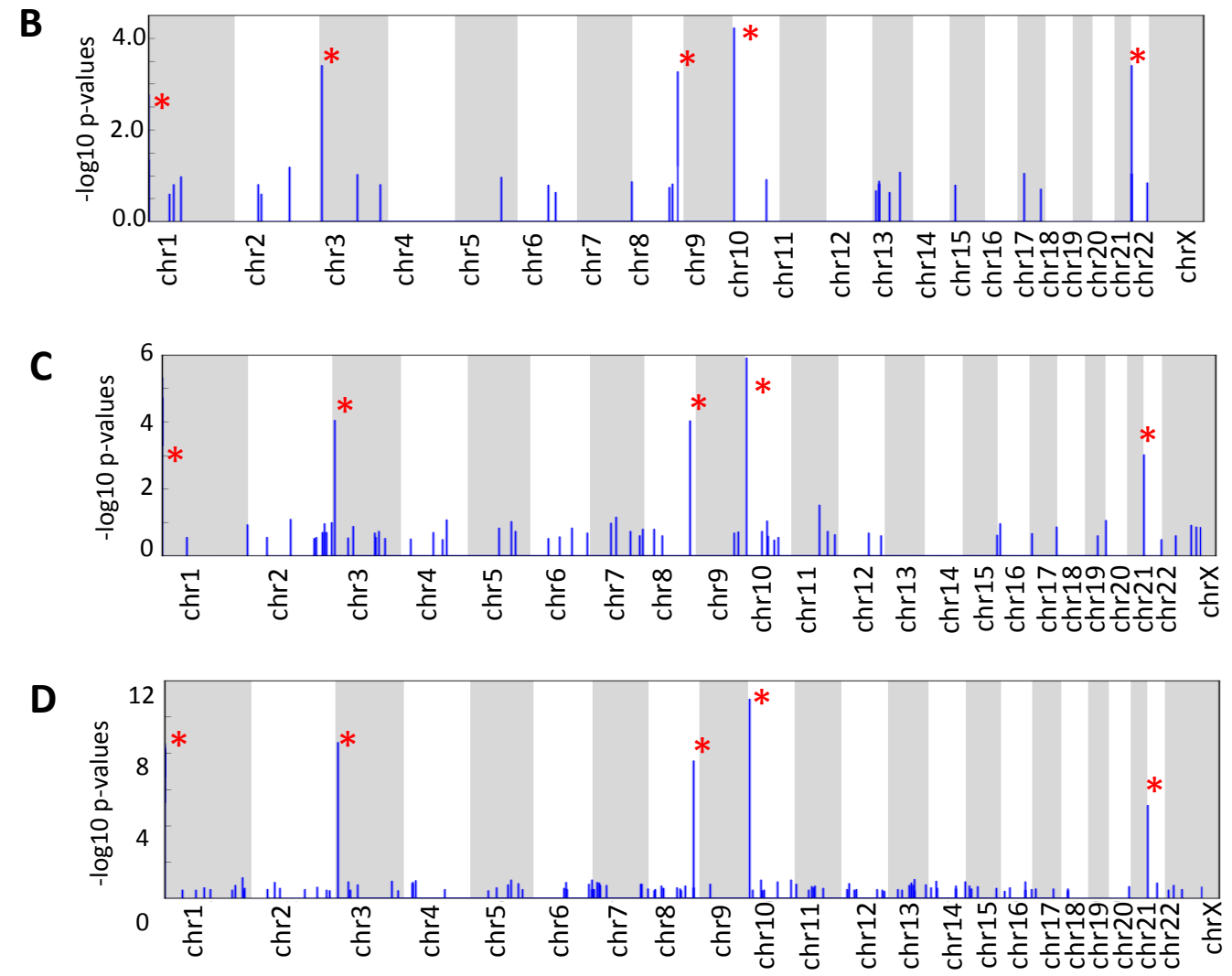
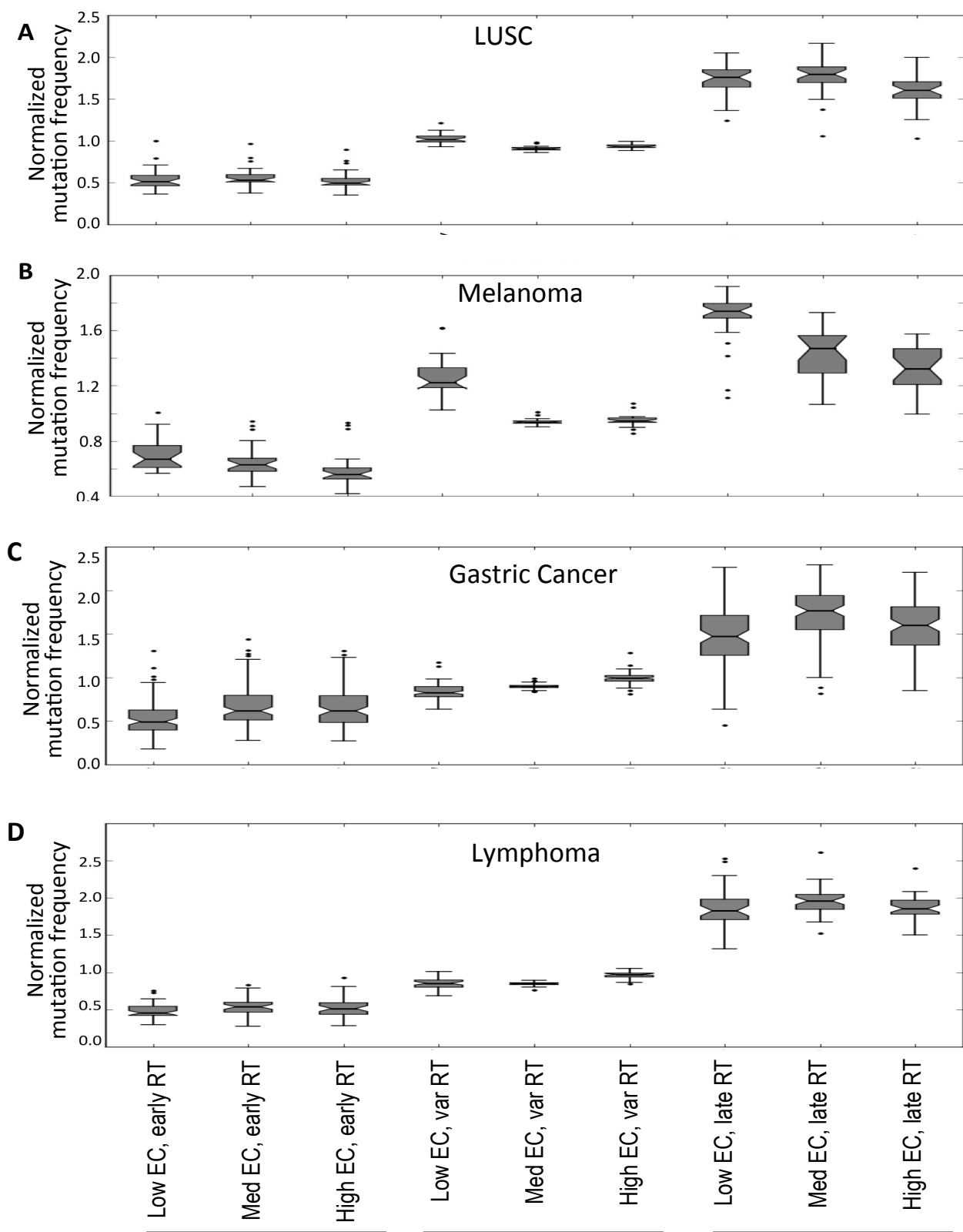


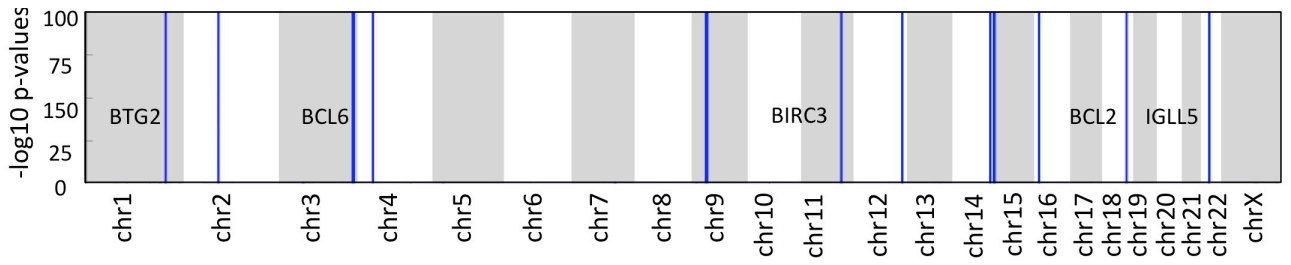
Chromosome	Start	End	Length	Spiked mutations
chr1	50050	50200	150	2
chr3	5000000	5000700	700	3
chr10	3000000	3000050	50	2
chr8	128750826	128751198	372	2
chr22	10000	12000	2000	5



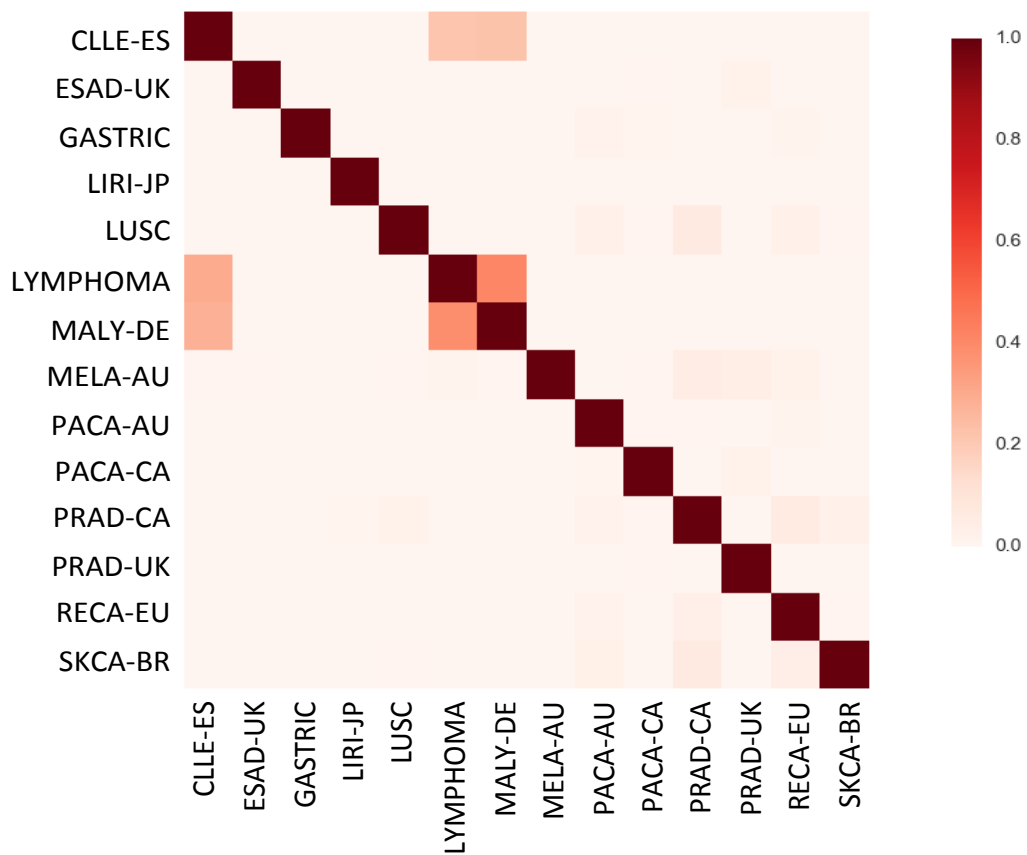
**Supplementary Figure 1: (A)** Regions spiked with artificial SASE **(B)** SASEs identified in randomly simulated genome of 30 samples with 3 samples containing SASE and mutation rate of 1/100000bps, spiked marked by asterisks. **(C)** SASEs identified in randomly simulated genome of 40 samples with 5 samples containing SASE and mutation rate of 1/100000bps, spiked marked by asterisks. **(D)** SASEs identified in randomly simulated genome of 50 samples with 10 samples containing SASE and mutation rate of 1/100000bps, spiked marked by asterisks.



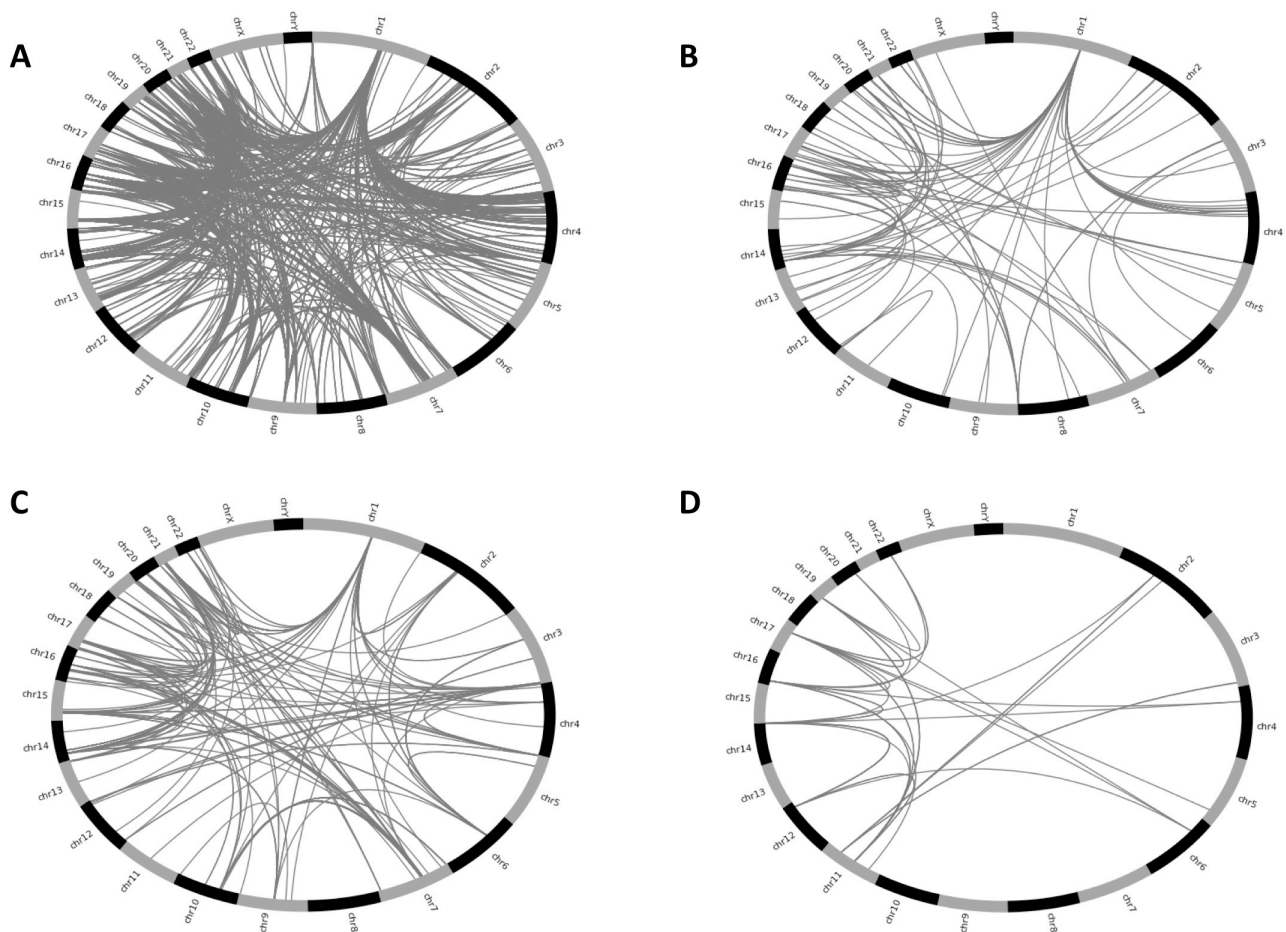
**Supplement Figure 2:** Mutational burden in equivariant regions (EVRs) based on combinations of evolutionary conservation (EC; low, medium, high) and replication timing (RT; early, variable, late) for (A) LUSC, (B) Melanoma, (C) Gastric cancer, and (D) Lymphoma cohorts. For each EVR, mutation frequency observed in each sample was normalized by the background mutation frequency in that sample.



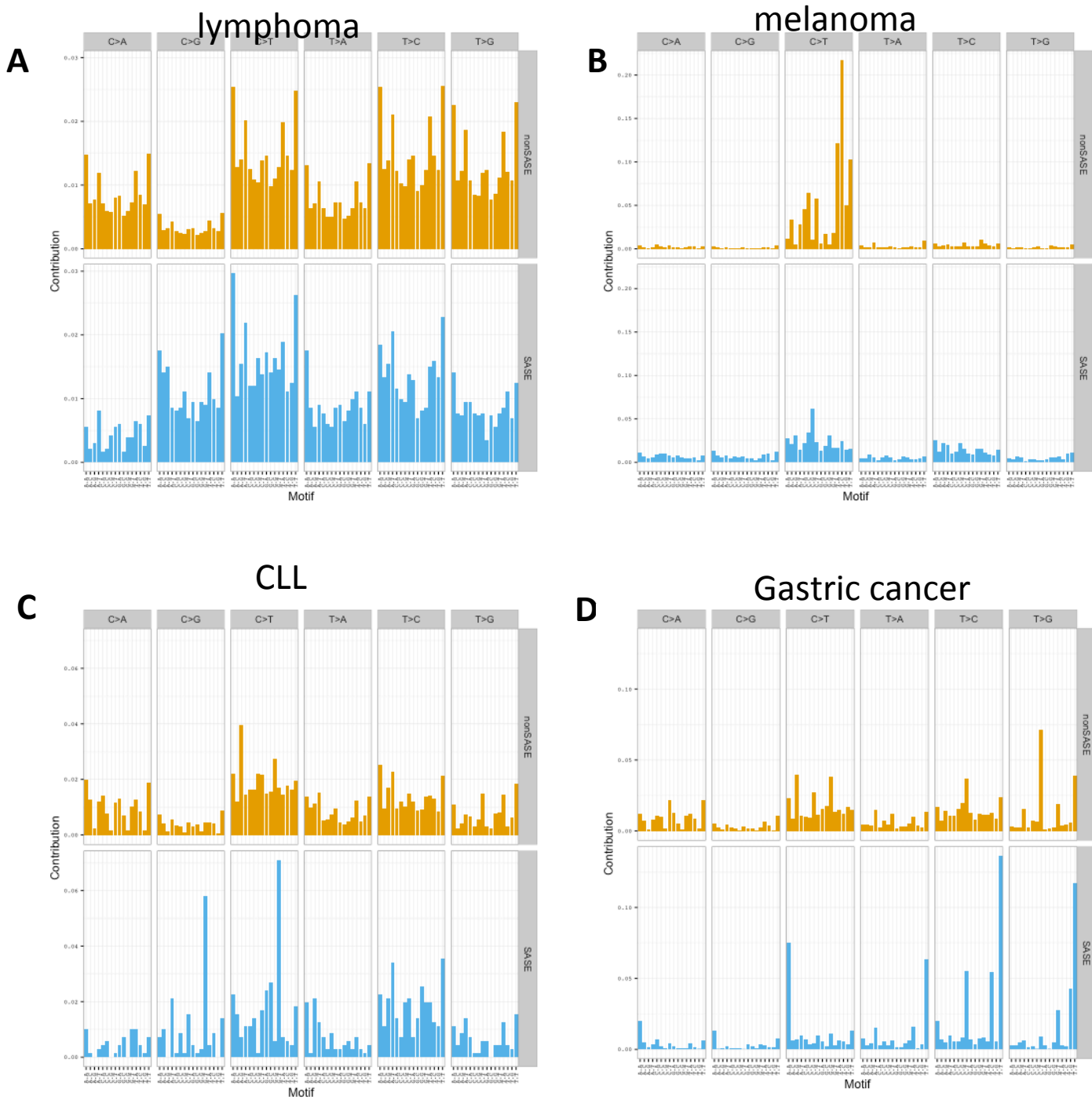
**Supplementary Figure 3:** Signature of accelerated somatic evolution in the lymphoma, MALY-DE, and CLL-ES combined cohort.



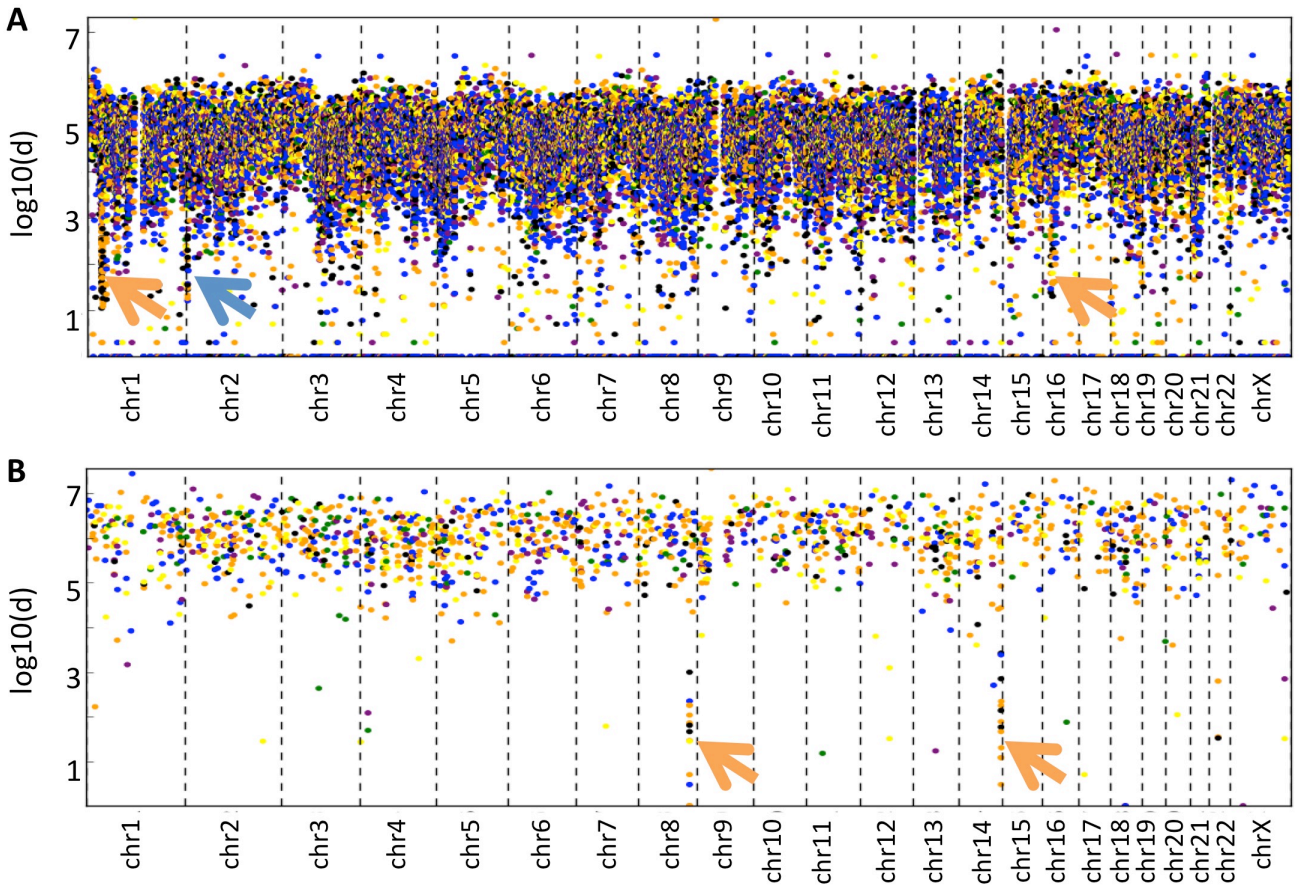
**Supplement Figure 4:** Heatmap of SASE overlaps between cohorts as a proportion of total SASEs in each cohort.



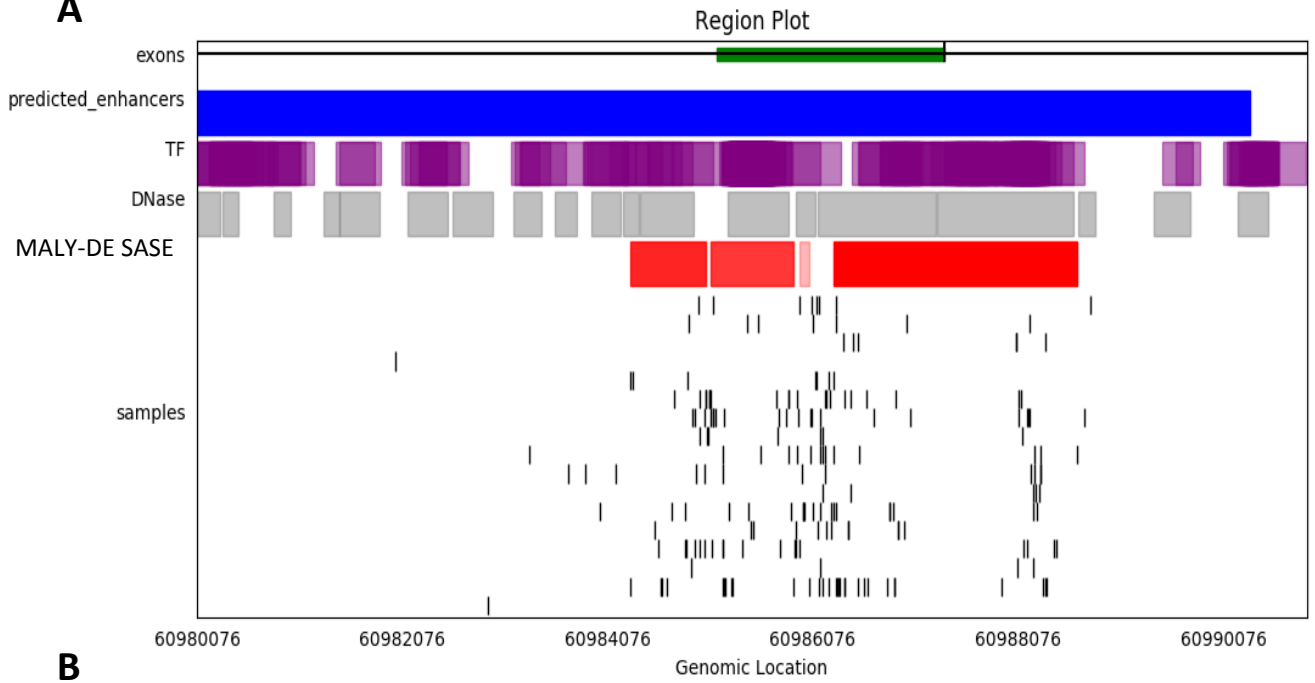
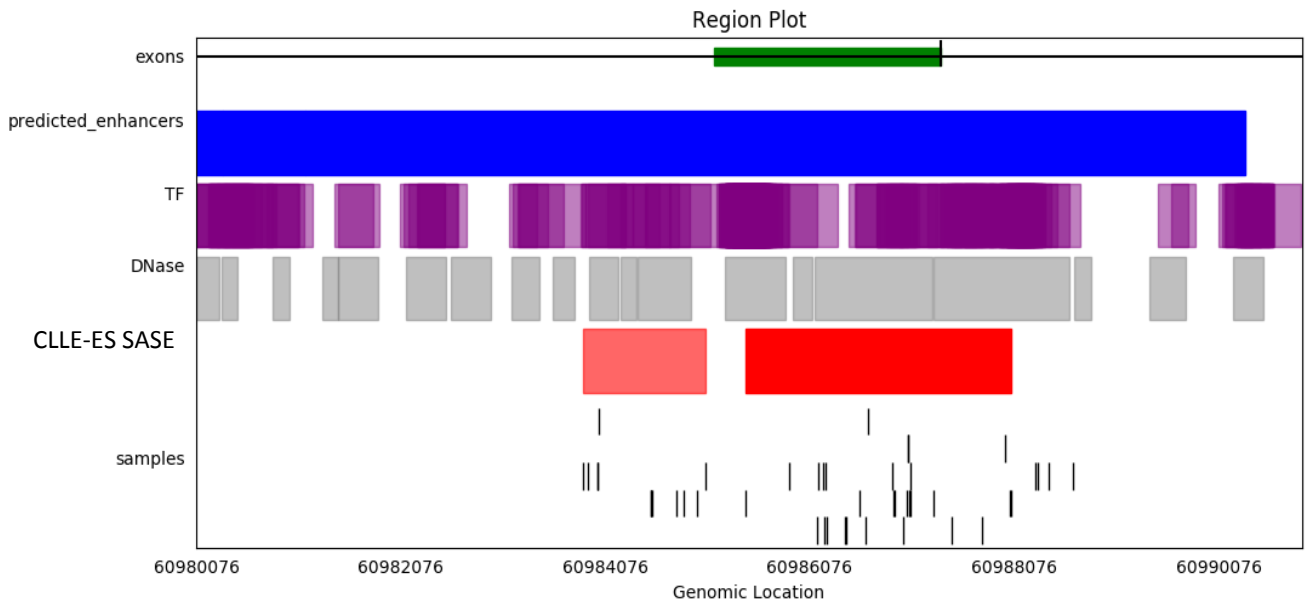
**Supplement Figure 5: (A)** Hi-C SASE-SASE interactions for melanoma cohort. **(B), (C), and (D)** show interactions for gastric, LUSC, and MALY-DE cohorts, respectively.



**Supplement Figure 6:** SASE-associated somatic mutation signatures for (A) lymphoma, (B) melanoma, (C) CLL, and (D) gastric cancer cohort.

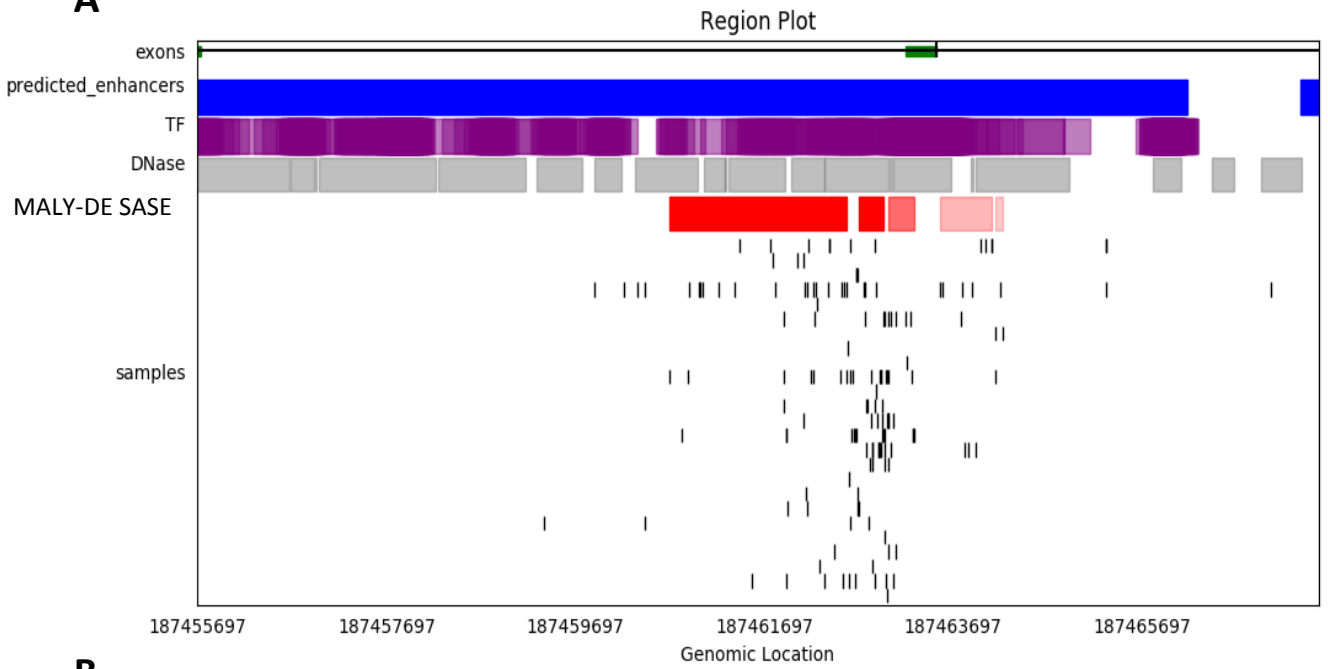
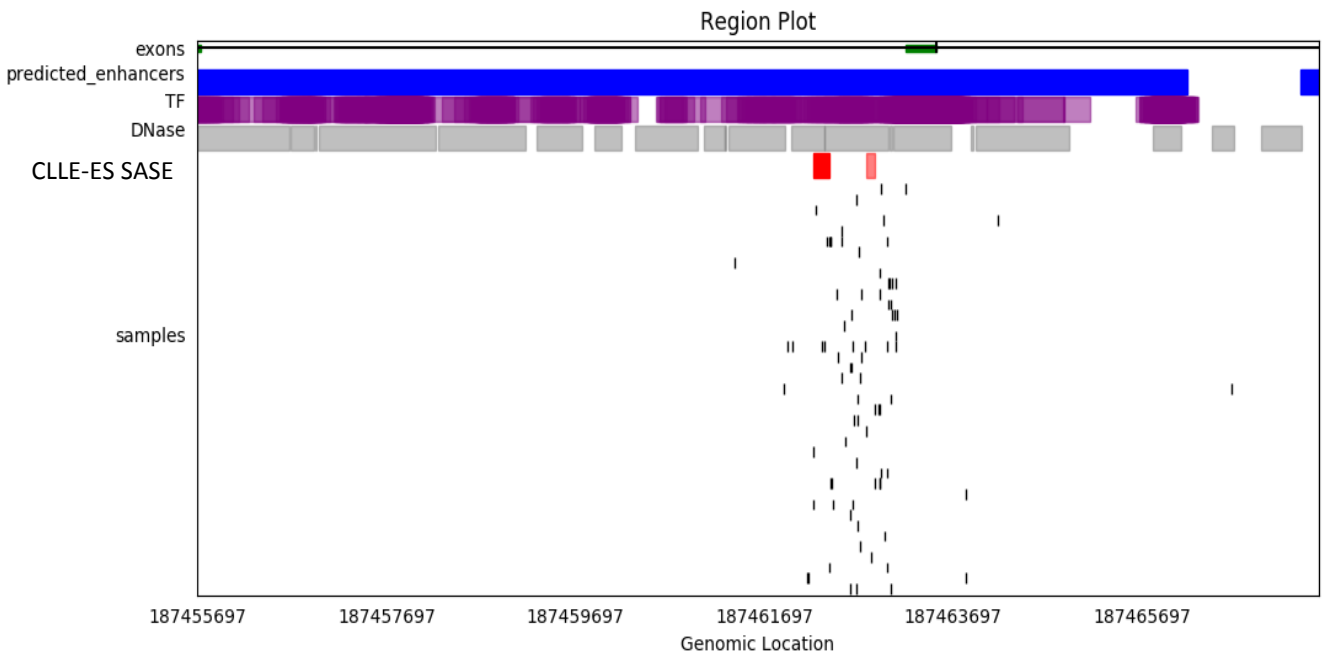


**Supplement Figure 7: (A)** Raindrop plot of intermutation distances observed in a LUSC sample with kataegis regions indicated by an orange arrow and kataegis-like regions indicated with a blue arrow. **(B)** Raindrop plot for MALY-DE sample.

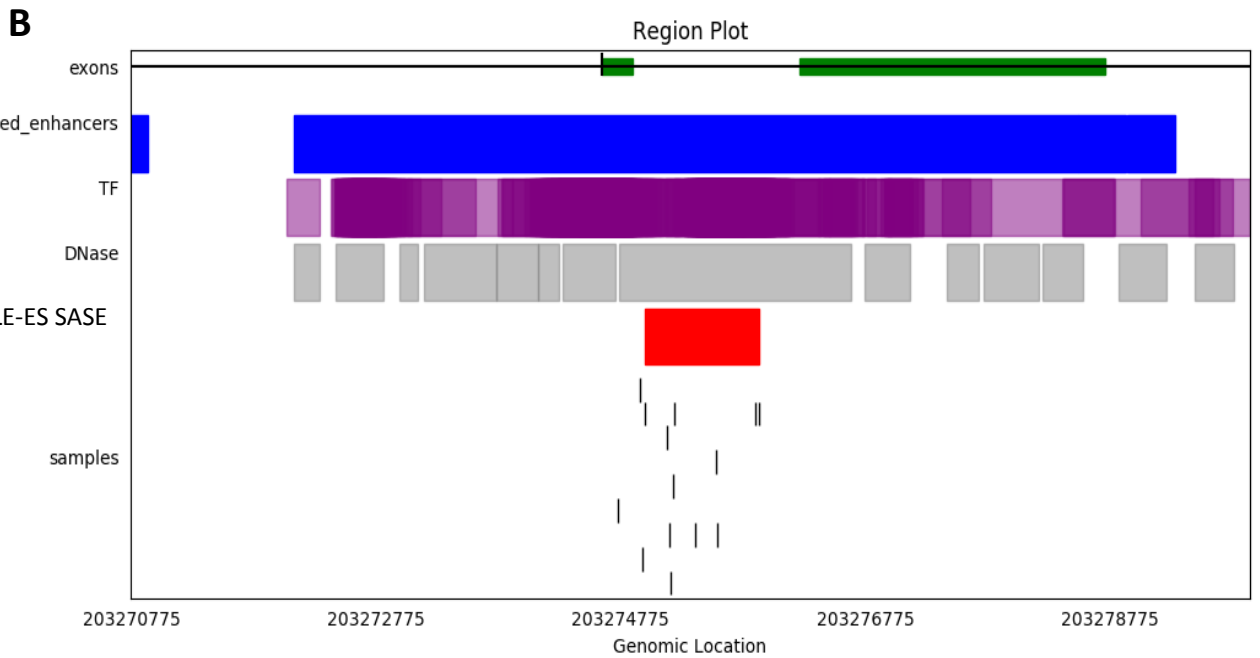
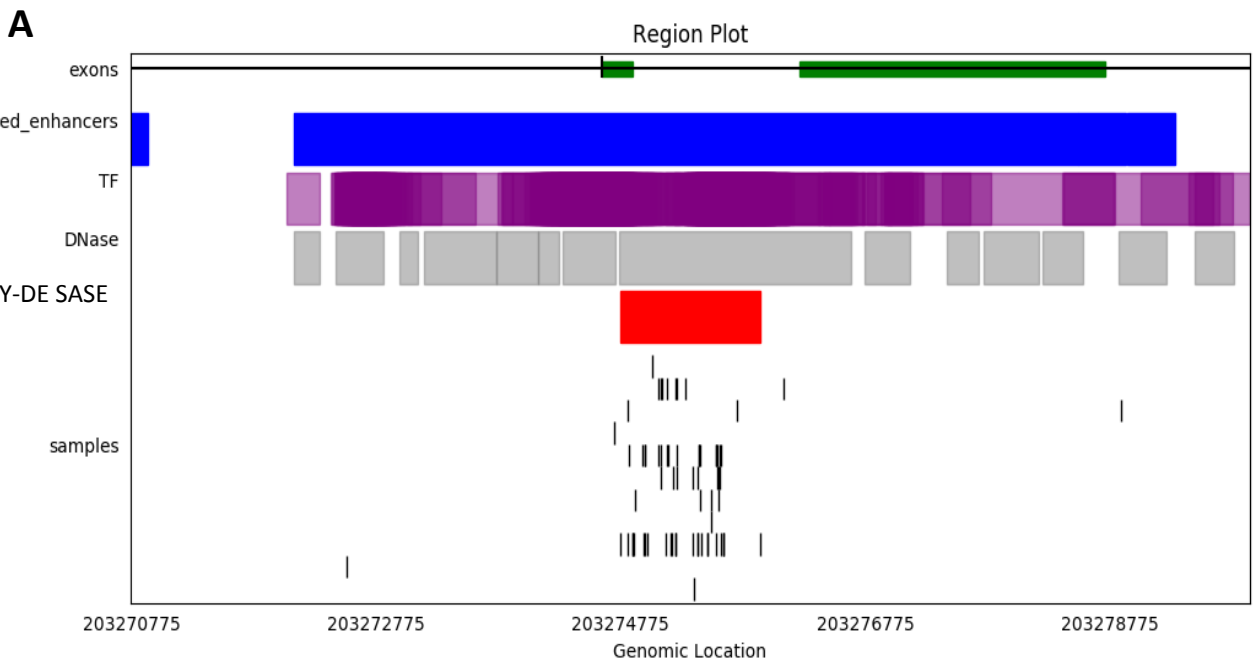
**A****B**

**Supplement Figure 8: (A)** Annotated MALY-DE SASE in BCL2 promoter. **(B)** Annotated CLLE-ES SASE in BCL2 promoter.

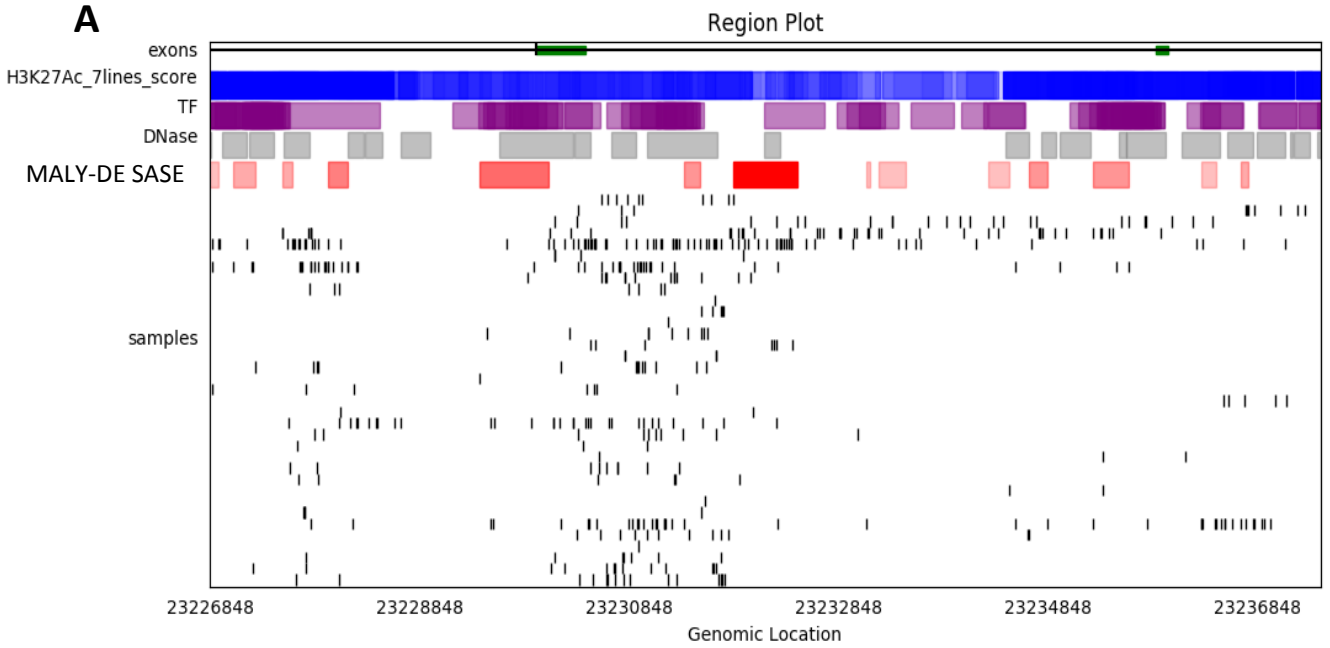
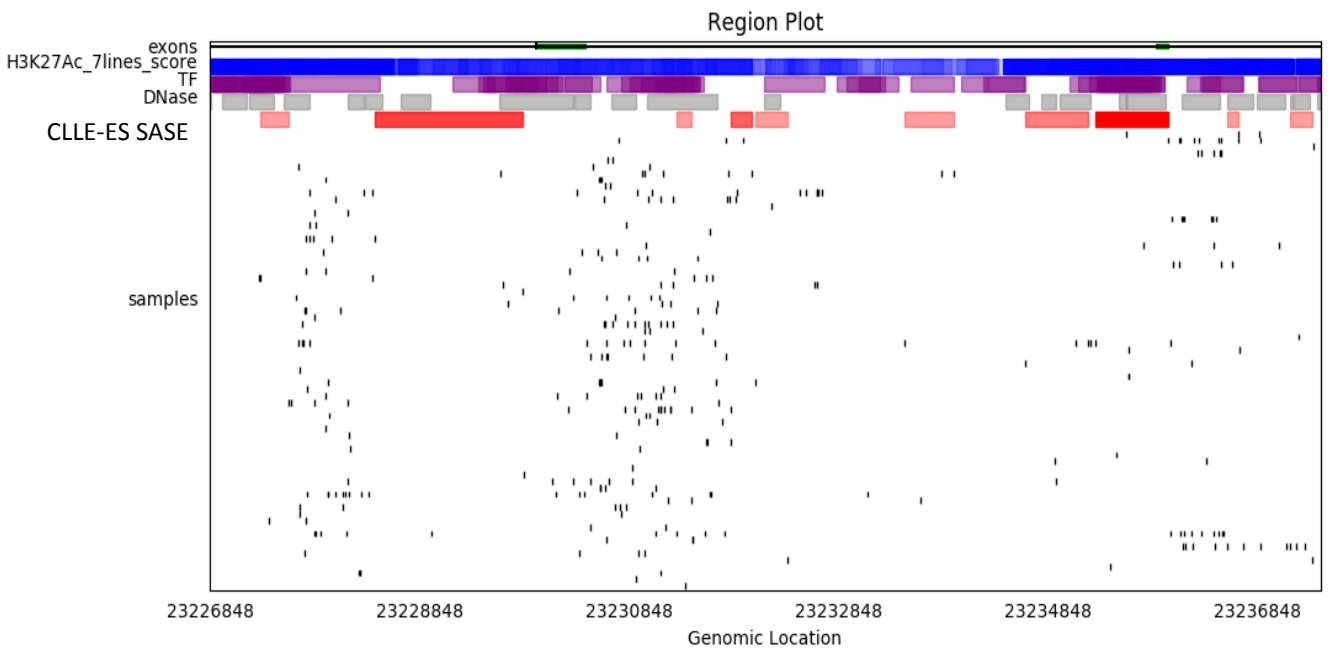


**A****B**

**Supplement Figure 9: (A)** Annotated MALY-DE SASE in BCL6 promoter. **(B)** Annotated CLLE-ES SASE in BCL6 promoter.



**Supplement Figure 10: (A)** Annotated MALY-DE SASE in BTG2 promoter. **(B)** Annotated CLLE-ES SASE in BTG2 promoter.

**A****B**

**Supplement Figure 11: (A)** Annotated MALY-DE SASE in IGLL5 promoter. **(B)** Annotated CLLE-ES SASE in IGLL5 promoter.