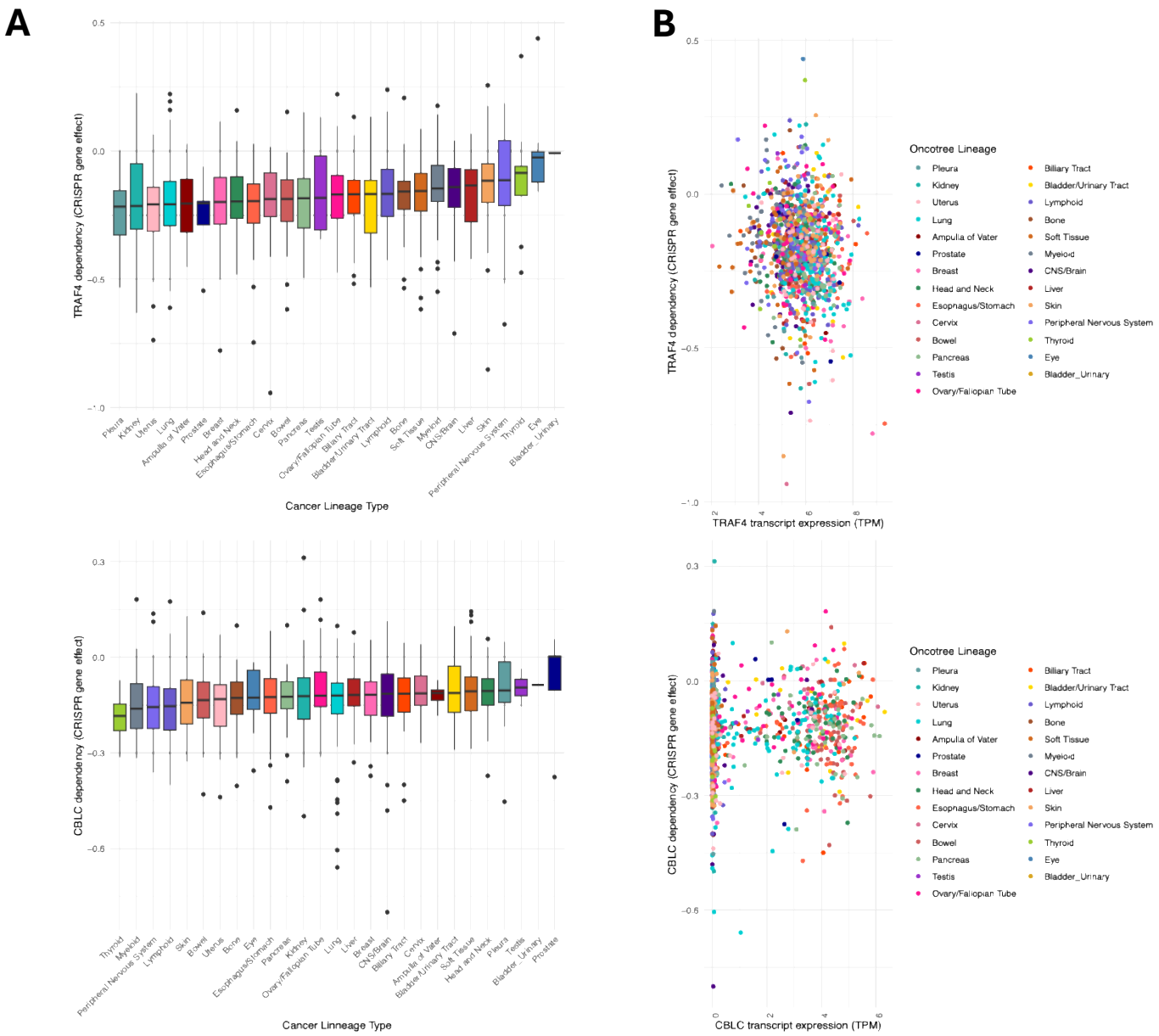
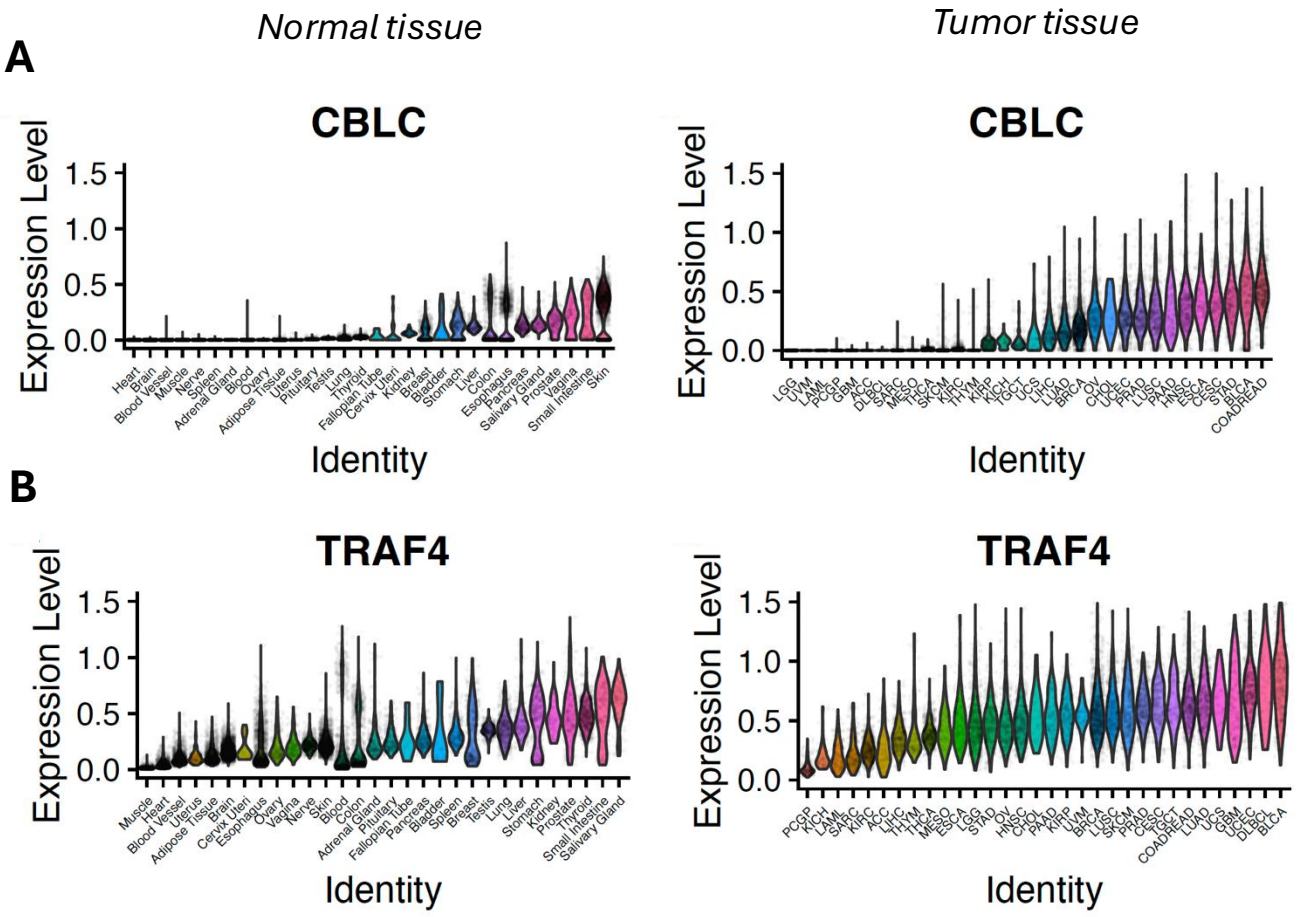
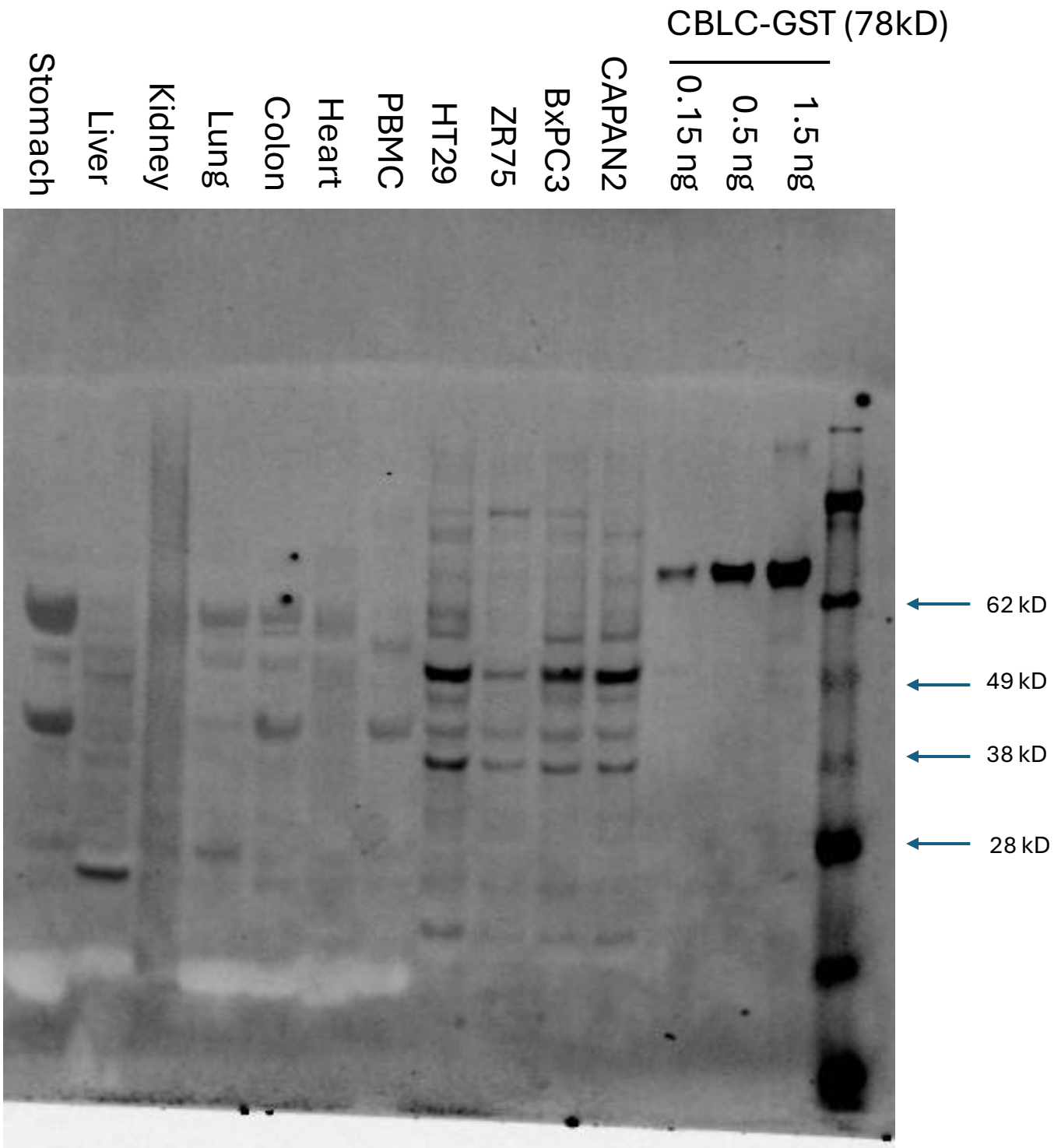
Supplemental Figure 1. Gene dependency of TRAF4 and CBLC by cancer lineage and transcript levels. **(A)** Boxplots show distribution of CRISPR knockdown effect in cancer cells lines grouped by cancer lineage. **(B)** Scatterplots show genetic dependency relative transcript abundance (TPM) for TRAF4 and CBLC colored by cancer lineage.



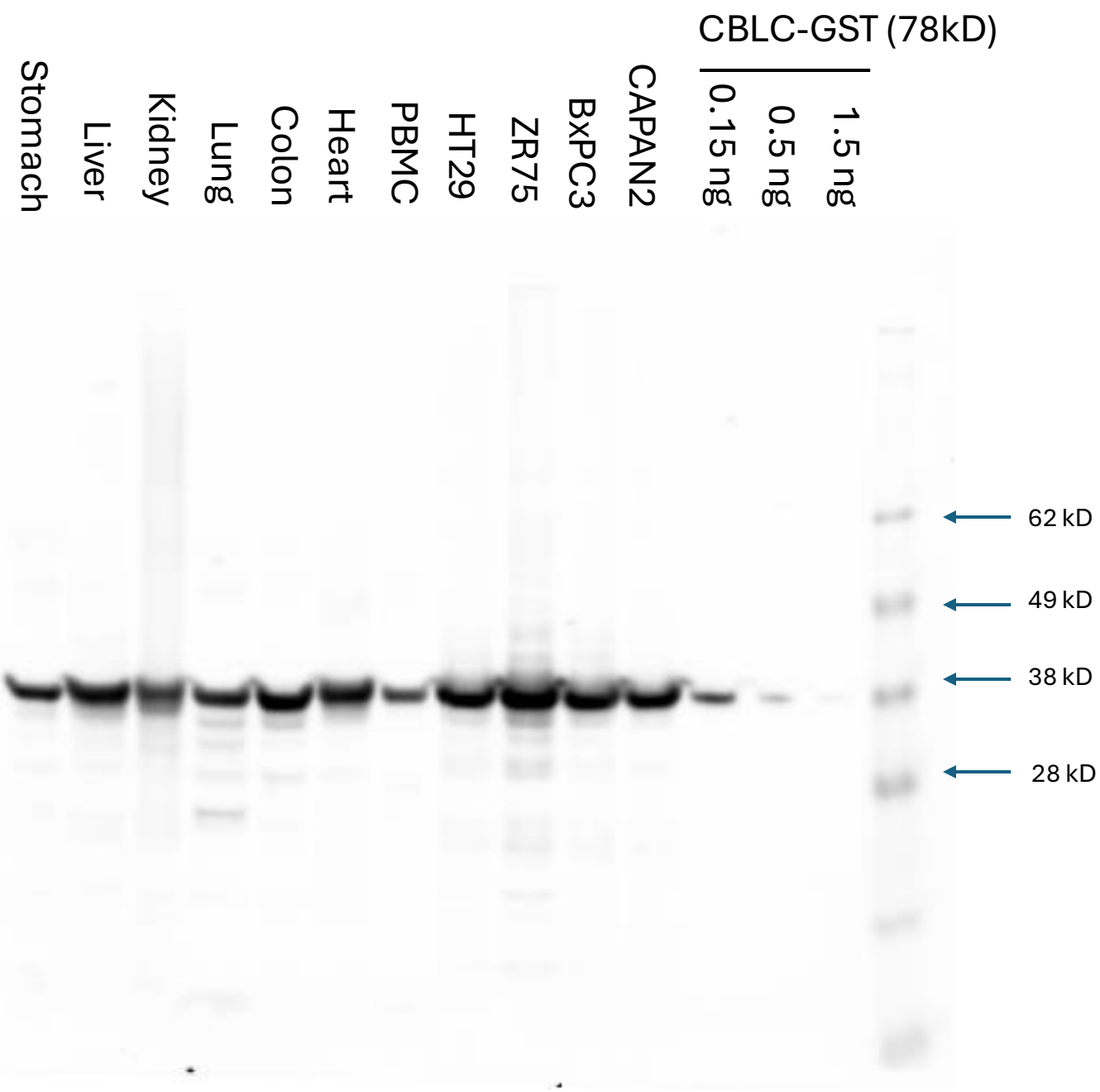
Supplemental Figure 2. Expanded transcriptomics profile. Violin plots show the expression of CBL-c (**A**) and TRAF-4 (**B**) stratified by tissue or tumor sample type.



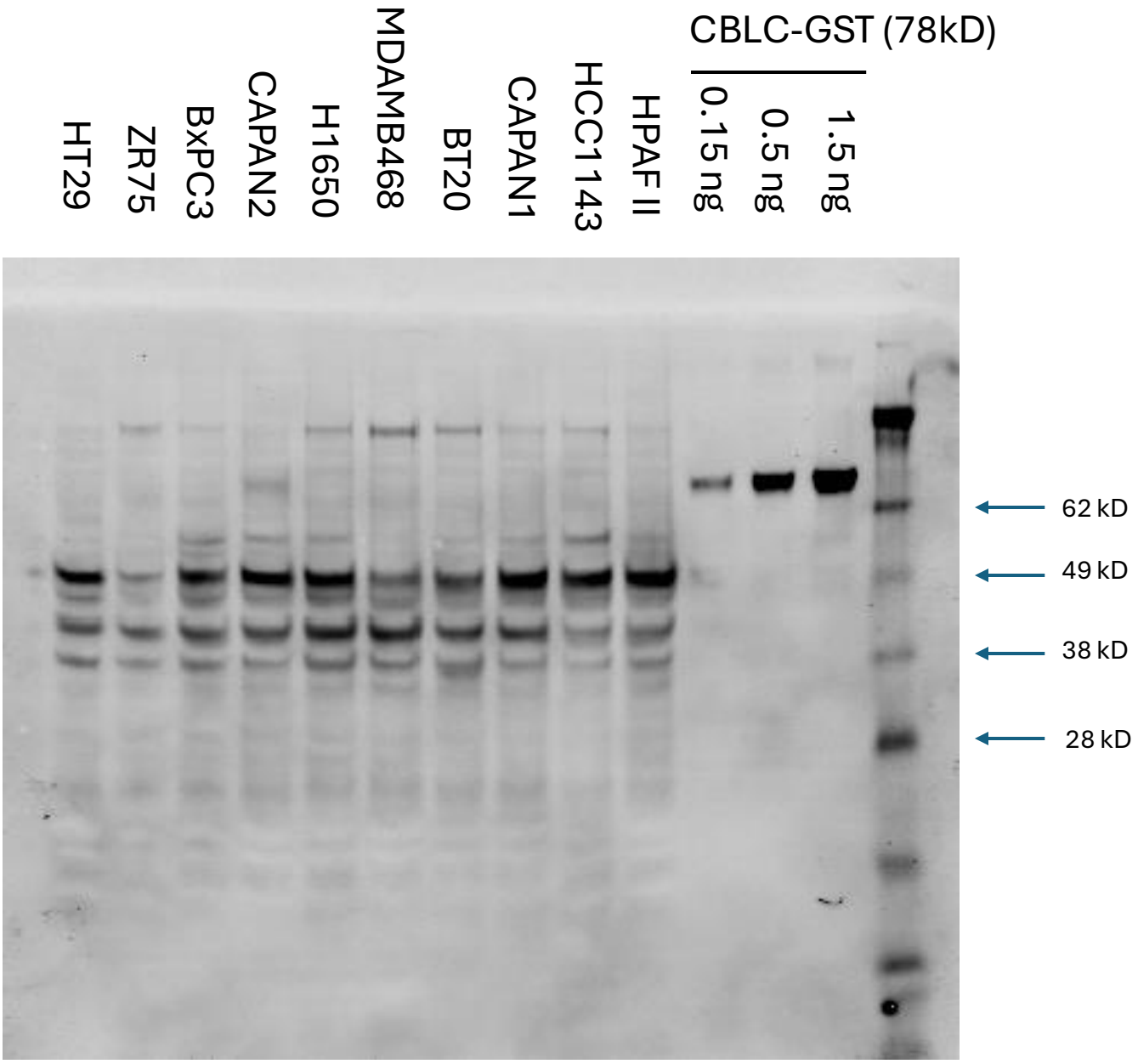
Supplemental Figure 3. Unedited Western blots for Figure 3A blot 1.
Immunoblot shows CBL-c protein levels across tumor specimens and cell lines.



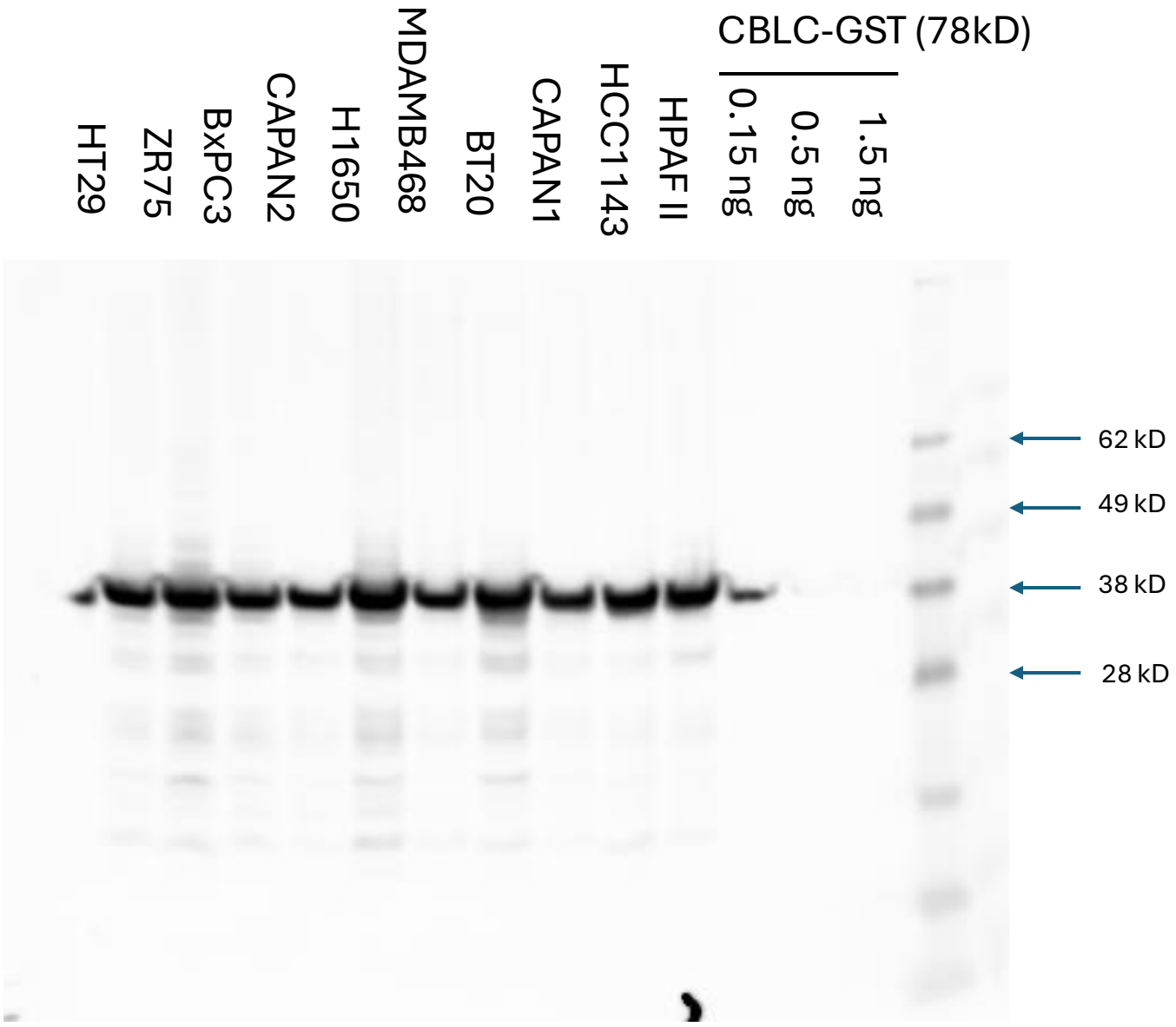
Supplemental Figure 4. Unedited Western blots for Figure 3A blot 1.
Immunoblot shows GADH protein levels across tumor specimens and cell lines.



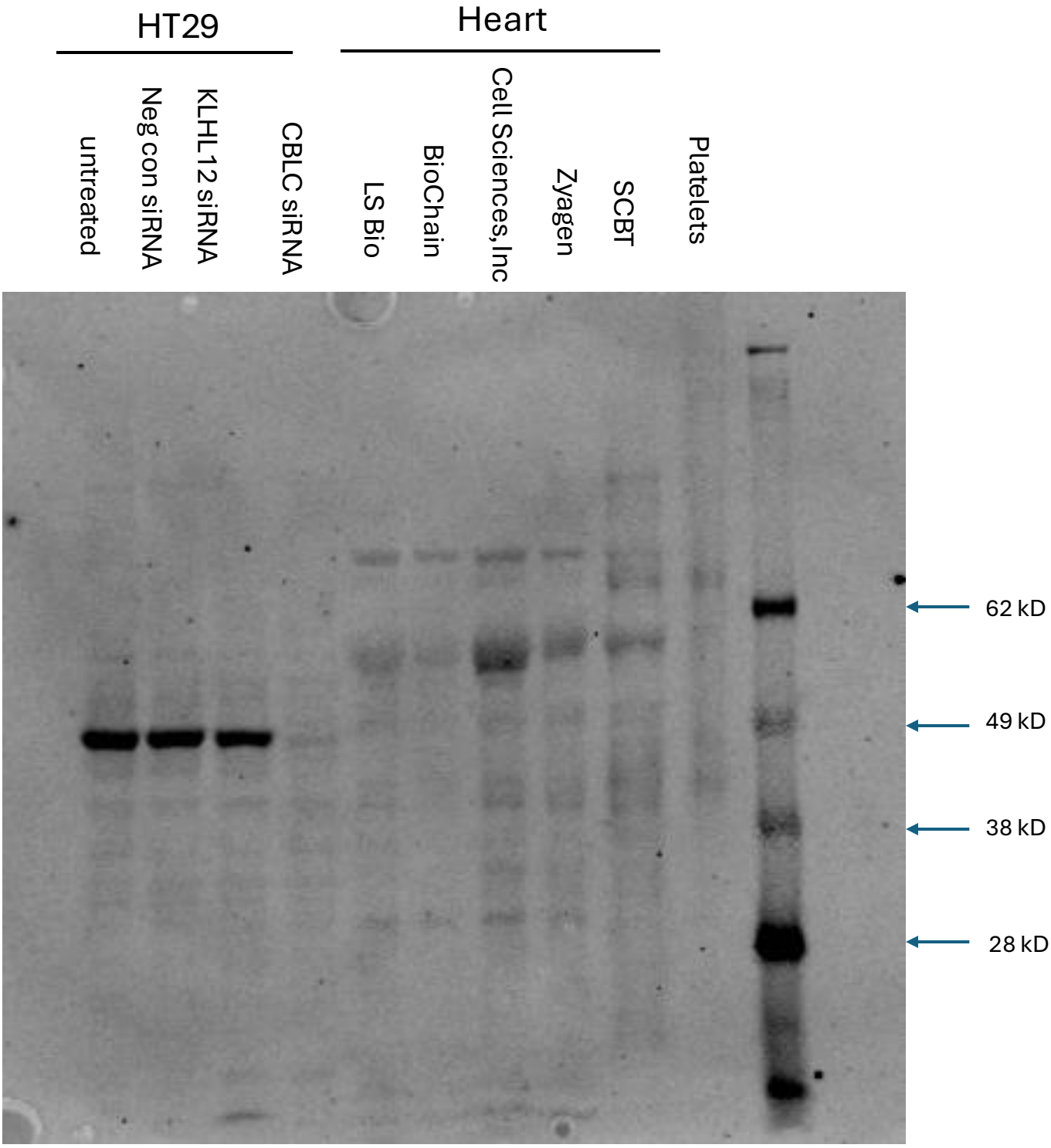
Supplemental Figure 5. Unedited Western blots for Figure 3A blot 2.
Immunoblot shows CBL-c protein levels across tumor specimens and cell lines.



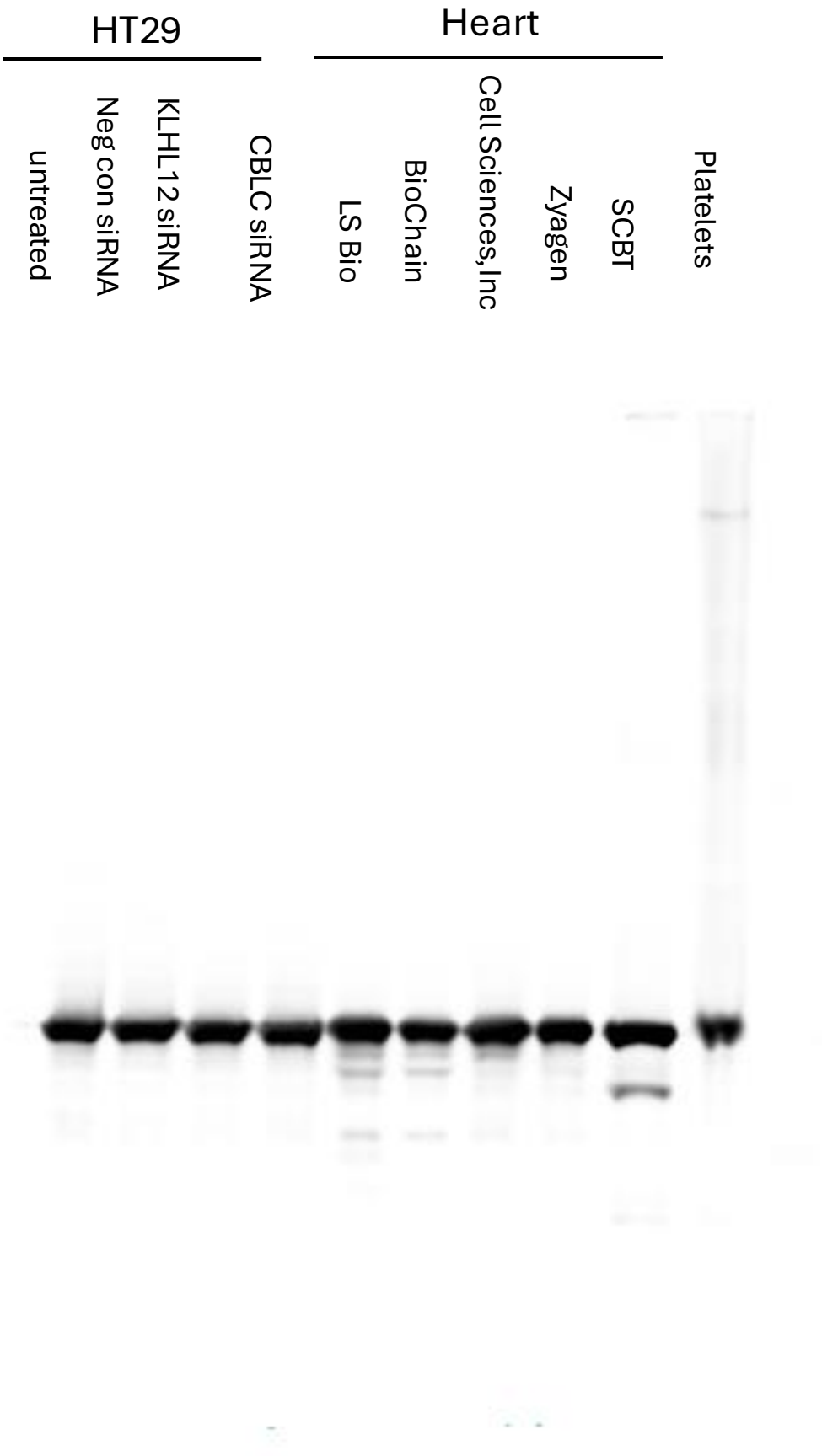
Supplemental Figure 6. Unedited Western blots for Figure 3A blot 2.
Immunoblot shows GAPDH protein levels across tumor specimens and cell lines.



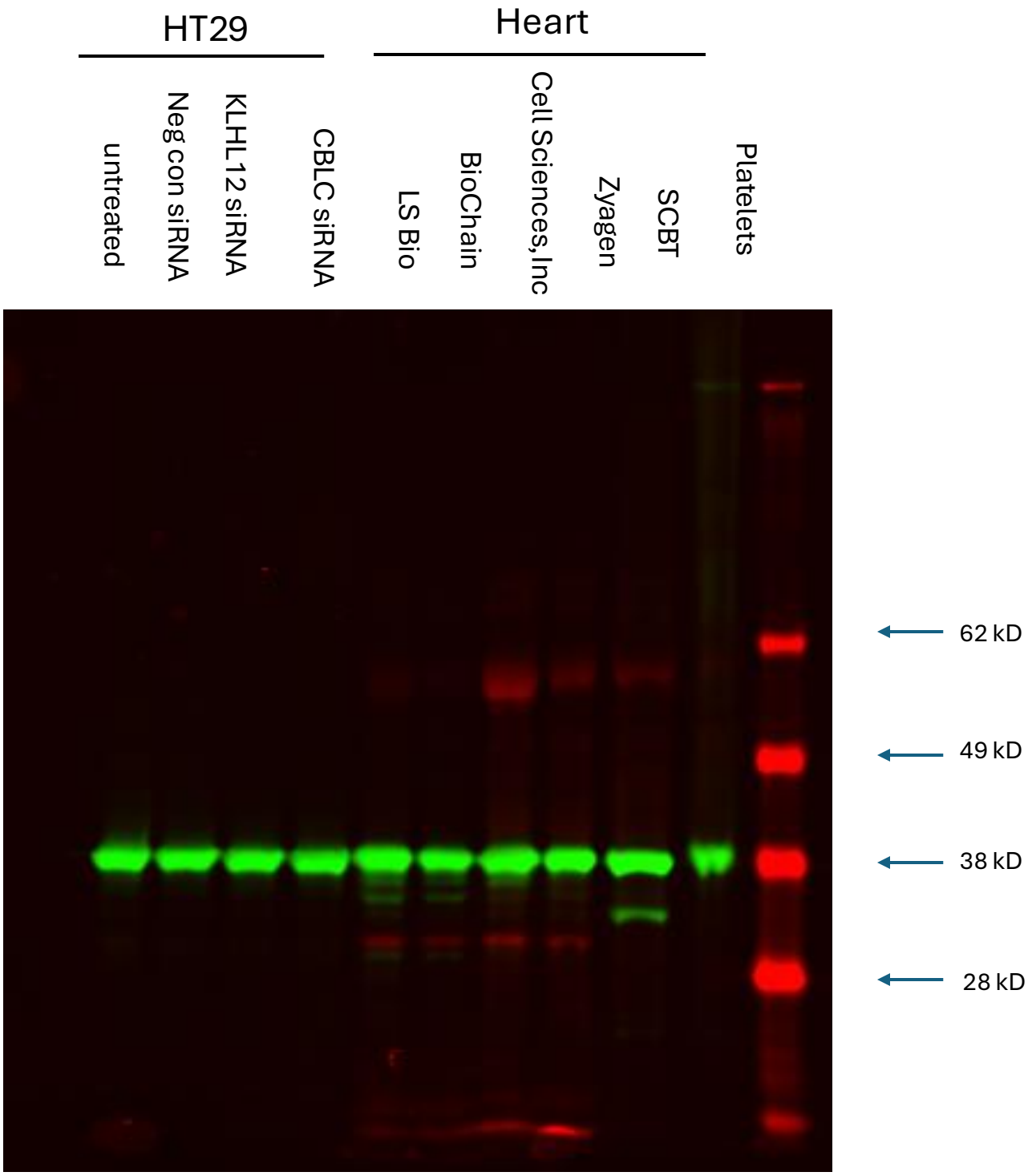
Supplemental Figure 7. Unedited Western blots for Figure 3B. Immunoblot shows CBL-c protein levels across heart tissue samples or in HT29 cells transfected with control or siRNAs targeting CBL-c or unrelated protein KLHL12.



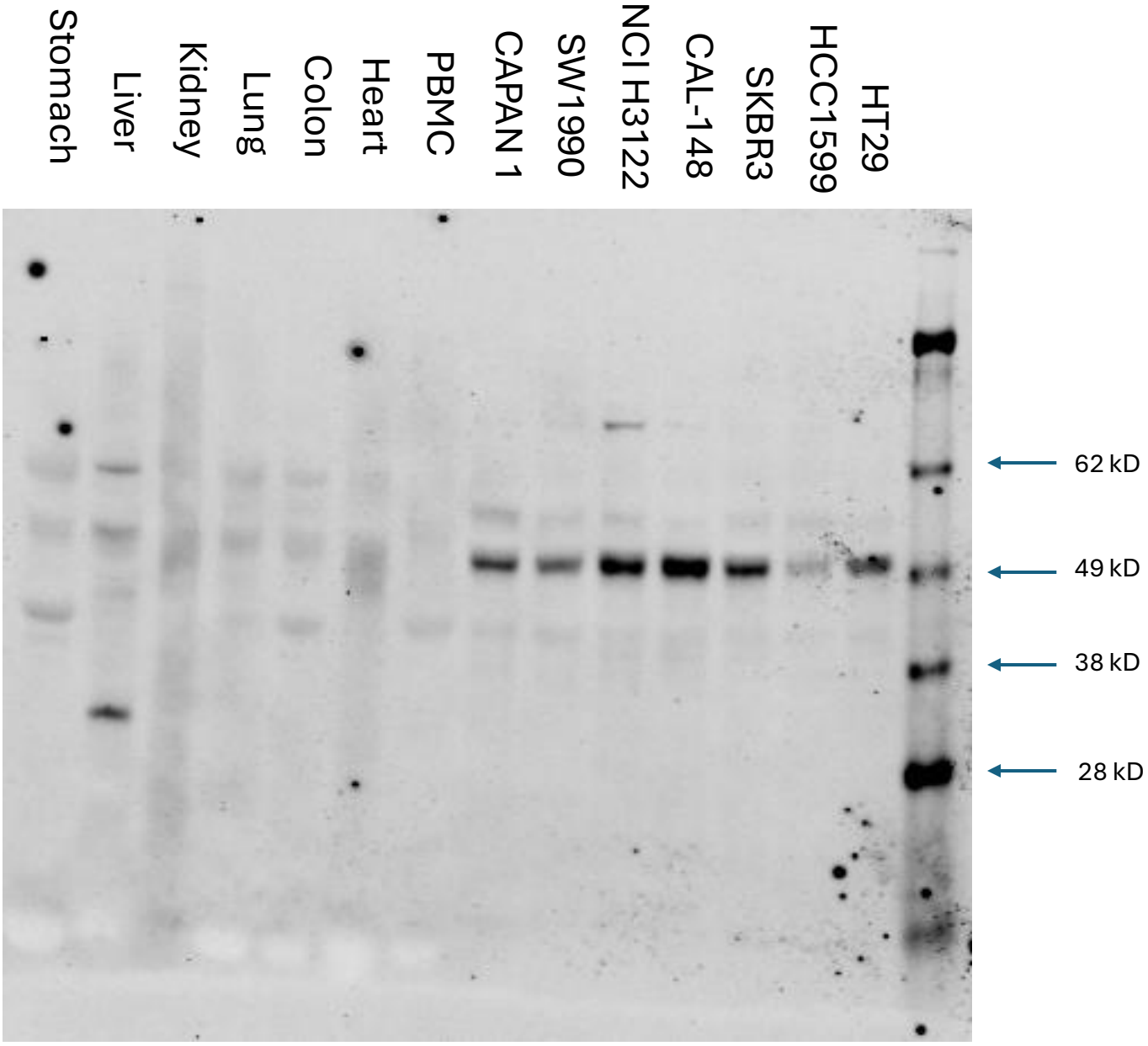
Supplemental Figure 8. Unedited Western blots for Figure 3B, converted to black and white for publication. Immunoblot shows GAPDH protein levels across heart tissue samples or in HT29 cells transfected with control or siRNAs targeting CBL-c or unrelated protein KLHL12.



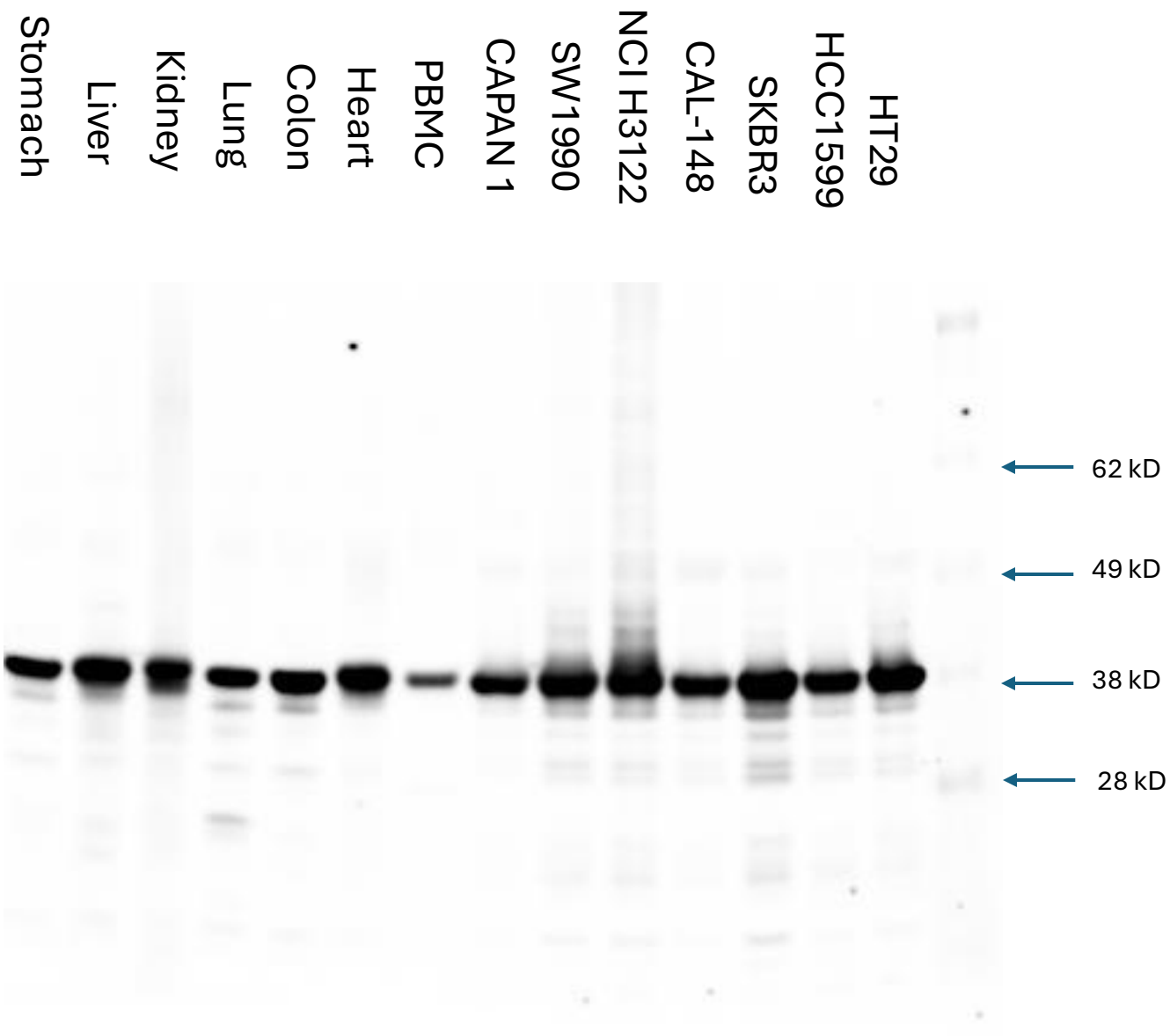
Supplemental Figure 9. Unedited Western blots for Figure 3B, original two-color image from the LiCOR to better illustrate molecular weight markers. Immunoblot shows GAPDH protein levels (green) across heart tissue samples or in HT29 cells transfected with control or siRNAs targeting CBL-c or unrelated protein KLHL12.



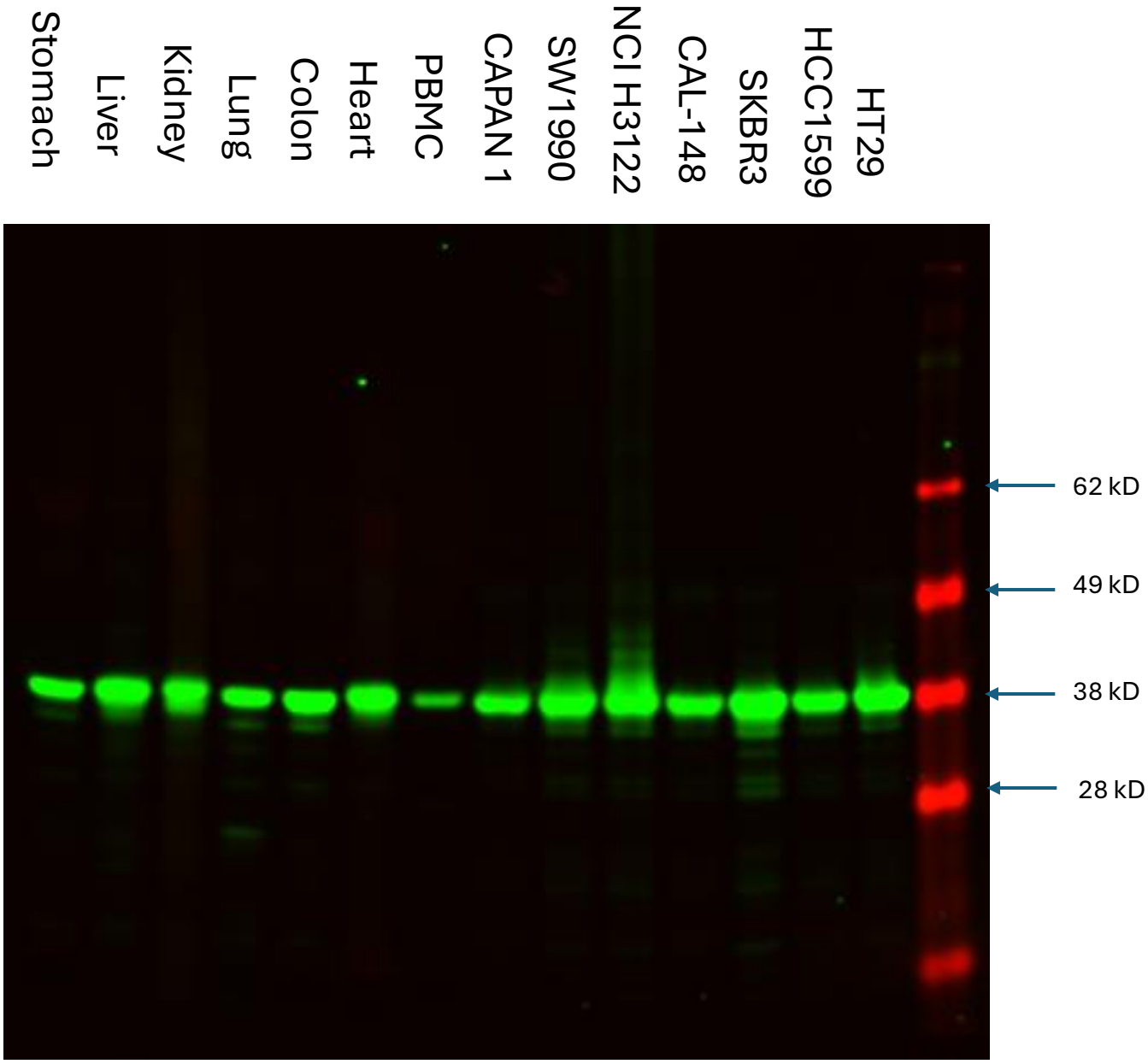
Supplemental Figure 10. Unedited Western blots for Figure 7A. Immunoblot shows TRAF-4 protein levels across tumor specimens and cell lines.



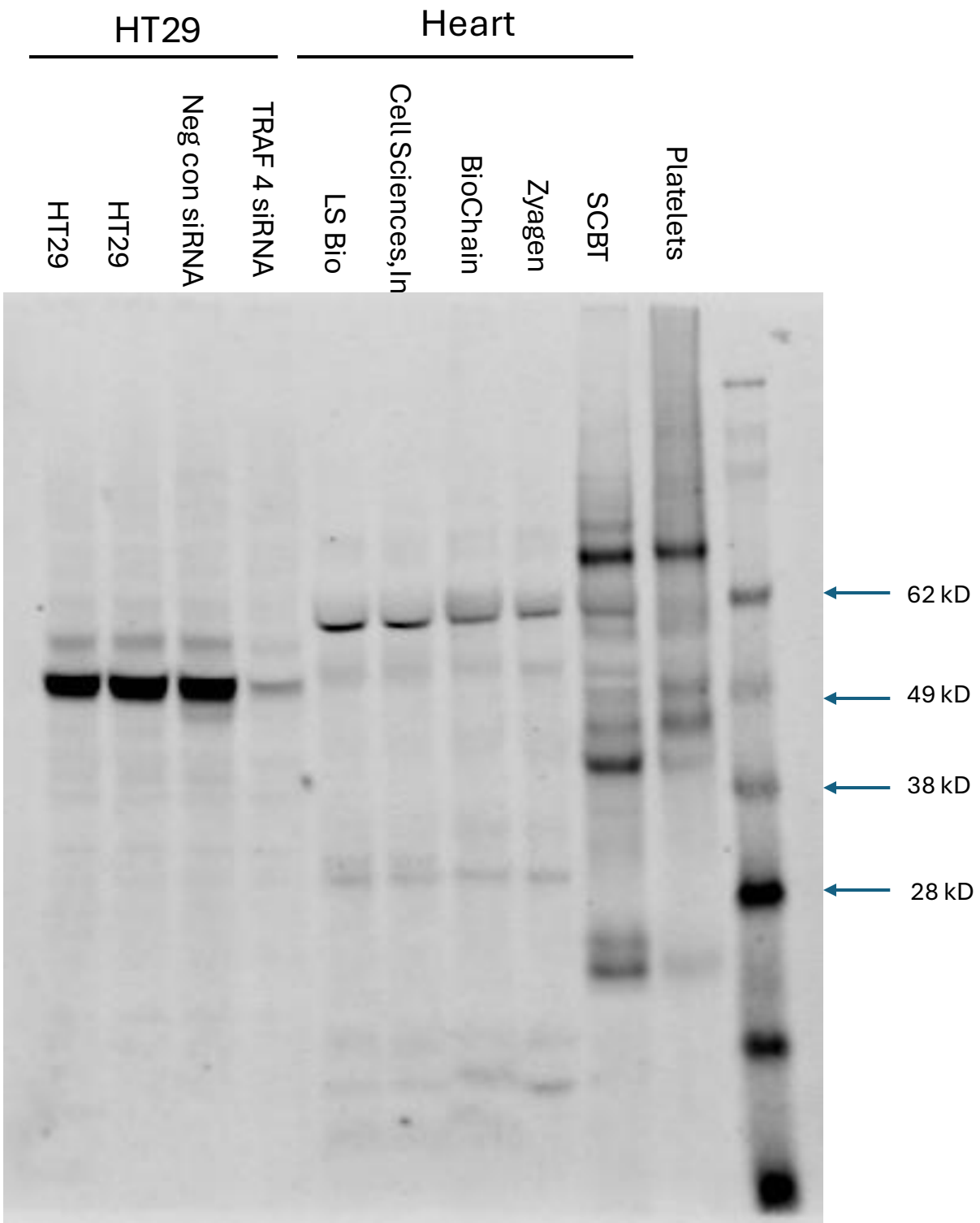
Supplemental Figure 11. Unedited Western blots for Figure 7A, converted to black and white for publication. Immunoblot shows GAPDH protein levels across tumor specimens and cell lines.



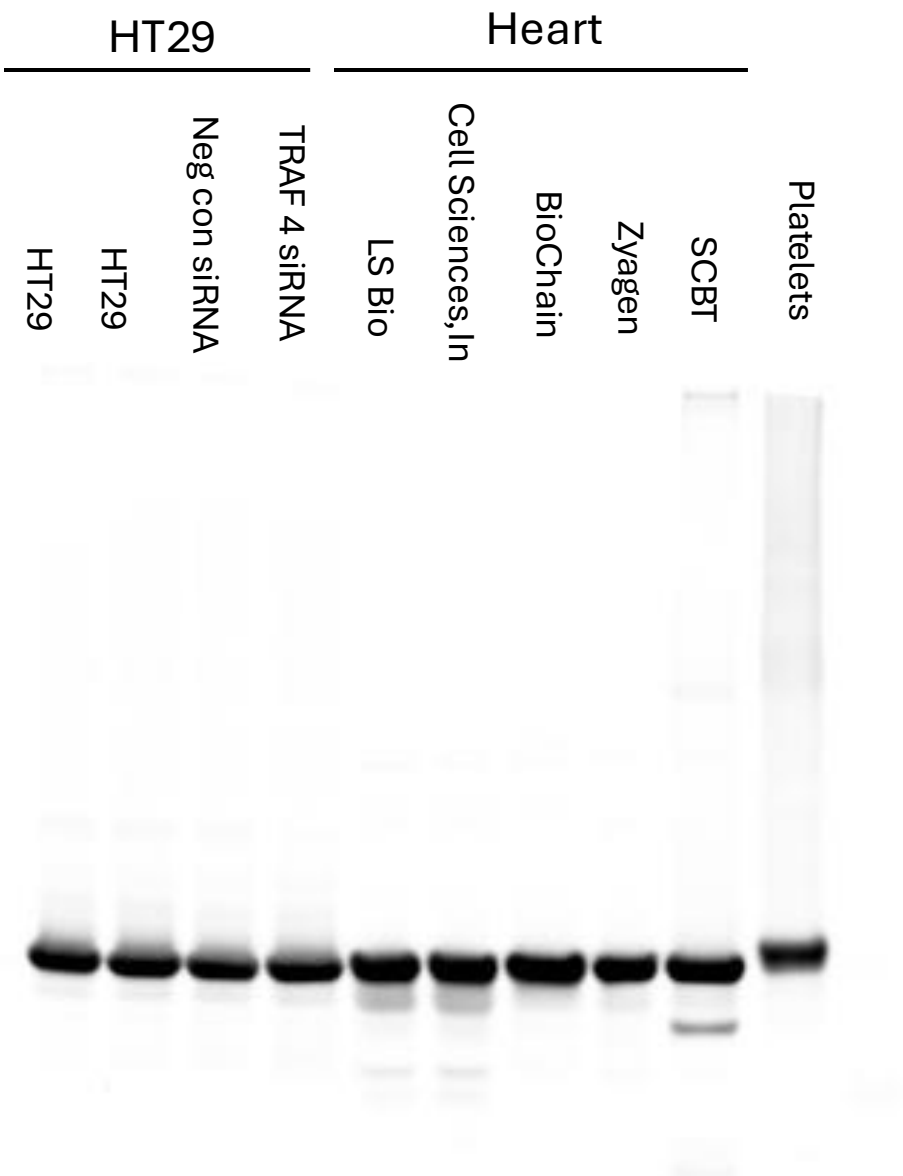
Supplemental Figure 12. Unedited Western blots for Figure 7A, original two-color image from the LiCOR to better illustrate molecular weight markers. Immunoblot shows GAPDH protein levels (green) across tumor specimens and cell lines.



Supplemental Figure 13. Unedited Western blots for Figure 7B. Immunoblot shows TRAF-4 protein levels across heart tissue samples and in HT29 cells transfected with control or TRAF-4-targeting siRNA.



Supplemental Figure 14. Unedited Western blots for Figure 7B, converted to black and white for publication. Immunoblot shows GAPDH protein levels across heart tissue samples and in HT29 cells transfected with control or TRAF-4-targeting siRNA.



Supplemental Figure 15. Unedited Western blots for Figure 7B, original two-color image from the LiCOR to better illustrate molecular weight markers. Immunoblot shows GAPDH protein levels (green) across tumor specimens and cell lines.