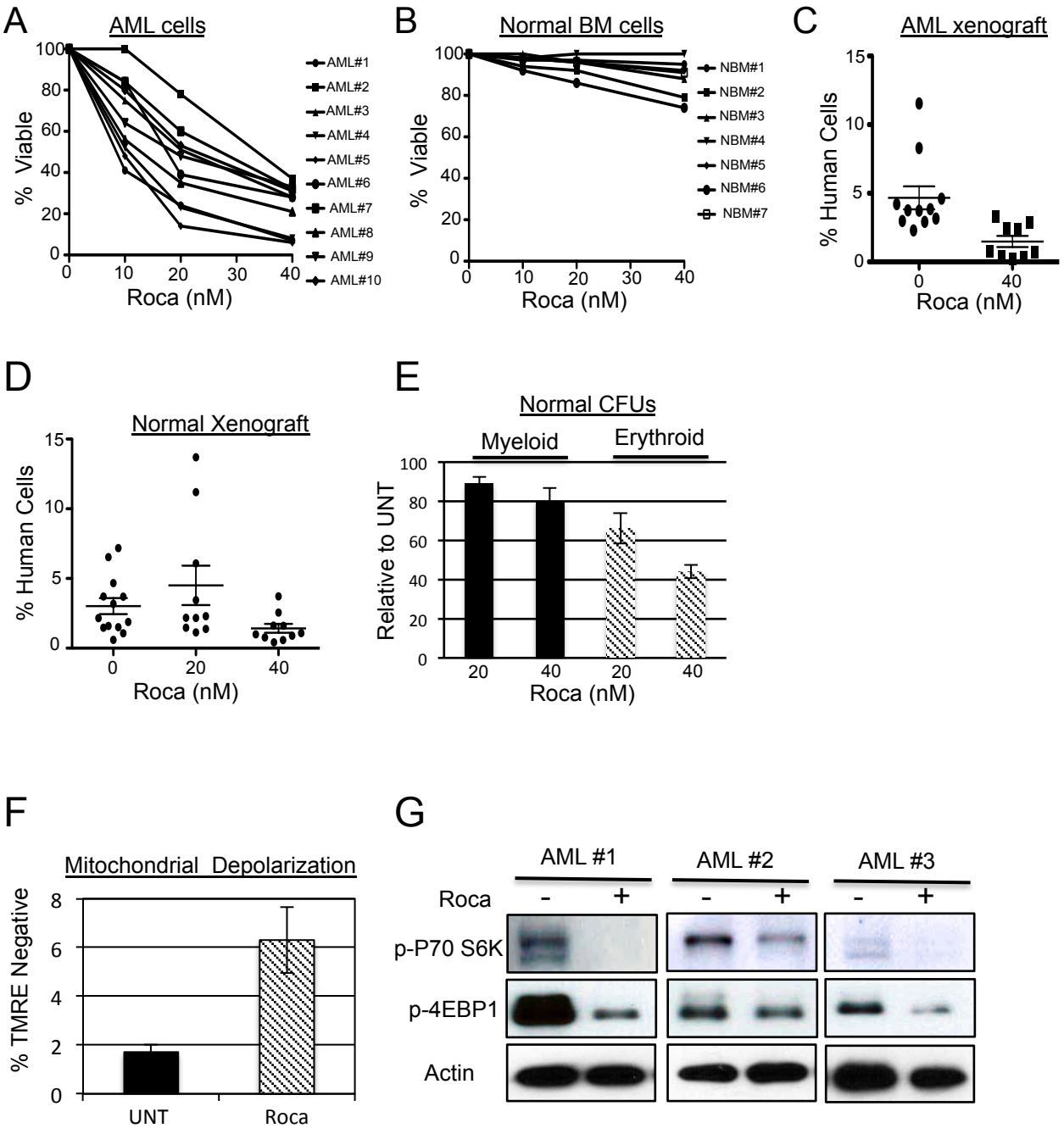
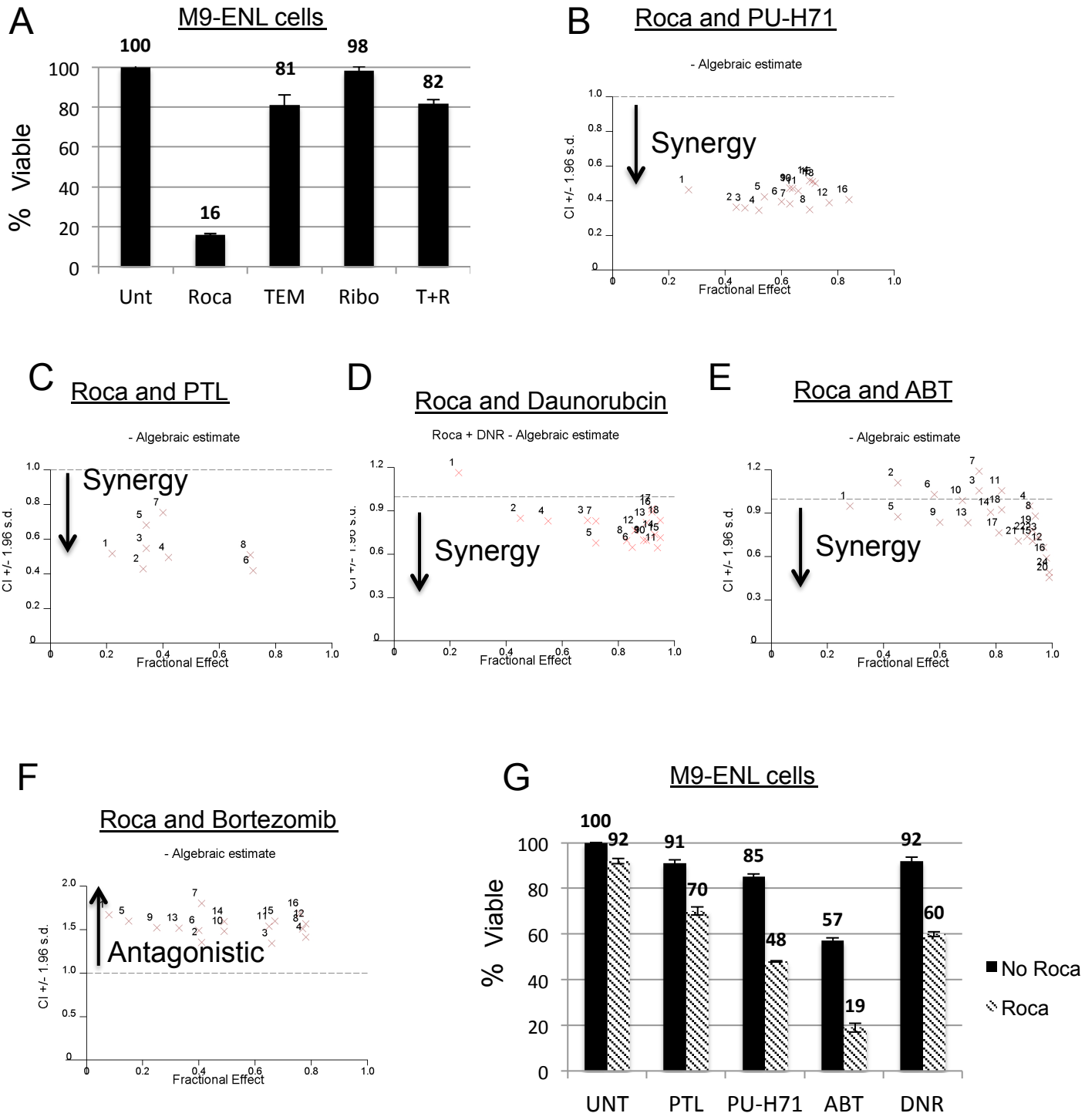
Supplemental Figure 1:



Supplemental Figure 1. A) Percentage of total viable hematopoietic cells obtained from primary human AML cells (N=10) exposed to indicated concentrations of rocaglamide. Cells were stained with annexin-V and 7-AAD and viability measured by a flow cytometer, viability values are relative to untreated controls. B) Percentage of total viable cells from healthy donors exposed to rocaglamide. C) Percentage engraftment achieved in NOG mice receiving AML cells D) Percentage engraftment achieved in NSG mice receiving hematopoietic cells from healthy donors after 48hrs culture with or without rocaglamide. E) Percentage of colony forming units (CFU) normalized to untreated controls, all assays done in triplicate, N=6. F) Percent of cells with depolarized mitochondria following treatment with 40nM rocaglamide (N=3). G) Whole cell lysates were generated from primary AML cells treated with 40nM rocaglamide for 24hrs for western blot analysis

Supplemental Figure 2



Supplemental Figure 2 . **A) Graph represents percent survival of M9 cells 48hrs after treatment with indicated drugs (Roca = 40nM Rocaglamide, TEM = 5ug/mL Temsirolimus, Ribo = 25uM Ribavarin, T+R = Temsirolimus and Ribavirin together)** B-F) Representative synergy plots generated using calculsyn software of indicated drugs in combination with rocagalmide. G) Graph represents percent survival of M9 leukemia cell treated simultaneously with indicated drugs. Dotted bars represent percent survival of compounds given individually. Striped bars represent the percent survival when compounds were given following 24hr pretreatment with rocaglamide.

Supplemental Figure 3

A

	Top Upstream Regulators	P-value of overlap
1	SIN3B	1.95E-10
2	MYC	9.66E-10
3	TP53	2.71E-09
4	HNF4A	1.05E-06
5	E2F1	1.17E-06

	Top Tox Lists	-log(p-value)
1	Renal Necrosis/Cell Death	1.4E-03
2	TGF-B Signaling	2.02E-03
3	Liver Necrosis/Cell Death	3.33E-03
4	p53 Signaling	3.99E-03
5	RAR Activation	4.73E-03

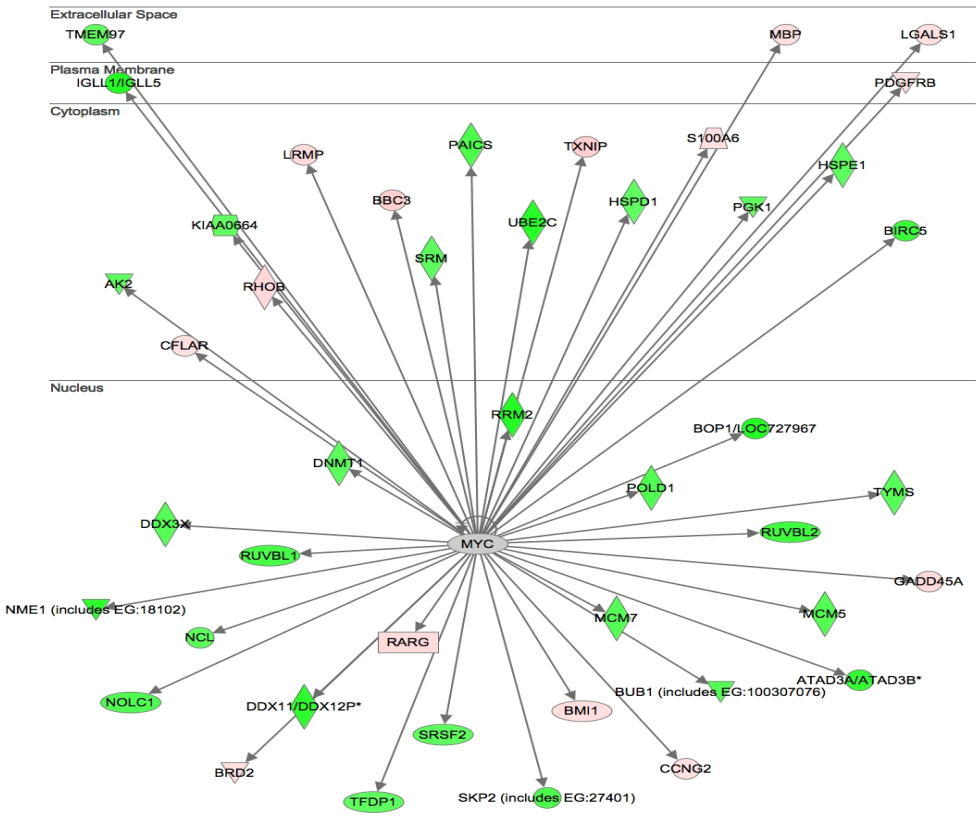
	Top Canonical Pathways	-log(p-value)
1	Molecular Mechanisms of Cancer	1.29E-05
2	ATM Signaling	4.34E-05
3	Hypoxia Signaling in the Cardiovascular System	6.2E-05
4	Glucocorticoid Receptor Signaling	5.74E-04
5	B Cell Receptor Signaling	1.28E-03

	Associated Network Functions
1	RNA Post-transcriptional Modification, Molecular Transport, Protein Trafficking
2	Cell Death, Nervous System Development and Function, Developmental Disorder
3	Cell Cycle, DNA replication, Recombination, and Repair
4	Cellular development, skeletal and muscular system development and function, embryonic development
5	Cell Death, Nucleic Acid Metabolism, Small Molecule Biochemistry

Supplemental Figure 3 A) Lists were generated from rocaglamide gene signature using IPA software B) MYC regulated genes are significantly down-regulated following treatment with rocaglamide, figure was generated using Ingenuity Pathway Analysis. C) Flow cytometry data from cell cycle analysis. D) Graph represents percent survival of cells treated with indicated concentrations JQ1.

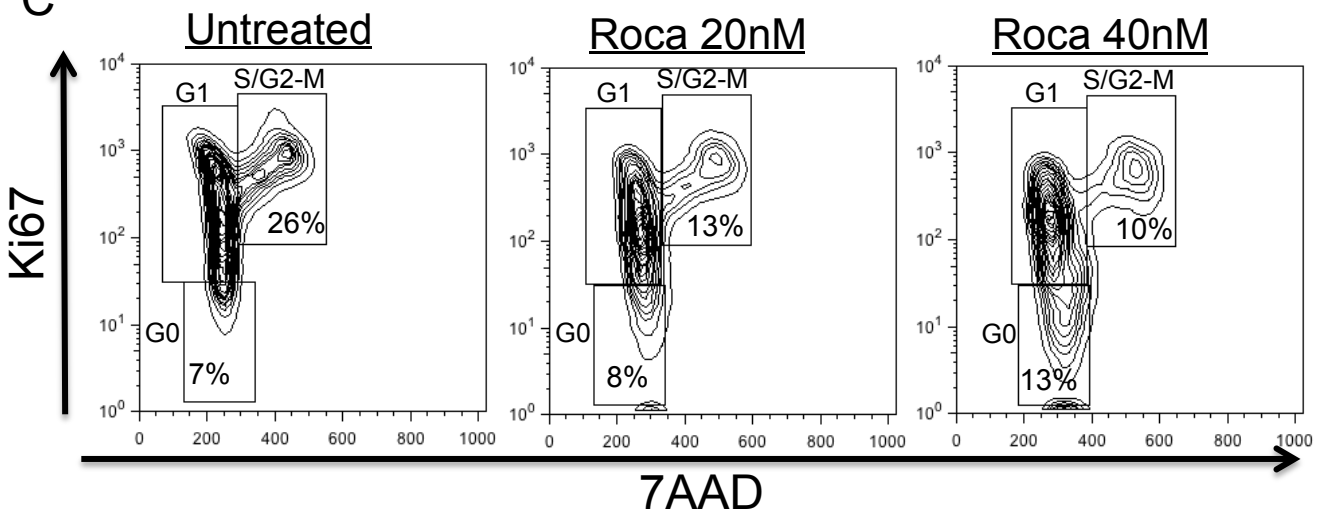
Supplemental Figure 3

B



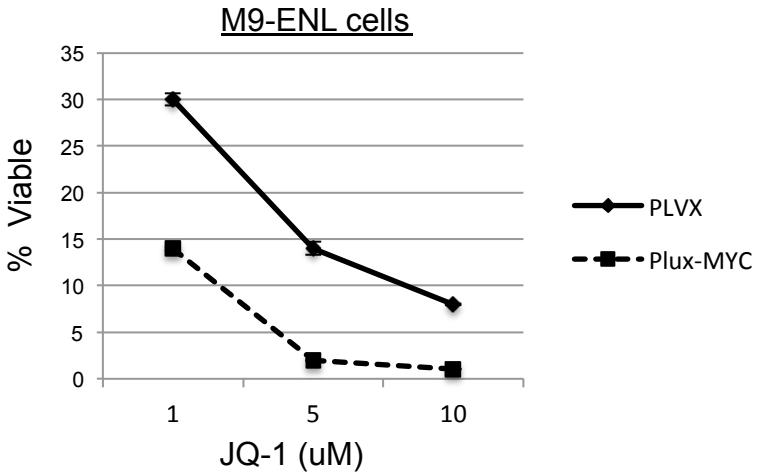
33 of 38 significantly deregulated Myc target genes are inhibited based on IPA analysis

C

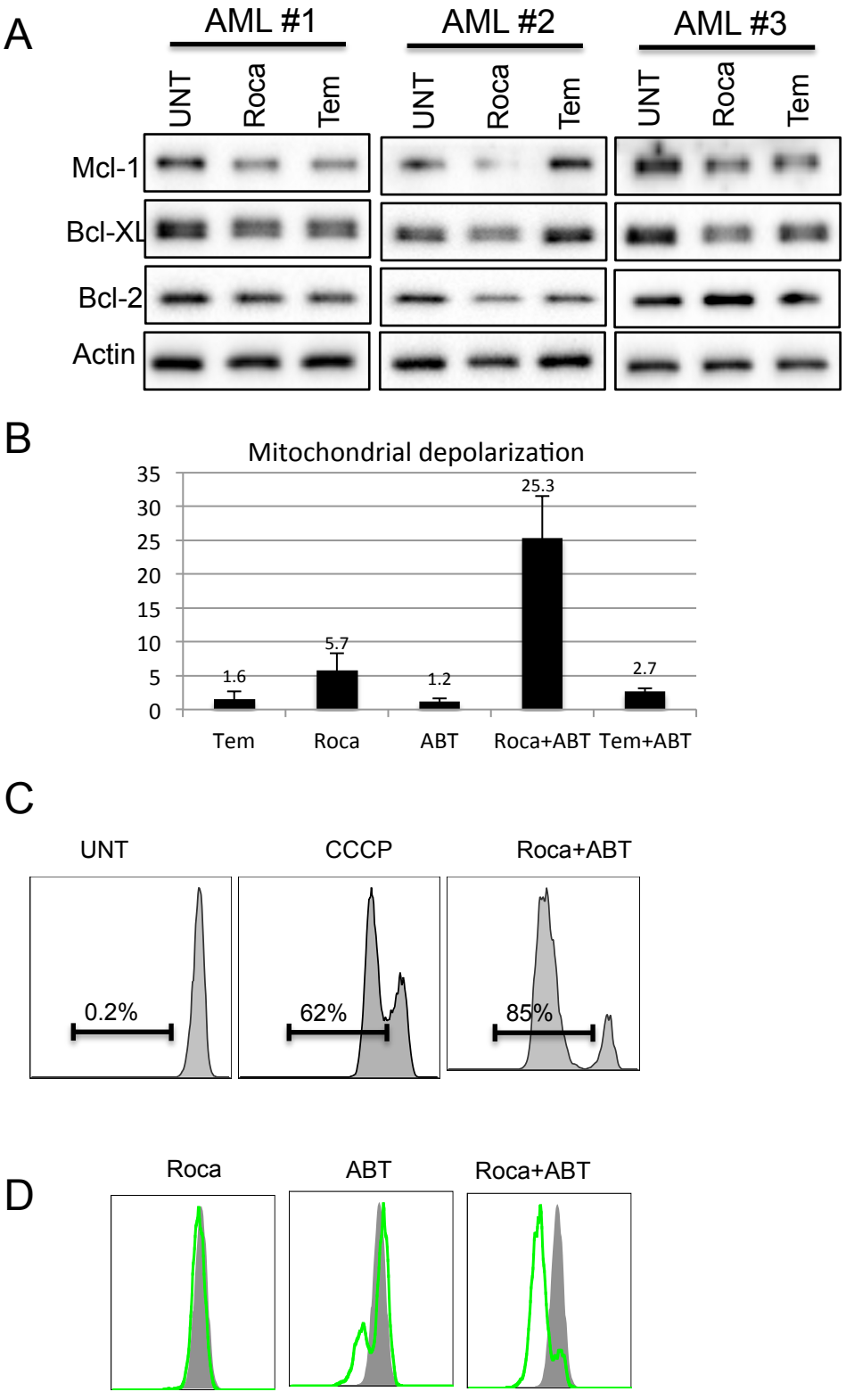


Supplemental Figure 3

D

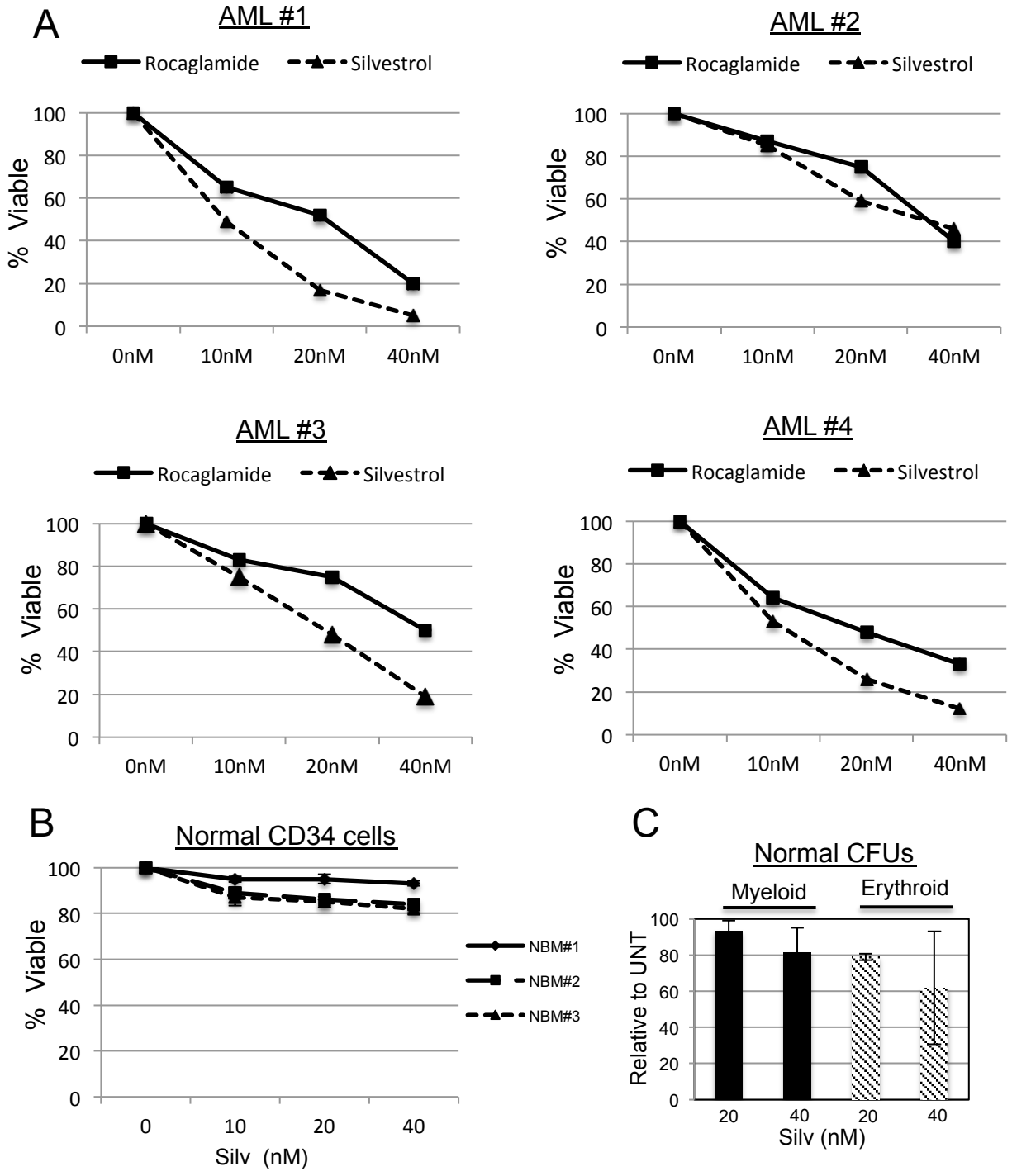


Supplemental Figure 4



Supplemental Figure 4: A) Whole cell lysates were generated from primary AML cells treated with 40nM Rocaglamide or 2.5mg/mL Temsirolimus for 24hrs for western blot analysis. B)Graphical representation of depolarization (N=3) of M9-cells treated with indicated drugs. **C) M9-ENL Cells were treated with indicated drugs, depolarized mitochondria was determined by flow cytometry following staining with TMRE dye. D) M9-ENL cells were incubated with indicated drugs followed by labeling with the fluorescent dye DCF which detects reactive oxygen species (ROS), and analysis by flow cytometry**

Supplemental Figure 5



Supplemental Figure 50. A) Percentage of CD34 viable hematopoietic cells in primary human AML cells exposed to rocaglamide or silvestrol. Cells were stained with annexin-V and 7-AAD and viability measured by a flow cytometer, viability values are relative to untreated controls. B)Percentage of viable CD34+ cells from healthy donors exposed to silvestrol C) Percentage of colony forming units (CFU) normalized to untreated controls, all assays done in triplicate, N=2.

Supplemental Figure 5

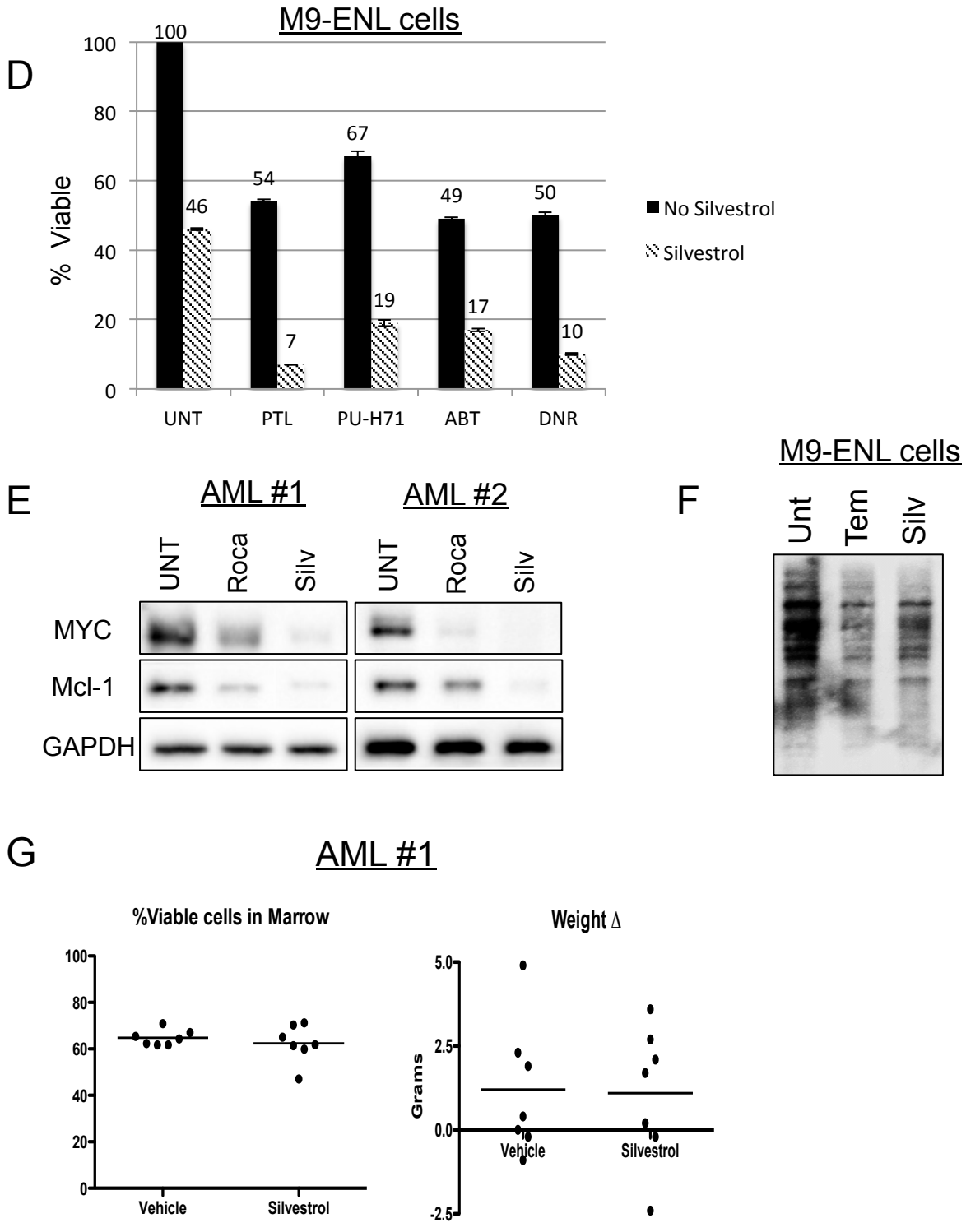
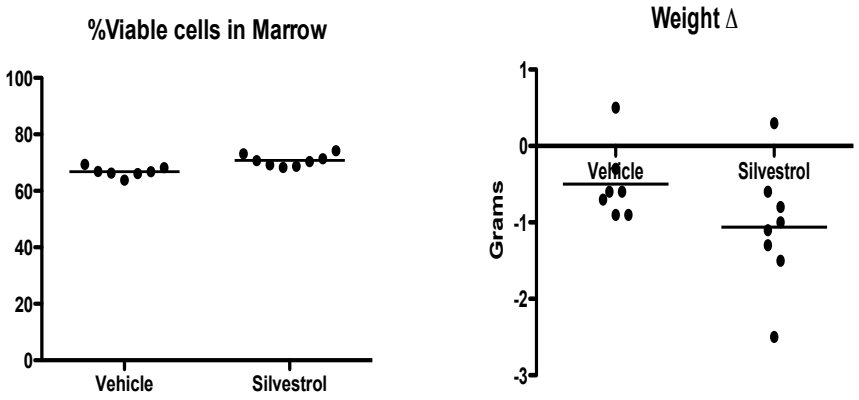


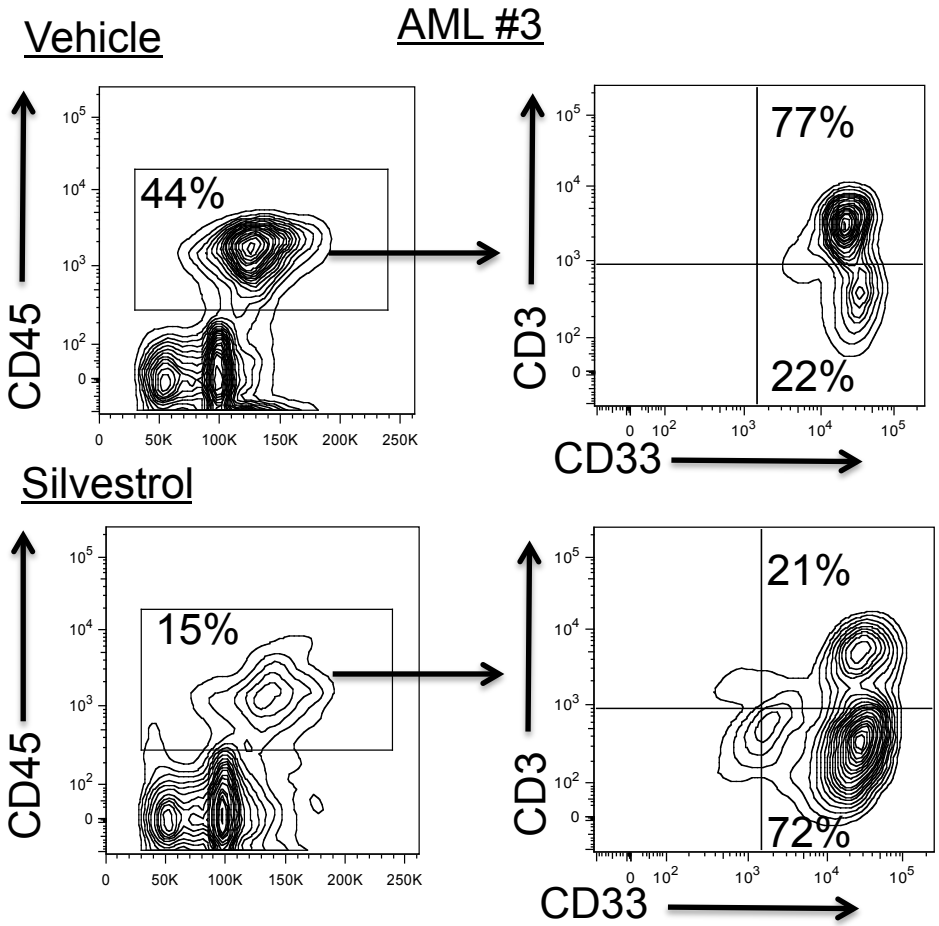
Figure 5. D) Graph represents percent survival of M9 leukemia cells treated with indicated drugs. Solid bars represent percent survival of compounds given individually. E) Whole cell lysates were generated from primary AML cells treated with rocaglamide or silvestrol for 24hrs for western blot analysis. F) Met-label experiment comparing translation after treatment with indicated compounds (5.0ug/mL Temsirolimus, 10nM Silvestrol) G)Percentage of bone marrow cells from silvestrol treated mice that were viable as determined by Dapi staining and flow cytometric analysis. Weight change before and after treatment with silvestrol. H) Representative flow cytometric analysis of AML#3 engraftment following drug analysis. I) Percentage of leukemic clone (CD33+ CD3+) from AML#3 present in marrow following indicated treatments.

Supplemental Figure 5:

G



H



I