Appendix – Table of Contents

Glutathione metabolism

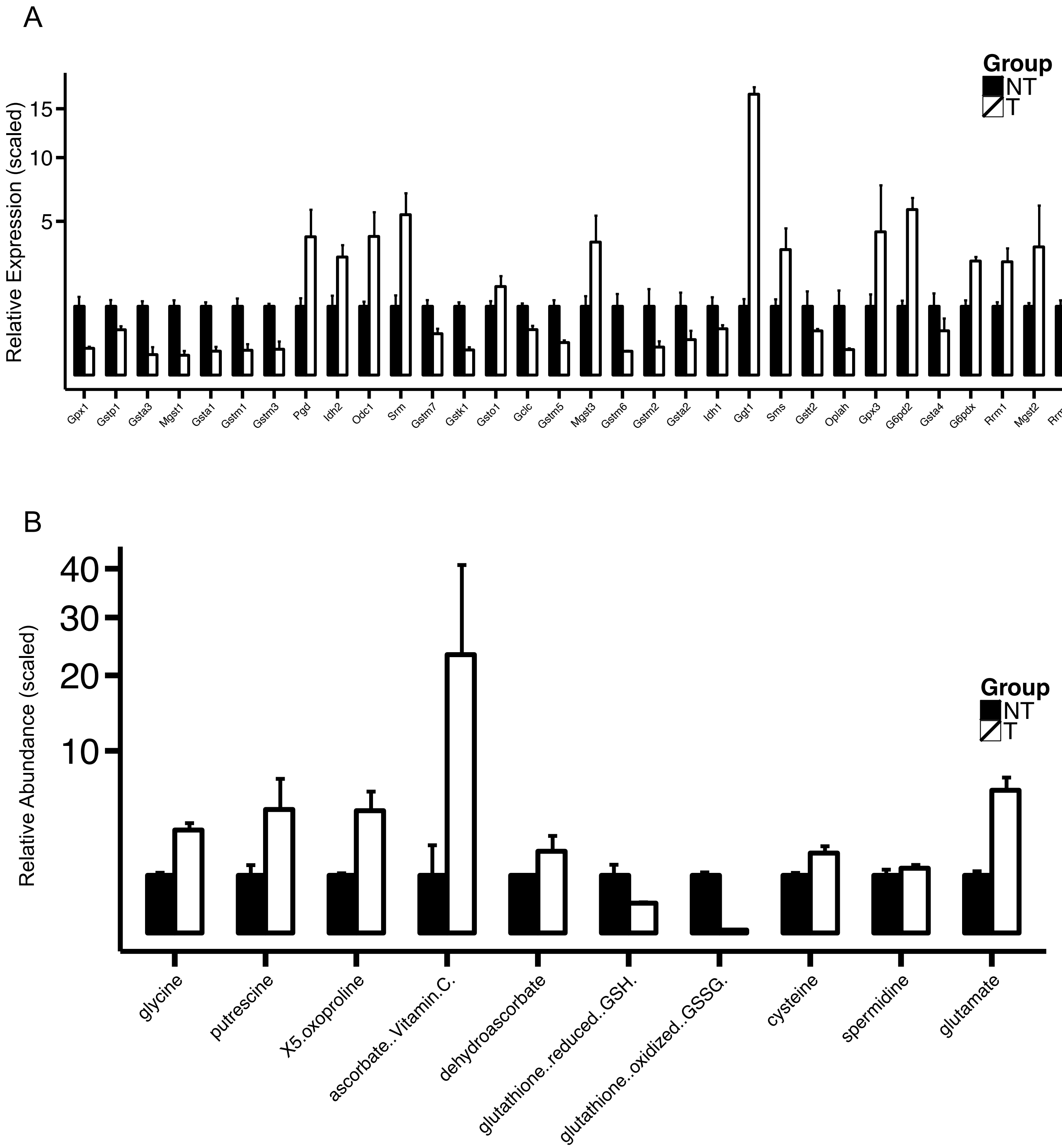

Figure S1. Barplots representing relative expression (A) and abundances (B) of significantly altered transcripts and metabolites, respectively, in LT2-MYC tumors compared to naïve livers, for the glutathione metabolism pathway. All data represented as normalized mean ± SEM, unpaired two-tailed t test, FDR adjusted $p < 0.05$.

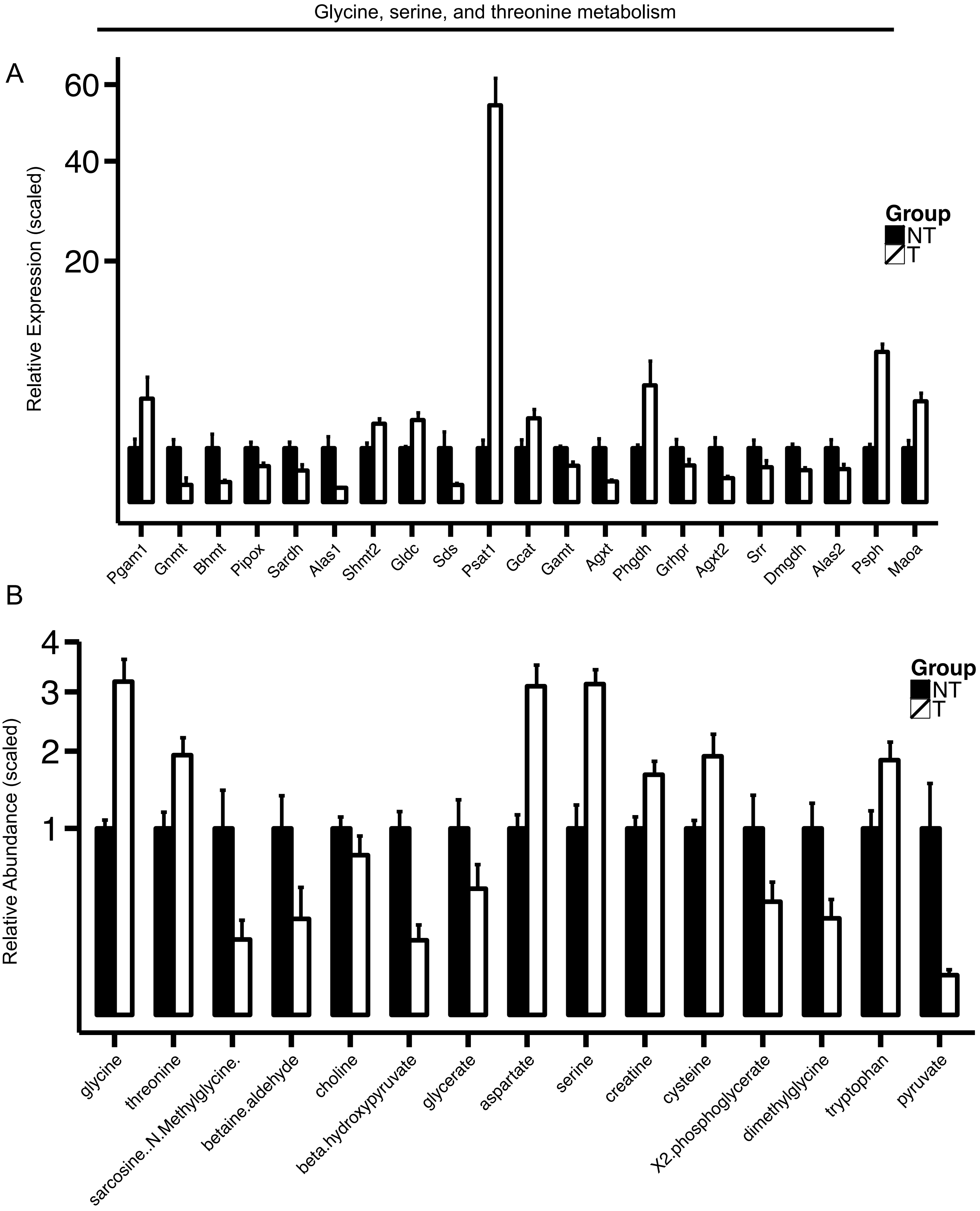

Figure S2. Barplots representing relative expression (A) and abundances (B) of significantly altered transcripts and metabolites, respectively, in LT2-MYC tumors compared to naïve livers, for the glycine, serine, and threonine metabolism pathway. All data represented as normalized mean ± SEM, unpaired two-tailed t test, FDR adjusted $p < 0.05$.

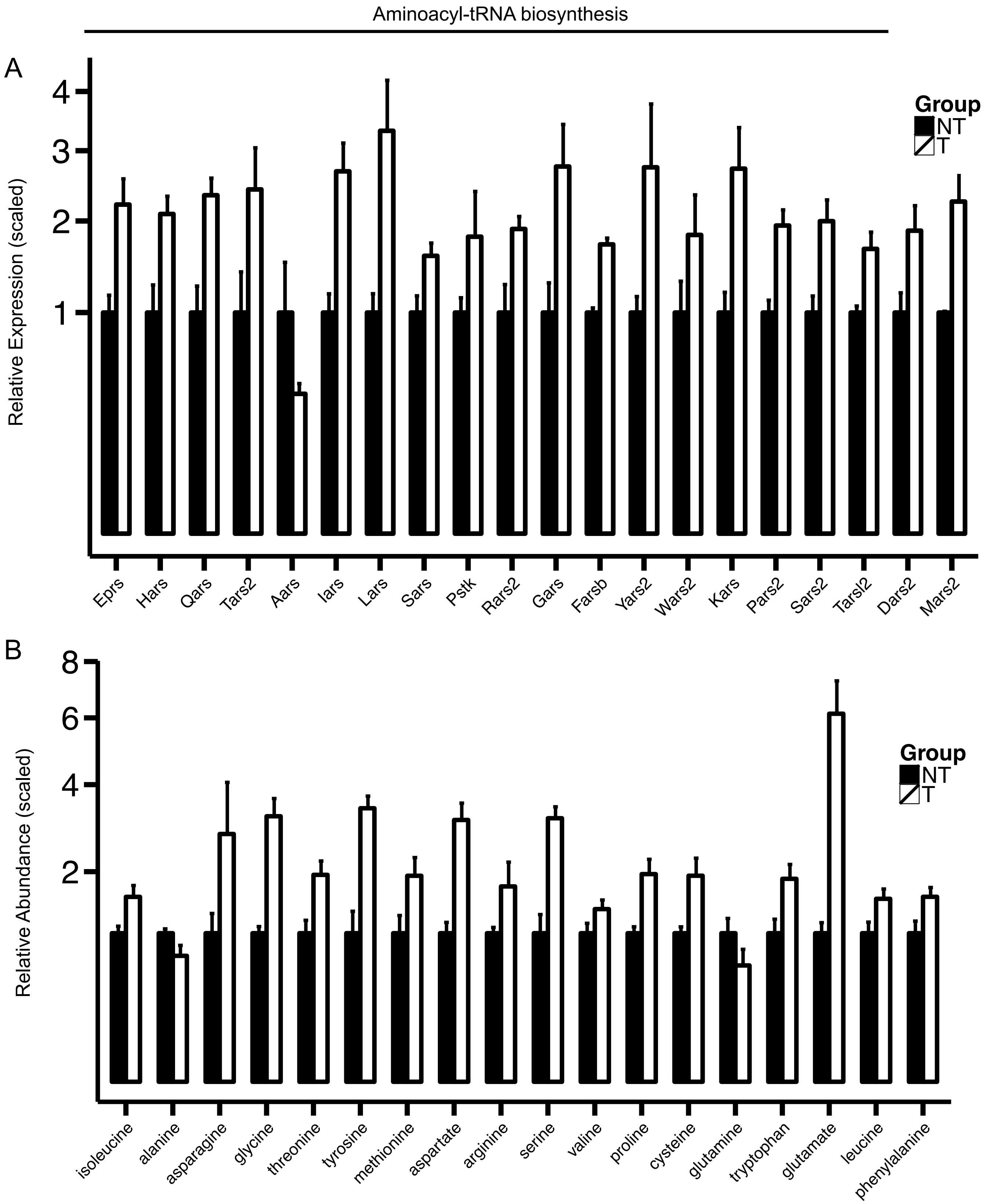

Figure S3. Barplots representing relative expression (A) and abundances (B) of significantly altered transcripts and metabolites, respectively, in LT2-MYC tumors compared to naïve livers, for the aminoacyl-tRNA biosynthesis pathway. All data represented as normalized mean ± SEM, unpaired two-tailed t test, FDR adjusted $p < 0.05$.

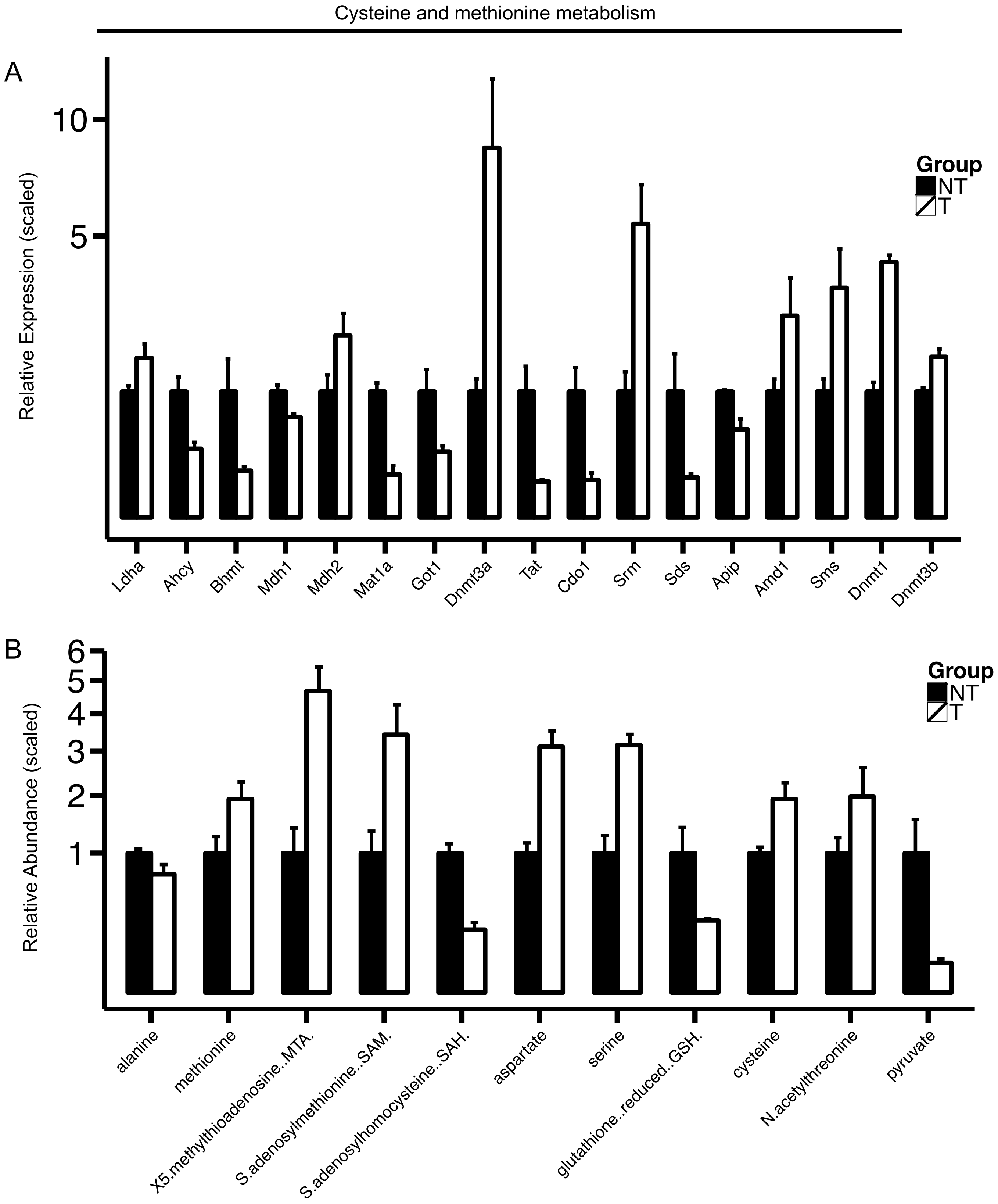

Figure S4. Barplots representing relative expression (A) and abundances (B) of significantly altered transcripts and metabolites, respectively, in LT2-MYC tumors compared to naïve livers, the cysteine and methionine metabolism pathway. All data represented as normalized mean ± SEM, unpaired two-tailed t test, FDR adjusted $p < 0.05$.

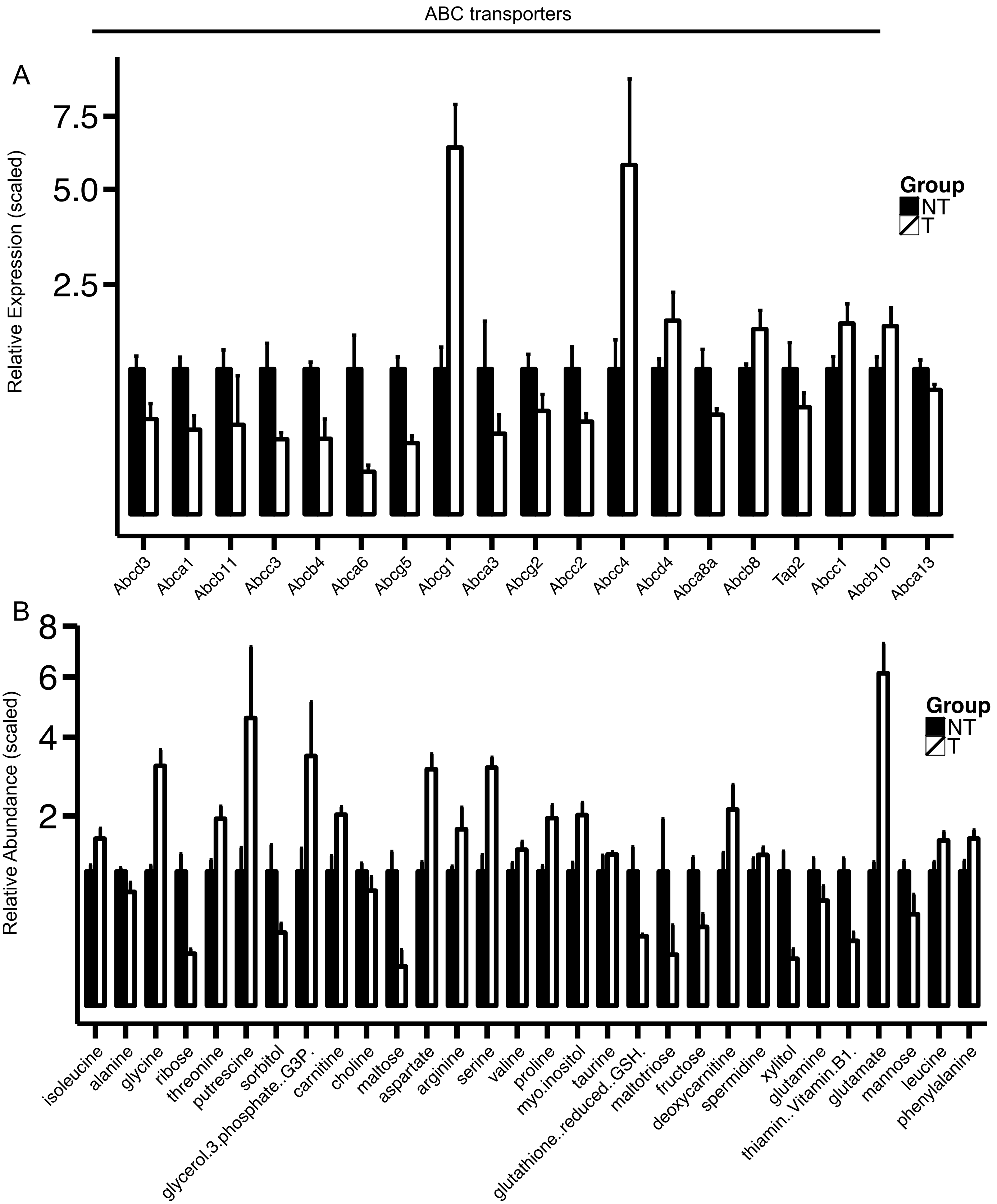

Figure S5. Barplots representing relative expression (A) and abundances (B) of significantly altered transcripts and metabolites, respectively, in LT2-MYC tumors compared to naïve livers, for the ABC transporters pathway. All data represented as normalized mean ± SEM, unpaired two-tailed t test, FDR adjusted $p < 0.05$.

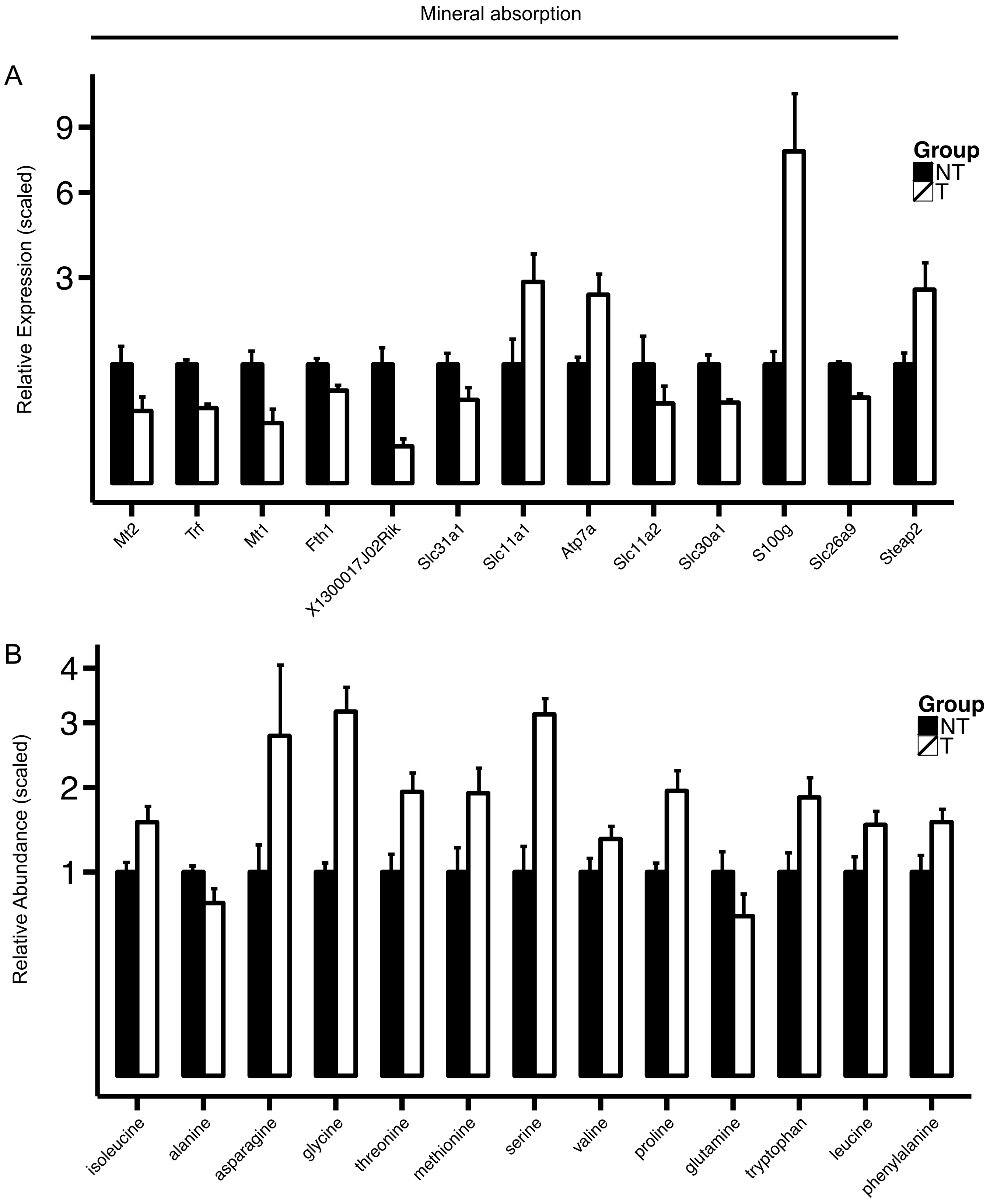

Figure S6. Barplots representing relative expression (A) and abundances (B) of significantly altered transcripts and metabolites, respectively, in LT2-MYC tumors compared to naïve livers, for the mineral absorption pathway. All data represented as normalized mean ± SEM, unpaired two-tailed t test, FDR adjusted $p < 0.05$.

Table S1. Metabolic pathways overrepresented in mRNA and metabolite profiling of LT2-MYC tumors. Fisher's exact test ($p < 0.05$) was performed using KEGG pathway classifications on global gene expression and metabolomics data from LT2-MYC tumors and LT2 controls.

Kegg Pathway	Significantly altered mRNAs	p value	Significantly altered metabolites	p value
Glutathione metabolism	32/52 (62%)	1.05E-12	10/11 (91%)	0.0293
Glycine, serine and threonine metabolism	21/39 (54%)	2.16E-07	15/18 (83%)	0.0304
Aminoacyl-tRNA biosynthesis	20/44 (45%)	1.25E-05	18/20 (90%)	0.0029
Cysteine and methionine metabolism	17/38 (45%)	7.13E-05	11/12 (92%)	0.0186
ABC transporters	19/46 (41%)	0.0001	30/40 (75%)	0.0276
Mineral absorption	13/44 (30%)	0.0302	13/15 (87%)	0.0255

Table S2. Summary output of TargetScanHuman (v6.2) predictions of GCLC 3’ UTR-binding miRNAs.

miRNA	conserved sites				poorly conserved sites				Total Context score
	Total	8mer	7mer-m8	7mer-1A	Total	8mer	7mer-m8	7mer-1A	
miR-18ab/4735-3p	1	1	0	0	0	0	0	0	-0.36
miR-101/101ab	1	0	0	1	1	0	1	0	-0.32
miR-190/190ab	0	0	0	0	1	0	1	0	-0.26
miR-193/193b/193a-3p	0	0	0	0	1	0	1	0	-0.25
miR-15abc/16/16abc/195/322/424/497/1907	0	0	0	0	1	0	1	0	-0.23
miR-30abcdef/30abe-5p/384-5p	1	0	1	0	0	0	0	0	-0.19
miR-216b/216b-5p	0	0	0	0	2	0	1	1	-0.18
miR-148ab-3p/152	0	0	0	0	1	0	0	1	-0.16
miR-133abc	1	0	0	1	0	0	0	0	-0.16
miR-24/24ab/24-3p	0	0	0	0	1	0	0	1	-0.15
miR-135ab/135a-5p	1	0	1	0	0	0	0	0	-0.15
miR-196abc	0	0	0	0	1	0	1	0	-0.15
miR-26ab/1297/4465	0	0	0	0	2	0	0	2	-0.13
miR-122/122a/1352	0	0	0	0	1	0	0	1	-0.13
miR-1ab/206/613	1	0	0	1	0	0	0	0	-0.12
miR-25/32/92abc/363/363-3p/367	0	0	0	0	1	0	0	1	-0.1
miR-144	1	0	0	1	0	0	0	0	-0.1
miR-137/137ab	0	0	0	0	1	0	0	1	-0.08
miR-216a	0	0	0	0	1	0	0	1	-0.04

TargetScanHuman, v6.2

Table S3. Summary of miRNA candidate expression in LT2 MYC tumors versus nontumor control liver. Data collection and statistical analysis described in [24].

Probe_ID	MicroRNA_Accession	LT2 MYC vs LT2 Ctrl_Log2Diff	LT2 MYC vs LT2 Ctrl_ttest	FDR
hsa-miR-18a_st1	MIMAT0000072	5.699199283	0.005656969	0.02765629
hsa-miR-18b_st1	MIMAT0001412	4.609599217	0.000805997	0.01472791
hsa-miR206_st1	NA	4.310055985	0.000240788	0.01059467
hsa-miR-18a-_st1	MIMAT0002891	3.281603521	0.001129219	0.01472791
hsa-miR-363-_st1	MIMAT0003385	2.353559808	0.001811416	0.01472791
mmu-miR-424_st2	MIMAT0000548	1.128166698	0.07236114	0.1799961
mmu-miR-363_st2	MIMAT0000708	0.953840582	0.422043475	0.5533693
hsa-miR-133a_st1	MIMAT0000427	0.775241322	0.427603581	0.5533693
hsa-miR-497_st1	MIMAT0002820	0.598273038	0.427336574	0.5533693
hsa-miR-195_st2	MIMAT0000461	0.54402918	0.11023725	0.2108887
hsa-miR-25_st2	MIMAT0000081	0.492606988	0.105356606	0.2107132
hsa-miR-206_st2	MIMAT0000462	0.338189617	0.678468901	0.7654521
hsa-miR-92b_st1	MIMAT0003218	0.173084081	0.703613719	0.7739751
hsa-miR30_st1	MIMAT0003218	0.144603505	0.735305352	0.783335
hsa-miR135_st2	NA	0.037548424	0.963089119	0.9630891
hsa-miR-152_st1	MIMAT0000438	-0.069132592	0.791092009	0.8094895
hsa-miR-24_st1	MIMAT0000080	-0.142812998	0.608518483	0.7046003
hsa-miR-148b_st2	MIMAT0000759	-0.228524171	0.490500587	0.5995007
hsa-miR-92_st1	MIMAT0000092	-0.23646842	0.206548133	0.336597
mmu-miR-322_st2	MIMAT0000549	-0.23704298	0.475595848	0.5978919
hsa-miR-137_st1	MIMAT0000429	-0.319967546	0.747728802	0.783335
hsa-miR-32_st1	MIMAT0000090	-0.384600313	0.13273963	0.243356
hsa-miR-30e-5p_st2	MIMAT0000692	-0.397422028	0.40977261	0.5533693
hsa-miR-15b_st1	MIMAT0000417	-0.412584831	0.351321823	0.53304
hsa-miR-190_st1	MIMAT0000458	-0.449961251	0.519155739	0.6173744
hsa-miR-26b_st1	MIMAT0000083	-0.533147329	0.102246677	0.2107132
hsa-miR-30b_st2	MIMAT0000420	-0.629193097	0.178651211	0.3023328
hsa-miR-16_st2	MIMAT0000069	-0.728576809	0.011194195	0.04925446
hsa-miR-384_st1	MIMAT0001075	-0.748400032	0.369486507	0.5419135
hsa-miR-15a_st1	MIMAT0000068	-0.773857833	0.105121924	0.2107132
hsa-miR-30c_st1	MIMAT0000244	-0.785497581	0.01445595	0.05297318
hsa-miR-30a-5p_st2	MIMAT0000087	-0.858964008	0.028126344	0.08839708
hsa-miR-101_st1	MIMAT0000099	-0.929845649	0.166367744	0.2928072
mmu-miR-30e-_st2	MIMAT0000249	-0.955060676	0.015651166	0.05297318
hsa-miR-144_st1	MIMAT0000436	-0.979559768	0.234576007	0.3686194
hsa-miR-30d_st1	MIMAT0000245	-1.042143704	0.004811522	0.02646337
hsa-miR-30e-3p_st1	MIMAT0000693	-1.05473302	0.014541182	0.05297318
hsa-miR-193a_st1	MIMAT0000459	-1.055925472	0.076430924	0.1799961
hsa-miR-26a_st2	MIMAT0000082	-1.118272573	0.002008351	0.01472791
hsa-miR-122a_st1	MIMAT0000421	-1.224268723	0.002563254	0.01611188
hsa-miR-30a-3p_st1	MIMAT0000088	-1.254547385	0.001340722	0.01472791
mmu-miR-101b_st1	MIMAT0000616	-1.53018606	0.033931224	0.0995316
hsa-miR-1_st1	MIMAT0000416	-1.724874854	0.077725586	0.1799961
hsa-miR-148a_st1	MIMAT0000243	-2.323421889	0.060621178	0.1667082

Table S4. Summary of MYC-dependent regulation of glutathione pathway genes. Columns 2-5 represent data described in [45]. ‘Protein Expression’ column summarizes Western Blot data in Figure 2D of this study.

Gene	Myc_indep_UP	Myc_dep_UP	Myc_indep_DN	Myc_dep_DN	Protein Expression
Gclc	no	no	yes	no	Dramatically decreased in tumors ($p < 0.001$)
Ggt1	yes	no	no	no	Very small, but significant, increase
Gss	no	no	no	no	No change
Glrx5	no	no	no	no	Large increase, significant at $p < 0.10$
Gsr	no	no	no	no	Very large increase, very significant
G6pdx	yes	no	no	no	Very large increase, very significant
Gls	no	yes	no	no	Previously shown to be upregulated (Yuneva et al 2012)
Gls2	no	no	yes	no	Previously shown to be downregulated (Yuneva et al 2012)