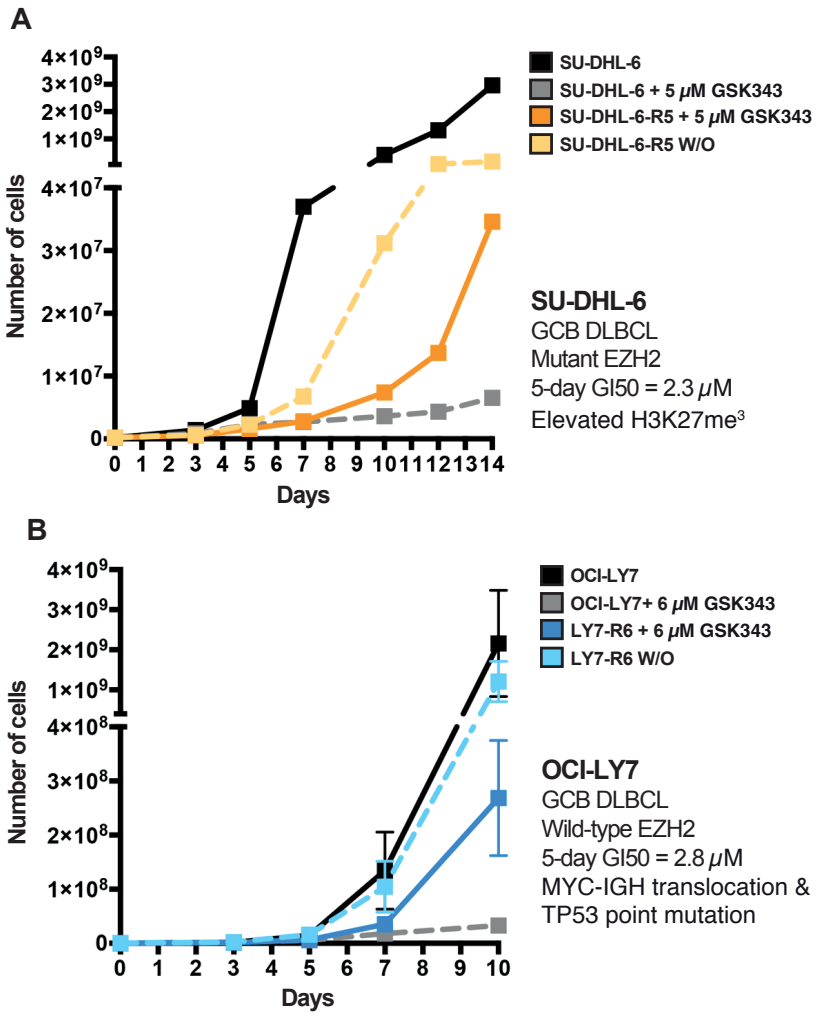
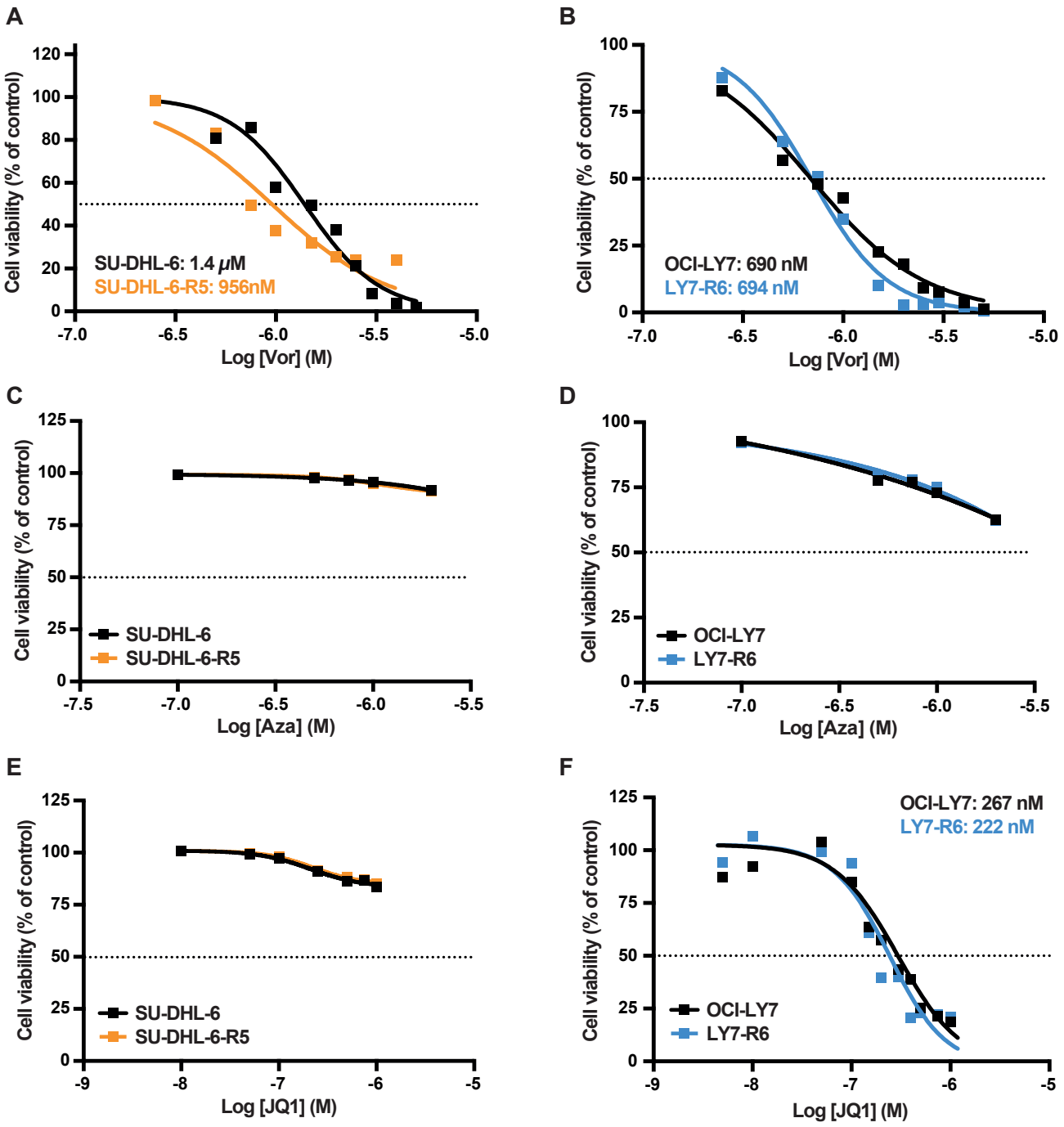
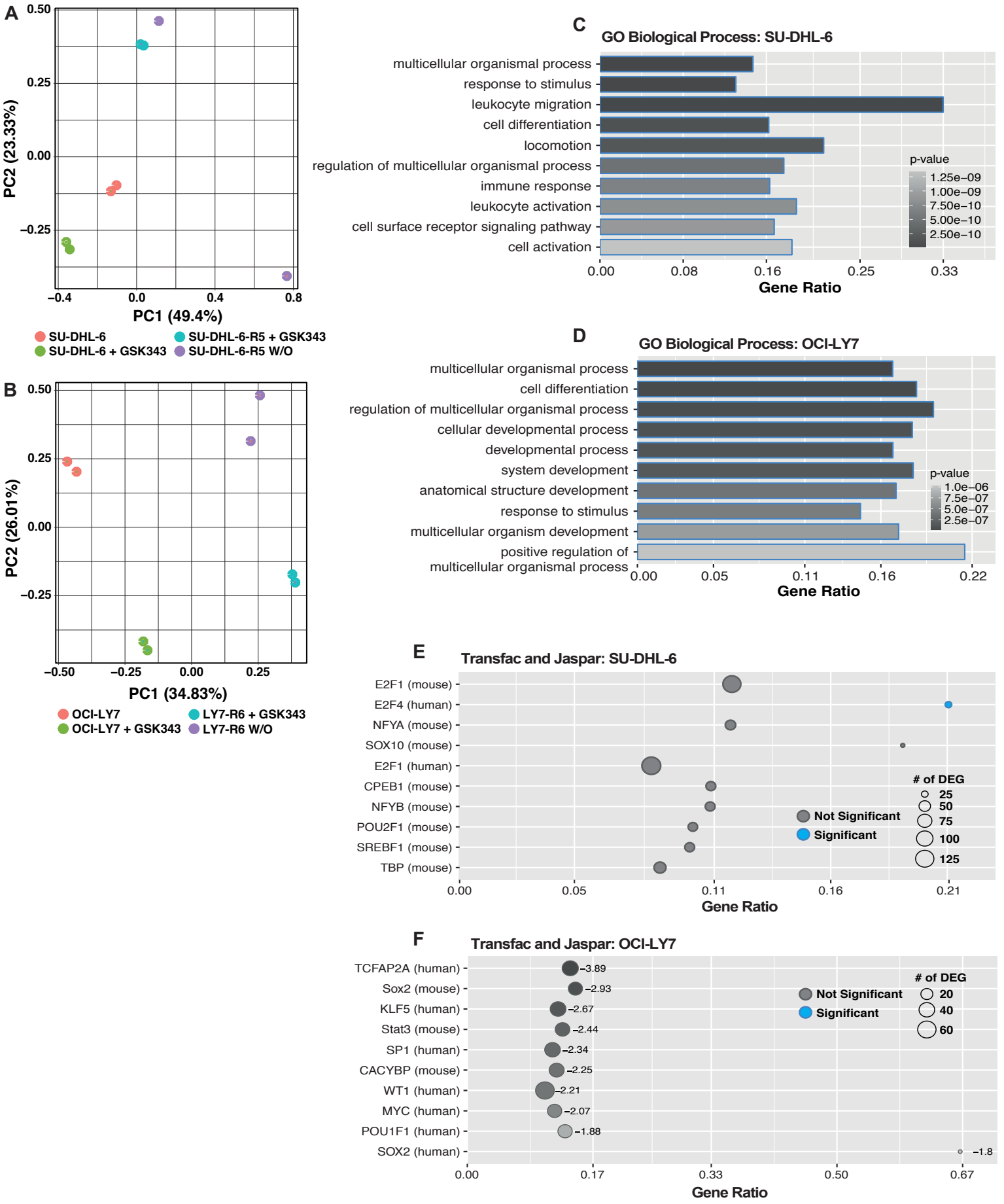


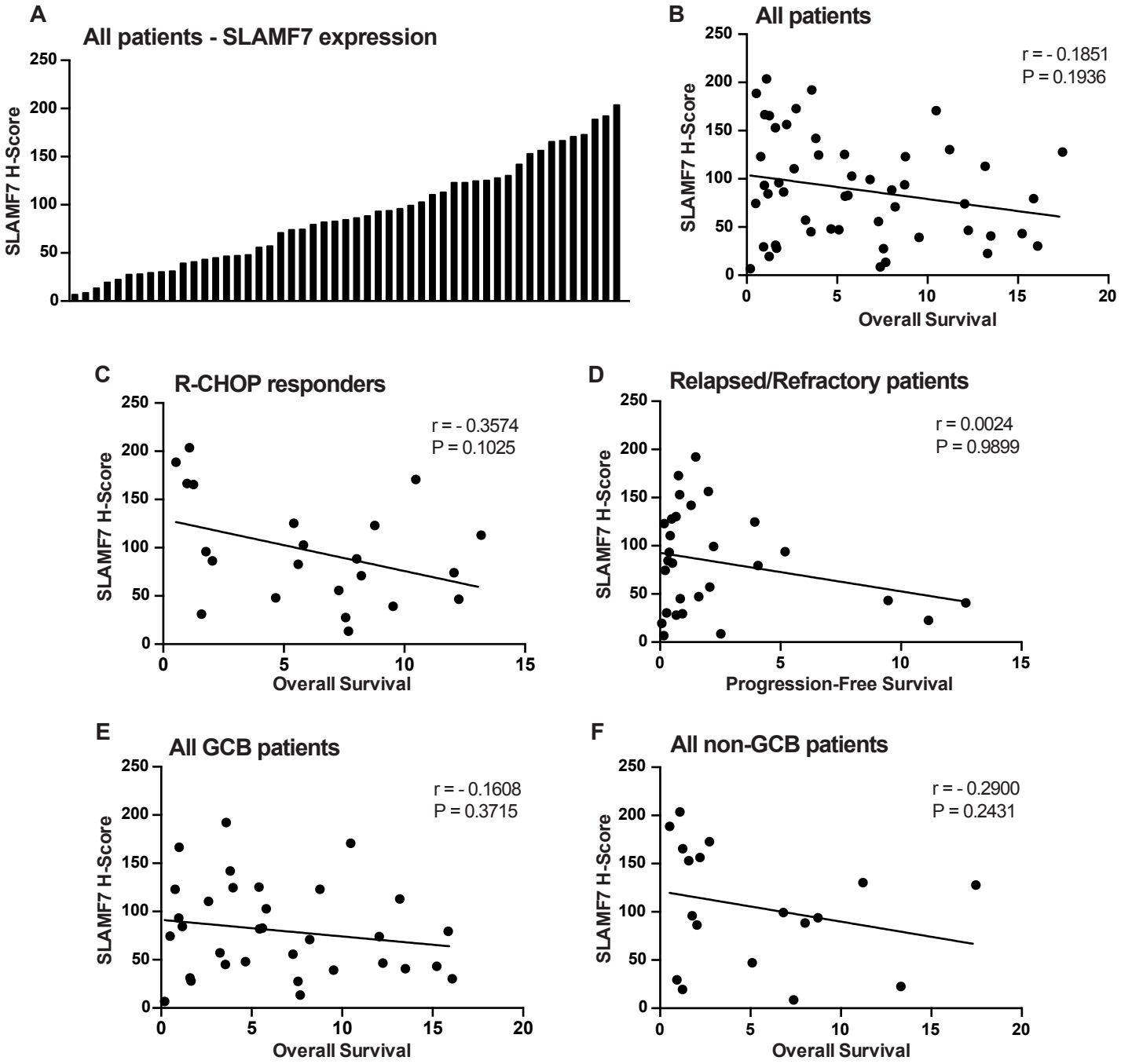
Supplementary Figure 1: Impact of EZH2i on proliferation rates in drug-sensitive and drug-resistant SU-DHL-6 and OCI-LY7 cell lines. (**A**) Cell growth curve of SU-DHL-6 and SU-DHL-6-R5 cells, in the presence and absence of GSK343. Cell numbers were counted at the indicated number of days post-seeding (n = 1). (**B**) Cell growth curve of OCI-LY7 and OCI-LY7-R6 cells, in the presence and absence of GSK343. Cell numbers were counted at the indicated number of days post-seeding. Mean values ± SD are plotted (n = 2).



Supplementary Figure 2: Sensitivity of SU-DHL-6 and OCI-LY7 parental and EZH2i-resistant cell lines to treatment with JQ1 and vorinostat. (**A-B**) Dose-response curve comparing vorinostat concentration between parental and EZH2i-resistant SU-DHL-6 (**A**) and OCI-LY7 (**B**) cells. IC50 values are indicated. (**C-D**) Dose-response curve comparing azacitadine concentration between parental and EZH2i-resistant SU-DHL-6 (**C**) and OCI-LY7 (**D**) cells. (**E-F**) Dose-response curve comparing JQ1 concentration between parental and EZH2i-resistant SU-DHL-6 (**E**) and OCI-LY7 (**F**) cells. All curves are expressed as percentage of viable cells versus the logarithmic concentration of the indicated drug. Mean values are plotted (n = 2 for all experiments).



Supplementary Figure 3: RNA-seq profiling or SU-DHL-6 and OCI-LY7 parental and EZH2i-resistant cells, in the presence and absence of GSK343. (**A-B**) PCA plots comparing the transcriptomes of indicated samples, spatially separated by the two most prominent transcriptional variables, in SU-DHL-6 (**A**) and OCI-LY7 (**B**) cells. (**C-D**) Functional enrichment analysis of normalized gene expression data was conducted through Gene Ontology (GO). Listed biological processes were significantly upregulated in SU-DHL-6-R5 cells compared to SU-DHL-6 cells (**C**), or in OCI-LY7-R6 cells compared to OCI-LY7 cells (**D**). (**E-F**) Transfac and Jaspar libraries were used to identify transcription factor binding profiles that were either enriched in SU-DHL-6-R5 cells compared to SU-DHL-6 cells (**E**) or enriched in OCI-LY7-R6 cells compared to OCI-LY7 cells (**F**). FDR (Padj < 0.05) was used to determine significance. All RNA-seq samples were processed in technical duplicates.



Supplementary Figure 4: Correlation of SLAMF7 expression and survival in a cohort of DLBCL patients. (**A**) Bar graph comparing expression of SLAMF7 across all patient samples. Each bar represents one patient (n = 51). All expression data are listed as H score values. (**B-F**) Spearman rank-order analysis correlating SLAMF7 expression and overall or progression-free survival (as indicated) in the following patient groups: all patients (**B**), R-CHOP responders (**C**), patients with relapsed/refractory disease (**D**), GCB DLBCL patients (**E**), and non-GCB DLBCL patients (**F**). P and r values are listed. Black trendlines represent linear regression.