Supplemental Figure Legends

Figure S1. Characterization of tumor histology.

A. Representative immunohistochemistry (IHC) for Atg7 in tumors at 14 weeks post tumor initiation. Arrow indicates stromal cell positive for Atg7 expression surrounded by Atg7-deficient tumor cells.

B. Western blot of Atg7 in tumors at 18 weeks post tumor initiation. Numbers identify individual mice. Note Atg7 expression in *atg7*$^{-/-}$ tumor tissue detected by Western blot due to the presence of *atg7* wild type stroma with *K-ras*$^{G12D/+}$*;atg7*$^{-/-}$ tumors.

C. Representative IHC for SP-C (top panel) and CCSP (bottom panel) of *K-ras*$^{G12D/+}$*;atg7*$^{+/+}$ and *K-ras*$^{G12D/+}$*;atg7*$^{-/-}$ tumors at 14 weeks.

Figure S2. Kinetics of autophagy parameter induction.

A and B. Representative IHC for LC3 (A) and p62 (B) of *K-ras*$^{G12D/+}$*;atg7*$^{+/+}$ and *K-ras*$^{G12D/+}$*;atg7*$^{-/-}$ tumors at the indicated times in high magnification. Red arrows in *K-ras*$^{G12D/+}$*;atg7*$^{+/+}$ point to autophagosomes and black arrows in *K-ras*$^{G12D/+}$*;atg7*$^{-/-}$ point to LC3 or p62 aggregates.

C. Quantification of tumor numbers at indicated times (n=3 mice for each time and genotype). Error bar represents SEM, $p>0.05$ (t-test).

Figure S3. Atg7 deficiency reduces K-ras-driven lung tumor burden.

Representative histology (H&E) of lung lobes at the indicated times were scanned with a Trestle/Zeiss MedMicro imaging system (n=3 mice for each time point and genotype).

Figure S4. Atg7 is required to sustain oncogenic signaling.

A and B. Representative IHC for P-MEK (A) and P-ERK (B) of *K-ras*$^{G12D/+}$;*atg7*$^{+/+}$ and *K-ras*$^{G12D/+}$;*atg7*$^{-/-}$ tumors at the indicated times (n=3 mice for each time point and genotype).

C. *K-ras*$^{G12D/+}$;*atg7*$^{+/+}$ and *K-ras*$^{G12D/+}$;*atg7*$^{-/-}$ tumors at 18 weeks were lysed and blotted with the indicated antibodies. Lung tissue from *K-ras*$^{+/+}$;*atg7*$^{+/+}$ and *K-ras*$^{+/+}$;*atg7*$^{-/-}$ mice are shown as controls.

Figure S5. Atg7 is required to maintain tumor cell proliferation.

A. Left panel: representative IHC for p53 in tumors at the indicated times (n=3 mice for each time point and genotype). Right panel: quantification of p53-positive cells in lung tumors. Error bar represents SEM. **p<0.01; ***p<0.001 (two-way ANOVA with Bonferroni post-test).

B. Left panel: representative IHC for p21 in tumors at indicated times (n=3 mice for each time point and genotype). Right panel: quantification of p21-positive cells in lung tumors. Error bar represents SEM. ***p<0.001 (two-way ANOVA with Bonferroni post-test).

C. Representative IHC for Ki67 in tumors at indicated times (n=3 mice for each time point and genotype).

Figure S6. Senescence and apoptosis are not the major causes of tumor atrophy.

A. Senescence β-galactosidase activity in the tumors at the indicated times (n=2 mice for each time point and genotype).

B. *K-ras*$^{G12D/+}$;*atg7*$^{+/+}$ and *K-ras*$^{G12D/+}$;*atg7*$^{-/-}$ tumors at 18 weeks were lysed and immunoblotted with an active caspase-3 antibody. An *H-ras*^{V12};*atg5*$^{-/-}$ allograft tumor (*7*) was used as positive control.

Figure S7. Kinetics of DNA damage response activation in *K-ras*$^{G12D/+}$ driven tumors.

Left panel: IHC staining for γ-H2AX of tumors at indicated times (n=3 mice for each genotype). Right panel: quantification of γ-H2AX-positive nuclei at the indicated times. Error bar represents SEM. *p<0.05; **p<0.01, ***p<0.001(two-way ANOVA with Bonferroni post-test).

Figure S8. Histology of tumors at 42 weeks.

A. Representative H&E and IHC for Atg7, p62, and LC3 in *K-ras*$^{G12D/+}$*;atg7*$^{+/+}$ (n=4 mice) and *K-ras*$^{G12D/+}$*;atg7*$^{-/-}$ (n=5 mice) tumors at 42 weeks. Red arrows in *K-ras*$^{G12D/+}$*;atg7*$^{+/+}$ tumors point to autophagosomes and black arrows in *K-ras*$^{G12D/+}$*;atg7*$^{-/-}$ tumors point to LC3 or p62 aggregates.

B. Representative IHC for CD68 in *K-ras*$^{G12D/+}$*;atg7*$^{+/+}$ (n=4 mice) and *K-ras*$^{G12D/+}$*;atg7*$^{-/-}$ (n=5 mice) in tumors at 42 weeks under low magnification showing crystalline macrophages within or around tumors or in air sacs.

C. Representative electron micrographs of *K-ras*$^{G12D/+}$*;atg7*$^{+/+}$ (n=2 mice) and *K-ras*$^{G12D/+}$ *atg7*$^{-/-}$ (n=2 mice) tumors at 42 weeks.

Figure S9. Cytokine expression levels in lungs from mice bearing *K-ras*$^{G12D/+}$ tumors.

Mouse cytokine array analysis was performed on lung tissue lysates at 20 weeks post tumor initiation. Analysis of pooled (n=3 mice for each genotype) tumor-bearing lung tissue for *atg7*$^{+/+}$ and *atg7*$^{-/-}$ samples is shown. *K-ras*$^{+/+}$*;atg7*$^{+/+}$ and *K-ras*$^{+/+}$*;atg7*$^{-/-}$ mice were used as controls.

Figure S10. *Atg7* deficiency reduces *p53*$^{-/-}$*;K-ras*$^{G12D/+}$ lung tumorigenesis.

Representative histology (H&E) of lung lobes at the indicated times post Cre administration were scanned with a Trestle/Zeiss MedMicro imaging system (n=3

mice for each time and genotype).

Figure S11. ***Atg7*** **deficiency causes mitochondrial accumulation in tumors.**

Tom20 IHC shows mitochondrial accumulation in *atg7*-deficient compared to *atg7* wild type tumors at the indicated times post Cre administration. (n=3 mice for each time point and genotype).

Figure S12. ***Atg7*** **deficiency causes lipid accumulation in tumors**.

Bodipy staining shows lipid droplet accumulation (green) in *atg7* deficient ($p53^{-/-}$;$K\text{-}ras^{G12D/+}$;$atg7^{-/-}$) but not *atg7* wild type ($p53^{-/-}$;$K\text{-}ras^{G12D/+}$;$atg7^{+/+}$) tumors at 18 weeks post tumor induction.

Figure S13. ***Atg7*** **deficiency does not affect TDCLs proliferation in normal growth medium.**

Viable cell number was determined for $atg7^{+/+}$ and $atg7^{-/-}$ TDCL in nutrient replete conditions. Viable cells were normalized to day 0. Error bar represents SEM. Four independent clones for each genotype were assessed. Error bar represents SEM.

Figure S14. ***Atg7*****-deficient TDCLs are sensitized to metabolic stress.**

A. Clonogenic survival assay of TDCLs following 3 days of starvation (HBSS) plus 4 days of recovery in normal growth medium.

B. Representative images show more cell death in $atg7^{-/-}$ compared to $atg7^{+/+}$ TDCLs under ischemia (5% O_2 and no glucose) conditions.

Figure S15. ***Atg7*** **deficiency in TDCLs causes more cell death and stromal infiltration in allograft tumors.**

Histology (H&E) shows more cell death in $atg7^{-/-}$ TDCL tumors compared to $atg7^{+/+}$ TDCL tumors (arrows point to necrotic cells). Trichrome staining of TDCLs

allograft tumors shows more stroma (blue staining) in *atg7*$^{-/-}$ tumors compared to *atg7*$^{+/+}$ tumors.

Figure S16. *Atg7* deficiency causes lipid accumulation in TDCLs.

A. TLC of lipids from *atg7* wild type and deficient TDCLs. MG: monoglycerides; DG: diglycerides; TG: triglycerides; FFA: free fatty acids; CE: cholesterol esters.

B. Quantification of lipids from (A).

C. Lipid (Bodipy=green) and nuclear (DAPI=blue) staining of starved (HBSS) TDCLs at the indicated times.

Figure S17. *Atg7* deficiency causes accumulation of defective mitochondria.

A. MM in TDCLs under normal conditions summarized in Fig. 4A. Numbers represent independent clones (n=10 for *atg7*$^{+/+}$; n=9 for *atg7*$^{-/-}$).

B. Relative MMP in TDCLs under normal conditions summarized in Fig. 4A. Numbers represent independent clones (n=10 for *atg7*$^{+/+}$; n=9 for *atg7*$^{-/-}$).

Figure S18. Autophagy deficiency alters intracellular metabolite levels.

Heatmap shows relative changes in pool sizes of a total of the 119 intracellular metabolites identified in *atg7*-wild type and *atg7*-deficient TDCLs under normal and starvation (HBSS) conditions. $\log_2$-transformed ion signals were normalized to those in un-starved (0hr) *atg7*-wild type in each pair (2 independent clones from each genotype).

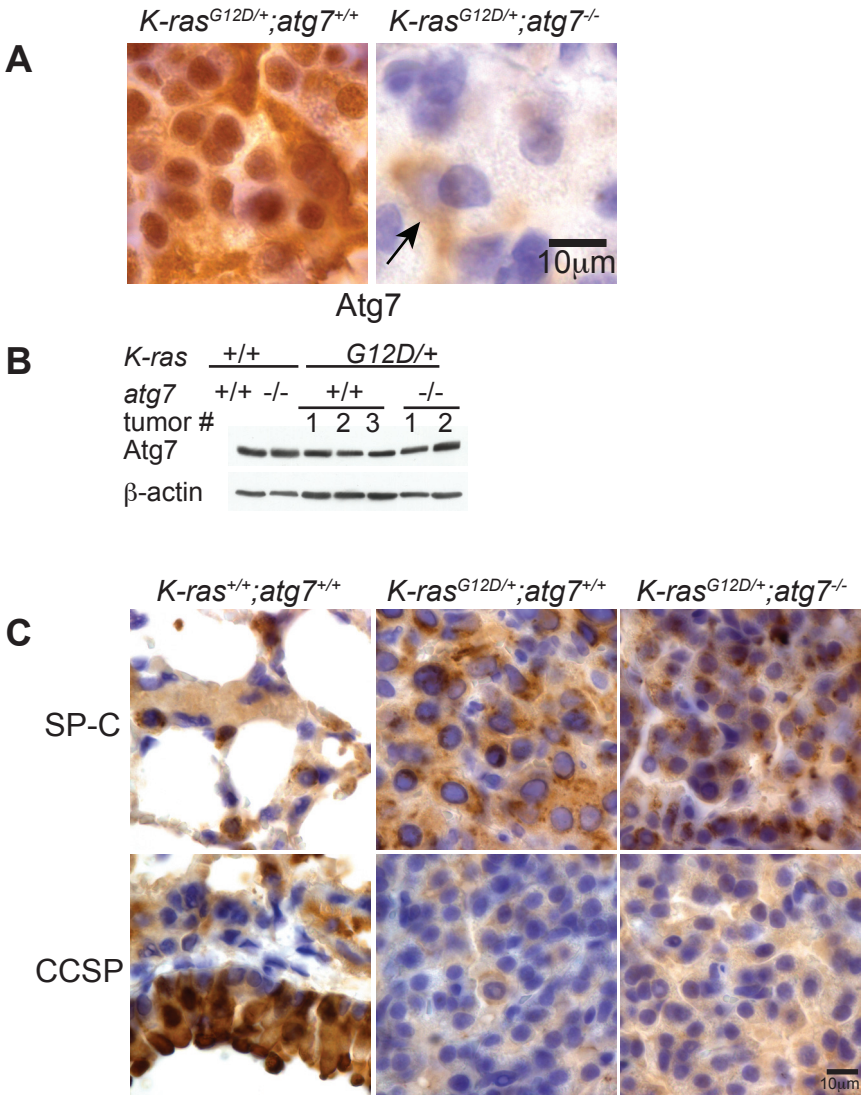
Figure S19. Autophagy deficiency changes intracellular metabolite levels.

Graphs show increased amino acid, glycolytic intermediates and NADH levels in 2 *atg7*-deficient compared to 2 *atg7*-wild type TDCLs at each indicated starvation (HBSS) time.

Figure S20. Autophagy is required for FAO and survival in starvation.

TDCLs were treated with HBSS for the indicated times in the presence of the CPT-1 inhibitor etomoxir (50μM) +/-pyruvate (1mM) and cells were returned to normal medium for 4 days, then stained with Giemsa.

Guo_Figure S1



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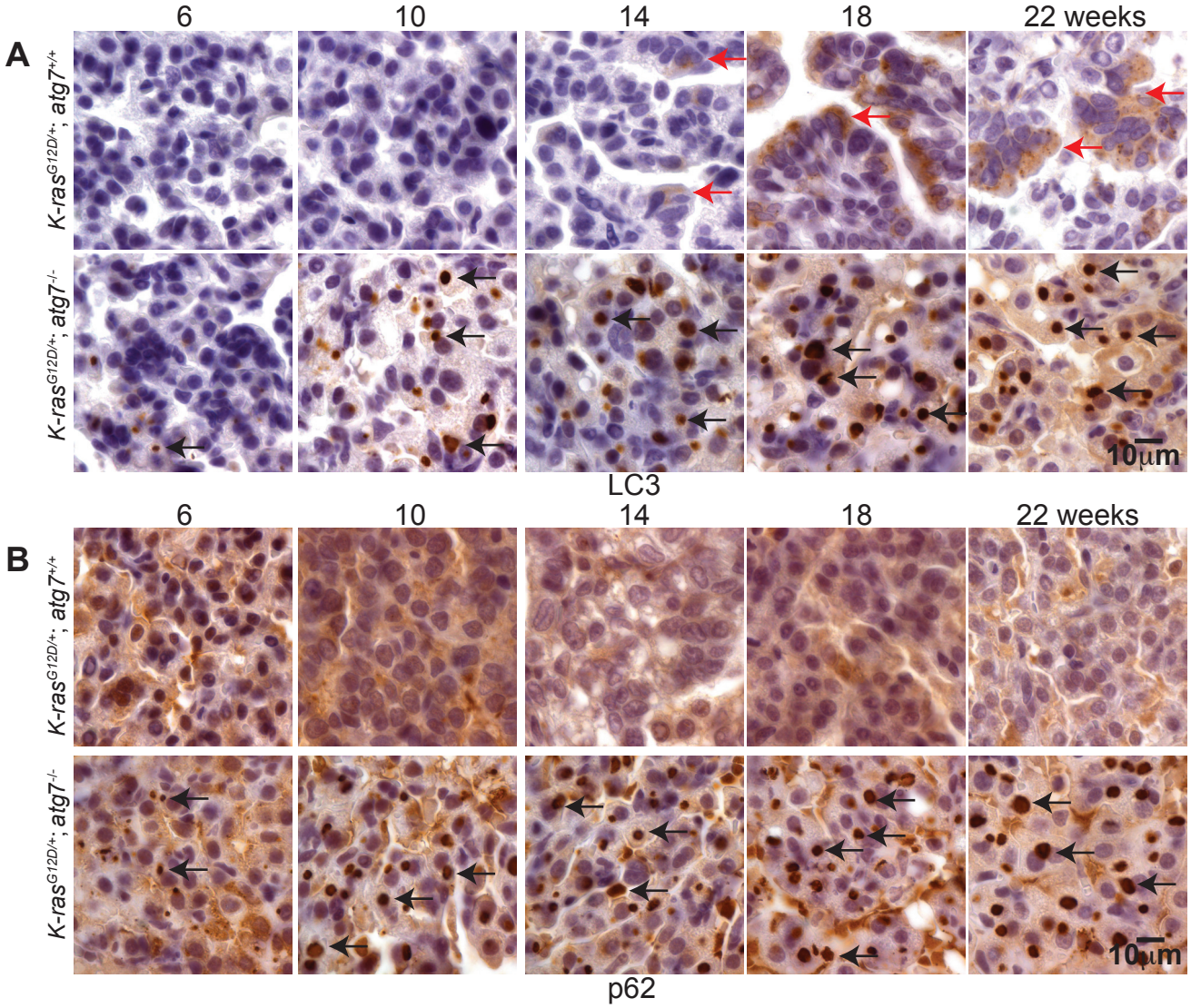

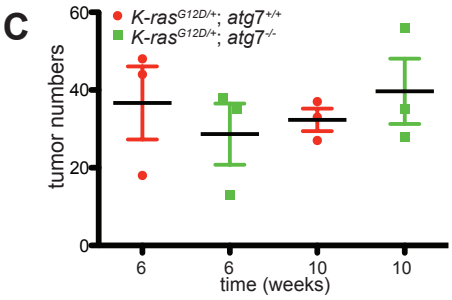

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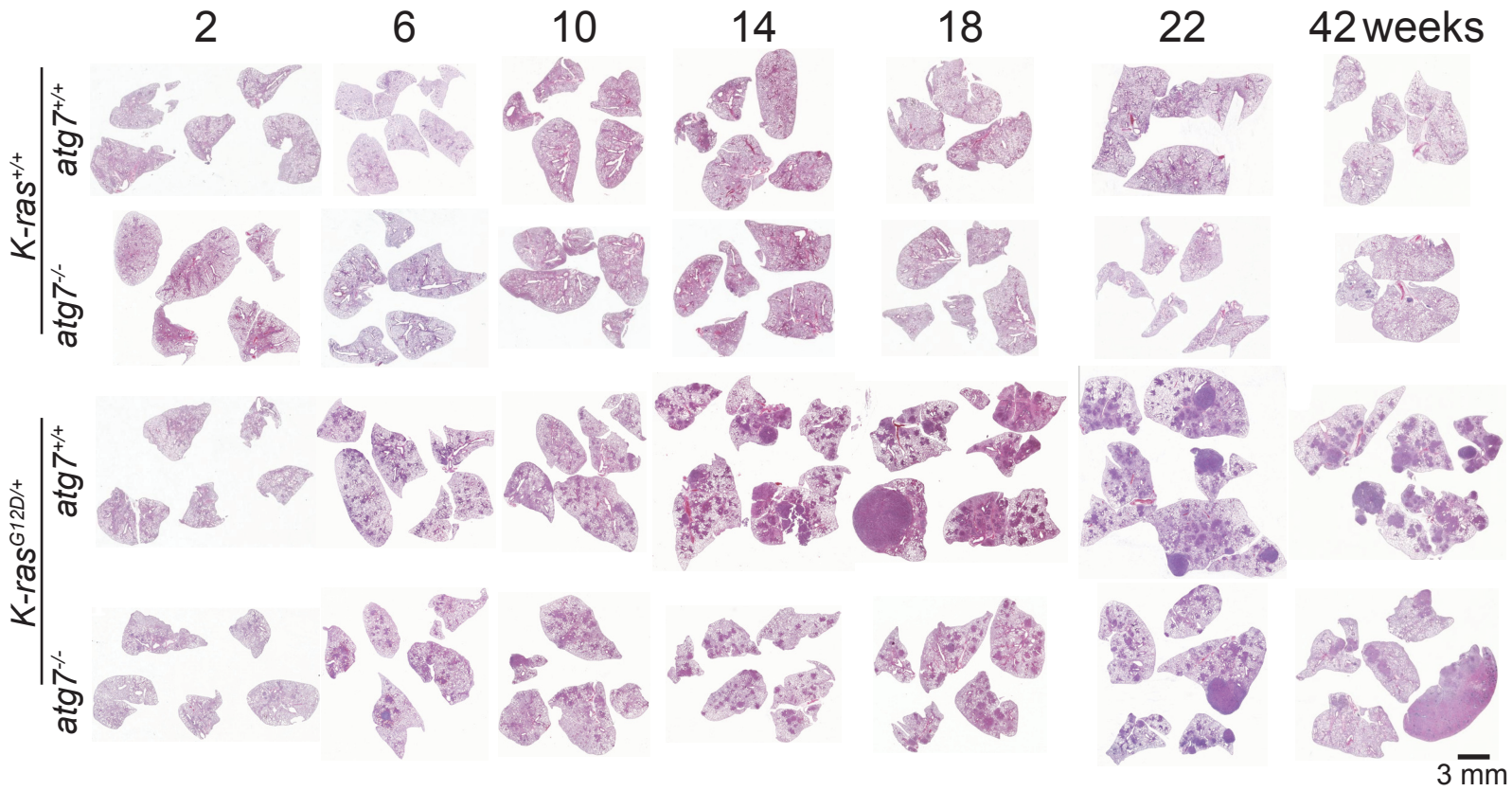

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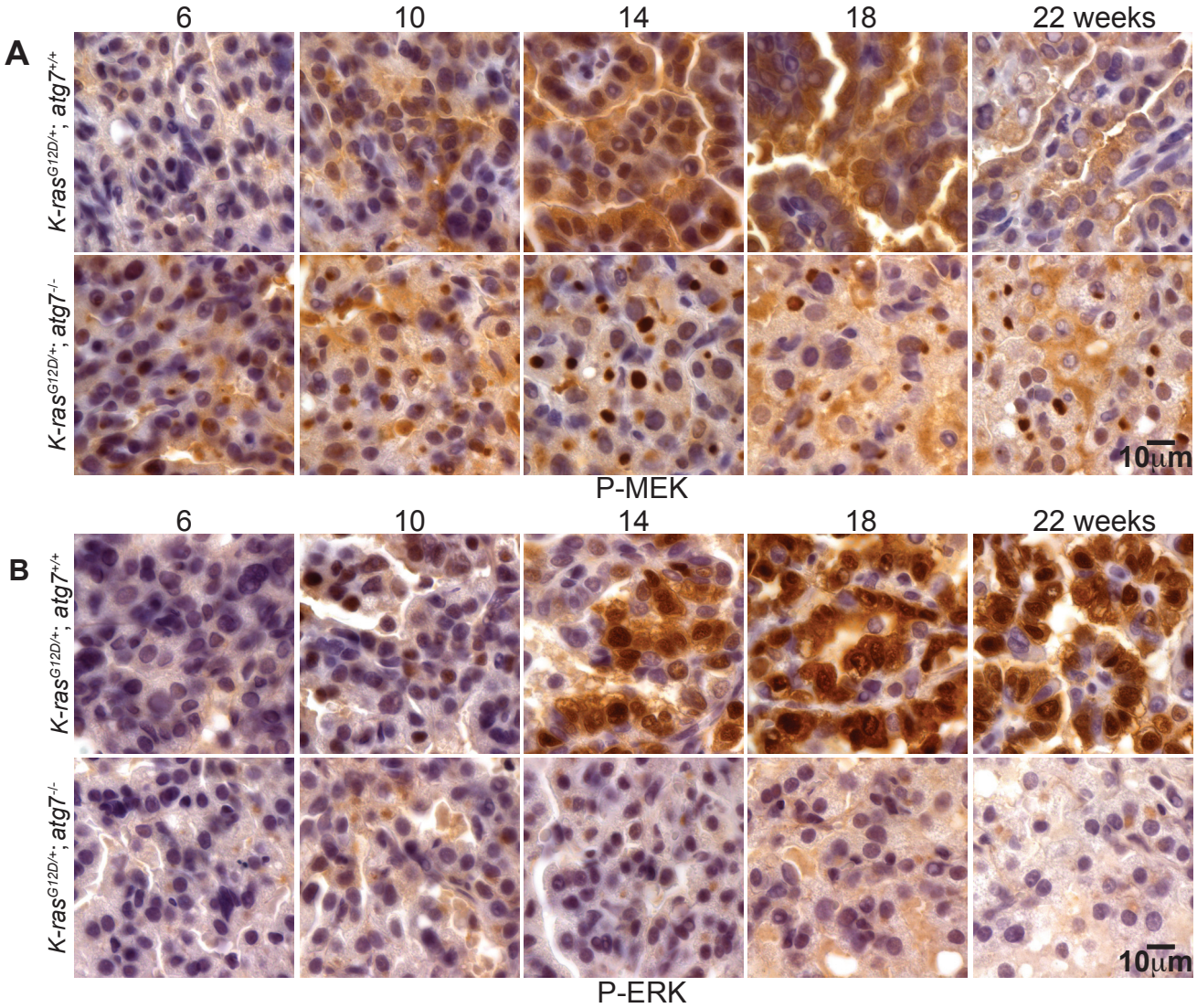

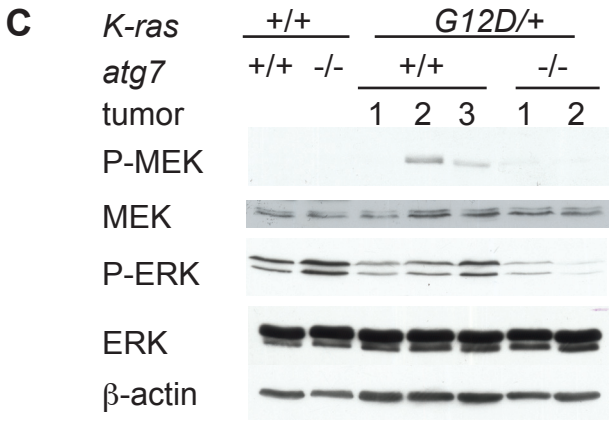

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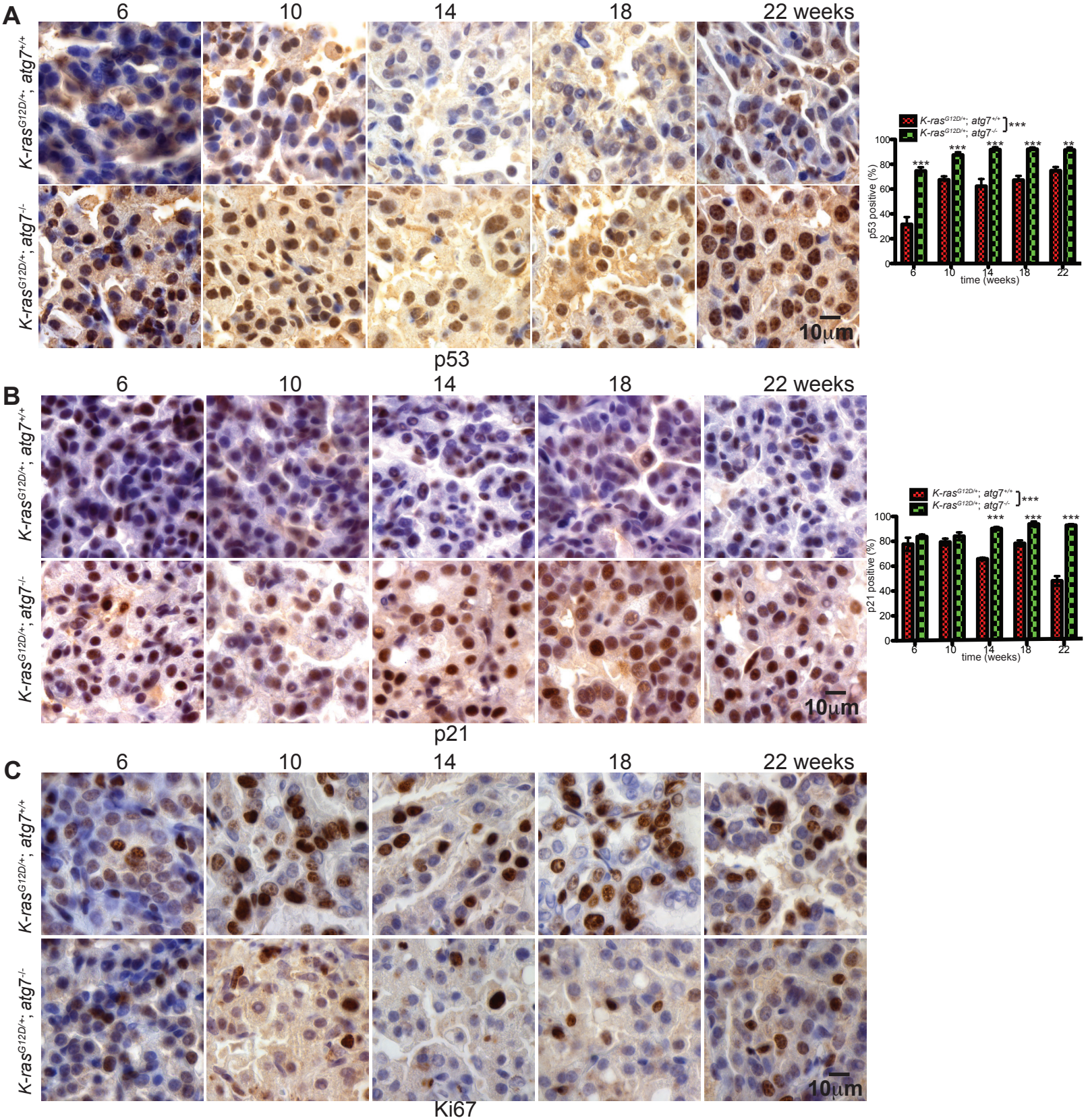

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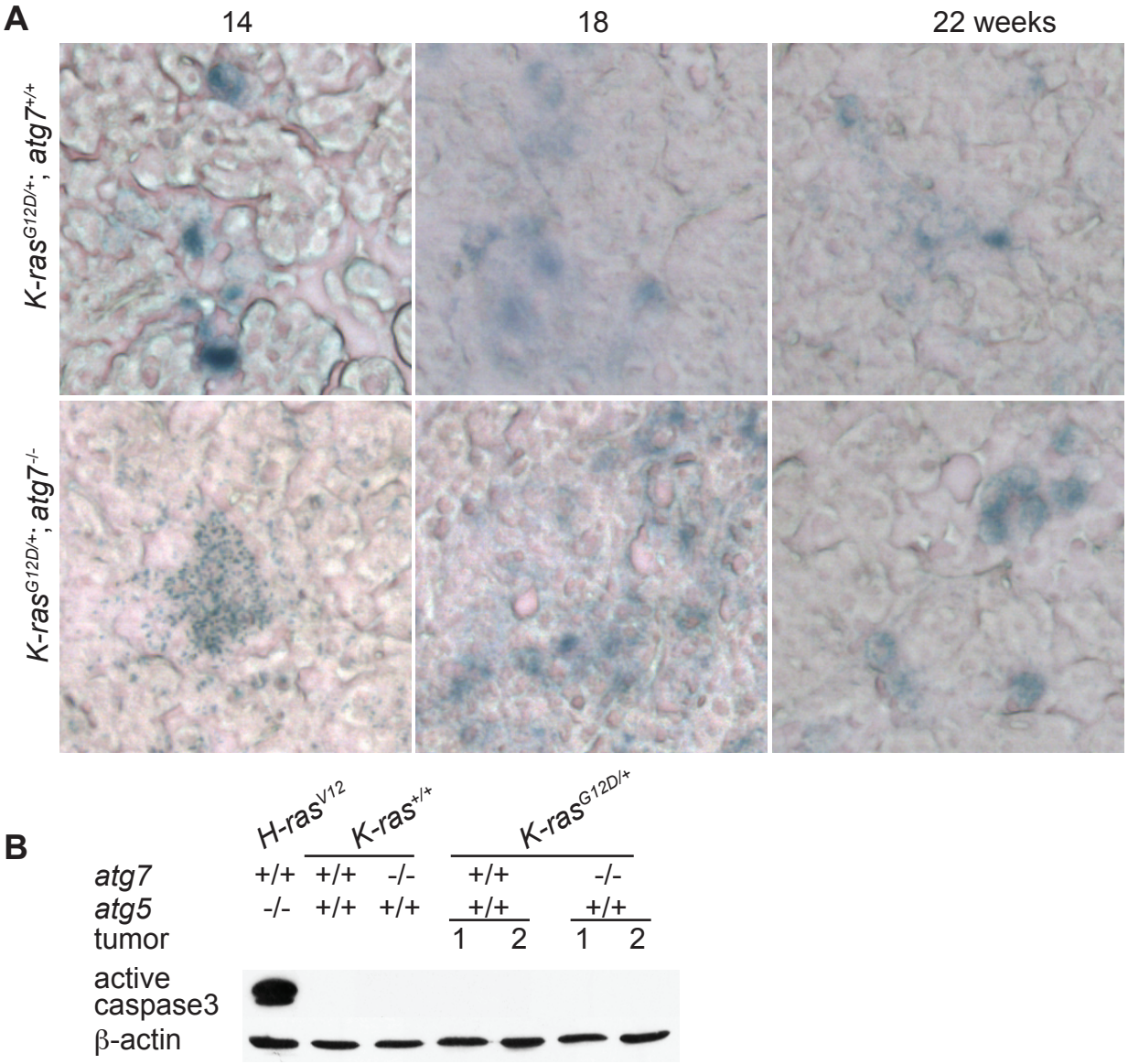

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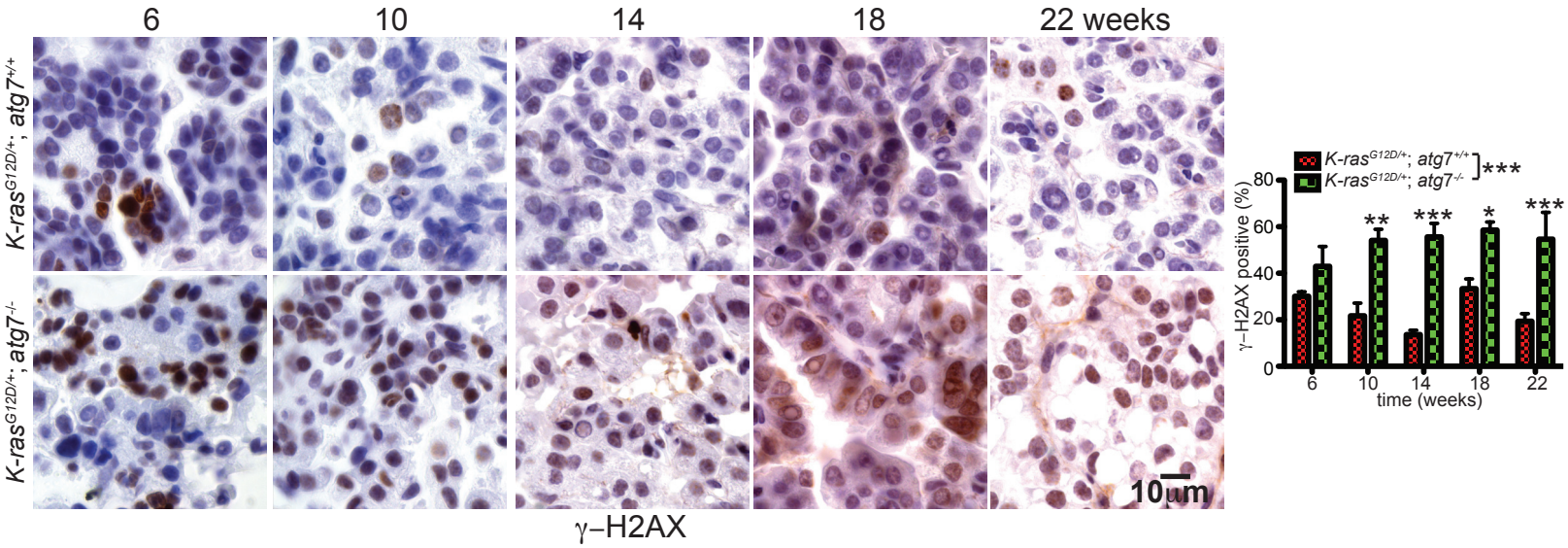

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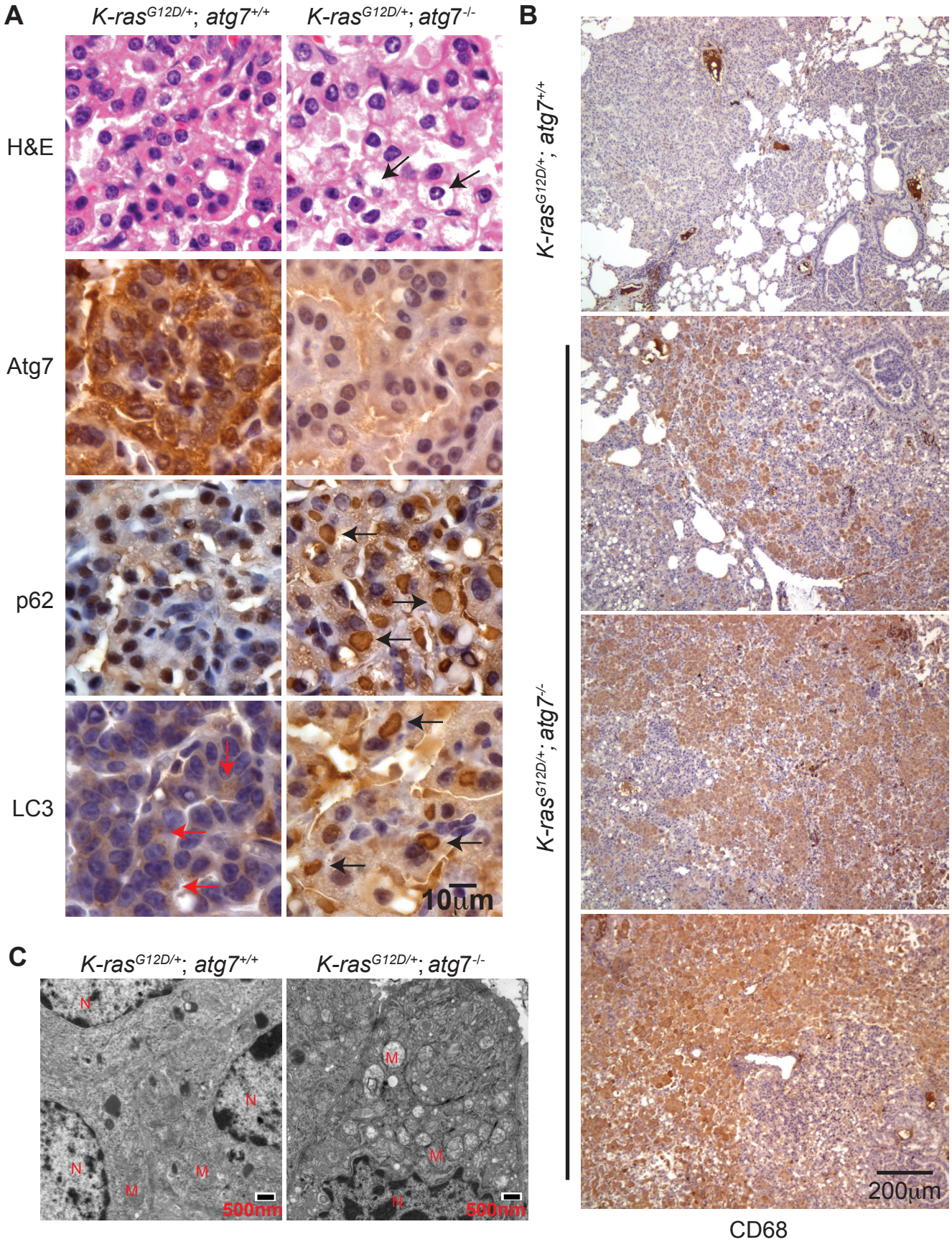

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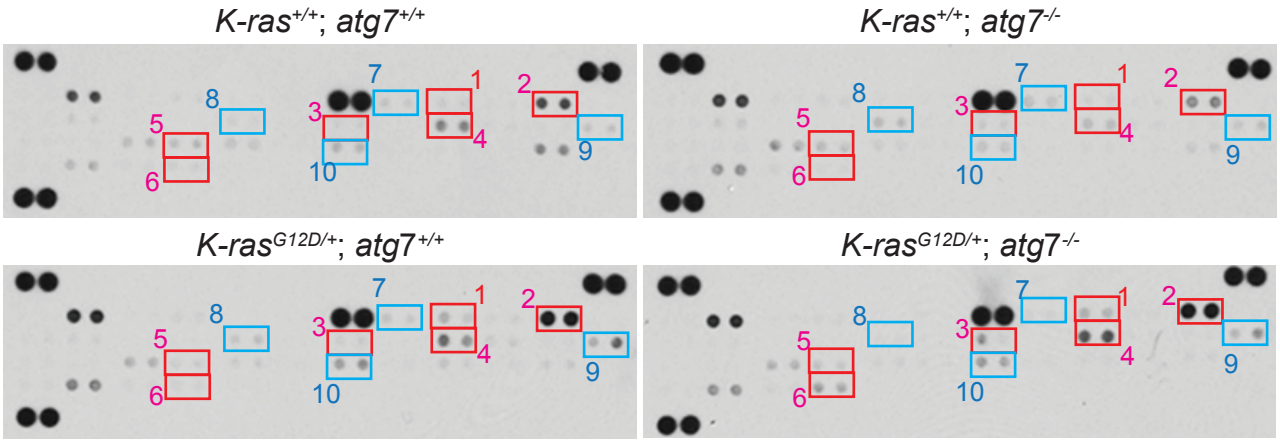
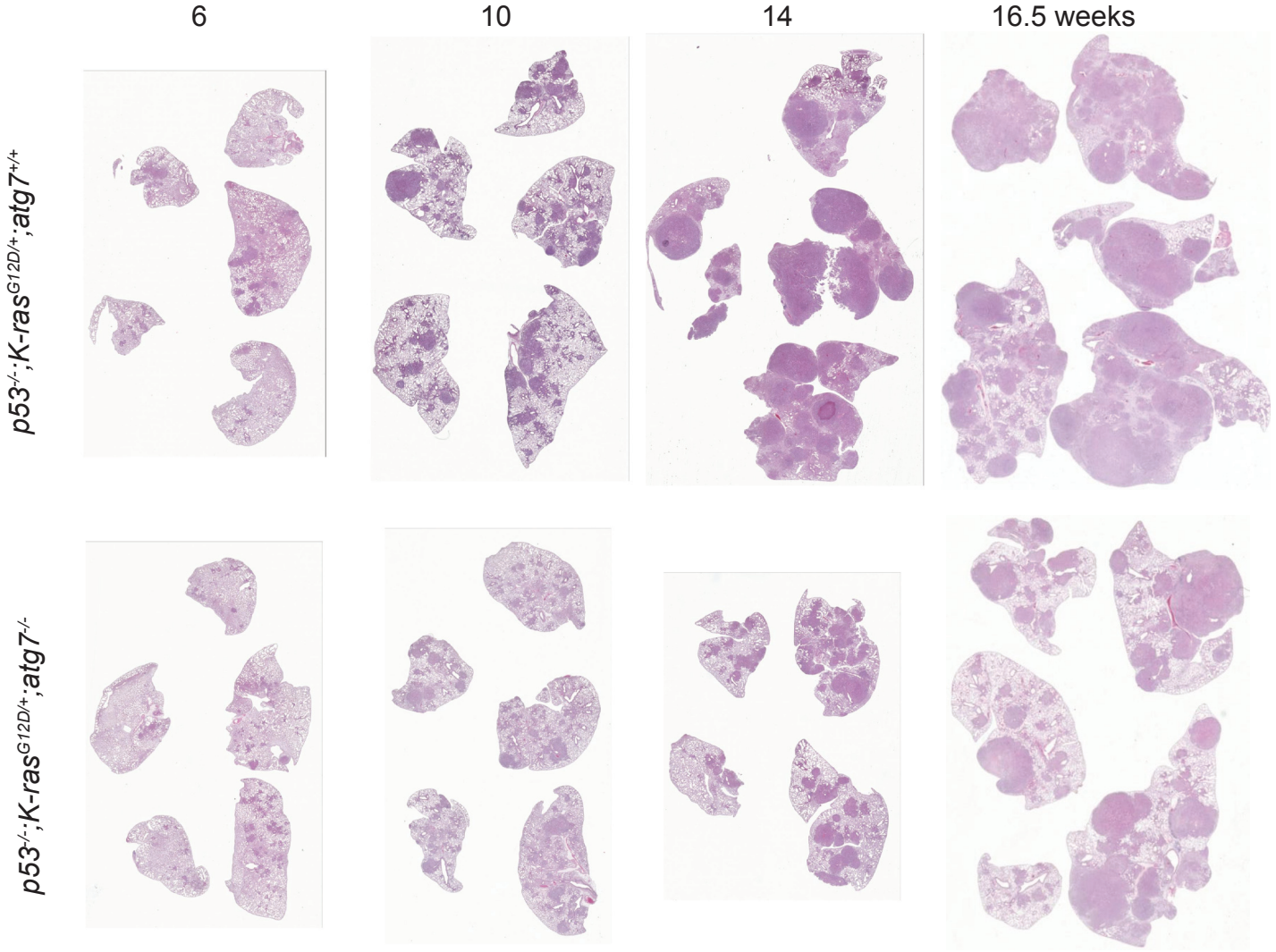


1-IL-1α; 2-IL1ra; 3-IL-13; 4-IL-16; 5-M-CSF; 6-TREM-1; 7-IFN-γ; 8-IL-7; 9-IL-27; 10-MIG

Guo_Figure S10



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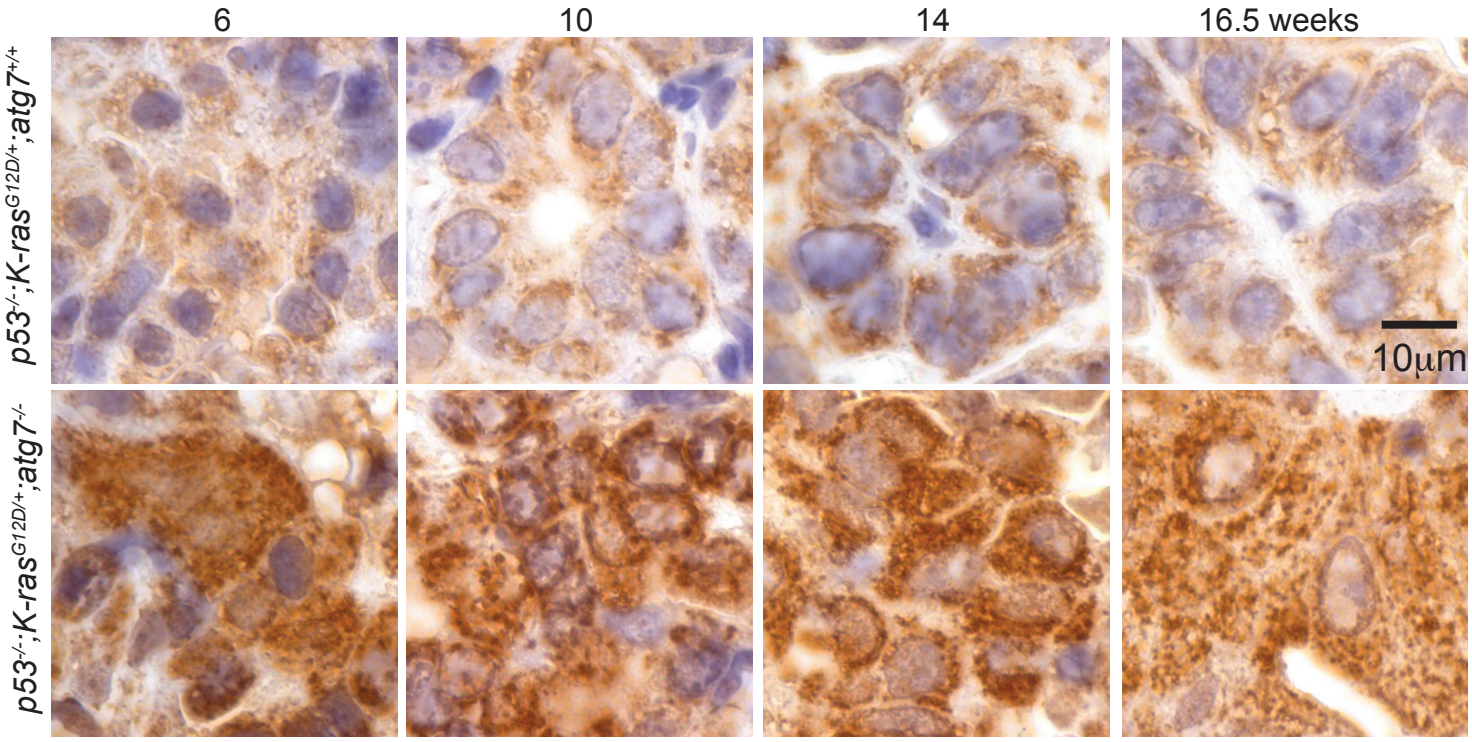
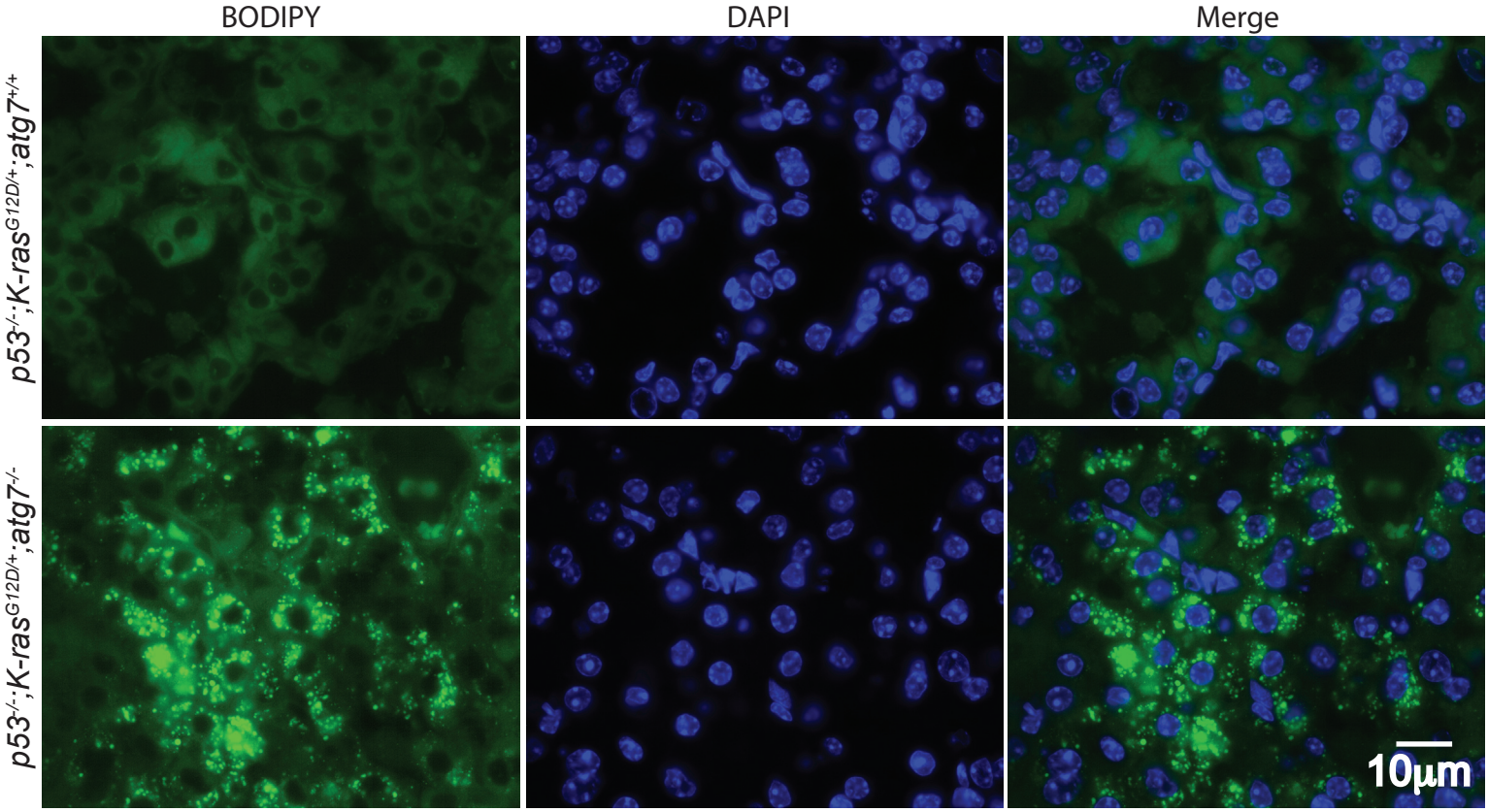


Figure S12



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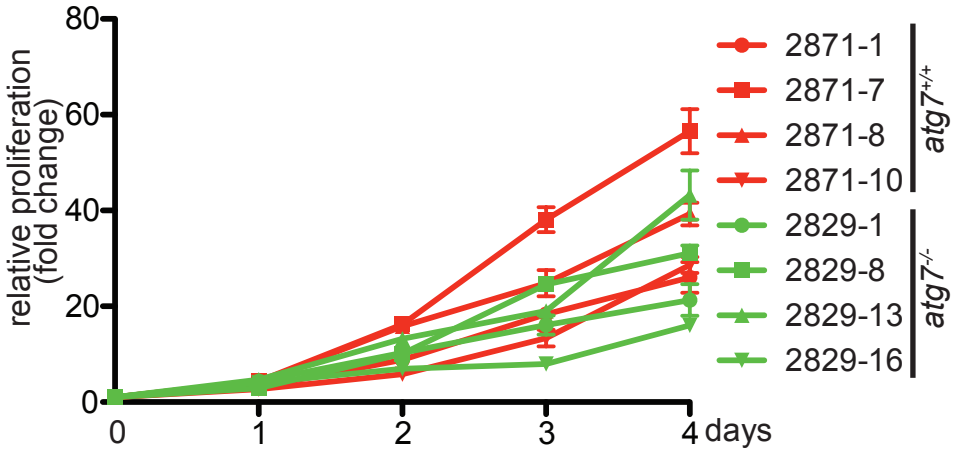

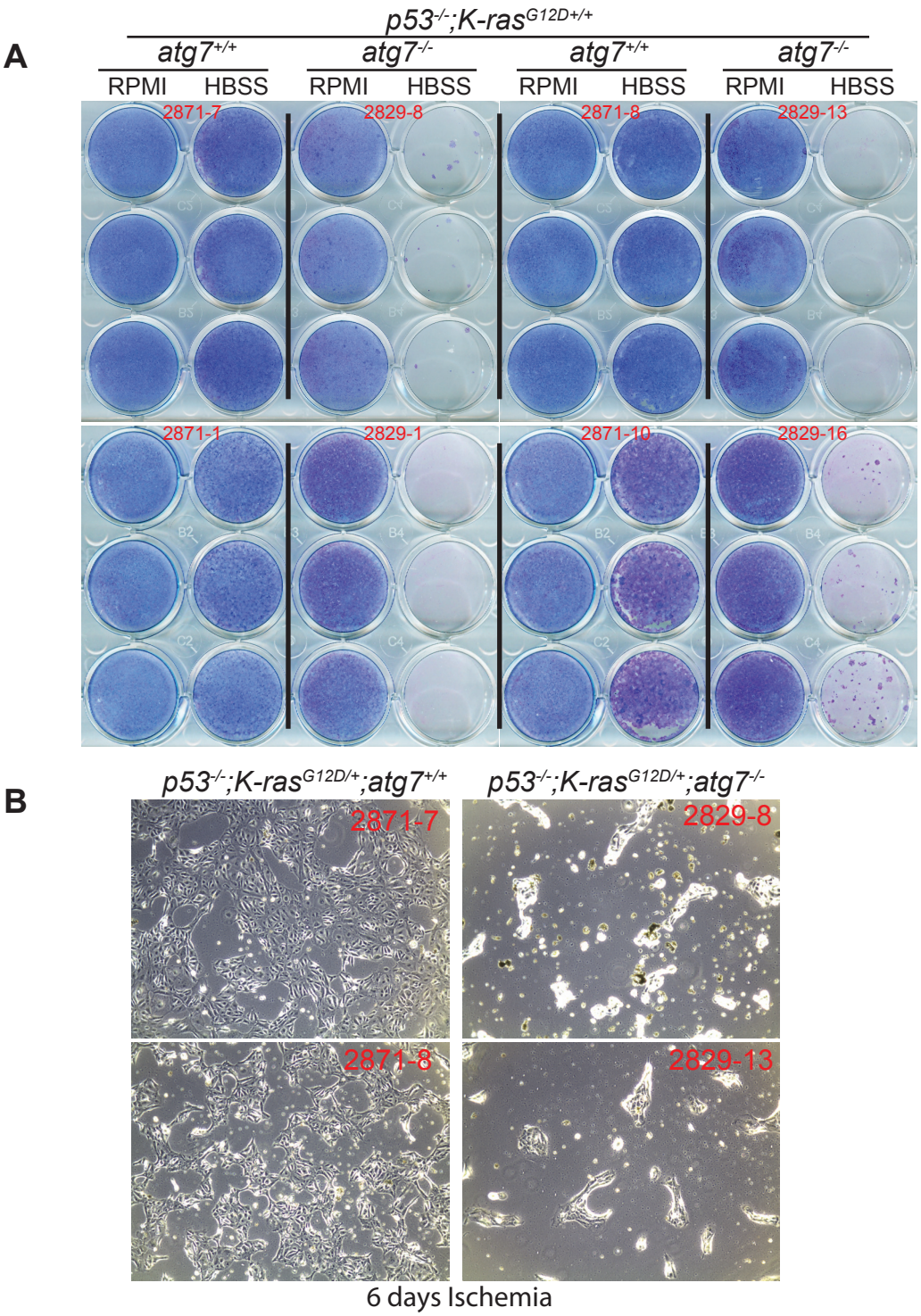
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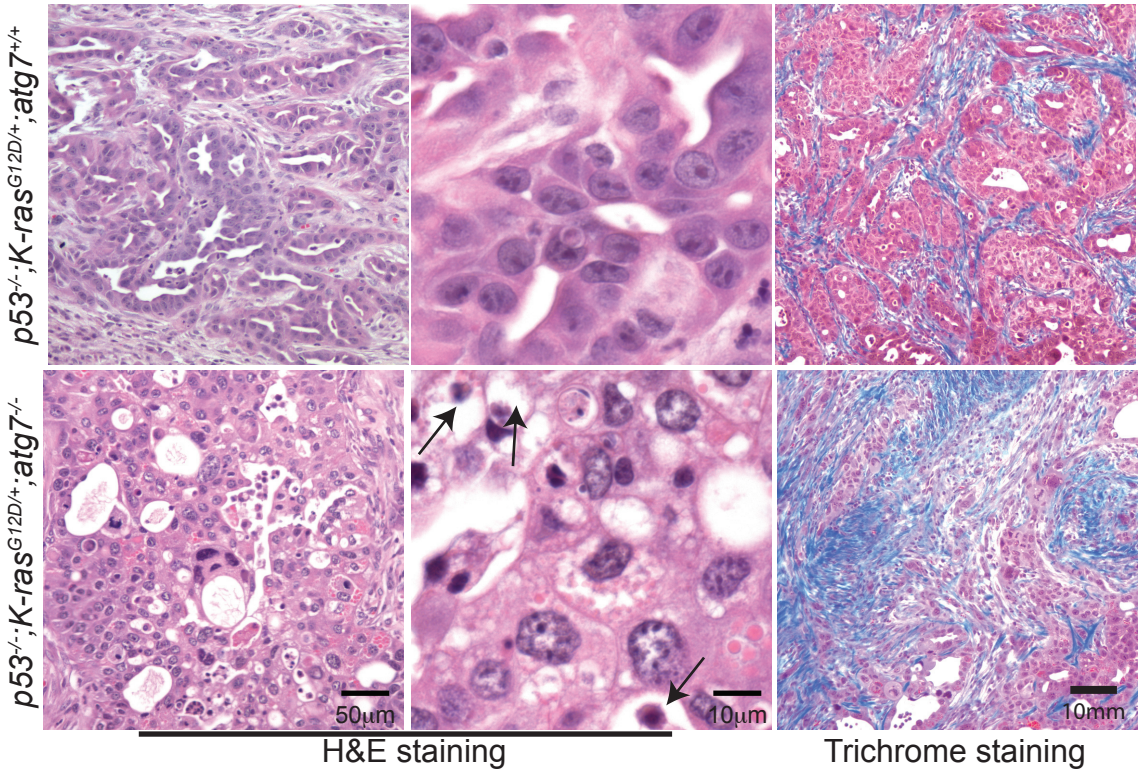
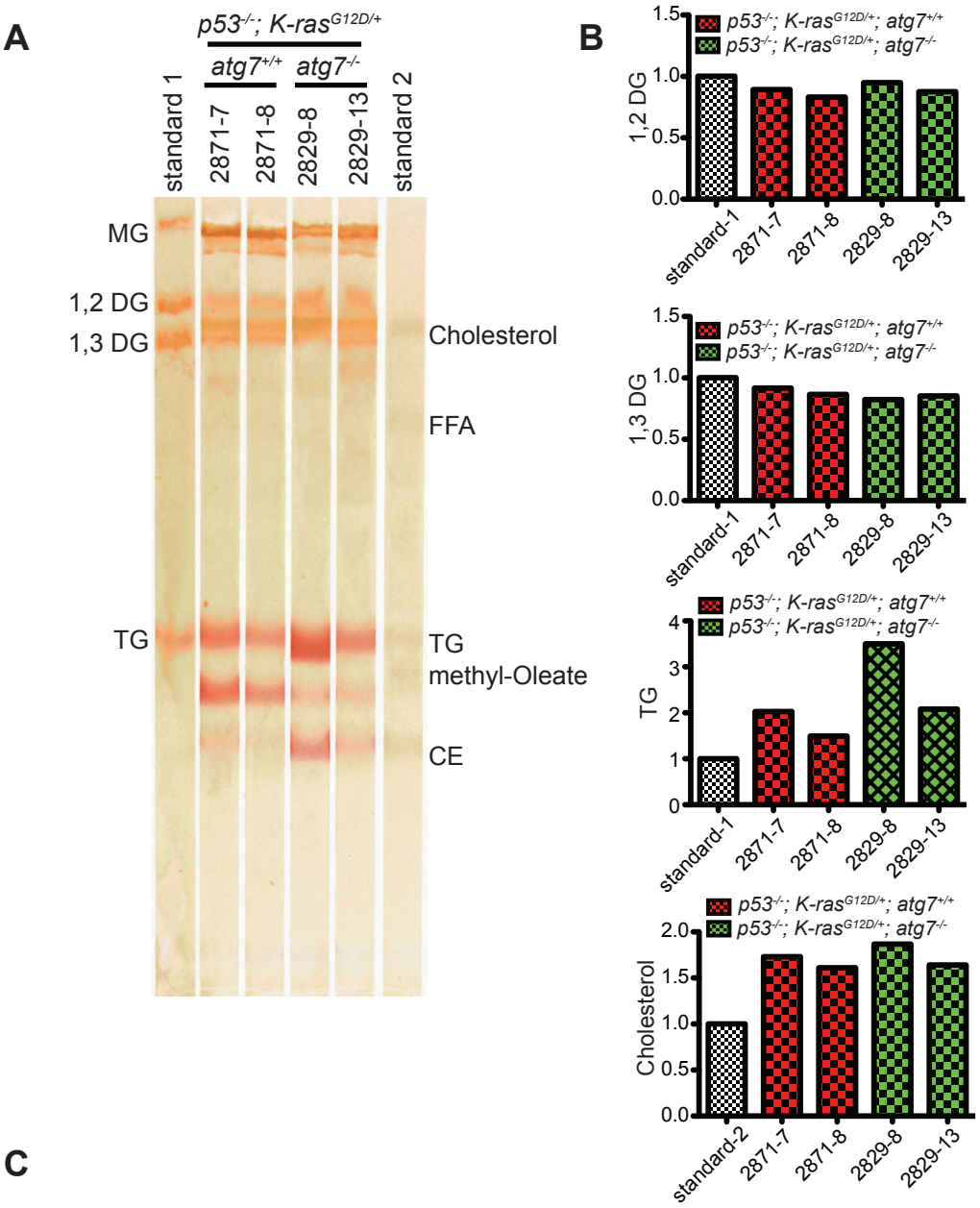
atg7+/+
atg7-/-
atg7+/+
atg7-/-
RPMI
HBSS
RPMI
HBSS
RPMI
HBSS
RPMI
HBSS
2871-7
2829-8
2871-8
2829-13
2871-1
2829-1
2871-10
2829-16
B
p53-/-;K-rasG12D/+;atg7+/+
p53-/-;K-rasG12D/+;atg7-/-
2871-7
2829-8
2871-8
2829-13
6 days Ischemia

Guo_Figure S15




A
p53-/-; K-rasG12D/+
atg7+/+
atg7-/-
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2871-7
2871-8
2829-8
2829-13
standard 2
MG
1,2 DG
1,3 DG
TG
Cholesterol
FFA
TG
methyl-Oleate
CE
B
p53-/-; K-rasG12D/+; atg7+/+
p53-/-; K-rasG12D/+; atg7-/-
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1,3 DG
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standard-2
2871-7
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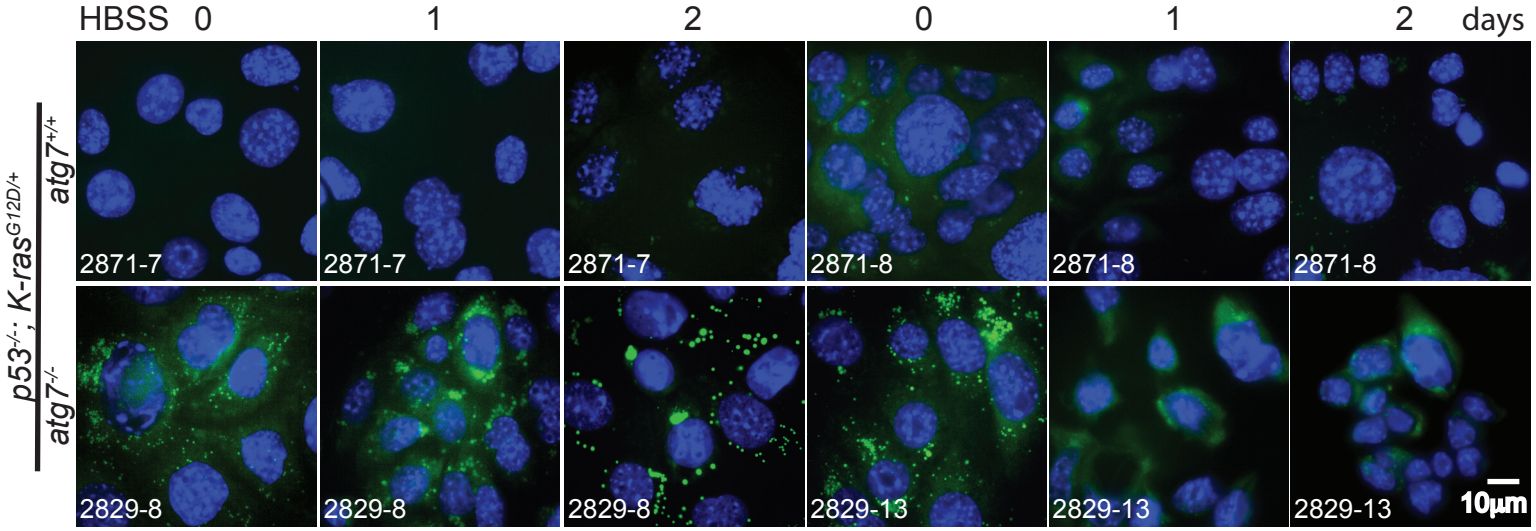
2829-8
2829-13


C
HBSS 0 1 2 0 1 2 days
p53-/-; K-rasG12D/+
atg7+/+
atg7-/-
2871-7
2871-7
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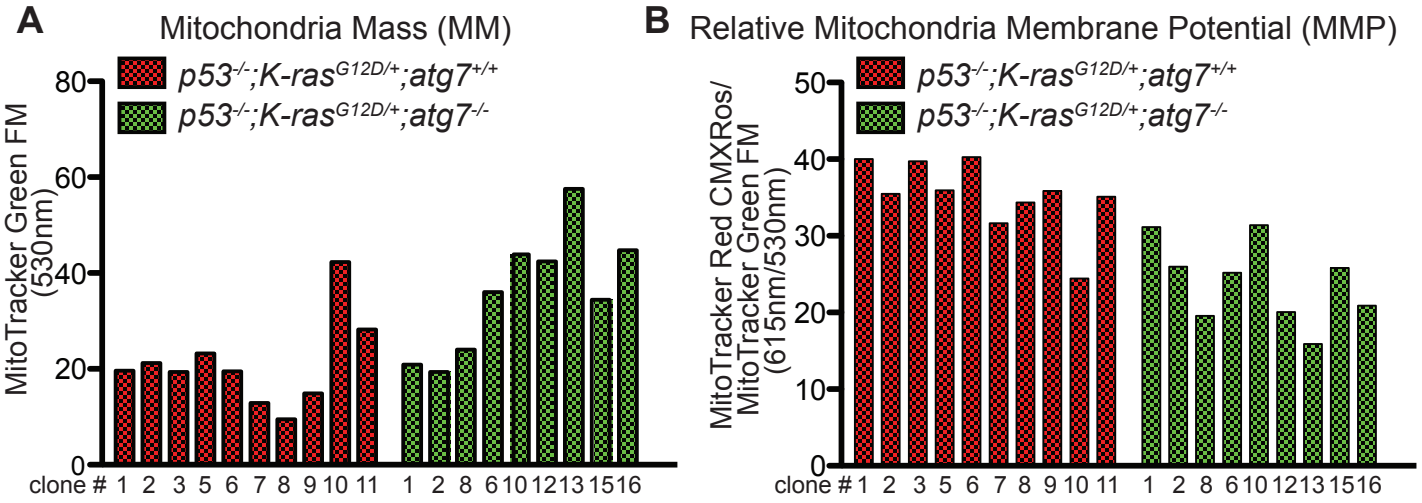
10μm

Guo_Figure S17



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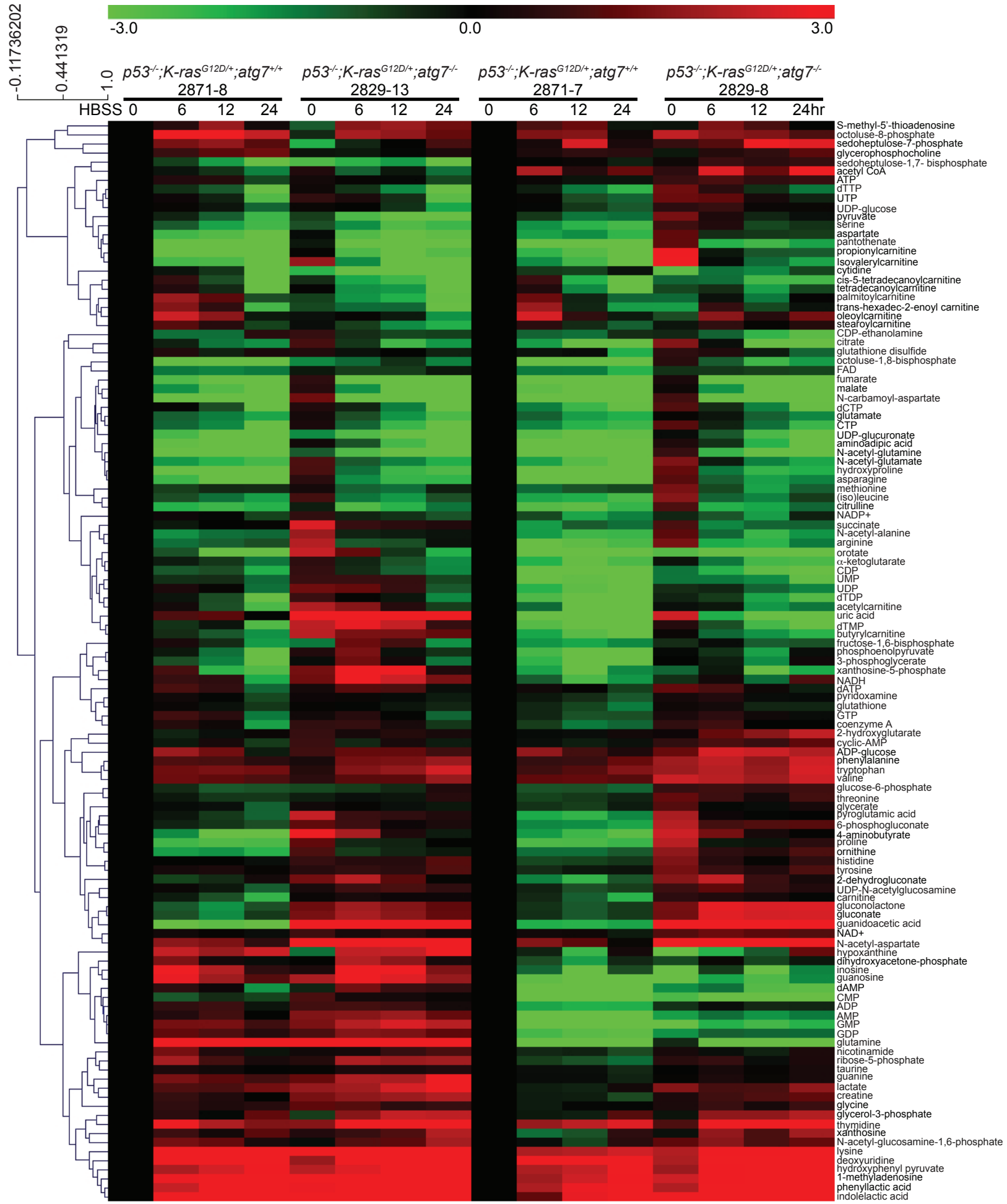

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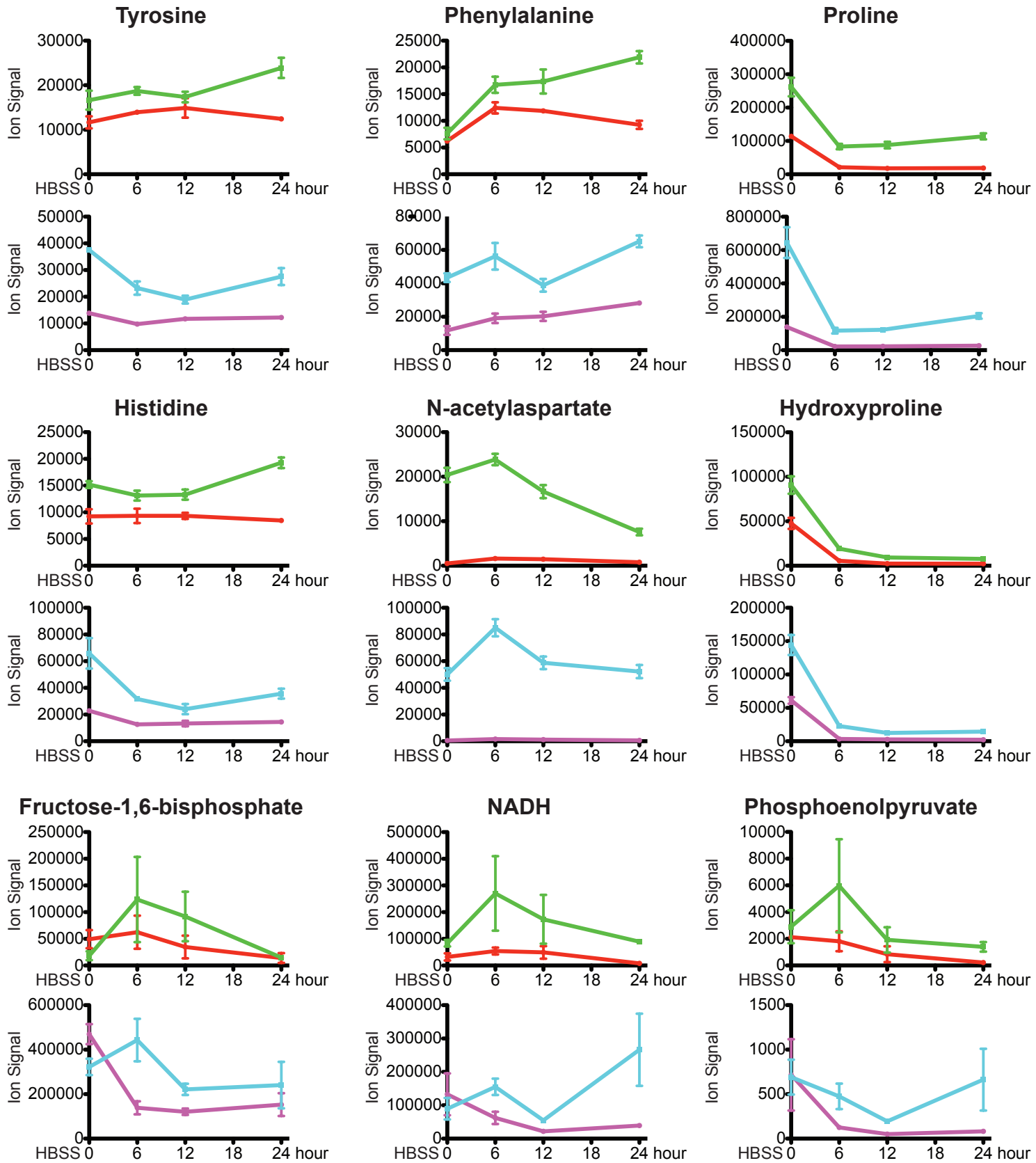

p53$^{-/-}$; *K-ras*$^{G12D/+}$; *atg7*$^{+/+}$ — 2871-7, 2871-8

p53$^{-/-}$; *K-ras*$^{G12D/+}$; *atg7*$^{-/-}$ — 2829-8, 2829-13

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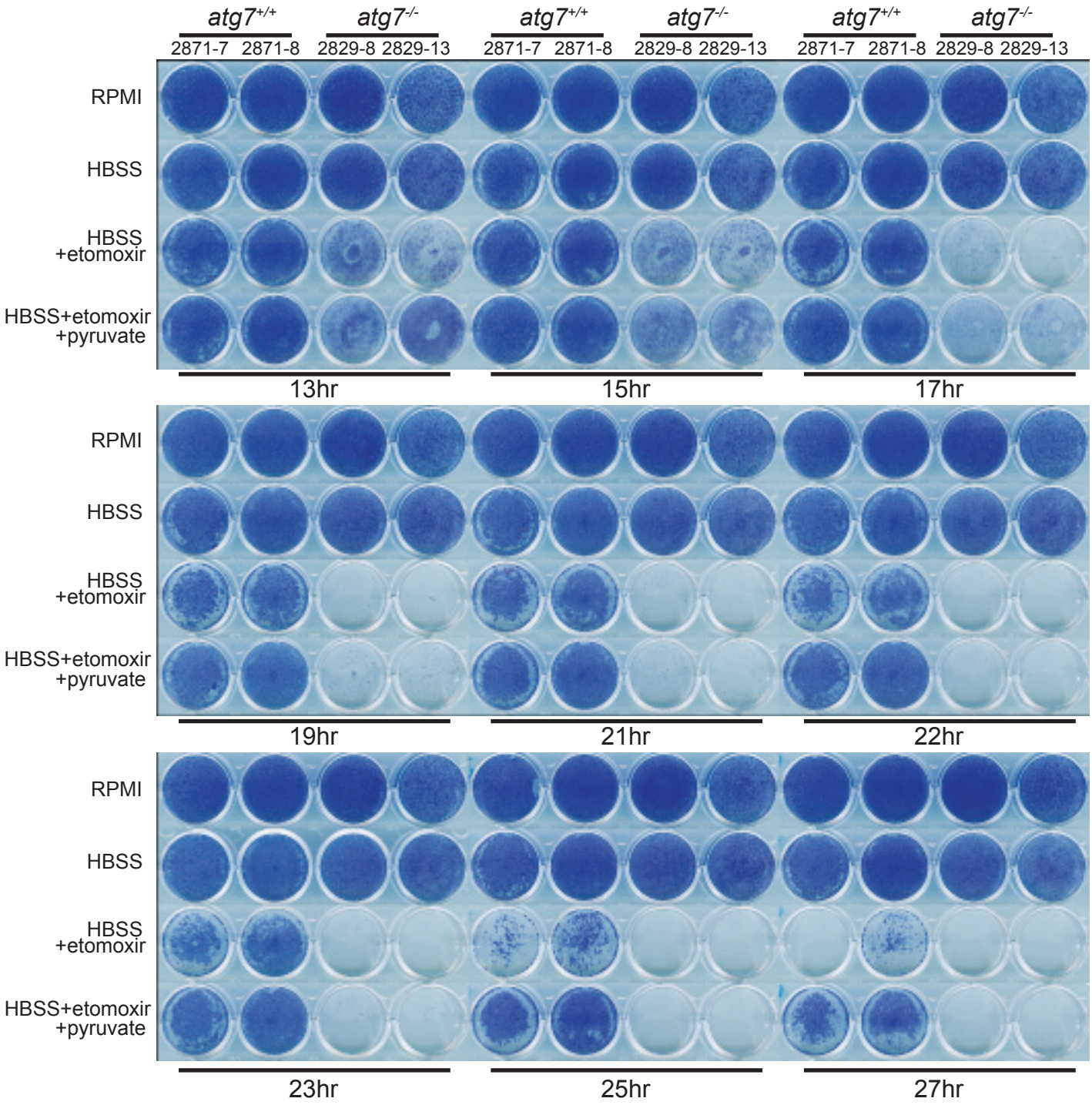

Table S1 Metabolite pool sizes in TDCLs under HBSS starvation

Genotype (Cell ID)	*p53*$^{-/-}$;*K-ras*$^{G12D/+}$;*atg7*$^{+/+}$ (2871-7)				*p53*$^{-/-}$;*K-ras*$^{G12D/+}$;*atg7*$^{-/-}$ (2829-8)				*p53*$^{-/-}$;*K-ras*$^{G12D/+}$;*atg7*$^{+/+}$ (2871-8)				*p53*$^{-/-}$;*K-ras*$^{G12D/+}$;*atg7*$^{-/-}$ (2829-13)			
HBSS / Metabolites	0h	6h	12h	24h	0h	6h	12h	24h	0h	6h	12h	24h	0h	6h	12h	24h
pyruvate	18216.6	14088.7	8439.0	3456.1	10850.4	3015.9	1795.5	1407.5	9959.3	6218.4	3823.0	4104.1	27272.1	13053.1	7462.4	9116.9
lactate	33911.5	68162.3	65196.1	89095.1	115478.3	128499.3	195650.6	332086.9	45439.3	36279.4	34501.8	53315.9	137519.4	86345.0	87120.6	149646.5
glycerate	2095.7	1997.6	1920.0	936.9	2415.3	2201.4	1925.6	1793.6	461.4	302.9	274.4	378.1	956.6	444.1	438.7	558.9
fumarate	6816.5	1080.6	399.2	117.3	10440.9	745.4	112.6	14.7	1375.9	90.4	37.6	24.6	1727.6	54.7	24.4	36.2
succinate	13111.4	11054.2	13392.7	13760.2	78334.4	22009.5	19400.6	17973.4	3167.2	893.6	1504.8	1290.8	6222.3	1058.3	1396.3	1416.3
pyroglutamic acid	57654.1	49816.6	35785.0	25611.4	292393.0	99418.2	90201.9	76798.2	185057.1	45576.2	38569.8	61740.8	750166.8	206382.9	181980.9	182315.4
N-acetyl-alanine	3335.6	1035.5	1341.7	1423.3	11981.1	2528.5	2740.5	2975.3	184.0	52.5	34.7	36.4	404.7	79.8	36.6	54.8
aspartate	42662.8	7922.3	6548.7	5292.5	40951.2	6661.3	3953.5	5747.7	30760.0	8375.5	9680.1	6511.2	70740.9	21066.4	19570.2	18560.4
malate	157604.5	48368.6	24163.4	9507.6	223859.8	48634.9	18849.8	12605.1	72131.8	9929.6	3933.5	1945.2	82056.5	21673.7	8316.4	7560.3
α-ketoglutarate	24552.2	20067.4	15719.4	9487.9	37709.8	18447.9	12574.1	7795.3	13394.7	3137.2	1707.9	2221.5	11777.6	5102.7	2412.3	2249.5
glutamate	196989.3	90154.5	70389.7	51551.8	236413.2	104824.7	58162.6	33026.9	260637.0	118526.3	72790.5	62842.3	278127.7	227818.4	119408.1	87187.4
2-hydroxyglutarate	9008.6	6793.8	8295.6	9961.0	15151.9	10984.7	12629.9	11082.6	3073.3	2946.1	2863.1	3616.1	3446.2	7321.8	9700.3	14999.4
guanine	187.1	518.3	407.0	344.8	441.6	790.2	751.1	1610.5	23296.0	21917.2	21926.1	17747.9	24654.8	29980.1	25382.0	28973.6
orotate	220.5	112.4	25.1	27.2	1133.1	522.8	143.7	50.9	4269.6	19.7	16.5	13.9	643.7	30.2	15.4	14.7
aminoadipic acid	1741.8	230.9	52.9	38.4	2032.6	887.2	307.4	57.3	1909.3	210.8	94.0	23.7	2525.9	1269.5	424.7	137.2
phenylalanine	6209.8	12423.7	11873.3	9250.9	7623.0	16744.6	17361.1	21902.6	11767.1	19080.9	20235.3	28262.2	43396.1	56189.6	38861.3	65129.5
phenyllactic acid	400.2	2019.7	3277.2	5483.5	2758.0	10430.9	24734.3	53641.7	494.7	2072.5	3371.5	12187.8	2124.3	8468.2	12912.2	41894.4
phosphoenolpyruvate	2121.2	1813.4	847.4	222.0	2904.2	5969.5	1917.3	1395.7	716.4	126.0	50.2	81.9	691.0	474.6	194.3	662.6
uric acid	88.4	177.9	194.1	87.5	7977.9	3363.2	6697.8	10114.8	3671.4	105.5	233.3	433.5	20046.5	884.3	194.9	282.4
pyridoxamine	261.8	302.1	256.3	146.0	291.2	290.3	250.3	216.1	714.3	610.0	488.0	346.5	855.6	989.6	669.6	683.5
dihydroxyacetone-phosphate	11484.8	32481.6	13783.7	10883.3	11454.9	50289.2	36445.0	14091.5	22158.1	11981.9	6204.6	16236.3	12367.1	24189.1	12693.2	18829.3
glycerol-3-phosphate	57494.2	86397.1	55209.5	131160.4	34863.3	176468.7	289145.0	274097.0	112992.7	95594.8	89533.0	237284.7	99594.5	368784.3	374318.9	494630.4
N-carbamoyl-aspartate	1261.7	69.4	27.8	20.6	3202.4	48.0	6.1	13.0	2734.9	6.7	4.1	4.0	5024.1	47.5	5.9	7.4
gluconolactone	1031.6	501.9	313.6	537.9	2597.0	3808.1	3080.4	2315.8	3540.4	2331.5	1713.4	2188.3	9576.0	23337.2	20842.2	21164.4
hydroxyphenyl pyruvate	117.8	480.1	664.2	917.1	540.1	728.1	1088.0	1464.0	99.4	410.8	502.7	1310.4	351.3	745.9	1063.8	2022.9
3-phosphoglycerate	26594.0	14091.2	9462.0	1639.6	24930.2	68678.0	31896.9	10324.1	20471.0	4327.6	2028.4	2318.6	20478.0	16416.5	6510.8	23543.2
citrate	116579.5	91337.2	44265.6	36155.1	219583.9	74580.7	21319.1	33539.4	13789.6	3831.5	853.3	32.1	41357.6	12766.8	37.2	18.2
N-acetyl-glutamine	2703.3	153.2	91.1	54.2	1289.8	429.7	274.1	142.7	2722.1	169.3	67.7	60.2	4499.6	544.3	268.0	175.0
N-acetyl-glutamate	1834.3	528.2	406.1	326.8	3628.2	880.8	637.4	446.5	1088.4	296.6	160.5	124.1	3159.6	893.7	380.8	282.9
2-dehydrogluconate	194.0	113.1	136.2	229.8	504.6	892.1	417.0	205.4	439.6	151.2	90.1	221.0	1356.4	2181.0	753.7	533.1
gluconate	26606.1	14029.2	8586.9	16544.5	73085.5	107105.1	83887.5	62397.1	65261.2	43778.6	31636.4	40639.6	169576.7	410693.1	364923.5	375040.1
tryptophan	2049.2	5219.2	5734.4	5372.6	2863.7	6071.1	6909.9	11583.5	3408.9	6043.5	7064.4	10126.0	12077.1	15342.4	11776.5	19847.3
pantothenate	75158.0	7840.8	6800.2	4067.8	64609.1	6524.2	4000.6	5144.5	22968.1	1904.5	1790.6	1560.4	52197.6	5183.2	4219.4	6128.2
deoxyuridine	40.2	1491.0	1720.4	1670.8	140.3	1256.4	2177.1	2988.2	69.1	895.5	1563.9	2672.1	283.8	1374.1	1370.7	2116.9
ribose-5-phosphate	4039.1	16071.1	7539.1	5027.4	5728.7	17082.1	14749.8	15385.8	21144.9	12635.3	10768.3	8761.2	30767.8	35164.9	19747.5	27292.6
thymidine	69.3	568.3	290.3	202.3	209.5	971.9	1912.9	3099.0	87.8	303.2	415.9	542.4	173.0	1785.6	2128.5	2904.6

glucose-6-phosphate	101416.9	71195.1	49644.0	51931.5	56537.5	62538.2	72091.4	136038.7	71990.2	37147.8	37806.5	31643.8	121244.7	130392.7	116835.7	128831.7
inosine	6459.1	69058.2	28366.0	9861.1	8265.9	86395.1	55593.9	18729.0	72402.1	31858.2	3893.2	39367.6	4028.2	44279.6	7246.0	24518.4
6-phosphogluconate	726.8	553.4	468.5	386.3	1649.4	1280.1	818.9	927.7	802.5	267.6	253.7	210.6	3671.2	1492.2	1656.5	1687.4
guanosine	148.7	1002.9	553.6	309.7	606.2	1262.1	928.0	509.8	10689.9	1446.4	822.1	1043.1	650.9	2756.4	1725.9	3517.3
xanthosine	304.8	536.0	358.2	668.9	420.8	511.6	614.9	1342.0	1131.2	457.0	575.9	1741.6	1026.6	3785.8	2161.6	4330.6
sedoheptulose-7-phosphate	12919.7	35730.1	43349.7	27409.6	3004.8	9533.0	12927.7	24345.9	10826.5	13211.7	64279.2	13557.3	18291.6	22383.9	117359.4	68757.9
S-methyl-5'-thioadenosine	153.2	220.6	533.7	180.2	72.4	475.3	549.7	394.3	500.8	979.3	1220.4	435.5	440.1	1427.8	966.6	520.7
N-acetyl-glucosamine-1,6-phosphate	1847.9	5001.0	4344.1	2356.0	1731.9	3758.6	4032.7	7308.5	3197.3	2976.7	1833.7	4618.4	7125.6	9961.2	6107.3	7584.7
glutathione	837952.0	927483.6	755012.1	529914.5	881677.7	821362.2	725213.9	615311.7	14574.1	10844.4	8277.0	5282.4	16479.3	17253.2	10707.3	10856.8
octoluse-8-phosphate	607.5	18250.7	10051.1	3063.2	435.7	2479.9	2022.9	1440.9	4445.3	12831.1	13367.7	5066.4	21652.8	14239.9	13123.8	8800.1
dTMP	205.9	135.1	179.8	31.9	976.4	1399.2	1031.5	338.7	2912.0	429.6	322.4	124.8	4038.0	1505.5	519.7	280.5
CMP	322.9	157.7	225.0	185.9	620.9	386.1	385.6	354.3	2130.4	34.0	28.5	31.8	360.3	235.5	127.3	115.5
UMP	3284.2	2219.3	2244.8	1379.6	5596.7	5634.0	5386.2	1851.8	31051.5	3277.1	4120.9	1353.0	11910.9	11604.9	9929.8	4062.6
cyclic-AMP	335.2	283.9	404.7	204.2	586.5	242.6	412.2	276.8	566.2	523.5	450.6	513.9	901.0	1098.6	971.9	1256.0
dAMP	120.2	185.0	133.8	36.1	91.4	325.4	207.5	187.5	572.6	50.9	69.4	46.9	179.6	228.4	85.7	80.4
fructose-1,6-bisphosphate	49371.3	62444.7	34727.2	14090.5	18271.6	123636.7	91827.3	14893.4	469767.4	138664.7	120965.3	152846.7	322499.6	443149.7	221452.6	240764.8
AMP	5191.5	7182.1	9451.3	5310.3	15199.6	16016.2	18568.1	12217.6	154463.7	10148.0	12650.1	9764.1	42360.0	62791.3	45984.5	57085.0
GMP	184.1	500.5	504.9	328.2	517.6	820.4	1086.2	840.2	8523.1	370.4	297.2	351.2	891.6	1979.1	1528.6	1923.9
xanthosine-5-phosphate	185.9	350.2	39.5	28.8	494.2	2760.4	1566.0	249.5	2549.8	676.3	63.9	844.1	1094.5	2151.9	295.4	635.9
sedoheptulose-1,7-bisphosphate	18167.1	10632.2	5015.3	1622.4	2922.8	3859.4	5097.8	1483.4	10760.9	11281.0	11817.5	8456.5	12294.9	18772.0	16132.9	17650.9
octoluse-1,8-bisphosphate	1030.9	133.7	70.0	17.6	340.8	435.9	698.0	359.7	1455.9	152.9	84.8	126.6	2115.7	683.4	275.3	409.0
dTDP	435.8	380.2	234.0	31.8	763.2	457.2	377.6	143.7	2540.9	411.9	218.6	138.5	1931.5	1562.2	662.1	388.2
CDP	1904.8	926.6	1009.1	453.2	3095.3	1343.7	879.4	622.3	9666.4	790.8	623.7	619.0	3735.8	2161.1	1318.8	1182.2
UDP	10661.7	13946.1	11395.5	4225.6	27612.4	25281.0	17601.0	5166.7	74743.9	16741.1	10289.8	9213.9	51763.2	56135.4	33234.0	25272.8
ADP	34720.3	54905.3	61183.8	30261.4	63426.4	64090.2	61137.6	40965.6	223746.0	58604.9	52938.5	53708.3	148071.1	208403.5	162075.5	165809.4
GDP	557.6	1285.0	1121.5	776.7	1080.3	1663.9	1574.6	1243.4	8314.1	1467.0	1201.0	1116.8	2527.6	3815.5	3614.2	3525.1
CDP-ethanolamine	669.9	264.5	270.6	977.4	1117.1	456.8	380.2	394.4	818.0	364.5	325.9	562.8	596.8	363.4	169.3	115.7
dCTP	1035.5	1003.8	554.5	70.5	1406.8	780.1	370.4	76.5	1117.5	397.8	221.8	144.9	2299.9	792.8	388.5	141.9
dTTP	9475.4	6448.3	4554.5	788.5	10760.3	6125.2	3109.6	867.6	8215.5	6601.9	3042.9	1736.1	21298.8	12186.0	5543.2	3070.3
CTP	43665.3	18859.3	14463.0	3167.1	55016.0	19303.4	8738.2	3103.8	27001.9	9208.4	6051.5	5263.7	56897.3	20956.2	10901.6	5358.2
UTP	213280.4	239440.6	166104.9	33238.4	339182.8	271064.1	145628.5	30510.8	176667.7	185774.9	95411.6	79262.4	442279.0	396131.8	213808.0	133392.1
dATP	618.4	1184.2	991.6	266.9	742.0	1302.8	1231.1	573.0	805.1	933.4	830.8	473.6	1865.1	1555.6	919.5	637.8
ATP	403929.7	556771.9	569672.0	227483.1	473404.6	431673.9	388361.1	227636.9	482473.9	535736.4	423895.9	420110.7	822665.3	938160.8	752780.0	822558.6
GTP	15168.9	27822.8	22443.3	5572.2	17535.4	21696.3	15795.7	6534.3	15817.9	11846.1	8095.7	8195.9	19881.4	23949.0	18360.8	14861.1
UDP-glucose	202362.7	214456.5	176216.5	88641.0	218694.0	203799.2	135591.5	52190.4	285310.2	279340.2	179809.7	138918.1	430260.3	480863.0	313643.5	310439.7
UDP-glucuronate	89314.1	15667.8	11073.9	7793.5	28384.4	14150.8	9983.8	2796.9	148461.2	21755.2	12903.1	19443.2	140862.6	71466.9	24685.7	13590.4
ADP-glucose	2173.1	7967.6	5733.4	1772.3	3938.1	5177.3	5077.8	3861.1	2779.3	9367.3	5138.8	3646.3	6737.4	16054.1	14690.1	12034.9
UDP-N-acetylglucosamine	302251.5	335083.2	257820.2	139319.7	371014.7	530571.5	577205.7	472745.5	388009.7	303556.3	202160.2	231939.9	681178.5	866001.3	638499.5	529818.0
glutathione disulfide	132348.2	179508.6	102816.4	166147.4	180259.7	120119.0	134430.1	103567.2	38951.2	34851.7	36555.6	9407.6	59809.8	53406.5	31976.2	17000.1
NAD+	37137.7	42876.7	39730.4	34564.6	66798.6	46061.6	53747.0	44727.7	38791.0	45232.7	44304.6	31573.5	80233.2	97436.1	84476.8	79822.2
NADH	32313.7	54400.9	49360.9	7957.7	83502.9	270180.6	173250.5	89512.5	132760.5	62193.7	21975.4	39040.4	89633.4	155262.8	54750.2	266405.5

NADP+	2601.0	2922.1	2556.0	1508.1	4136.8	1992.0	1719.5	1321.2	3194.7	1783.5	835.8	1111.1	2387.0	1601.0	893.9	2506.6
coenzyme A	5290.2	7448.5	5979.3	1432.1	8330.9	8695.7	6554.2	3332.8	16759.8	10092.2	6129.9	7193.1	26468.8	30255.1	16988.8	16897.9
FAD	426.3	160.3	145.8	158.8	360.6	261.4	260.4	365.9	1190.9	438.9	428.0	269.6	780.3	765.0	706.9	683.4
acetyl CoA	639.0	567.2	419.8	216.1	873.4	289.3	545.6	254.7	136.5	569.6	189.5	331.6	205.4	843.8	332.4	1405.5
4-aminobutyrate	158.3	51.1	18.0	17.0	1272.4	636.3	208.1	130.2	921.5	260.9	174.9	129.8	4913.4	2480.4	1128.6	949.7
serine	11579.8	5649.3	3081.1	2125.7	6102.3	3630.7	1811.2	2246.5	20395.0	6276.5	4374.3	3613.9	36289.1	27608.9	11386.5	13368.4
proline	113989.3	21104.7	17909.3	18885.6	261670.5	83154.7	87686.2	113835.9	138729.5	22200.5	22949.5	27202.0	644877.5	117133.6	122276.7	205044.6
valine	372.4	941.8	845.9	749.1	558.8	800.1	810.7	1276.8	701.3	1583.2	1638.7	1480.8	3726.3	3240.7	2628.3	3829.8
guanidoacetic acid	278.9	28.0	38.9	35.3	17826.6	13866.0	9255.6	8695.6	1788.1	430.1	396.9	472.5	24304.5	20937.9	16251.0	14186.4
threonine	5405.9	4657.6	3450.2	3407.3	4324.5	4962.4	4700.8	7786.0	11879.2	6863.7	7418.1	9029.0	27769.6	21009.6	14131.5	22126.2
nicotinamide	1422.3	3875.2	1949.2	1249.6	1645.0	1710.3	2393.0	2740.8	3574.1	2620.8	2794.3	1965.2	4350.4	3304.2	2794.3	4588.2
taurine	85876.2	111281.0	100082.5	85008.3	90438.3	110653.3	107543.6	118533.4	36290.5	33967.9	33454.5	26365.7	35729.2	44182.0	38989.0	44909.1
creatine	65762.7	107591.6	87895.8	66556.9	179590.2	214082.3	236638.2	285066.3	117052.1	96274.7	94345.8	64406.7	152384.5	210676.6	234717.2	268727.1
hydroxyproline	47582.2	5555.0	2439.4	2319.1	90666.0	19174.7	9299.4	7628.1	61187.2	3490.8	2732.5	2230.1	144188.3	22688.0	12496.3	14470.7
(iso)leucine	22812.1	12214.7	9009.8	6244.3	42360.1	8730.0	6584.6	11966.1	80507.5	20852.9	19371.7	14027.6	249563.6	35717.7	27321.1	49028.2
ornithine	1025.8	283.6	309.3	229.5	2049.6	632.3	756.3	864.4	1585.0	640.7	633.4	755.4	5186.0	2409.5	2241.4	3156.0
asparagine	26212.1	4972.3	2916.3	2363.9	38856.4	8334.9	5303.0	5535.3	84259.9	10224.3	8141.6	7735.2	177620.7	38995.0	23086.1	28488.0
hypoxanthine	460.0	2303.3	1636.4	2453.3	184.2	2220.6	2340.4	5045.7	4875.9	3757.4	964.9	5802.3	167.6	1109.8	2348.4	11675.6
lysine	3.6	81.5	214.0	157.2	65.1	89.9	169.1	330.5	39.4	163.8	175.1	216.6	171.3	301.5	295.0	536.5
glutamine	139.3	4989.9	7540.0	7570.6	2848.7	4489.2	6345.3	11997.3	99319.9	4601.3	5249.8	5019.2	71384.4	4969.1	3283.5	2851.5
methionine	4633.0	2765.1	3303.3	3250.7	5586.8	2084.8	1861.0	3645.2	5014.5	2124.2	2580.5	2826.1	13847.8	2795.3	1337.2	2304.8
histidine	9236.9	9336.4	9338.1	8474.5	15202.8	13129.1	13308.4	19276.3	22767.3	12652.9	13265.2	14459.0	65884.0	31630.1	24077.6	35647.5
arginine	2526.4	1018.6	1168.4	1353.5	11319.2	1241.0	1307.8	2260.4	10865.7	1332.8	1504.8	1843.1	29909.0	2689.4	2332.7	4010.4
citrulline	1413.3	326.3	272.4	322.9	1138.6	218.5	309.8	549.5	5509.0	825.5	752.5	1123.7	10848.4	1263.4	1404.9	2382.3
tyrosine	11664.1	13940.8	14882.4	12446.7	16639.2	18724.2	17351.2	23896.1	13857.2	9781.4	11711.0	12233.7	37517.5	23256.6	18941.1	27565.8
cytidine	96585.7	85615.4	62789.6	11012.0	20801.0	4386.2	2967.1	3498.6	2187.3	1371.4	1288.8	1936.4	296.3	861.1	721.6	1248.9
glycerophosphocholine	468913.7	808453.8	1022655.6	1210675.6	414888.8	403921.8	458402.1	606181.1	958055.2	1224366.3	1495265.9	1402594.2	809082.6	1344119.3	1524597.5	2102559.4
1-methyladenosine	188.0	1280.1	2717.7	2645.5	3280.5	4112.0	5157.3	7289.9	451.5	1689.9	2454.2	3567.2	2423.9	3285.7	4701.5	9793.3
glycine	57.4	88.9	75.9	82.2	126.7	120.4	85.7	94.5	927.2	758.9	903.1	905.6	1183.3	1598.3	1122.2	1605.1
carnitine	6467.4	5255.4	3373.9	1322.3	7096.8	8059.2	7265.9	7250.4	3388.3	2429.3	1572.7	739.9	5106.7	4647.2	4051.6	3285.1
acetylcarnitine	7274.7	8579.5	3835.2	1236.0	31349.5	22366.4	10359.3	4379.5	13886.0	5856.5	1620.3	1115.9	12772.1	11797.6	4078.5	5304.8
propionylcarnitine	4043.0	463.7	361.6	150.0	4242.1	664.1	492.4	610.3	1485.3	307.6	219.0	111.8	10654.8	1279.9	741.5	708.8
butyrylcarnitine	651.1	448.6	313.4	198.2	3032.3	1822.9	1797.1	1510.1	1612.2	414.1	232.6	170.2	1783.4	685.3	483.8	351.5
Isovalerylcarnitine	330.0	58.6	55.3	18.5	1120.3	105.8	35.7	28.9	186.3	58.8	33.9	6.7	1836.1	178.4	79.7	48.7
cis-5-tetradecanoylcarnitine	229.0	369.2	121.3	20.1	156.6	58.2	43.8	2.3	315.0	549.5	73.6	25.5	135.5	128.3	55.9	56.5
tetradecanoylcarnitine	1277.2	1762.7	928.0	155.3	1309.2	395.6	371.9	141.5	1270.4	1699.4	412.7	142.7	721.4	876.0	349.0	720.0
trans-hexadec-2-enoyl carnitine	741.5	2228.9	1160.0	131.5	415.5	307.5	320.4	80.6	571.6	2057.5	426.1	158.4	156.5	953.7	317.2	514.5
palmitoylcarnitine	3173.1	11350.1	6943.5	1686.1	1861.8	935.8	752.4	410.9	2481.4	6224.5	1887.6	1077.7	1051.9	2229.9	922.3	2563.5
oleoylcarnitine	1136.5	6112.7	3616.9	965.4	1033.7	1215.3	946.4	345.4	759.5	4444.8	1197.5	633.0	409.9	2411.4	1085.4	2035.8
stearoylcarnitine	1134.6	2386.3	1619.1	655.5	1057.4	677.0	360.0	271.7	910.3	1342.2	636.7	413.3	797.7	1430.2	960.7	1276.6
N-acetyl-aspartate	508.3	1609.3	1453.1	794.0	20387.9	23869.7	16654.6	7569.4	545.2	1637.9	1187.4	595.0	50063.6	85022.7	58750.9	52184.6

indolelactic acid	12.3	154.9	237.5	528.0	213.6	1515.0	3428.2	7700.5	47.2	107.9	317.4	1181.3	1039.9	1550.0	2758.7	8579.8
nicotinate	308.1	603.3	638.8	393.7	428.8	485.5	577.6	747.7								
thymine	172.3	288.4	300.1	263.2	279.4	293.3	556.6	963.3								
ascorbic acid	27.1	29.9	34.1	23.0	59.4	212.0	271.7	580.6								
D-erythrose-4-phosphate	3447.1	3102.8	2719.2	1979.3	1763.7	1965.7	2342.4	4854.4								
dUTP	736.9	342.5	189.2	33.5	110.7	149.2	161.3	47.0								
choline	3020.9	4484.4	4247.3	2100.6	1481.7	1317.7	1449.3	1366.4								
adenine	115.0	1150.0	1058.3	455.8	365.0	713.7	744.5	1041.8								
methylnicotinamide	152.8	1783.6	831.4	446.8	283.3	1798.6	1426.3	719.7								
N-acetyl ornithine	2851.7	3535.1	3311.3	2589.6	2581.6	2842.8	3115.2	2928.1								
glucosamine	2531.1	2211.7	1429.9	1079.2	2365.3	1581.9	1322.4	1637.3								
acetyl lysine	113.2	279.4	184.9	164.2	1385.8	530.6	285.5	231.2								
dodecanoylcarnitine	352.0	311.1	170.2	21.9	444.9	64.5	81.1	42.8								
dimethylglycine	966.3	1632.0	1683.0	1756.0	947.6	817.9	843.9	1032.6								
indole									81.7	197.1	154.1	262.3	323.4	411.6	339.3	666.5
2-hydroxy-2-methyl butanedioic acid									2354.1	2165.0	1941.8	1948.0	3761.5	3537.2	2702.4	3525.2
acetylphosphate									1287.7	271.4	267.2	348.0	766.9	1072.7	475.9	522.4
xanthine									116.0	70.7	155.2	631.0	153.7	38.5	56.7	158.0
dihydroorotate									479.2	4.7	4.1	4.0	773.2	7.3	5.9	7.4
phenylpyruvate									304.5	487.5	659.6	895.8	385.1	939.3	901.3	1379.8
glyceraldehdye-3-phosphate									1694.5	820.7	857.3	674.5	2154.0	2361.3	2124.9	2279.5
3-phosphoserine									1222.2	52.0	8.1	4.0	5189.3	185.2	11.0	7.4
creatine phosphate									6191.6	3715.3	1740.7	559.7	22660.5	20411.4	11178.0	11085.6
2,3-diphosphoglyceric acid									2202.7	701.9	221.7	290.7	759.0	413.2	188.2	93.5
dUMP									421.1	167.4	160.6	88.7	720.2	155.0	34.0	12.0
aminoimidazole carboxamide ribonucleotide									1183.1	1210.0	1607.9	239.7	1689.2	2174.6	1520.2	554.1
IMP									28261.6	6695.2	1043.3	16622.3	2398.1	6661.7	1038.4	2194.8
S-adenosyl-L-homocysteine									7229.4	7503.8	8979.5	1811.5	5682.6	11347.7	5734.9	2607.0
5-phosphoribosyl-1-pyrophosphate									66.3	57.5	99.7	4.0	714.2	601.0	161.4	27.5
adenosine-5'-phosphosulfate									145.4	771.4	1026.7	625.9	230.4	329.8	678.5	439.5
folate									70.9	4.7	4.1	4.0	1344.1	25.6	10.3	7.4
FMN									362.6	71.8	51.8	23.5	124.0	137.5	82.0	55.5
dephospho-CoA									732.1	439.7	293.8	320.1	995.8	1129.4	708.9	726.6
NADPH									12946.5	8419.1	8588.1	6211.5	20540.5	17532.2	11308.0	4756.6
3-hydroxy-3-methylglutaryl-CoA									243.6	128.7	23.4	10.1	405.9	380.9	152.0	65.8
3-hydroxyanthranic acid									9301.9	7333.7	5474.3	5405.6	15004.5	21226.5	19373.8	23190.6
cystathionine									2308.0	884.4	679.4	450.3	59752.8	35009.2	14597.4	11420.1
thiamine									170.1	29.8	21.9	23.4	4843.0	39.1	39.7	16.4
S-adenosyl methionine									7603.3	26131.5	23866.9	11700.5	8472.7	28164.4	18097.6	17081.4
alanine									45133.0	2781.5	2723.2	2392.9	78898.9	7862.5	3340.6	4502.1
lauroylcarnitine									461.1	338.0	102.2	23.3	196.1	173.7	52.9	77.1

Table S1: Metabolite pool sizes for all detected metabolites in TDCLs in response to HBSS starvation. A total of the 159 intracellular metabolites (ion signals) identified in *atg7*-wild type and *atg7*-deficient TDCLs under normal and starvation (HBSS) conditions are shown.