

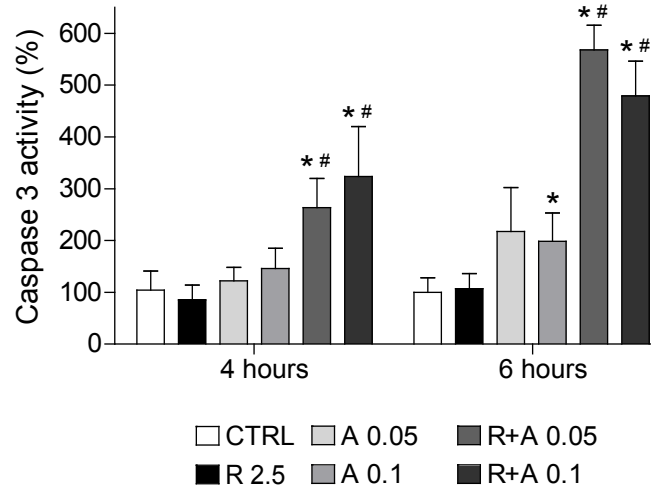
Supplementary materials: Regorafenib alteration of the BCL-xL/MCL-1 ratio provides a therapeutic opportunity for BH3-mimetics in hepatocellular carcinoma models

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Table S1. Patient's data.

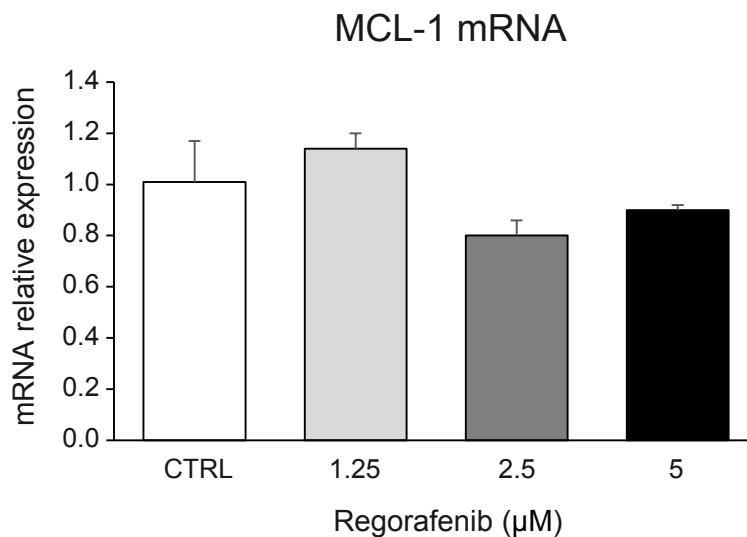
GENDER	AGE	Underlying liver disease	ETHIOLOGY	Virus hepatitis	AFP (ngr/mL)	TUMOR SIZE (cm)	Tumor	Vascular Invasion
M	67	cirrhosis	alcohol	NO		4,5	single	NA
M	54	cirrhosis	VHC+VHB+alcohol	VHC+VHB	15	1,3	single	NA
M	50	cirrhosis	VHC+alcohol	VHC	19	1,4	single	NA
M	61	chronic hepatitis	VHC	VHC	20	1,8	single	Yes
M	33	chronic hepatitis	VHB	VHB	4	1,1	single	No
F	61	cirrhosis	VHC	VHC	11	2,1	single	No
M	56	cirrhosis	VHC	VHC	2	5,2 (principal)	multinodular	No
M	68	cirrhosis	alcohol	No	1515	5	single	Yes, microvascular
M	61	cirrhosis	alcohol	No	2	3,5	single+1 satellite	No
M	47	cirrhosis	VHC	VHC	6	2,5	single	No
M	75	cirrhosis	VHC	VHC	23	1,1 (principal)	binodular	No
F	69	cirrhosis	VHC	VHC	7	1,2	single	Yes, microvascular
M	78	cirrhosis	VHC	VHC		4,5	single	No
M	73	cirrhosis	VHC	VHC	2	2,1	single	No
M	67	cirrhosis	VHC	VHC	22	2,1	single	No
M	63	cirrhosis	VHC	VHC	2	2,2	single	No
M	63	chronic hepatitis	VHC	VHC	9	6	single	No
M	48	cirrhosis	VHC	VHC	7	7,5	single	Yes, peritumoral
M	64	cirrhosis	alcohol	NO	6	4,5	single	No
M	68	healthy liver	NA	NO	NA	NA	NA	NA
F	70	healthy liver	NA	NO	NA	NA	NA	NA
F	47	healthy liver	NA	NO	NA	NA	NA	NA
F	50	healthy liver	NA	NO	NA	NA	NA	NA
F	55	healthy liver	NA	NO	NA	NA	NA	NA
M	36	healthy liver	NA	NO	NA	NA	NA	NA
M	36	healthy liver	NA	NO	NA	NA	NA	NA
M	55	healthy liver	NA	NO	NA	NA	NA	NA
M	37	healthy liver	NA	NO	NA	NA	NA	NA
F	73	healthy liver	NA	NO	NA	NA	NA	NA

Supplemental Figure 1



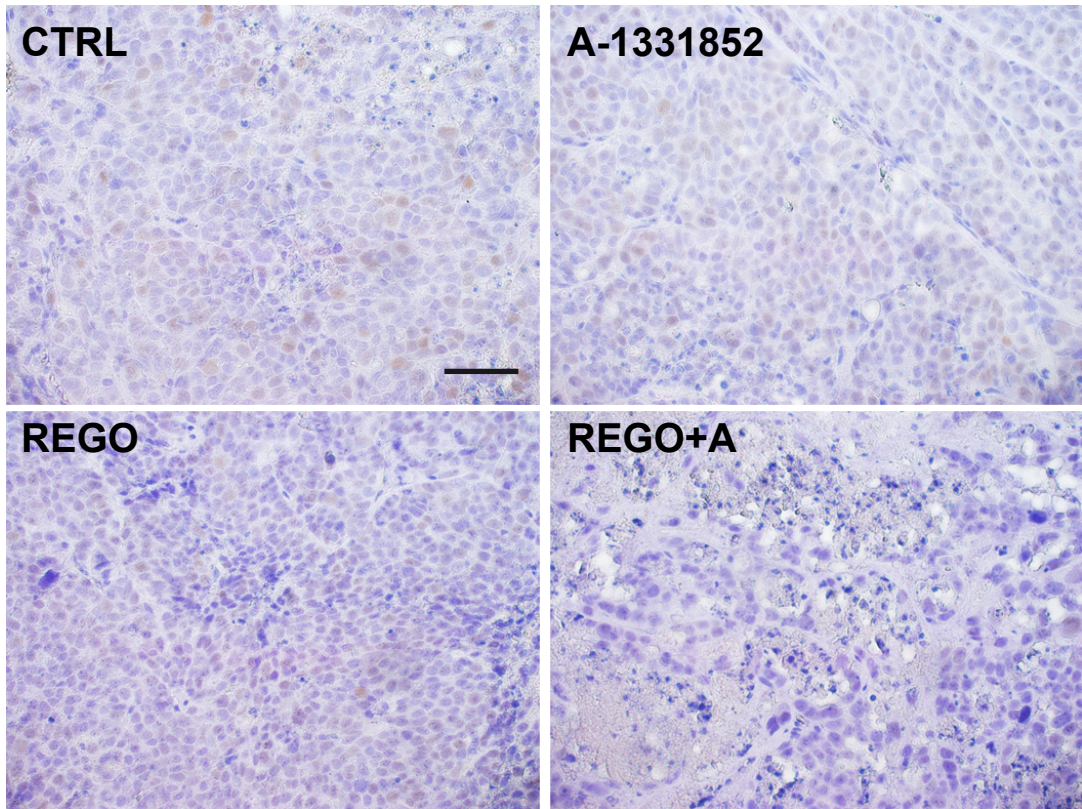
HepG2 cells were exposed to regorafenib (R, 2.5 μM) with or without A-1331852 (A, 0.1-0.05 μM) and caspase-3 activity was determined fluorimetrically at four and six hours. * $P < 0.05$ vs. control cells, # $P < 0.05$ vs. regorafenib-treated cells. (n=3)

Supplemental Figure 2



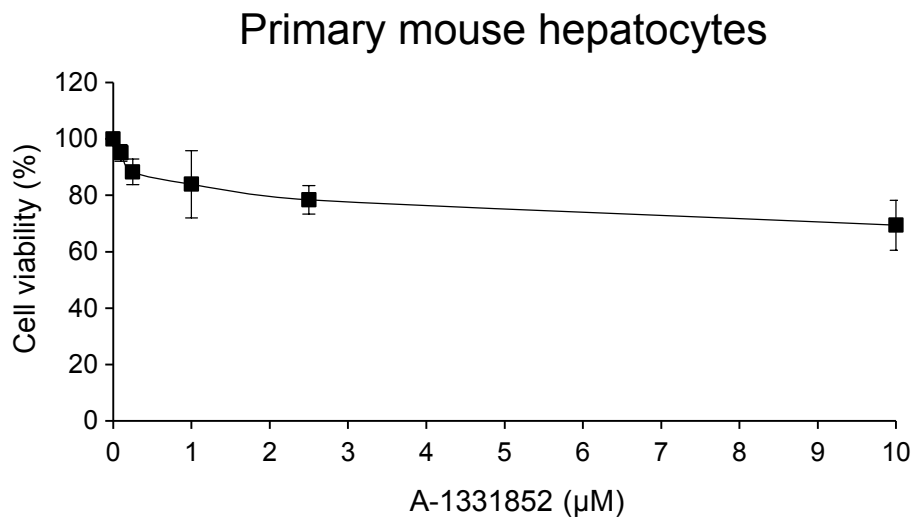
HepG2 cells were exposed to regorafenib (R, 1-5 μM) for 16 h and mRNA levels of MCL-1 were determined by qPCR. (n=2)

Supplemental Figure 3



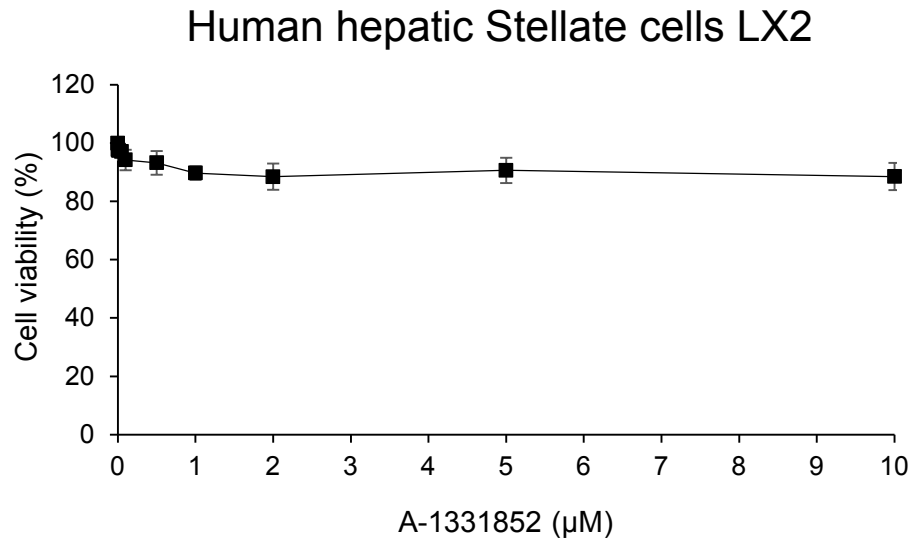
Representative images of Ki-67 expression in tumor samples from BCLC9 PDXs (scale bar, 50 μ m).

Supplemental Figure 4



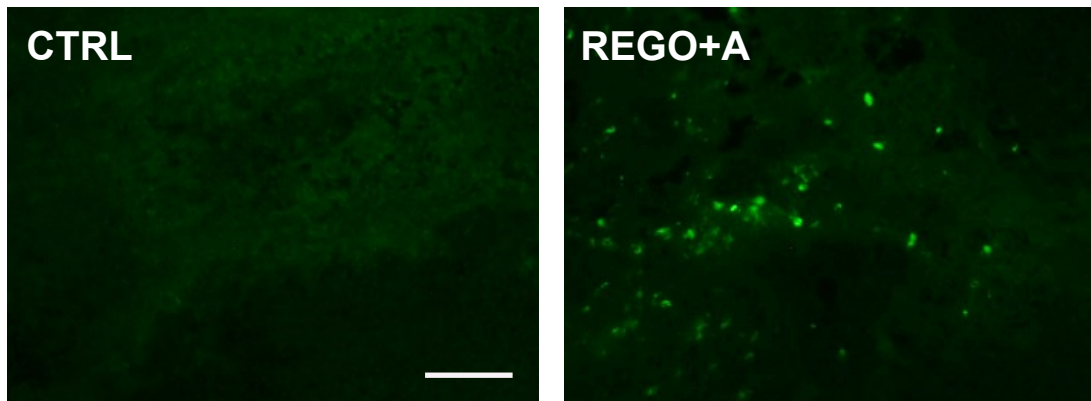
Primary mouse hepatocytes cultured on collagen plates were exposed to A-1331852 at different concentrations (up to 10 μ M) and MTT assays performed 16 h. (n=4)

Supplemental Figure 5



Human hepatic Stellate cells LX2 were exposed to A-1331852 at different concentrations (up to 10 µM) and MTT assays performed 16 h. (n=4)

Supplemental Figure 6



Representative images of TUNEL staining in tumor samples from R HEPG2 CDXs (scale bar, 100 µm).

The whole western blot

Figure 2F

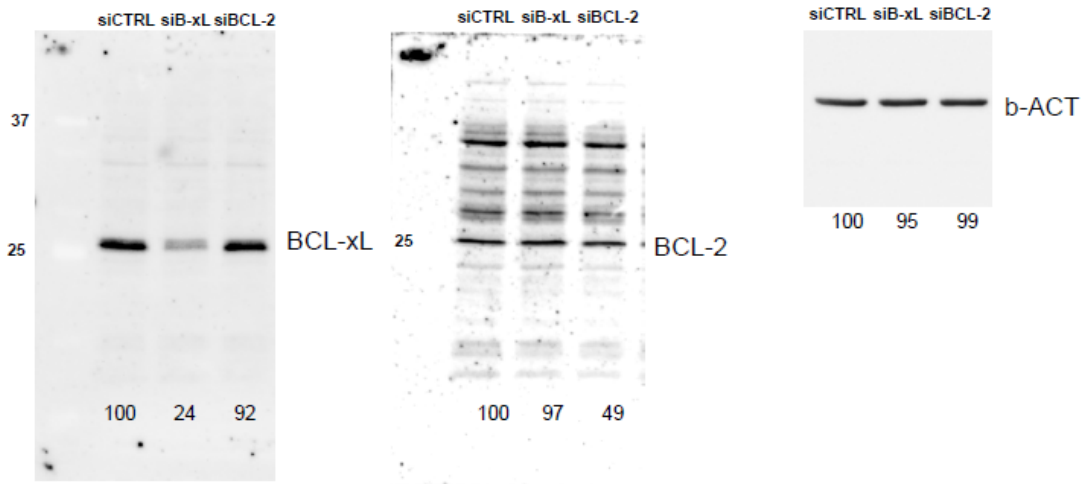


Figure 4B

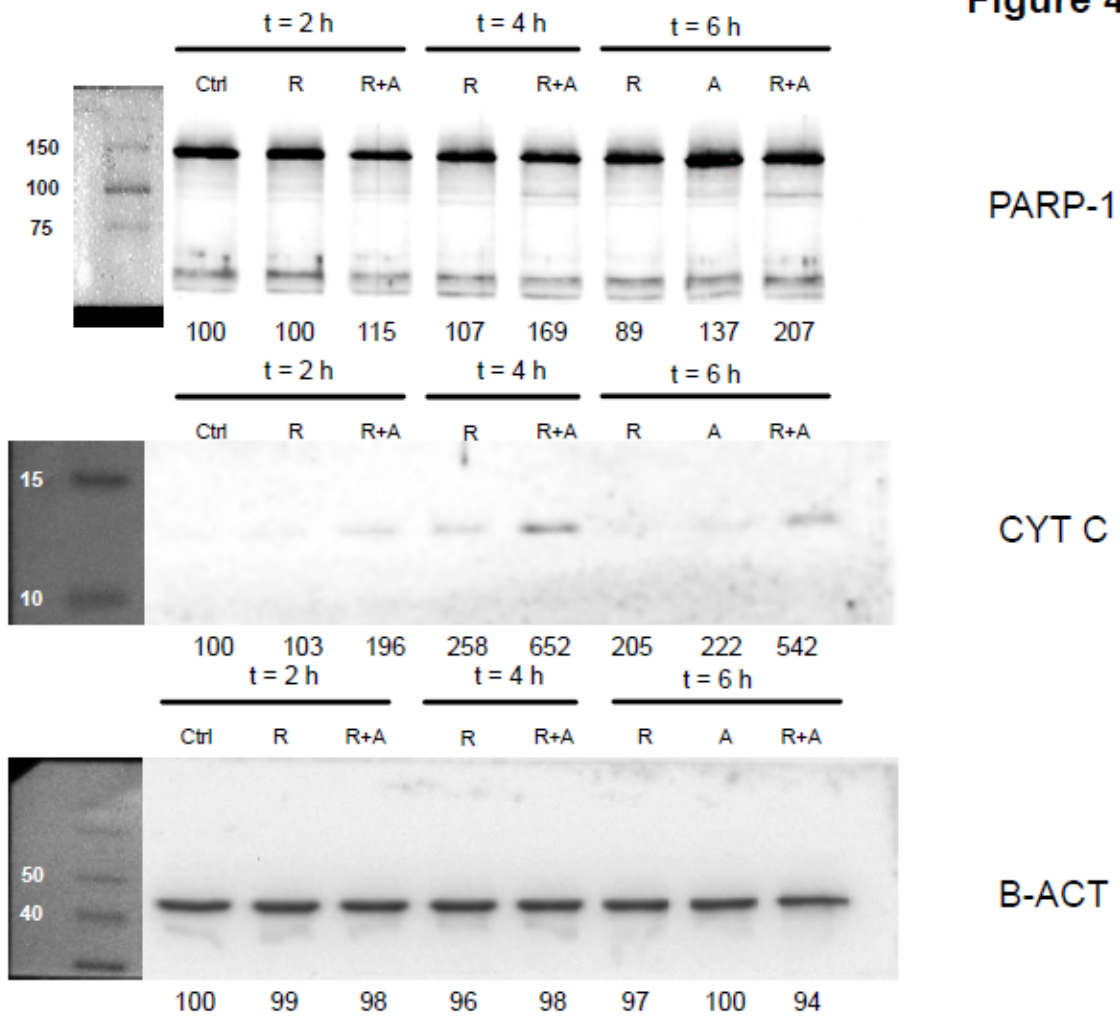


Figure 5A

HEP3B

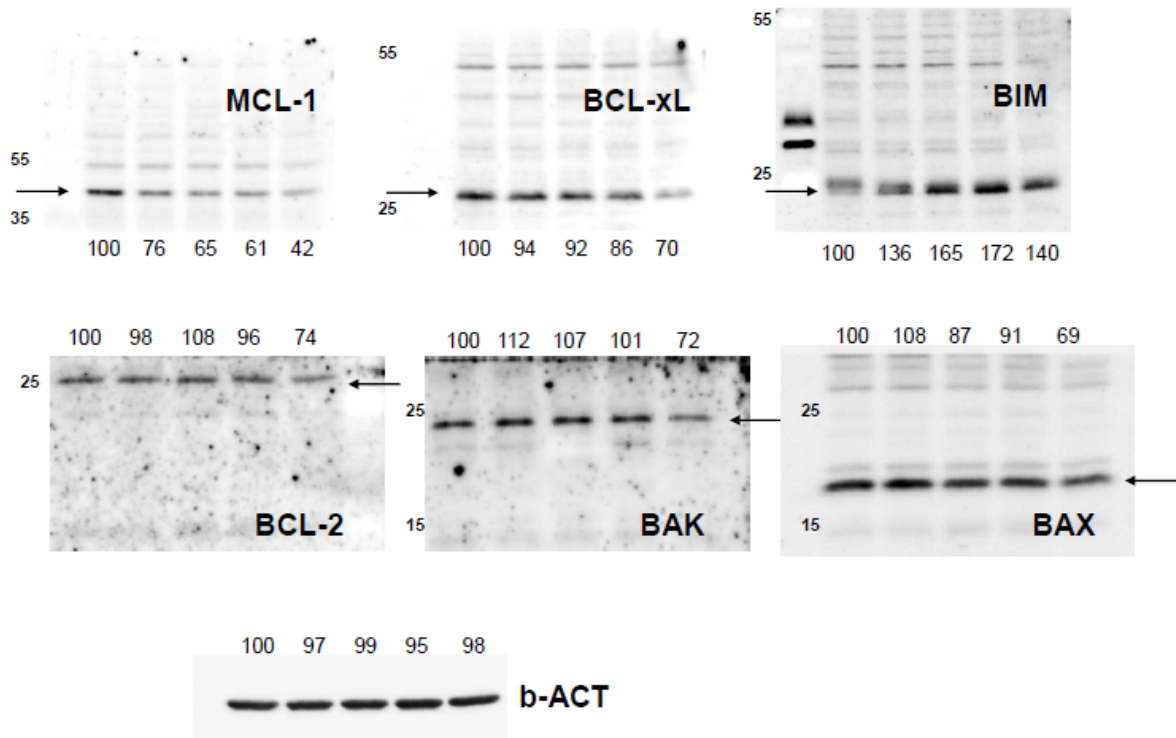


Figure 5A

HEPG2

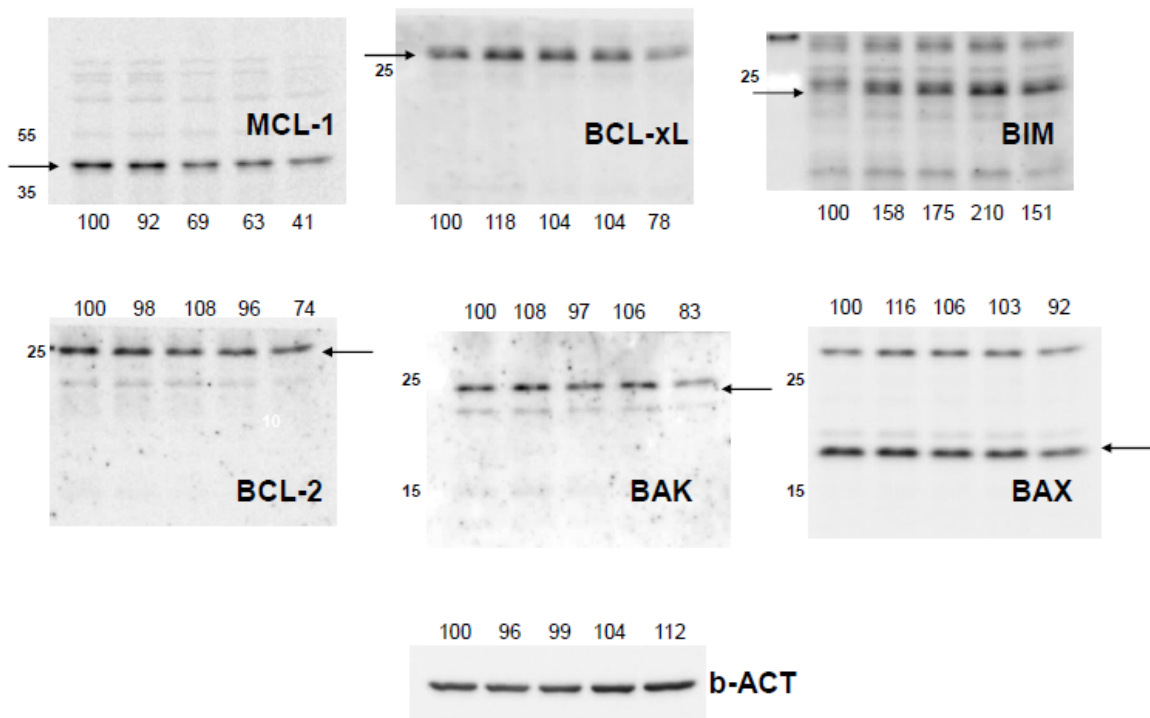


Figure 7A

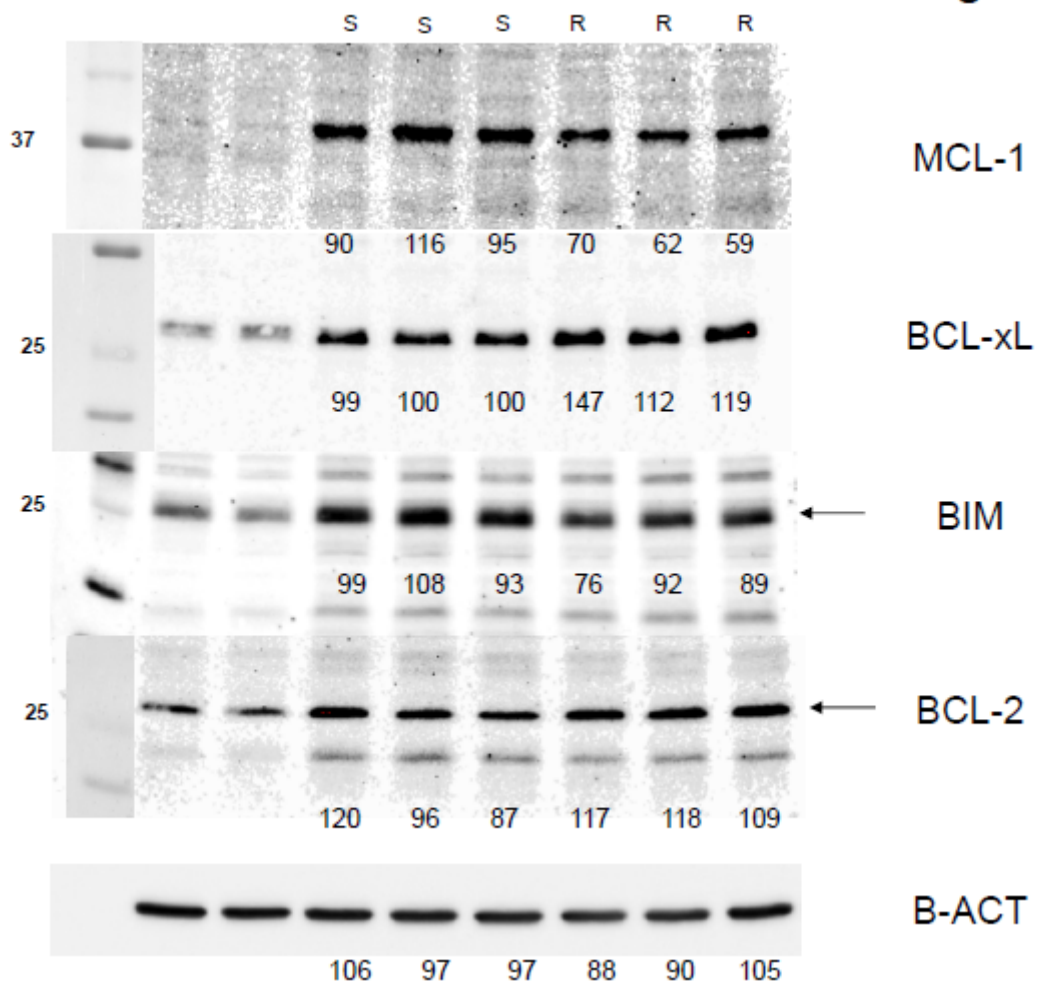
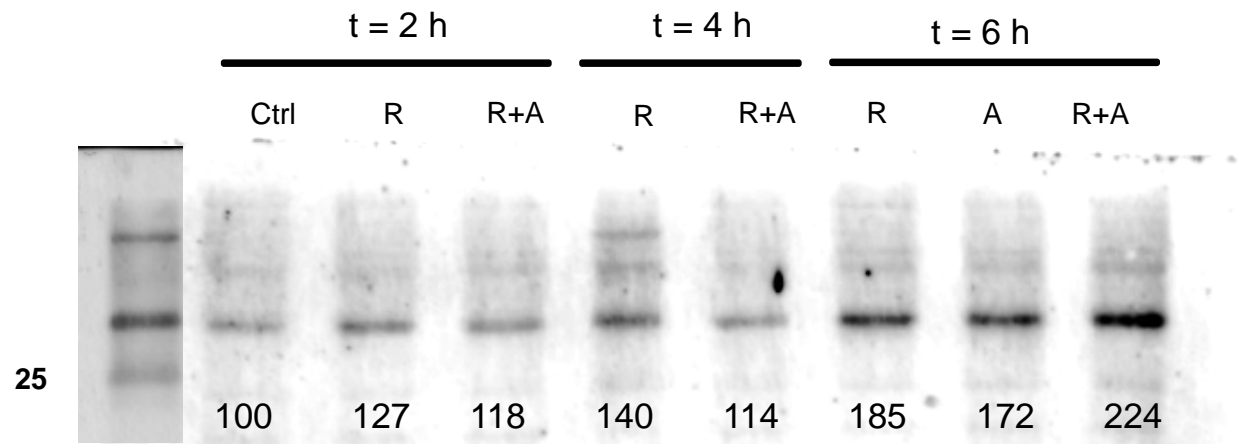
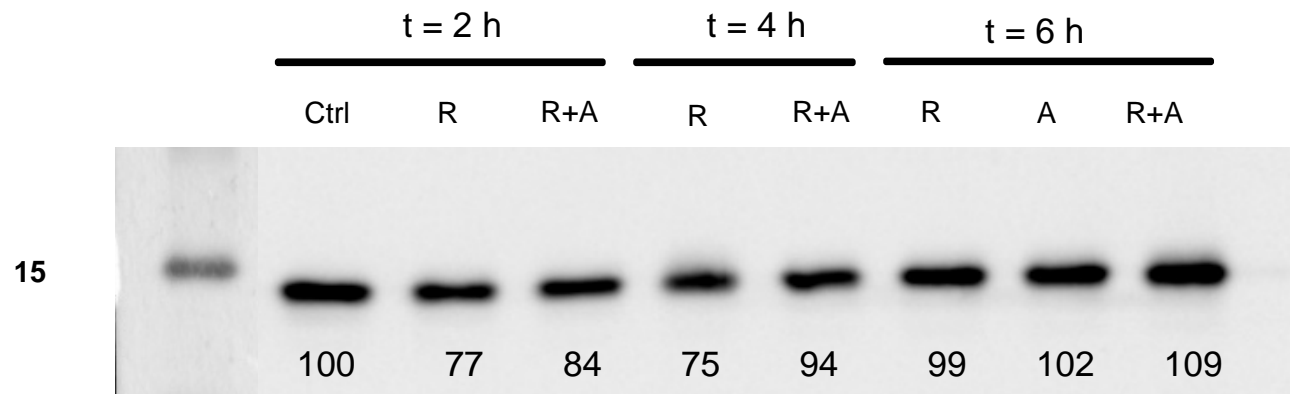


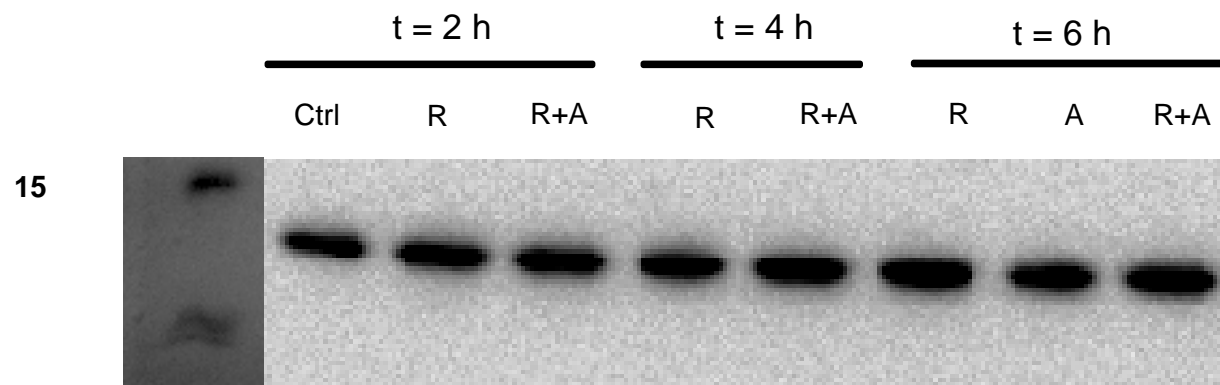
Figure 4B



BAX MITO

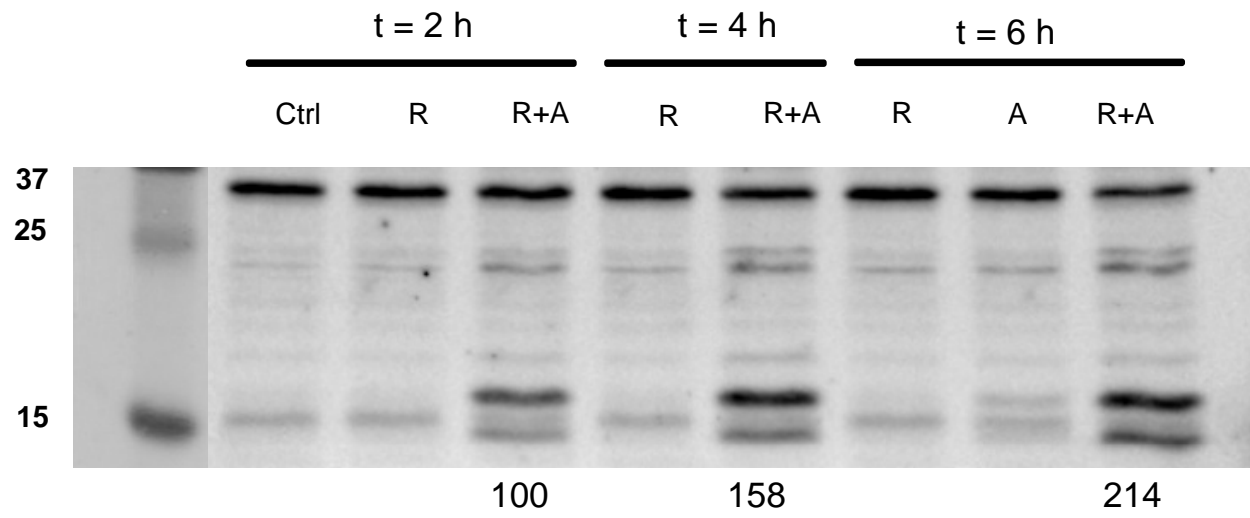


TOM20 MITO



CYT C TOT

Figure 4B



CASP-3 TOT

Figure 4C

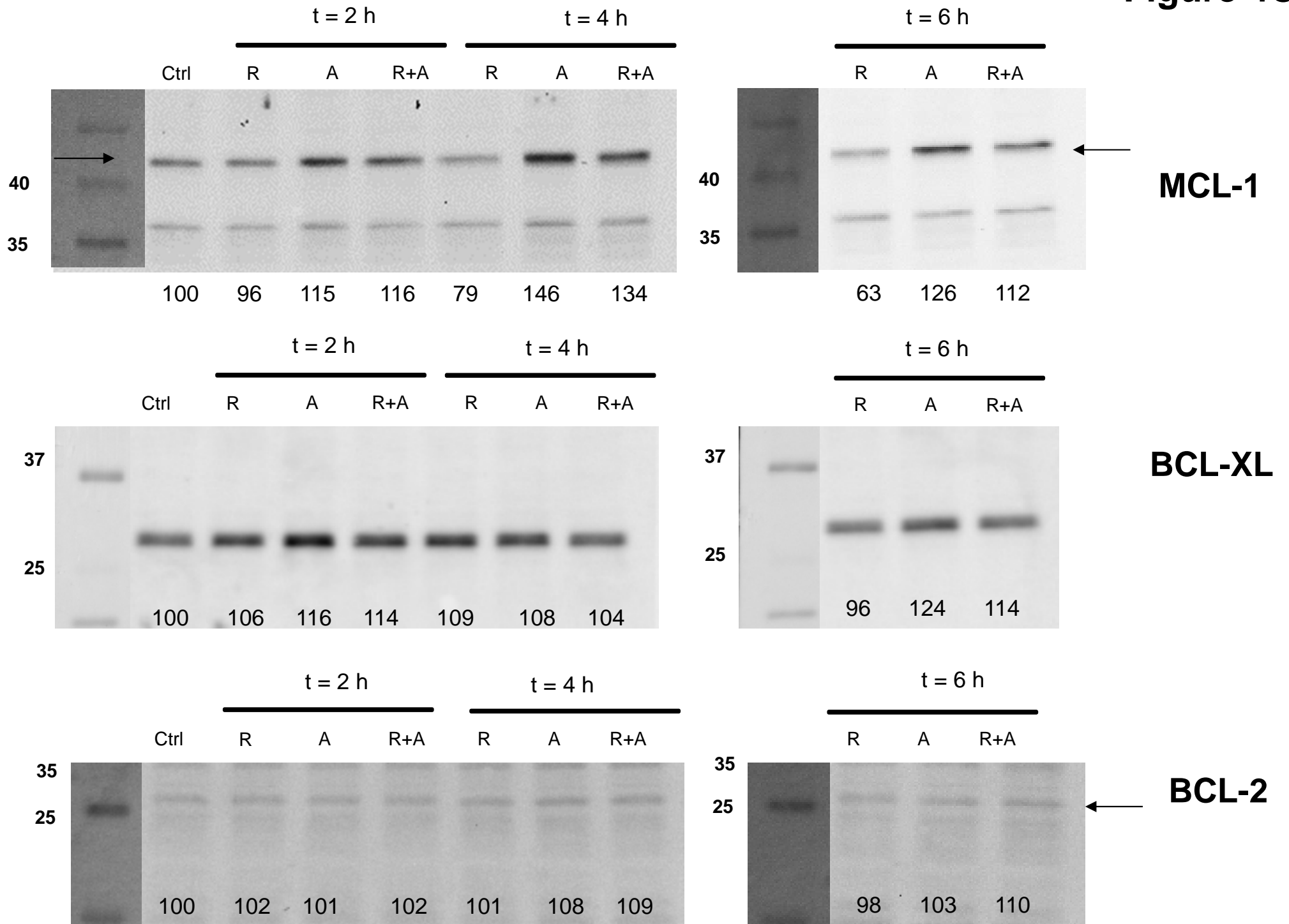


Figure 4C

