

Supplemental Figure Legends

Figure S1: A cluster of 59 differentially expressed genes (17 upregulated and 42 downregulated more than 2-fold, see ‘Supplemental Table I’) separates wild-type E μ -myc lymphomas from TRAIL-R-deficient (TRAIL-R^{+/-} and TRAIL-R^{-/-}) E μ -myc lymphomas, but does not distinguish between TRAIL-R^{+/-} and TRAIL-R^{-/-} E μ -myc lymphomas. Total RNA was isolated from wild-type, TRAIL-R^{+/-} and TRAIL-R^{-/-} E μ -myc lymphomas (N=5 each genotype) and hybridized to an affymetrix MOE430A 2.0 chip. Data was analyzed using the GeneSpring FX software and genes with a fold change of at least 2-fold and P<0.05 (One-Way ANOVA) were used for expression-based clustering.

Figure S2: Treatment of cells with JSI-124 (curcubitacin I) enhances TRAIL-mediated cell death. (A) Interferon alpha (IFN- α) triggers phosphorylation at Tyr705 of Stat3 in the murine fibrosarcoma cell line L929 but not treatment with TRAIL. Treatment of cells with the phosphotyrosine-stat3 inhibitor JSI-124 triggers synergistic cell killing with TRAIL as determined by trypan blue staining (B) and FITC-Vad-FMK/PI analysis (C). Immunofluorescence (D) of the stat3-target surviving and activated caspase 3 in the human colorectal carcinoma cell line HCT116 suggest reduced nuclear survivin expression (Cy2, green) following treatment with 50 nM JSI-124 and increased activation of caspase-3 (Cy3, red) following combination treatment with TRAIL and JSI-124. Cell nuclei are visualized with DAPI (blue). The average or representative results of two independent experiments are shown. Treatment of HCT116 cells with the combination of TRAIL and JSI-124 (E) for 16 hours triggers synergistic apoptosis as measured by DNA-fragmentation (Sub-G1 %) compared to either treatment alone.

Supplemental Figures

Figure S1

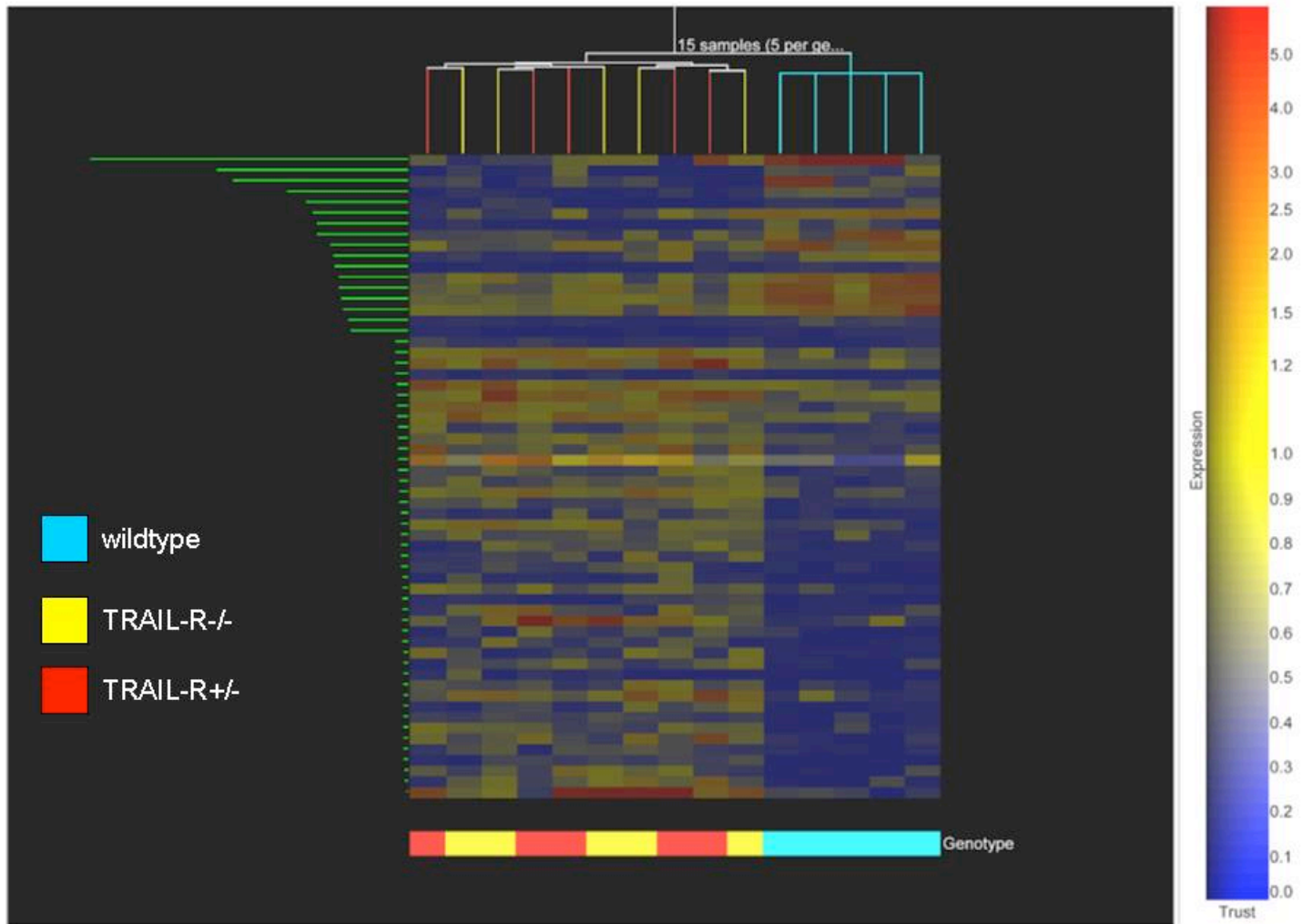
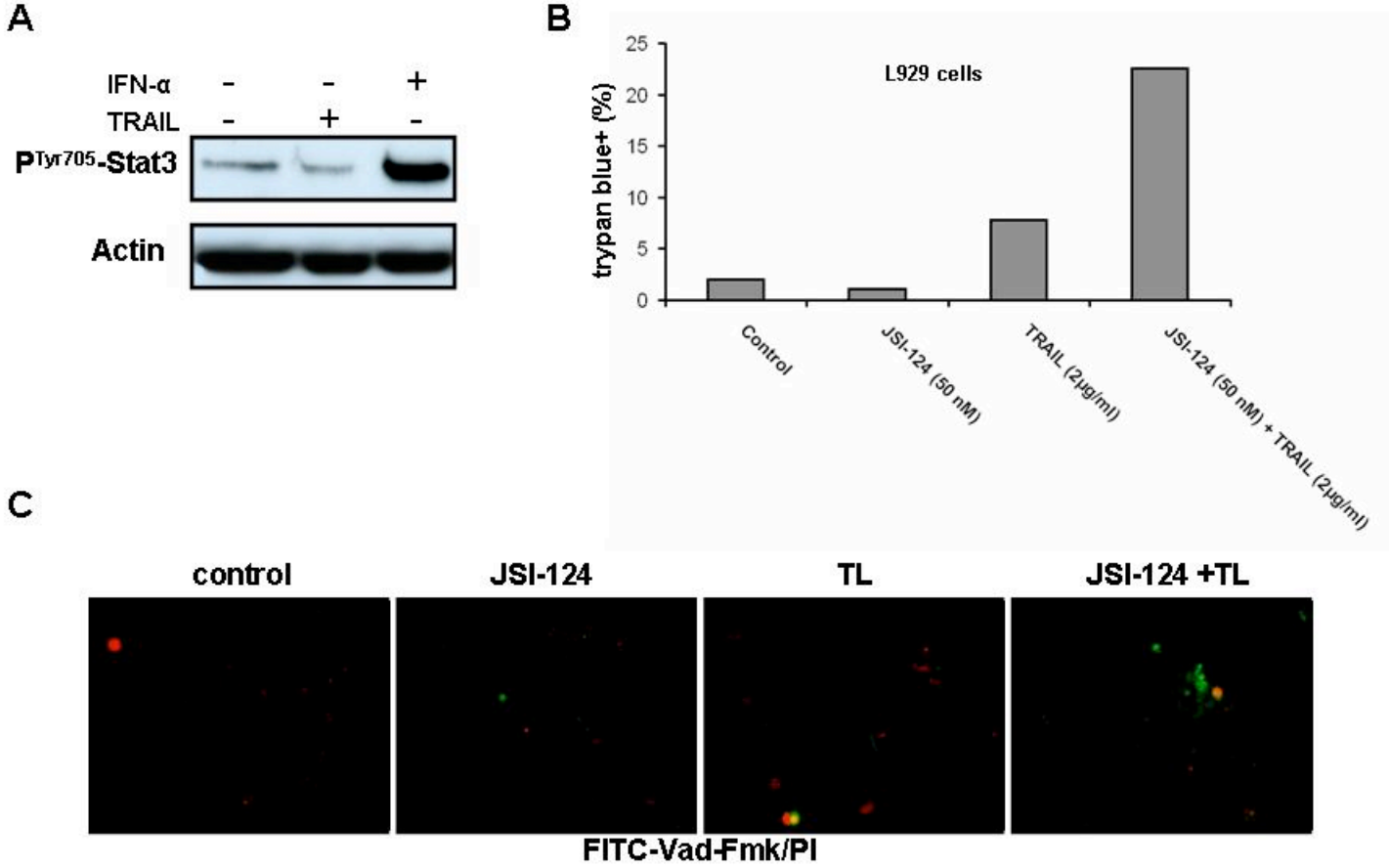
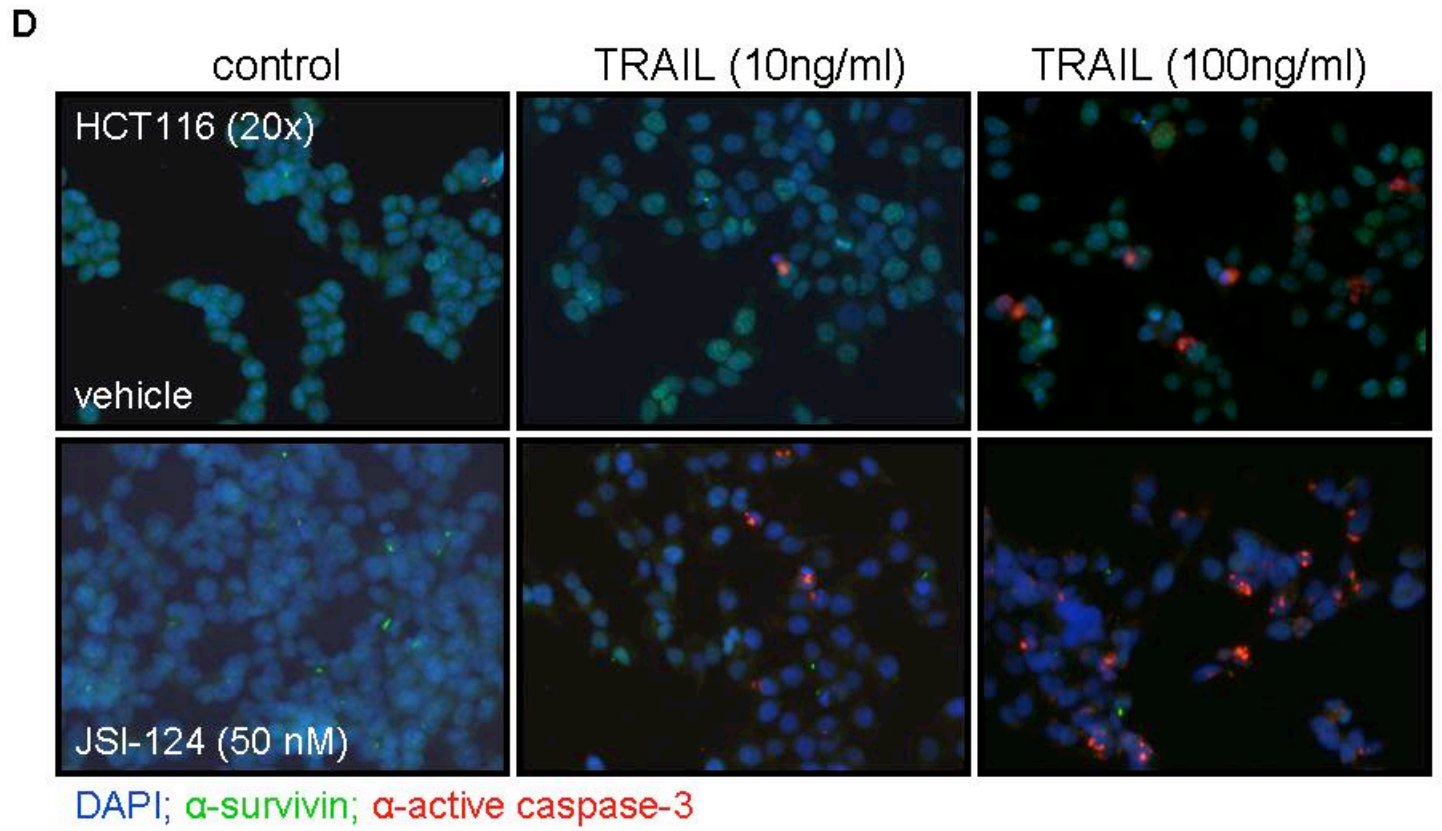
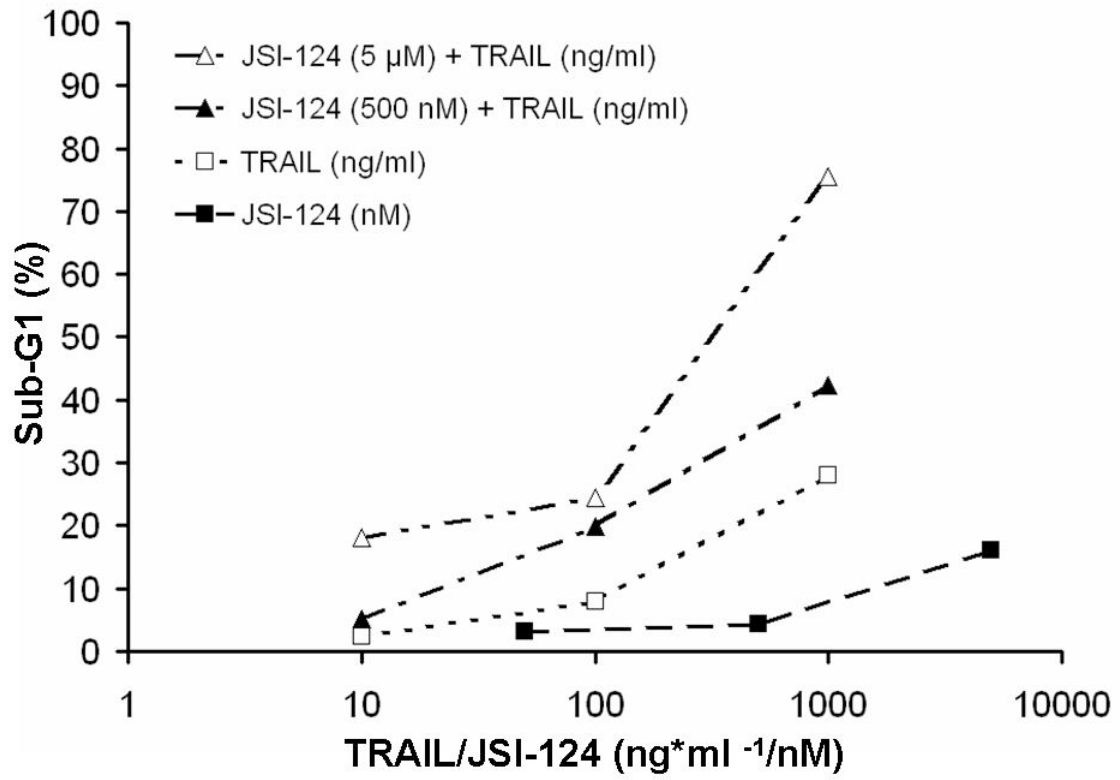


Figure S2





E



Supplemental Table I: Genes upregulated more than 2-fold in wild-type E μ -myc lymphomas relative to TRAIL-R-deficient E μ -myc lymphomas

Gene Name	Fold change¹	Description
1460423_x_at	11.85	Ig kappa chain
1420721_at	7.115	RIKEN cDNA 4921536K21 gene
1424303_at	6.511	expressed sequence AV216087
1418558_at	4.523	retina and anterior neural fold homeobox
1452318_a_at	3.901	heat shock protein 1B
1433483_s_at	3.793	expressed sequence C86187
1425426_a_at	3.54	myocyte enhancer factor 2A
1452453_a_at	3.418	calcium/calmodulin-dependent protein kinase II alpha
1460469_at	3.388	tumor necrosis factor receptor superfamily, member 9
1456212_x_at	2.989	suppressor of cytokine signaling 3
1434772_at	2.778	adenosine A2b receptor
1421241_at	2.735	nerve growth factor receptor (TNFR superfamily, member 16)
1427127_x_at	2.62	heat shock protein 1B
1427126_at	2.474	heat shock protein 1B
1455899_x_at	2.462	suppressor of cytokine signaling 3
1420508_at	2.253	sema domain, immunoglobulin domain (Ig), short basic domain
1423603_at	2.292	zink finger protein, multitype 1
1428359_s_at	2.146	RIKEN cDNA 1810010M01 gene
1424638_at	2.174	cyclin-dependent kinase inhibitor 1A (P21)
1418943_at	2.162	RIKEN cDNA B230120H23 gene (MALTK)

¹ Fold change relative TRAIL-R^{-/-} E μ -myc lymphomas

Supplemental Tables

Supplemental Table I: **Genes downregulated more than 2-fold in wild-type Eμ-myc lymphomas relative to TRAIL-R-deficient Eμ-myc lymphomas**

Gene Name	Fold change ¹	Description
1431913_a_at	0.489	phosphodiesterase 3A, cGMP inhibited
1460327_at	0.487	G-protein coupled receptor 88
1448842_at	0.484	cysteine dioxygenase-1, cytosolic
1437531_at	0.481	transient receptor potential cation channel, subfamily M, member
1424700_at	0.454	transmembrane protein 38B
1452308_a_at	0.438	ATPase, Na ⁺ /K ⁺ transporting, alpha 2 polypeptide
1424553_at	0.429	Gup1, glycerol uptake/transporter homolog (yeast)
1449910_at	0.415	RIKEN cDNA 2210418010 gene
1449417_at	0.396	Ameloblastin
1433924_at	0.392	Peg3 mRNA for zinc finger protein
1438182_x_at	0.389	ankyrin repeat and SOCS box-containing protein 6
1436388_a_at	0.381	RIKEN cDNA 3830406C13 gene
1452561_at	0.379	Latrophilin mRNA, (cDNA clone IMAGE:30549106)
1420335_at	0.354	disrupted meiotic cDNA 1 homolog
1424493_s_at	0.352	UDP glycosyltransferases 3 family, polypeptide A1
1427968_at	0.319	TGIF homeobox 1
1425256_a_at	0.302	DIX domain containing 1
1427509_at	0.273	gene model 937, (NCBI)
1422977_at	0.273	glycoprotein Ib, beta polypeptide
1450369_at	0.266	factor in the germline alpha
1449088_at	0.261	fructose biphosphatase 2
1456461_at	0.256	Erwing sarcoma breakpoint region 1
1417276_at	0.253	tubby-like protein 2
1430457_at	0.24	decay accelerating factor 2
1449832_at	0.237	RIKEN cDNA 1700091H14 gene
1417389_at	0.235	glypican 1
1422150_at	0.233	H6 homeo box 3
1426562_a_at	0.208	olfactomedin 1
1421482_at	0.2	Bartter syndrome, infantile, with sensorineural deafness (Barttin)
1454267_a_at	0.184	protease, serine, 32
1437054_x_at	0.181	protamine 1
1420544_at	0.18	germinal center expressed transcript 2
1426340_at	0.18	solute carrier family 1, (glial high affinity glutamate transporter), 1
1422051_a_at	0.18	gamma-aminobutyric acid (GABA-B) receptor, 1

1452065_at	0.179	cDNA sequence BC027127
1435837_at	0.176	crystallin, alpha B
1423381_at	0.165	RIKEN cDNA 4921521F21 gene
1427315_at	0.159	transmembrane emp24 protein transport domain containing 7
1434553_at	0.158	transmembrane protein 56
1423331_a_at	0.116	poliovirus receptor related-3
1420444_at	0.108	solute carrier family 22 (organic cation transporter), member 3
1449347_a_at	0.0523	X-linked lymphocyte-regulated 4B, X-linked lymphocyte regulated

¹ Fold change relative TRAIL-R-/- Eμ-*myc* lymphomas