val vs. Gln	> 0.9999
Asp vs. Phe	0.937	Leu vs. Gln	> 0.9999	Val vs. Ser	> 0.9999

Val vs. Lac	0.2927	Asp vs. Lac	> 0.9999	Met vs. Gln	> 0.9999
Gln vs. Ser	> 0.9999	Glu vs. Pro	0.112	Met vs. Ser	> 0.9999
Gln vs. Lac	0.1755	Glu vs. Leu	0.9991	Met vs. Lac	< 0.0001
Ser vs. Lac	0.2106	Glu vs. Lys	> 0.9999	Phe vs. Trp	> 0.9999
<b>8h</b>		Glu vs. Met	0.9998	Phe vs. Tyr	> 0.9999
Ala vs. Asn	> 0.9999	Glu vs. Phe	0.9982	Phe vs. Val	> 0.9999
Ala vs. Asp	> 0.9999	Glu vs. Trp	0.9995	Phe vs. Gln	> 0.9999
Ala vs. Glu	0.0007	Glu vs. Tyr	0.9994	Phe vs. Ser	> 0.9999
Ala vs. Pro	0.9801	Glu vs. Val	0.9996	Phe vs. Lac	< 0.0001
Ala vs. Leu	< 0.0001	Glu vs. Gln	0.9968	Trp vs. Tyr	> 0.9999
Ala vs. Lys	< 0.0001	Glu vs. Ser	0.9927	Trp vs. Val	> 0.9999
Ala vs. Met	< 0.0001	Glu vs. Lac	< 0.0001	Trp vs. Gln	> 0.9999
Ala vs. Phe	< 0.0001	Pro vs. Leu	0.0034	Trp vs. Ser	> 0.9999
Ala vs. Trp	< 0.0001	Pro vs. Lys	0.0069	Trp vs. Lac	< 0.0001
Ala vs. Tyr	< 0.0001	Pro vs. Met	0.0054	Tyr vs. Val	> 0.9999
Ala vs. Val	< 0.0001	Pro vs. Phe	0.0026	Tyr vs. Gln	> 0.9999
Ala vs. Gln	< 0.0001	Pro vs. Trp	0.0041	Tyr vs. Ser	> 0.9999
Ala vs. Ser	< 0.0001	Pro vs. Tyr	0.004	Tyr vs. Lac	< 0.0001
Ala vs. Lac	> 0.9999	Pro vs. Val	0.0046	Val vs. Gln	> 0.9999
Asn vs. Asp	> 0.9999	Pro vs. Gln	0.002	Val vs. Ser	> 0.9999
Asn vs. Glu	0.0003	Pro vs. Ser	0.0013	Val vs. Lac	< 0.0001
Asn vs. Pro	0.9347	Pro vs. Lac	0.6621	Gln vs. Ser	> 0.9999
Asn vs. Leu	< 0.0001	Leu vs. Lys	> 0.9999	Gln vs. Lac	< 0.0001
Asn vs. Lys	< 0.0001	Leu vs. Met	> 0.9999	Ser vs. Lac	< 0.0001
Asn vs. Met	< 0.0001	Leu vs. Phe	> 0.9999	<b>24h</b>	
Asn vs. Phe	< 0.0001	Leu vs. Trp	> 0.9999	Ala vs. Asn	0.0104
Asn vs. Trp	< 0.0001	Leu vs. Tyr	> 0.9999	Ala vs. Asp	< 0.0001
Asn vs. Tyr	< 0.0001	Leu vs. Val	> 0.9999	Ala vs. Glu	< 0.0001
Asn vs. Val	< 0.0001	Leu vs. Gln	> 0.9999	Ala vs. Pro	< 0.0001
Asn vs. Gln	< 0.0001	Leu vs. Ser	> 0.9999	Ala vs. Leu	< 0.0001
Asn vs. Ser	< 0.0001	Leu vs. Lac	< 0.0001	Ala vs. Lys	< 0.0001
Asn vs. Lac	> 0.9999	Lys vs. Met	> 0.9999	Ala vs. Met	< 0.0001
Asp vs. Glu	0.0005	Lys vs. Phe	> 0.9999	Ala vs. Phe	< 0.0001
Asp vs. Pro	0.9669	Lys vs. Trp	> 0.9999	Ala vs. Trp	< 0.0001
Asp vs. Leu	< 0.0001	Lys vs. Tyr	> 0.9999	Ala vs. Tyr	< 0.0001
Asp vs. Lys	< 0.0001	Lys vs. Val	> 0.9999	Ala vs. Val	< 0.0001
Asp vs. Met	< 0.0001	Lys vs. Gln	> 0.9999	Ala vs. Gln	< 0.0001
Asp vs. Phe	< 0.0001	Lys vs. Ser	> 0.9999	Ala vs. Ser	< 0.0001
Asp vs. Trp	< 0.0001	Lys vs. Lac	< 0.0001	Ala vs. Lac	< 0.0001
Asp vs. Tyr	< 0.0001	Met vs. Phe	> 0.9999	Asn vs. Asp	0.9964
Asp vs. Val	< 0.0001	Met vs. Trp	> 0.9999	Asn vs. Glu	< 0.0001
Asp vs. Gln	< 0.0001	Met vs. Tyr	> 0.9999	Asn vs. Pro	< 0.0001
Asp vs. Ser	< 0.0001	Met vs. Val	> 0.9999	Asn vs. Leu	< 0.0001

Asn vs. Lys	< 0.0001	Leu vs. Met	> 0.9999	Ser vs. Lac	< 0.0001
Asn vs. Met	< 0.0001	Leu vs. Phe	> 0.9999	<b>48h</b>	
Asn vs. Phe	< 0.0001	Leu vs. Trp	> 0.9999	Ala vs. Asn	< 0.0001
Asn vs. Trp	< 0.0001	Leu vs. Tyr	> 0.9999	Ala vs. Asp	< 0.0001
Asn vs. Tyr	< 0.0001	Leu vs. Val	> 0.9999	Ala vs. Glu	< 0.0001
Asn vs. Val	< 0.0001	Leu vs. Gln	> 0.9999	Ala vs. Pro	< 0.0001
Asn vs. Gln	< 0.0001	Leu vs. Ser	> 0.9999	Ala vs. Leu	< 0.0001
Asn vs. Ser	< 0.0001	Leu vs. Lac	< 0.0001	Ala vs. Lys	< 0.0001
Asn vs. Lac	0.0263	Lys vs. Met	> 0.9999	Ala vs. Met	< 0.0001
Asp vs. Glu	< 0.0001	Lys vs. Phe	> 0.9999	Ala vs. Phe	< 0.0001
Asp vs. Pro	0.0092	Lys vs. Trp	> 0.9999	Ala vs. Trp	< 0.0001
Asp vs. Leu	< 0.0001	Lys vs. Tyr	> 0.9999	Ala vs. Tyr	< 0.0001
Asp vs. Lys	< 0.0001	Lys vs. Val	> 0.9999	Ala vs. Val	< 0.0001
Asp vs. Met	< 0.0001	Lys vs. Gln	0.9987	Ala vs. Gln	< 0.0001
Asp vs. Phe	< 0.0001	Lys vs. Ser	0.993	Ala vs. Ser	< 0.0001
Asp vs. Trp	< 0.0001	Lys vs. Lac	< 0.0001	Ala vs. Lac	< 0.0001
Asp vs. Tyr	< 0.0001	Met vs. Phe	> 0.9999	Asn vs. Asp	< 0.0001
Asp vs. Val	< 0.0001	Met vs. Trp	> 0.9999	Asn vs. Glu	< 0.0001
Asp vs. Gln	< 0.0001	Met vs. Tyr	> 0.9999	Asn vs. Pro	< 0.0001
Asp vs. Ser	< 0.0001	Met vs. Val	> 0.9999	Asn vs. Leu	< 0.0001
Asp vs. Lac	0.5006	Met vs. Gln	> 0.9999	Asn vs. Lys	< 0.0001
Glu vs. Pro	< 0.0001	Met vs. Ser	> 0.9999	Asn vs. Met	< 0.0001
Glu vs. Leu	0.0002	Met vs. Lac	< 0.0001	Asn vs. Phe	< 0.0001
Glu vs. Lys	0.0033	Phe vs. Trp	> 0.9999	Asn vs. Trp	< 0.0001
Glu vs. Met	0.0003	Phe vs. Tyr	> 0.9999	Asn vs. Tyr	< 0.0001
Glu vs. Phe	0.0005	Phe vs. Val	> 0.9999	Asn vs. Val	< 0.0001
Glu vs. Trp	0.0003	Phe vs. Gln	> 0.9999	Asn vs. Gln	< 0.0001
Glu vs. Tyr	0.0004	Phe vs. Ser	> 0.9999	Asn vs. Ser	< 0.0001
Glu vs. Val	0.0002	Phe vs. Lac	< 0.0001	Asn vs. Lac	0.995
Glu vs. Gln	< 0.0001	Trp vs. Tyr	> 0.9999	Asp vs. Glu	< 0.0001
Glu vs. Ser	< 0.0001	Trp vs. Val	> 0.9999	Asp vs. Pro	> 0.9999
Glu vs. Lac	< 0.0001	Trp vs. Gln	> 0.9999	Asp vs. Leu	< 0.0001
Pro vs. Leu	< 0.0001	Trp vs. Ser	> 0.9999	Asp vs. Lys	< 0.0001
Pro vs. Lys	< 0.0001	Trp vs. Lac	< 0.0001	Asp vs. Met	< 0.0001
Pro vs. Met	< 0.0001	Tyr vs. Val	> 0.9999	Asp vs. Phe	< 0.0001
Pro vs. Phe	< 0.0001	Tyr vs. Gln	> 0.9999	Asp vs. Trp	< 0.0001
Pro vs. Trp	< 0.0001	Tyr vs. Ser	> 0.9999	Asp vs. Tyr	< 0.0001
Pro vs. Tyr	< 0.0001	Tyr vs. Lac	< 0.0001	Asp vs. Val	< 0.0001
Pro vs. Val	< 0.0001	Val vs. Gln	> 0.9999	Asp vs. Gln	< 0.0001
Pro vs. Gln	< 0.0001	Val vs. Ser	> 0.9999	Asp vs. Ser	< 0.0001
Pro vs. Ser	< 0.0001	Val vs. Lac	< 0.0001	Asp vs. Lac	0.0016
Pro vs. Lac	0.9701	Gln vs. Ser	> 0.9999	Glu vs. Pro	< 0.0001
Leu vs. Lys	> 0.9999	Gln vs. Lac	< 0.0001	Glu vs. Leu	< 0.0001

Glu vs. Lys	< 0.0001	Phe vs. Trp	> 0.9999	Asn vs. Trp	< 0.0001
Glu vs. Met	< 0.0001	Phe vs. Tyr	> 0.9999	Asn vs. Tyr	< 0.0001
Glu vs. Phe	< 0.0001	Phe vs. Val	> 0.9999	Asn vs. Val	< 0.0001
Glu vs. Trp	< 0.0001	Phe vs. Gln	0.9953	Asn vs. Gln	< 0.0001
Glu vs. Tyr	< 0.0001	Phe vs. Ser	0.9597	Asn vs. Ser	< 0.0001
Glu vs. Val	< 0.0001	Phe vs. Lac	< 0.0001	Asn vs. Lac	< 0.0001
Glu vs. Gln	< 0.0001	Trp vs. Tyr	> 0.9999	Asp vs. Glu	< 0.0001
Glu vs. Ser	< 0.0001	Trp vs. Val	> 0.9999	Asp vs. Pro	< 0.0001
Glu vs. Lac	< 0.0001	Trp vs. Gln	0.9972	Asp vs. Leu	< 0.0001
Pro vs. Leu	< 0.0001	Trp vs. Ser	0.9711	Asp vs. Lys	< 0.0001
Pro vs. Lys	< 0.0001	Trp vs. Lac	< 0.0001	Asp vs. Met	< 0.0001
Pro vs. Met	< 0.0001	Tyr vs. Val	> 0.9999	Asp vs. Phe	< 0.0001
Pro vs. Phe	< 0.0001	Tyr vs. Gln	0.9988	Asp vs. Trp	< 0.0001
Pro vs. Trp	< 0.0001	Tyr vs. Ser	0.9831	Asp vs. Tyr	< 0.0001
Pro vs. Tyr	< 0.0001	Tyr vs. Lac	< 0.0001	Asp vs. Val	< 0.0001
Pro vs. Val	< 0.0001	Val vs. Gln	> 0.9999	Asp vs. Gln	< 0.0001
Pro vs. Gln	< 0.0001	Val vs. Ser	0.9972	Asp vs. Ser	< 0.0001
Pro vs. Ser	< 0.0001	Val vs. Lac	< 0.0001	Asp vs. Lac	0.026
Pro vs. Lac	0.0034	Gln vs. Ser	> 0.9999	Glu vs. Pro	< 0.0001
Leu vs. Lys	0.9997	Gln vs. Lac	< 0.0001	Glu vs. Leu	< 0.0001
Leu vs. Met	> 0.9999	Ser vs. Lac	< 0.0001	Glu vs. Lys	< 0.0001
Leu vs. Phe	> 0.9999	<b>72h</b>		Glu vs. Met	< 0.0001
Leu vs. Trp	> 0.9999	Ala vs. Asn	< 0.0001	Glu vs. Phe	< 0.0001
Leu vs. Tyr	> 0.9999	Ala vs. Asp	< 0.0001	Glu vs. Trp	< 0.0001
Leu vs. Val	> 0.9999	Ala vs. Glu	< 0.0001	Glu vs. Tyr	< 0.0001
Leu vs. Gln	> 0.9999	Ala vs. Pro	< 0.0001	Glu vs. Val	< 0.0001
Leu vs. Ser	0.9966	Ala vs. Leu	< 0.0001	Glu vs. Gln	< 0.0001
Leu vs. Lac	< 0.0001	Ala vs. Lys	< 0.0001	Glu vs. Ser	< 0.0001
Lys vs. Met	> 0.9999	Ala vs. Met	< 0.0001	Glu vs. Lac	< 0.0001
Lys vs. Phe	> 0.9999	Ala vs. Phe	< 0.0001	Pro vs. Leu	< 0.0001
Lys vs. Trp	> 0.9999	Ala vs. Trp	< 0.0001	Pro vs. Lys	< 0.0001
Lys vs. Tyr	> 0.9999	Ala vs. Tyr	< 0.0001	Pro vs. Met	< 0.0001
Lys vs. Val	0.9997	Ala vs. Val	< 0.0001	Pro vs. Phe	< 0.0001
Lys vs. Gln	0.8765	Ala vs. Gln	< 0.0001	Pro vs. Trp	< 0.0001
Lys vs. Ser	0.6815	Ala vs. Ser	< 0.0001	Pro vs. Tyr	< 0.0001
Lys vs. Lac	< 0.0001	Ala vs. Lac	< 0.0001	Pro vs. Val	< 0.0001
Met vs. Phe	> 0.9999	Asn vs. Asp	0.0184	Pro vs. Gln	< 0.0001
Met vs. Trp	> 0.9999	Asn vs. Glu	< 0.0001	Pro vs. Ser	< 0.0001
Met vs. Tyr	> 0.9999	Asn vs. Pro	< 0.0001	Pro vs. Lac	0.0002
Met vs. Val	> 0.9999	Asn vs. Leu	< 0.0001	Leu vs. Lys	0.9998
Met vs. Gln	0.9997	Asn vs. Lys	< 0.0001	Leu vs. Met	> 0.9999
Met vs. Ser	0.9931	Asn vs. Met	< 0.0001	Leu vs. Phe	> 0.9999
Met vs. Lac	< 0.0001	Asn vs. Phe	< 0.0001	Leu vs. Trp	> 0.9999

Leu vs. Tyr	> 0.9999	Met vs. Trp	> 0.9999	Trp vs. Gln	0.9892
Leu vs. Val	> 0.9999	Met vs. Tyr	> 0.9999	Trp vs. Ser	0.9316
Leu vs. Gln	0.9986	Met vs. Val	> 0.9999	Trp vs. Lac	< 0.0001
Leu vs. Ser	0.9818	Met vs. Gln	0.9957	Tyr vs. Val	> 0.9999
Leu vs. Lac	< 0.0001	Met vs. Ser	0.9618	Tyr vs. Gln	0.9905
Lys vs. Met	> 0.9999	Met vs. Lac	< 0.0001	Tyr vs. Ser	0.937
Lys vs. Phe	> 0.9999	Phe vs. Trp	> 0.9999	Tyr vs. Lac	< 0.0001
Lys vs. Trp	> 0.9999	Phe vs. Tyr	> 0.9999	Val vs. Gln	0.9988
Lys vs. Tyr	> 0.9999	Phe vs. Val	> 0.9999	Val vs. Ser	0.9835
Lys vs. Val	0.9997	Phe vs. Gln	0.9814	Val vs. Lac	< 0.0001
Lys vs. Gln	0.7549	Phe vs. Ser	0.903	Gln vs. Ser	> 0.9999
Lys vs. Ser	0.5199	Phe vs. Lac	< 0.0001	Gln vs. Lac	< 0.0001
Lys vs. Lac	< 0.0001	Trp vs. Tyr	> 0.9999	Ser vs. Lac	< 0.0001
Met vs. Phe	> 0.9999	Trp vs. Val	> 0.9999		

EFig.2l two-way ANOVA (n=3)

Source of Variation	% of total variation	P value
Interaction	22.73	< 0.0001
Row Factor	1.529	< 0.0001
Column Factor	71.75	< 0.0001

<b>2h</b>		Val vs. Phe	> 0.9999	Ala vs. Lys	< 0.0001
Asn vs. Val	> 0.9999	Val vs. Glu	0.9949	Ala vs. Phe	< 0.0001
Asn vs. Thr	> 0.9999	Val vs. Trp	> 0.9999	Ala vs. Glu	< 0.0001
Asn vs. Ala	< 0.0001	Val vs. Gln	> 0.9999	Ala vs. Trp	< 0.0001
Asn vs. Pro	0.0367	Val vs. Ser	0.9921	Ala vs. Gln	< 0.0001
Asn vs. Asp	0.4782	Val vs. Lac	0.0041	Ala vs. Ser	< 0.0001
Asn vs. Met	0.7768	Thr vs. Ala	< 0.0001	Ala vs. Lac	< 0.0001
Asn vs. Lys	0.9996	Thr vs. Pro	0.0918	Pro vs. Asp	< 0.0001
Asn vs. Phe	> 0.9999	Thr vs. Asp	0.2729	Pro vs. Met	< 0.0001
Asn vs. Glu	0.8135	Thr vs. Met	0.5567	Pro vs. Lys	0.365
Asn vs. Trp	> 0.9999	Thr vs. Lys	> 0.9999	Pro vs. Phe	0.0216
Asn vs. Gln	0.9841	Thr vs. Phe	> 0.9999	Pro vs. Glu	< 0.0001
Asn vs. Ser	0.7809	Thr vs. Glu	0.6025	Pro vs. Trp	0.0042
Asn vs. Lac	0.0444	Thr vs. Trp	0.9995	Pro vs. Gln	0.0002
Val vs. Thr	0.9989	Thr vs. Gln	0.9166	Pro vs. Ser	< 0.0001
Val vs. Ala	< 0.0001	Thr vs. Ser	0.5616	Pro vs. Lac	> 0.9999
Val vs. Pro	0.0033	Thr vs. Lac	0.1083	Asp vs. Met	> 0.9999
Val vs. Asp	0.9124	Ala vs. Pro	< 0.0001	Asp vs. Lys	0.06
Val vs. Met	0.9917	Ala vs. Asp	< 0.0001	Asp vs. Phe	0.5997
Val vs. Lys	0.9291	Ala vs. Met	< 0.0001	Asp vs. Glu	> 0.9999

Asp vs. Trp	0.8854	Asn vs. Trp	0.9945	Pro vs. Gln	0.0001
Asp vs. Gln	0.9988	Asn vs. Gln	0.8092	Pro vs. Ser	< 0.0001
Asp vs. Ser	> 0.9999	Asn vs. Ser	0.3723	Pro vs. Lac	0.1673
Asp vs. Lac	< 0.0001	Asn vs. Lac	> 0.9999	Asp vs. Met	> 0.9999
Met vs. Lys	0.1815	Val vs. Thr	0.9996	Asp vs. Lys	0.0349
Met vs. Phe	0.8668	Val vs. Ala	< 0.0001	Asp vs. Phe	0.991
Met vs. Glu	> 0.9999	Val vs. Pro	0.0054	Asp vs. Glu	> 0.9999
Met vs. Trp	0.9866	Val vs. Asp	0.902	Asp vs. Trp	0.9685
Met vs. Gln	> 0.9999	Val vs. Met	0.6919	Asp vs. Gln	> 0.9999
Met vs. Ser	> 0.9999	Val vs. Lys	0.8704	Asp vs. Ser	> 0.9999
Met vs. Lac	< 0.0001	Val vs. Phe	> 0.9999	Asp vs. Lac	0.2078
Lys vs. Phe	0.9978	Val vs. Glu	0.9709	Met vs. Lys	0.01
Lys vs. Glu	0.2091	Val vs. Trp	> 0.9999	Met vs. Phe	0.9241
Lys vs. Trp	0.9483	Val vs. Gln	0.9995	Met vs. Glu	> 0.9999
Lys vs. Gln	0.5519	Val vs. Ser	0.9446	Met vs. Trp	0.8409
Lys vs. Ser	0.1843	Val vs. Lac	0.9973	Met vs. Gln	0.9966
Lys vs. Lac	0.4065	Thr vs. Ala	< 0.0001	Met vs. Ser	> 0.9999
Phe vs. Glu	0.894	Thr vs. Pro	0.1051	Met vs. Lac	0.0808
Phe vs. Trp	> 0.9999	Thr vs. Asp	0.3062	Lys vs. Phe	0.5937
Phe vs. Gln	0.9952	Thr vs. Met	0.1319	Lys vs. Glu	0.0744
Phe vs. Ser	0.8699	Thr vs. Lys	0.9998	Lys vs. Trp	0.7329
Phe vs. Lac	0.0265	Thr vs. Phe	0.9818	Lys vs. Gln	0.2574
Glu vs. Trp	0.9913	Thr vs. Glu	0.4767	Lys vs. Ser	0.052
Glu vs. Gln	> 0.9999	Thr vs. Trp	0.9956	Lys vs. Lac	> 0.9999
Glu vs. Ser	> 0.9999	Thr vs. Gln	0.8238	Phe vs. Glu	0.999
Glu vs. Lac	< 0.0001	Thr vs. Ser	0.3897	Phe vs. Trp	> 0.9999
Trp vs. Gln	> 0.9999	Thr vs. Lac	> 0.9999	Phe vs. Gln	> 0.9999
Trp vs. Ser	0.9872	Ala vs. Pro	< 0.0001	Phe vs. Ser	0.9968
Trp vs. Lac	0.0053	Ala vs. Asp	< 0.0001	Phe vs. Lac	0.9491
Gln vs. Ser	> 0.9999	Ala vs. Met	< 0.0001	Glu vs. Trp	0.9942
Gln vs. Lac	0.0003	Ala vs. Lys	< 0.0001	Glu vs. Gln	> 0.9999
Ser vs. Lac	< 0.0001	Ala vs. Phe	< 0.0001	Glu vs. Ser	> 0.9999
		Ala vs. Glu	< 0.0001	Glu vs. Lac	0.3495
<b>4h</b>		Ala vs. Trp	< 0.0001	Trp vs. Gln	> 0.9999
Asn vs. Val	0.9994	Ala vs. Gln	< 0.0001	Trp vs. Ser	0.9858
Asn vs. Thr	> 0.9999	Ala vs. Ser	< 0.0001	Trp vs. Lac	0.983
Asn vs. Ala	< 0.0001	Ala vs. Lac	< 0.0001	Gln vs. Ser	> 0.9999
Asn vs. Pro	0.1125	Pro vs. Asp	< 0.0001	Gln vs. Lac	0.7087
Asn vs. Asp	0.2908	Pro vs. Met	< 0.0001	Ser vs. Lac	0.275
Asn vs. Met	0.1234	Pro vs. Lys	0.5699		
Asn vs. Lys	0.9999	Pro vs. Phe	0.001	<b>8h</b>	
Asn vs. Phe	0.9786	Pro vs. Glu	< 0.0001	Asn vs. Val	0.9786
Asn vs. Glu	0.4579	Pro vs. Trp	0.0022	Asn vs. Thr	> 0.9999

Asn vs. Ala	< 0.0001	Ala vs. Lac	< 0.0001	Gln vs. Ser	> 0.9999
Asn vs. Pro	0.0022	Pro vs. Asp	< 0.0001	Gln vs. Lac	0.9857
Asn vs. Asp	0.1351	Pro vs. Met	< 0.0001	Ser vs. Lac	0.8986
Asn vs. Met	0.0055	Pro vs. Lys	0.1828		
Asn vs. Lys	0.9782	Pro vs. Phe	< 0.0001	<b>24h</b>	
Asn vs. Phe	0.1637	Pro vs. Glu	< 0.0001	Asn vs. Val	0.8779
Asn vs. Glu	0.2994	Pro vs. Trp	< 0.0001	Asn vs. Thr	> 0.9999
Asn vs. Trp	0.863	Pro vs. Gln	< 0.0001	Asn vs. Ala	< 0.0001
Asn vs. Gln	0.6205	Pro vs. Ser	< 0.0001	Asn vs. Pro	< 0.0001
Asn vs. Ser	0.3499	Pro vs. Lac	< 0.0001	Asn vs. Asp	0.5429
Asn vs. Lac	0.9998	Asp vs. Met	0.9989	Asn vs. Met	0.1056
Val vs. Thr	0.8583	Asp vs. Lys	0.0013	Asn vs. Lys	> 0.9999
Val vs. Ala	< 0.0001	Asp vs. Phe	> 0.9999	Asn vs. Phe	0.9978
Val vs. Pro	< 0.0001	Asp vs. Glu	> 0.9999	Asn vs. Glu	0.9983
Val vs. Asp	0.9352	Asp vs. Trp	0.9941	Asn vs. Trp	0.9739
Val vs. Met	0.3089	Asp vs. Gln	0.9999	Asn vs. Gln	0.0439
Val vs. Lys	0.2201	Asp vs. Ser	> 0.9999	Asn vs. Ser	0.0025
Val vs. Phe	0.9555	Asp vs. Lac	0.6423	Asn vs. Lac	0.0369
Val vs. Glu	0.9919	Met vs. Lys	< 0.0001	Val vs. Thr	0.9738
Val vs. Trp	> 0.9999	Met vs. Phe	0.9976	Val vs. Ala	< 0.0001
Val vs. Gln	> 0.9999	Met vs. Glu	0.9806	Val vs. Pro	< 0.0001
Val vs. Ser	0.9957	Met vs. Trp	0.585	Val vs. Asp	> 0.9999
Val vs. Lac	> 0.9999	Met vs. Gln	0.8388	Val vs. Met	0.9853
Thr vs. Ala	< 0.0001	Met vs. Ser	0.9686	Val vs. Lys	0.9705
Thr vs. Pro	0.0098	Met vs. Lac	0.086	Val vs. Phe	> 0.9999
Thr vs. Asp	0.0435	Lys vs. Phe	0.0018	Val vs. Glu	> 0.9999
Thr vs. Met	0.0011	Lys vs. Glu	0.0052	Val vs. Trp	> 0.9999
Thr vs. Lys	0.9992	Lys vs. Trp	0.0817	Val vs. Gln	0.9228
Thr vs. Phe	0.055	Lys vs. Gln	0.0257	Val vs. Ser	0.4065
Thr vs. Glu	0.1182	Lys vs. Ser	0.007	Val vs. Lac	< 0.0001
Thr vs. Trp	0.6045	Lys vs. Lac	0.5713	Thr vs. Ala	< 0.0001
Thr vs. Gln	0.3326	Phe vs. Glu	> 0.9999	Thr vs. Pro	< 0.0001
Thr vs. Ser	0.1454	Phe vs. Trp	0.9969	Thr vs. Asp	0.7756
Thr vs. Lac	0.9913	Phe vs. Gln	> 0.9999	Thr vs. Met	0.2343
Ala vs. Pro	< 0.0001	Phe vs. Ser	> 0.9999	Thr vs. Lys	> 0.9999
Ala vs. Asp	< 0.0001	Phe vs. Lac	0.6979	Thr vs. Phe	> 0.9999
Ala vs. Met	< 0.0001	Glu vs. Trp	0.9998	Thr vs. Glu	> 0.9999
Ala vs. Lys	< 0.0001	Glu vs. Gln	> 0.9999	Thr vs. Trp	0.9977
Ala vs. Phe	< 0.0001	Glu vs. Ser	> 0.9999	Thr vs. Gln	0.112
Ala vs. Glu	< 0.0001	Glu vs. Lac	0.8627	Thr vs. Ser	0.0085
Ala vs. Trp	< 0.0001	Trp vs. Gln	> 0.9999	Thr vs. Lac	0.0124
Ala vs. Gln	< 0.0001	Trp vs. Ser	> 0.9999	Ala vs. Pro	< 0.0001
Ala vs. Ser	< 0.0001	Trp vs. Lac	0.9995	Ala vs. Asp	< 0.0001



Ala vs. Met	< 0.0001	Asp vs. Lys	0.7623	Lys vs. Ser	0.0078
Ala vs. Lys	< 0.0001	Asp vs. Phe	0.9946	Lys vs. Lac	0.0134
Ala vs. Phe	< 0.0001	Asp vs. Glu	0.9935	Phe vs. Glu	> 0.9999
Ala vs. Glu	< 0.0001	Asp vs. Trp	0.9998	Phe vs. Trp	> 0.9999
Ala vs. Trp	< 0.0001	Asp vs. Gln	0.9971	Phe vs. Gln	0.5206
Ala vs. Gln	< 0.0001	Asp vs. Ser	0.7767	Phe vs. Ser	0.0921
Ala vs. Ser	< 0.0001	Asp vs. Lac	< 0.0001	Phe vs. Lac	0.0007
Ala vs. Lac	< 0.0001	Met vs. Lys	0.2237	Glu vs. Trp	> 0.9999
Pro vs. Asp	< 0.0001	Met vs. Phe	0.742	Glu vs. Gln	0.5027
Pro vs. Met	< 0.0001	Met vs. Glu	0.7259	Glu vs. Ser	0.0862
Pro vs. Lys	< 0.0001	Met vs. Trp	0.9149	Glu vs. Lac	0.0008
Pro vs. Phe	< 0.0001	Met vs. Gln	> 0.9999	Trp vs. Gln	0.7598
Pro vs. Glu	< 0.0001	Met vs. Ser	0.9966	Trp vs. Ser	0.2119
Pro vs. Trp	< 0.0001	Met vs. Lac	< 0.0001	Trp vs. Lac	0.0002
Pro vs. Gln	< 0.0001	Lys vs. Phe	> 0.9999	Gln vs. Ser	0.9999
Pro vs. Ser	< 0.0001	Lys vs. Glu	> 0.9999	Gln vs. Lac	< 0.0001
Pro vs. Lac	0.0382	Lys vs. Trp	0.9972	Ser vs. Lac	< 0.0001
Asp vs. Met	> 0.9999	Lys vs. Gln	0.1059		

**Extended Data Figure 3****EFig.3b** two-way ANOVA (n=3)

Source of Variation	% of total variation	P value
Interaction	11.47	0.1990
Row Factor	46.83	< 0.0001
Column Factor	13.02	0.0207

Tukey's multiple comparisons test	P Value		
shGFP		hPSC CM vs. 8902 CM	0.2225
hPSC CM vs. 8902 CM	0.0134	hPSC CM vs. ctrl	0.8256
hPSC CM vs. ctrl	0.0007	8902 CM vs. ctrl	0.9988
8902 CM vs. ctrl	0.9980	shGPT2 #1	
shGPT1 #1		hPSC CM vs. 8902 CM	0.9975
hPSC CM vs. 8902 CM	0.2074	hPSC CM vs. ctrl	0.6996
hPSC CM vs. ctrl	0.5773	8902 CM vs. ctrl	0.9991
8902 CM vs. ctrl	> 0.9999	shGPT2 #2	
shGPT1 #2		hPSC CM vs. 8902 CM	0.6228
		hPSC CM vs. ctrl	0.8817
		8902 CM vs. ctrl	> 0.9999

**EFig.3c** One-way ANOVA, F=3.811, p<0.0157 (n=3)

Tukey's multiple comparisons test	Adjusted p Value		
ShGFP vs. ShGPT1 1	0.0339	ShGFP vs. ShGPT2 2	0.0443
ShGFP vs. ShGPT1 2	0.0622	ShGFP vs. ctrl media	0.0129
ShGFP vs. ShGPT2 1	0.0742	ShGPT1 1 vs. ShGPT1 2	0.9996
		ShGPT1 1 vs. ShGPT2 1	0.9985

ShGPT1 1 vs. ShGPT2 2	> 0.9999	ShGPT1 2 vs. ctrl media	0.9687
ShGPT1 1 vs. ctrl media	0.9967	ShGPT2 1 vs. ShGPT2 2	0.9998
ShGPT1 2 vs. ShGPT2 1	> 0.9999	ShGPT2 1 vs. ctrl media	0.9502
ShGPT1 2 vs. ShGPT2 2	> 0.9999	ShGPT2 2 vs. ctrl media	0.9896

## EFig.3d Two-way ANOVA (n=3)

Source of Variation	% of total variation	P value	
Interaction	40.5	< 0.0001	
Row Factor	9.769	< 0.0001	
Column Factor	49.17	< 0.0001	
Tukey's multiple comparisons test	p Value		<b>Ala (M0)</b>
<b>Lactate (M0)</b>			Mock vs. 1mM Ala (12C)
Mock vs. 1mM Ala (12C)	0.0001		< 0.0001
Mock vs. 1mM 13C Ala	0.2133		Mock vs. 1mM 13C Ala
1mM Ala (12C) vs. 1mM 13C Ala	0.0086		< 0.0001
			<b>Ala 13C (M3)</b>
<b>lactate (M3)</b>			Mock vs. 1mM Ala (12C)
Mock vs. 1mM Ala (12C)	0.9999		0.9999
Mock vs. 1mM 13C Ala	0.2416		Mock vs. 1mM 13C Ala
1mM Ala (12C) vs. 1mM 13C Ala	0.2353		< 0.0001
			1mM Ala (12C) vs. 1mM 13C Ala
			< 0.0001

## EFig.3e Two-way ANOVA (n=3)

Source of Variation	% of total variation	p value	
Interaction	64.43	< 0.0001	
Row Factor	28.77	< 0.0001	
Column Factor	6.234	< 0.0001	
Tukey's multiple comparisons test	Adjusted p Value		<b>Ala 13C</b>
<b>Ala</b>			Mock vs. 1mM Ala (12C)
Mock vs. 1mM Ala (12C)	< 0.0001		> 0.9999
Mock vs. 1mM 13C Ala	0.0045		Mock vs. 1mM 13C Ala
1mM Ala (12C) vs. 1mM 13C Ala	< 0.0001		< 0.0001
			1mM Ala (12C) vs. 1mM 13C Ala
			< 0.0001

## EFig.3f Two-way ANOVA (n=3)

Source of Variation	% of total variation	P value	
heavy metabolite	0.000423	0.9314	
label	37.44	< 0.0001	
Interaction: heavy metabolite x label	62.04	< 0.0001	
Tukey's multiple comparisons test	P Value		Ctrl vs. 1mM Pyr 13C
<b>Ala M0</b>			> 0.9999
Ctrl vs. 1mM Pyr	0.8038		Ctrl vs. 1mM Ala
			< 0.0001
			Ctrl vs. 1mM Ala 13C
			0.9169

1mM Pyr vs. 1mM Pyr 13C	0.862	Ctrl vs. 1mM Pyr 13C	0.8196
1mM Pyr vs. 1mM Ala	< 0.0001	Ctrl vs. 1mM Ala	> 0.9999
1mM Pyr vs. 1mM Ala 13C	0.9984	Ctrl vs. 1mM Ala 13C	< 0.0001
1mM Pyr 13C vs. 1mM Ala	< 0.0001	1mM Pyr vs. 1mM Pyr 13C	0.8196
1mM Pyr 13C vs. 1mM Ala 13C	0.9526	1mM Pyr vs. 1mM Ala	> 0.9999
1mM Ala vs. 1mM Ala 13C	< 0.0001	1mM Pyr vs. 1mM Ala 13C	< 0.0001
		1mM Pyr 13C vs. 1mM Ala	0.8196
<b>Ala M3</b>		1mM Pyr 13C vs. 1mM Ala 13C	< 0.0001
Ctrl vs. 1mM Pyr	> 0.9999	1mM Ala vs. 1mM Ala 13C	< 0.0001

## EFig.3g Two-way ANOVA (n=3)

Source of Variation	% of total variation	P value
heavy metabolite	0.3134	0.0109
label	37.58	< 0.0001
Interaction: heavy metabolite x label	61.92	< 0.0001

Tukey's multiple comparisons test	Adjusted P Value		
Ala M0		Ala M3	
Ctrl vs. 1mM Pyr	0.2818	Ctrl vs. 1mM Pyr	> 0.9999
Ctrl vs. 1mM Pyr 13C	0.9946	Ctrl vs. 1mM Pyr 13C	0.4401
Ctrl vs. 1mM Ala	< 0.0001	Ctrl vs. 1mM Ala	> 0.9999
Ctrl vs. 1mM Ala 13C	0.4479	Ctrl vs. 1mM Ala 13C	< 0.0001
1mM Pyr vs. 1mM Pyr 13C	0.4415	1mM Pyr vs. 1mM Pyr 13C	0.4362
1mM Pyr vs. 1mM Ala	< 0.0001	1mM Pyr vs. 1mM Ala	> 0.9999
1mM Pyr vs. 1mM Ala 13C	0.9939	1mM Pyr vs. 1mM Ala 13C	< 0.0001
1mM Pyr 13C vs. 1mM Ala	< 0.0001	1mM Pyr 13C vs. 1mM Ala	0.4357
1mM Pyr 13C vs. 1mM Ala 13C	0.6493	1mM Pyr 13C vs. 1mM Ala 13C	< 0.0001
1mM Ala vs. 1mM Ala 13C	< 0.0001	1mM Ala vs. 1mM Ala 13C	< 0.0001

## EFig.3h Two-way ANOVA (n=3)

Source of Variation	% of total variation	P value
heavy metabolite	0.3376	0.003
label	37.8	< 0.0001
Interaction: heavy metabolite x label	61.76	< 0.0001

Tukey's multiple comparisons test	P Value		
Ala M0		Ctrl vs. 1mM Ala	< 0.0001
Ctrl vs. 1mM Pyr	0.1163	Ctrl vs. 1mM Ala 13C	0.1613
Ctrl vs. 1mM Pyr 13C	0.9409	1mM Pyr vs. 1mM Pyr 13C	0.3066
		1mM Pyr vs. 1mM Ala	< 0.0001

1mM Pyr vs. 1mM Ala 13C	0.9991	Ctrl vs. 1mM Ala	> 0.9999
1mM Pyr 13C vs. 1mM Ala	< 0.0001	Ctrl vs. 1mM Ala 13C	< 0.0001
1mM Pyr 13C vs. 1mM Ala 13C	0.408	1mM Pyr vs. 1mM Pyr 13C	0.3149
1mM Ala vs. 1mM Ala 13C	< 0.0001	1mM Pyr vs. 1mM Ala	> 0.9999
Ala M3		1mM Pyr vs. 1mM Ala 13C	< 0.0001
Ctrl vs. 1mM Pyr	> 0.9999	1mM Pyr 13C vs. 1mM Ala	0.3143
Ctrl vs. 1mM Pyr 13C	0.3217	1mM Pyr 13C vs. 1mM Ala 13C	< 0.0001
		1mM Ala vs. 1mM Ala 13C	< 0.0001

## EFig.3k Unpaired two-tailed t-test (n=6)

p-value mock vs. 1mM Ala = 0.6086

## EFig.3l One-way ANOVA, F=24.57, p=0.0040 (n=4)

Tukey's multiple comparisons test	P Value		
Ctrl vs. 1mM Ala	0.0534	1mM Ala vs. 10mM Pyr	0.0601
Ctrl vs. 1mM Pyr	0.0243	1mM Ala vs. 10mM Lac	0.1116
Ctrl vs. 10mM Pyr	0.0528	1mM Pyr vs. 10mM Pyr	0.2285
Ctrl vs. 10mM Lac	0.4053	1mM Pyr vs. 10mM Lac	0.0533
1mM Ala vs. 1mM Pyr	0.0205	10mM Pyr vs. 10mM Lac	0.0511

## EFig.3m One-way ANOVA, F=24.78, p=0.0092 (n=3)

Tukey's multiple comparisons test	P Value		
Ctrl vs. 1mM Ala	0.0063	1mM Ala vs. 10mM Pyr	0.0279
Ctrl vs. 1mM Pyr	0.0689	1mM Ala vs. 10mM Lac	0.7917
Ctrl vs. 10mM Pyr	0.0231	1mM Pyr vs. 10mM Pyr	0.4226
Ctrl vs. 10mM Lac	0.9981	1mM Pyr vs. 10mM Lac	0.1978
1mM Ala vs. 1mM Pyr	0.1088	10mM Pyr vs. 10mM Lac	0.0384

## EFig.3n Two-way ANOVA (n=3)

Source of Variation	% of total variation	p value
Interaction	0.4078	0.157
Row Factor	0.2177	0.3469
Column Factor	98.25	< 0.0001

Tukey's multiple comparisons test	Adjusted p Value	Lactate (M3)	
Lactate (M0)		Mock vs. 1mM Ala (12C)	> 0.9999
Mock vs. 1mM Ala (12C)	0.1402	Mock vs. 1mM 13C Ala	0.4927
Mock vs. 1mM 13C Ala	0.25	1mM Ala (12C) vs. 1mM 13C Ala	0.4888
1mM Ala (12C) vs. 1mM 13C Ala	0.9261		

**Extended Data Figure6**

EFig.6a Unpaired two-tailed T-test, p-values (n=3)

Cit M0 Ala vs Mock :	0.0009
Cit M2 Ala vs Mock :	0.0169

EFig.6h Unpaired two-tailed T-test, p-values (n=3)

3PG M3 Ala vs Mock :	0.035515
3PSer M3 Ala vs Mock :	0.004078
Ser M3 Ala vs Mock :	0.017177
Gly M2 Ala vs Mock :	0.012271

EFig.6i Unpaired two-tailed t-test (n=3)

3PG Ala vs Mock :	0.0355
3PSer Ala vs Mock :	0.0041

EFig.6j Unpaired two-tailed t-test (n=3)

3PG Ala vs Mock :	0.0005
3PSer Ala vs Mock :	<0.0001

**Extended Data Figure7**

EFig.7c Two-way ANOVA (n= 13 for shGFP; n=12 for shATG5#1, shATG7#1 and #2; n=10 for shATG5#2)

Source of Variation	% of total variation	p value
Interaction	18.34	< 0.0001
Row Factor	12.79	0.0011
Column Factor	0.3974	0.4346

Tukey's multiple comparisons test	pValue		
		shATG5 1 vs. shATG7 2	0.0697
		shATG5 2 vs. shATG7 1	0.9851
<b>Autophagosomes</b>			
shGFP vs. shATG5 1	0.0067	shATG5 2 vs. shATG7 2	0.4035
shGFP vs. shATG5 2	0.0009	shATG7 1 vs. shATG7 2	0.6932
shGFP vs. shATG7 1	< 0.0001		
shGFP vs. shATG7 2	< 0.0001		
shATG5 1 vs. shATG5 2	0.9406		
shATG5 1 vs. shATG7 1	0.6631	<b>Autolysosomes</b>	

shGFP vs. shATG5 1	0.7598	shATG5 1 vs. shATG7 1	0.5642
shGFP vs. shATG5 2	0.2345	shATG5 1 vs. shATG7 2	0.9905
shGFP vs. shATG7 1	0.9978	shATG5 2 vs. shATG7 1	0.1274
shGFP vs. shATG7 2	0.9507	shATG5 2 vs. shATG7 2	0.6323
shATG5 1 vs. shATG5 2	0.8747	shATG7 1 vs. shATG7 2	0.8367

EFig.7g One-way ANOVA:  $F=10.87$ ,  $p=0.0010$  (n=4)

Tukey's multiple comparisons test	P Value	hPSC#2-shGFP vs. hPSC#2-shATG5	0.0268
Ctrl vs. hPSC#2-shGFP	0.0006	hPSC#2-shGFP vs. hPSC#2-shATG7	0.0154
Ctrl vs. hPSC#2-shATG5	0.1539	hPSC#2-shATG5 vs. hPSC#2-shATG7	0.9886
Ctrl vs. hPSC#2-shATG7	0.2487		

EFig.7h One-way ANOVA:  $F=14.92$   $p<0.0001$  (n=4 for ctrl, 8988T, 1mM Ala, hPSC groups; n=3 for hPSC shATG5 #2, hPSC shATG7 #1, hPSC shATG5 #2 + Ala, hPSC shATG7 #1 + Ala and hPSC + Ala)

Tukey's multiple comparisons test	p Value	1mM Ala vs. hPSC shATG5 #2 + Ala	0.9678
ctrl vs. 8988T	0.9969	1mM Ala vs. hPSC shATG7 #1 + Ala	0.9988
ctrl vs. 1mM Ala	0.0004	1mM Ala vs. hPSC + Ala	0.9000
ctrl vs. hPSC	0.0003	hPSC vs. hPSC shATG5 #2	0.0176
ctrl vs. hPSC shATG5 #2	0.9090	hPSC vs. hPSC shATG7 #1	0.0035
ctrl vs. hPSC shATG7 #1	0.9992	hPSC vs. hPSC shATG5 #2 + Ala	0.9864
ctrl vs. hPSC shATG5 #2 + Ala	< 0.0001	hPSC vs. hPSC shATG7 #1 + Ala	0.9998
ctrl vs. hPSC shATG7 #1 + Ala	0.0002	hPSC vs. hPSC + Ala	0.9444
ctrl vs. hPSC + Ala	< 0.0001	hPSC shATG5 #2 vs. hPSC shATG7 #1	0.9988
8988T vs. 1mM Ala	0.0026	hPSC shATG5 #2 vs. hPSC shATG5 #2 + Ala	0.0041
8988T vs. hPSC	0.0018	hPSC shATG5 #2 vs. hPSC shATG7 #1 + Ala	0.0105
8988T vs. hPSC shATG5 #2	0.9992	hPSC shATG5 #2 vs. hPSC + Ala	0.0023
8988T vs. hPSC shATG7 #1	> 0.9999	hPSC shATG7 #1 vs. hPSC shATG5 #2 + Ala	0.0009
8988T vs. hPSC shATG5 #2 + Ala	0.0005	hPSC shATG7 #1 vs. hPSC shATG7 #1 + Ala	0.0023
8988T vs. hPSC shATG7 #1 + Ala	0.0013	hPSC shATG7 #1 vs. hPSC + Ala	0.0005
8988T vs. hPSC + Ala	0.0003	hPSC shATG5 #2 + Ala vs. hPSC shATG7 #1 + Ala	> 0.9999
1mM Ala vs. hPSC	> 0.9999	hPSC shATG5 #2 + Ala vs. hPSC + Ala	> 0.9999
1mM Ala vs. hPSC shATG5 #2	0.0244	hPSC shATG7 #1 + Ala vs. hPSC + Ala	0.9989
1mM Ala vs. hPSC shATG7 #1	0.0049		

EFig.7i One-way ANOVA:  $F=22.69$ ,  $p=0.0016$  (n=3)

Tukey's multiple comparisons test	Adjusted p Value
hPSC - ShGFP vs. hPSC - ShATG5	0.002
hPSC - ShGFP vs. hPSC - ShATG7	0.004
hPSC - ShATG5 vs. hPSC - ShATG7	0.7353

EFig.7j Unpaired two-tailed T-test, p-value (n=3)

ctrl media vs. hPSC	0.0062	hPSC vs. hPSC shATG5	0.0428
ctrl media vs. hPSC shATG5	0.0196	hPSC vs. hPSC shATG7	0.0477
ctrl media vs. hPSC shATG7	0.0028	hPSC shATG5 vs. hPSC shATG7	0.5691

## EFig.7k Unpaired two-tailed T-test, p-value (n=3)

hPSC #2 vs.	hPSC #2 shATG7	0.021311
hPSC #2 vs.	hPSC #2 10uM CQ	0.020612
hPSC #2 shATG5	hPSC #2 shATG7	0.299999

## EFig.7m Unpaired two-tailed T-test, p-value (n=3)

mPSC shGFP vs.	mPSC shATG5	<0.0001	mPSC shGFP vs.	mPSC CQ	0.0001
mPSC shGFP vs.	mPSC shATG7	0.0003	mPSC vs.	mPSC CQ	0.0110
mPSC shGFP vs.	mPSC	0.3879	mPSC shATG5 vs.	mPSC shATG7	0.0011

## EFig.7n One-way ANOVA for last time-point: F=13.77, p&lt;0.0001 (n=4)

Tukey's multiple comparisons test	P Value	shATG5 #1 vs. shATG7 #1	0.1284
shGFP vs. shATG5 #1	0.0103	shATG5 #1 vs. shATG7 #2	0.0719
shGFP vs. shATG5 #2	0.0124	shATG5 #2 vs. shATG7 #1	0.1510
shGFP vs. shATG7 #1	0.6657	shATG5 #2 vs. shATG7 #2	0.0604
shGFP vs. shATG7 #2	< 0.0001	shATG7 #1 vs. shATG7 #2	0.0005
shATG5 #1 vs. shATG5 #2	> 0.9999		

## EFig.7o One-way ANOVA: F=0.3049, p=0.8669 (n=3)

Tukey's multiple comparisons test	p Value	hPSC shATG5 #1 vs. hPSC shATG7 #1	> 0.9999
hPSC shGFP vs. hPSC shATG5 #1	0.9166	hPSC shATG5 #2 vs. hPSC shATG7 #2	0.9413
hPSC shGFP vs. hPSC shATG5 #2	0.9956	hPSC shATG5 #2 vs. hPSC shATG7 #1	0.9897
hPSC shGFP vs. hPSC shATG7 #1	0.919	hPSC shATG5 #2 vs. hPSC shATG7 #2	0.9984
hPSC shGFP vs. hPSC shATG7 #2	> 0.9999	hPSC shATG7 #1 vs. hPSC shATG7 #2	0.9432
hPSC shATG5 #1 vs. hPSC shATG5 #2	0.989		

## EFig.7p One-way ANOVA: F=0.30889, p=0.6937 (n=3)

Tukey's multiple comparisons test	p Value
mPSC shGFP vs. mPSC shATG5	0.6879
mPSC shGFP vs. mPSC shATG7	0.9727
mPSC shATG5 vs. mPSC shATG7	0.8117

**Extended Data Figure8**

## EFig.8a One-way ANOVA, F=9.134, p=0.0005 (n=6)

Tukey's multiple comparisons test	P Value	Ala vs. 8988T CM	0.0004
Ctrl vs. Ala	0.0079	Ala vs. hPSC CM	0.0069
Ctrl vs. 8988T CM	0.5763	8988T CM vs. hPSC CM	0.6148
Ctrl vs. hPSC CM	> 0.9999		



**EFig.8b** One-way ANOVA,  $F=70.76$ ,  $p<0.0001$  (n=4)

Tukey's multiple comparisons test	P Value	10% serum vs. hPSC2 CM	0.0192
ctrl vs. 10% serum	< 0.0001	10% serum vs. 8T CM	< 0.0001
ctrl vs. hPSC2 CM	< 0.0001	hPSC2 CM vs. 8T CM	< 0.0001
ctrl vs. 8T CM	0.9996		

**EFig.8c** One-way ANOVA,  $F=28.89$ ,  $p<0.0001$  (n=3)

Tukey's multiple comparisons test	P Value	8902 CM vs. hPSC 2 CM	0.1392
ctrl vs. 8902 CM	0.4219	8902 CM vs. 10% serum	< 0.0001
ctrl vs. hPSC 2 CM	0.0091	hPSC 2 CM vs. 10% serum	0.0022
ctrl vs. 10% serum	< 0.0001		

**EFig.8d** One-way ANOVA:  $F=8.022$ ,  $p=0.0001$  (n=4)

Tukey's multiple comparisons test	P Value	hPSC shGFP vs. ctrl media	0.0420
8T vs. hPSC shGFP	0.0501	ShATG5 vs. ShATG7	0.4224
8T vs. ShATG5	0.7837	ShATG5 vs. full gluc	0.2982
8T vs. ShATG7	0.9956	ShATG5 vs. low gluc + Ala	0.1327
8T vs. full gluc	0.0190	ShATG5 vs. ctrl media	0.7376
8T vs. low gluc + Ala	0.0066	ShATG7 vs. full gluc	0.0048
8T vs. ctrl media	> 0.9999	ShATG7 vs. low gluc + Ala	0.0016
hPSC shGFP vs. ShATG5	0.5458	ShATG7 vs. ctrl media	0.9980
hPSC shGFP vs. ShATG7	0.0133	full gluc vs. low gluc + Ala	0.9989
hPSC shGFP vs. full gluc	0.9992	full gluc vs. ctrl media	0.0158
hPSC shGFP vs. low gluc + Ala	0.9634	low gluc + Ala vs. ctrl media	0.0054

**EFig.8e** One-way ANOVA:  $F=10.67$ ,  $p<0.0001$  (n=8)

Tukey's multiple comparisons test	P Value	hpsc cm vs. CTRL Media	0.0011
8t cm vs. hpsc cm	0.0011	hpsc ShATG5 cm vs. hpsc ShATG7 cm	0.9967
8t cm vs. hpsc ShATG5 cm	0.9997	hpsc ShATG5 cm vs. 10% serum	0.0005
8t cm vs. hpsc ShATG7 cm	0.9548	hpsc ShATG5 cm vs. 0% + ala	0.0041
8t cm vs. 10% serum	0.0001	hpsc ShATG5 cm vs. CTRL Media	0.9998
8t cm vs. 0% + ala	0.0012	hpsc ShATG7 cm vs. 10% serum	0.0031
8t cm vs. CTRL Media	> 0.9999	hpsc ShATG7 cm vs. 0% + ala	0.0227
hpsc cm vs. hpsc ShATG5 cm	0.0037	hpsc ShATG7 cm vs. CTRL Media	0.9577
hpsc cm vs. hpsc ShATG7 cm	0.0208	10% serum vs. 0% + ala	0.9925
hpsc cm vs. 10% serum	0.9942	10% serum vs. CTRL Media	0.0001
hpsc cm vs. 0% + ala	> 0.9999	0% + ala vs. CTRL Media	0.0013

**EFig.8f** One-way ANOVA:  $F=18.72$ ,  $p<0.0001$  (n=6 for 0% serum + Ala; n=10 for the remaining groups)

Tukey's multiple comparisons test	P Value	hpsc cm vs. hpsc ShATG5 cm	0.0001
8902 cm vs. hpsc cm	0.0030	hpsc cm vs. hpsc ShATG7 cm	0.0001
8902 cm vs. hpsc ShATG5 cm	0.9538	hpsc cm vs. 10% serum	0.1156
8902 cm vs. hpsc ShATG7 cm	0.9546	hpsc cm vs. 0% + ala	> 0.9999
8902 cm vs. 10% serum	< 0.0001	hpsc cm vs. ctrl media	0.0007
8902 cm vs. 0% + ala	0.0202	hpsc ShATG5 cm vs. hpsc ShATG7 cm	> 0.9999
8902 cm vs. ctrl media	0.9519	hpsc ShATG5 cm vs. 10% serum	< 0.0001

hpsc ShATG5 cm vs. 0% + ala	0.0015	hpsc ShATG7 cm vs. ctrl media	> 0.9999
hpsc ShATG cm vs. ctrl media	> 0.9999	10% serum vs. 0% + ala	0.2018
hpsc ShATG7 cm vs. 10% serum	< 0.0001	10% serum vs. ctrl media	< 0.0001
hpsc ShATG7 cm vs. 0% + ala	0.0015	0% + ala vs. ctrl media	0.0042

**EFig.8g** One-way ANOVA:  $F=54.24$ ,  $p<0.0001$  (n=3)

Tukey's multiple comparisons test	P Value	hPSC-shATG5 vs. hPSC-shATG5 + 1mM Ala	< 0.0001
ctrl vs. hPSC-ShGFP	< 0.0001	hPSC-shATG5 vs. hPSC-shATG7	0.2809
ctrl vs. hPSC-shATG5	0.9911	hPSC-shATG5 vs. hPSC-shATG7 + 1mM Ala	< 0.0001
ctrl vs. hPSC-shATG5 + 1mM Ala	< 0.0001	hPSC-shATG5 vs. complete media	< 0.0001
ctrl vs. hPSC-shATG7	0.0937	hPSC-shATG5 + 1mM Ala vs. hPSC-shATG7	< 0.0001
ctrl vs. hPSC-shATG7 + 1mM Ala	< 0.0001	hPSC-shATG5 + 1mM Ala vs. hPSC-shATG7 + 1mM Ala	0.4439
ctrl vs. complete media	< 0.0001	hPSC-shATG5 + 1mM Ala vs. complete media	0.9650
hPSC-ShGFP vs. hPSC-shATG5	< 0.0001	hPSC-shATG7 vs. hPSC-shATG7 + 1mM Ala	< 0.0001
hPSC-ShGFP vs. hPSC-shATG5 + 1mM Ala	0.2194	hPSC-shATG7 vs. complete media	0.0001
hPSC-ShGFP vs. hPSC-shATG7	0.0018	hPSC-shATG7 + 1mM Ala vs. complete media	0.1159
hPSC-ShGFP vs. hPSC-shATG7 + 1mM Ala	0.0063		
hPSC-ShGFP vs. complete media	0.6710		

**EFig.8h** One-way ANOVA:  $F=58.91$   $p<0.0001$  (n=3)

Tukey's multiple comparisons test	p Value	shGFP CM vs. shATG7 CM	0.0395
ctrl media (no serum) vs. shGFP CM	0.0002	shGFP CM vs. complete media	0.0003
ctrl media (no serum) vs. shATG5 CM	0.0151	shATG5 CM vs. shATG7 CM	> 0.9999
ctrl media (no serum) vs. shATG7 CM	0.0156	shATG5 CM vs. complete media	< 0.0001
ctrl media (no serum) vs. complete media	< 0.0001	shATG7 CM vs. complete media	< 0.0001
shGFP CM vs. shATG5 CM	0.0408		

**EFig.8i** One-way ANOVA:  $F=13.45$ ,  $p=0.0005$  (n=3)

Tukey's multiple comparisons test	p Value	shGFP CM vs. shATG7 CM	0.5864
ctrl media (no serum) vs. shGFP CM	0.0108	shGFP CM vs. complete media	0.1048
ctrl media (no serum) vs. shATG5 CM	0.1296	shATG5 CM vs. shATG7 CM	> 0.9999
ctrl media (no serum) vs. shATG7 CM	0.1084	shATG5 CM vs. complete media	0.0088
ctrl media (no serum) vs. complete media	0.0002	shATG7 CM vs. complete media	0.0105
shGFP CM vs. shATG5 CM	0.5202		

**EFig.8j** One-way ANOVA:  $F=11,35$   $p=0.0002$  (n=4)

Tukey's multiple comparisons test	p Value	1mM Ala vs. 1mM Lac	0.0115
ctrl (0.5mM Glc) vs. 1mM Ala	0.0085	1mM Ala vs. full glc	> 0.9999
ctrl (0.5mM Glc) vs. 1mM Pyr	0.0013	1mM Pyr vs. 1mM Lac	0.0018
ctrl (0.5mM Glc) vs. 1mM Lac	0.9999	1mM Pyr vs. full glc	0.9017
ctrl (0.5mM Glc) vs. full glc	0.0070	1mM Lac vs. full glc	0.0095
1mM Ala vs. 1mM Pyr	0.8623		

**EFig.8k** One-way ANOVA:  $F=15.07$   $p<0.0001$  (n=4)

Tukey's multiple comparisons test	P Value		
ctrl (0.5mM Glc) vs. 1mM Ala	0.0060	1mM Ala vs. 1mM Lac	0.0028
ctrl (0.5mM Glc) vs. 1mM Pyr	0.0008	1mM Ala vs. full glc	0.9658
ctrl (0.5mM Glc) vs. 1mM Lac	0.9938	1mM Pyr vs. 1mM Lac	0.0004
ctrl (0.5mM Glc) vs. full glc	0.0018	1mM Pyr vs. full glc	0.9926
1mM Ala vs. 1mM Pyr	0.8219	1mM Lac vs. full glc	0.0008

EFig.8l One-way ANOVA:  $F=9,797$   $p=0.0004$  (n=4)

Tukey's multiple comparisons test	P Value		
0.5mM Gluc vs. 0.5mM Gluc + 1mM Ala	0.0323	0.5mM Gluc + 1mM Ala vs. 0.5mM Gluc + 1mM Lac	0.1496
0.5mM Gluc vs. 0.5mM Gluc + 1mM Pyr	0.0044	0.5mM Gluc + 1mM Ala vs. Full media	0.4176
0.5mM Gluc vs. 0.5mM Gluc + 1mM Lac	0.9115	0.5mM Gluc + 1mM Pyr vs. 0.5mM Gluc + 1mM Lac	0.0229
0.5mM Gluc vs. Full media	0.0010	0.5mM Gluc + 1mM Pyr vs. Full media	0.9395
0.5mM Gluc + 1mM Ala vs. 0.5mM Gluc + 1mM Pyr	0.8385	0.5mM Gluc + 1mM Lac vs. Full media	0.0053

EFig.8m Two-way ANOVA (n=3)

Source of Variation	% of total variation	P value
Interaction	11.49	0.0005
Row Factor	32.61	< 0.0001
Column Factor	45.71	< 0.0001

Tukey's multiple comparisons test	p Value		
<b>shGFP</b>			
low serum vs. hPSC CM	< 0.0001	hPSC CM vs. 8T CM	0.3507
low serum vs. 8T CM	0.4710	hPSC CM vs. Full serum	0.2107
low serum vs. Full serum	< 0.0001	hPSC CM vs. Ala	0.0616
low serum vs. Ala	0.0060	8T CM vs. Full serum	0.0018
hPSC CM vs. 8T CM	0.0054	8T CM vs. Ala	0.9021
hPSC CM vs. Full serum	0.9595	Full serum vs. Ala	0.0001
hPSC CM vs. Ala	0.7902	<b>shGPT2 1</b>	
8T CM vs. Full serum	0.0007	low serum vs. hPSC CM	< 0.0001
8T CM vs. Ala	0.2208	low serum vs. 8T CM	0.0005
Full serum vs. Ala	0.4202	low serum vs. Full serum	< 0.0001
<b>shGPT1 1</b>			
low serum vs. hPSC CM	0.6757	low serum vs. Ala	< 0.0001
low serum vs. 8T CM	0.9737	hPSC CM vs. 8T CM	0.0701
low serum vs. Full serum	0.0005	hPSC CM vs. Full serum	0.5273
low serum vs. Ala	0.9653	hPSC CM vs. Ala	0.9999
hPSC CM vs. 8T CM	0.9503	8T CM vs. Full serum	0.0009
hPSC CM vs. Full serum	0.0258	8T CM vs. Ala	0.0972
hPSC CM vs. Ala	0.2907	Full serum vs. Ala	0.4387
8T CM vs. Full serum	0.0034	<b>shGPT2 2</b>	
8T CM vs. Ala	0.7177	low serum vs. hPSC CM	0.0004
Full serum vs. Ala	< 0.0001	low serum vs. 8T CM	0.0216
<b>shGPT1 2</b>			
low serum vs. hPSC CM	0.0493	low serum vs. Full serum	< 0.0001
low serum vs. 8T CM	0.8653	low serum vs. Ala	< 0.0001
low serum vs. Full serum	< 0.0001	hPSC CM vs. 8T CM	0.6821
low serum vs. Ala	> 0.9999	hPSC CM vs. Full serum	0.0736
		hPSC CM vs. Ala	0.6732
		8T CM vs. Full serum	0.0020
		8T CM vs. Ala	0.0771
		Full serum vs. Ala	0.6699

**Extended Data Figure9**

EFig.9b Two-tailed t-tests performed for each time-point (n=10)

<b>p-value at day:</b>	<b>7</b>	<b>10</b>	<b>14</b>	<b>18</b>	<b>21</b>	<b>25</b>	<b>28</b>
8988T vs. 8T+hPSC-ShGFP	0.0000	0.0002	0.0000	0.0000	0.0001	0.0000	0.0001
8T+hPSC-ShATG5 vs. 8T+hPSC-ShGFP	0.0035	0.1258	0.0867	0.0820	0.0356	0.0072	0.0516
8T+hPSC-ShATG7 vs. 8T+hPSC-ShGFP	0.0057	0.0194	0.0275	0.1151	0.1493	0.0371	0.1293
hPSC vs. 8T+hPSC-ShGFP	0.0058	0.7893	0.0502	0.4836	0.5813	0.3776	0.2476
<b>p-value at day:</b>	<b>32</b>	<b>35</b>	<b>39</b>	<b>42</b>	<b>46</b>	<b>49</b>	<b>53</b>
8988T vs. 8T+hPSC-ShGFP	0.0001	0.0000	0.0009	0.0091	0.0055	0.0072	0.0269
8T+hPSC-ShATG5 vs. 8T+hPSC-ShGFP	0.1749	0.0410	0.1400	0.0819	0.0446	0.0887	0.1044
8T+hPSC-ShATG7 vs. 8T+hPSC-ShGFP	0.0384	0.0226	0.0209	0.1099	0.0264	0.0477	0.1001
hPSC vs. 8T+hPSC-ShGFP	0.4817	0.1423	0.0852	0.1027	0.1374	0.1742	0.2367
<b>p-value at day:</b>	<b>56</b>	<b>60</b>	<b>63</b>	<b>67</b>	<b>70</b>	<b>74</b>	
8988T vs. 8T+hPSC-ShGFP	0.0469	0.0438	0.1012	0.0968	0.1287	0.1442	
8T+hPSC-ShATG5 vs. 8T+hPSC-ShGFP	0.2277	0.1432	0.3806	0.3127	0.3344	0.3019	
8T+hPSC-ShATG7 vs. 8T+hPSC-ShGFP	0.1188	0.1351	0.2547	0.1596	0.2602	0.2836	
hPSC vs. 8T+hPSC-ShGFP	0.2662	0.2910	0.5014	0.3409	0.4277	0.4178	

EFig.9c One-way ANOVA: F=8.68, p&lt;0.0001 (n=10 for MiaPaCa2 only, MiaPaCa2+hPSC-ShGFP, MiaPaCa2+hPSC-ShATG5 and MiaPaCa2+hPSC-ShATG7; n=5 for hPSC only)

Tukey's multiple comparisons test	p Value	Comparison	p Value
Mia vs. Mia+hPSC-ShGFP	< 0.0001	Mia+hPSC-ShGFP vs. Mia+hPSC-ShATG7	0.002
Mia vs. Mia+hPSC-ShATG5	0.3856	Mia+hPSC-ShGFP vs. hPSC only	0.0005
Mia vs. Mia+hPSC-ShATG7	0.7352	Mia+hPSC-ShATG5 vs. Mia+hPSC-ShATG7	0.9778
Mia vs. hPSC only	0.9994	Mia+hPSC-ShATG5 vs. hPSC only	0.4463
Mia+hPSC-ShGFP vs. Mia+hPSC-ShATG5	0.0099	Mia+hPSC-ShATG7 vs. hPSC only	0.735

EFig.9d Log-rank (Mantel-Cox) test, comparisons by pairs (n=10)

MiaPaCa2 vs. MiaPaCa2+hPSC-shGFP: Chi square=17.89 p-value&lt;0.0001

MiaPaCa2+hPSC-shGFP vs. MiaPaCa2+hPSC-shATG5: Chi square=5.654, p-value=0.00174

MiaPaCa2+hPSC-shGFP vs. MiaPaCa2+hPSC-shATG7: Chi square=4.019, p-value=0.045

MiaPaCa2+hPSC-shATG5 vs. MiaPaCa2+hPSC-shATG7: Chi square=0.7871, p-value=0.375

EFig.9e Two-tailed t-tests performed for each time-point (n=10)

<b>p-value at day:</b>	<b>6</b>	<b>9</b>	<b>13</b>	<b>16</b>	<b>20</b>	<b>23</b>	<b>27</b>	<b>30</b>
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MiaPaCa2 vs. Mia+hPSC-ShGFP	0.0249	0.0037	0.0001	0.0002	0.0002	0.0008	0.0003	0.0000
MiaPaCa2+hPSC-ShATG5 vs. Mia+hPSC-ShGFP	0.2946	0.4342	0.0071	0.0052	0.0088	0.0093	0.0551	0.0177
MiaPaCa2+hPSC-ShATG7 vs. Mia+hPSC-ShGFP	0.0636	0.0960	0.0037	0.0287	0.0033	0.0705	0.1008	0.4414
hPSC vs. MiaPaCa2+hPSC-ShGFP	0.1014	0.0262	0.0041	0.0046	0.0047	0.0099	0.0062	0.0004
<b>p-value at day:</b>	<b>34</b>	<b>38</b>	<b>42</b>	<b>44</b>	<b>48</b>	<b>51</b>	<b>55</b>	
MiaPaCa2 vs. Mia+hPSC-ShGFP	0.0000	0.0007	0.0010	0.0014	0.0001	0.0033	0.0113	
MiaPaCa2+hPSC-ShATG5 vs. Mia+hPSC-ShGFP	0.0088	0.2006	0.3241	0.1026	0.1407	0.3739	0.3409	
MiaPaCa2+hPSC-ShATG7 vs. Mia+hPSC-ShGFP	0.4766	0.1320	0.1446	0.1172	0.0905	0.0733	0.0320	
hPSC vs. MiaPaCa2+hPSC-ShGFP	0.0001	0.0048	0.0068	0.0056	0.0003	0.0058	0.0127	

EFig.9h One-way ANOVA:  $F=0.5944$ ,  $p=0.5814$  (n=2 for shATG7; n=3 for shATG5 and n=4 for shGFP)

Tukey's multiple comparisons test	Adjusted p Value
shGFP vs. shATG5	0.5982
shGFP vs. shATG7	> 0.9999
shATG5 vs. shATG7	0.6915

### Extended Data Figure 10

EFig.10b One-way ANOVA:  $F=7.668$ ,  $p=0.0006$  (n=5)

Tukey's multiple comparisons test	p Value
MiaPaCa vs. MiaPaca + hPSC-shGFP	0.0252
MiaPaCa vs. Miapaca + hPSC-shATG5	> 0.9999
MiaPaCa vs. Miapaca + hPSC-shATG7	0.6185
MiaPaCa vs. hPSC - ShGFP	0.5613
MiaPaca + hPSC-shGFP vs. Miapaca + hPSC-shATG5	0.0283
MiaPaca + hPSC-shGFP vs. Miapaca + hPSC-shATG7	0.001
MiaPaca + hPSC-shGFP vs. hPSC - ShGFP	0.0008
Miapaca + hPSC-shATG5 vs. Miapaca + hPSC-shATG7	0.5859
Miapaca + hPSC-shATG5 vs. hPSC - ShGFP	0.5289
Miapaca + hPSC-shATG7 vs. hPSC - ShGFP	> 0.9999

EFig.10c Log-rank (Mantel-Cox) test, comparisons by pairs (n=5).

MiaPaCa2 vs. MiaPaCa2+hPSC-shGFP: Chi square=4.782, p-value=0.0288

MiaPaCa2+hPSC-shGFP vs. MiaPaCa2+hPSC-shATG5: Chi square=4.841, p-value=0.0278

MiaPaCa2+hPSC-shGFP vs. MiaPaCa2+hPSC-shATG7: Chi square=9.851, p-value=0.0017

MiaPaCa2+hPSC-shATG5 vs. MiaPaCa2+hPSC-shATG7: Chi square=0.8667, p-value=0.3519

EFig. 10d Two-tailed t-tests performed for each time-point (n=5)

<b>p-value at week:</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
MiaPaCa2 vs. Mia+ hPSC-shGFP	0.0652	0.0631	0.0891	0.0427	0.0636
MiaPaCa2+ hPSC-shATG5 vs. Mia+ hPSC-shGFP	0.6837	0.0654	0.0470	0.0454	0.0988
MiaPaCa2+ hPSC-shATG7 vs. Mia+ hPSC-shGFP	0.0972	0.0177	0.0097	0.0032	0.0142