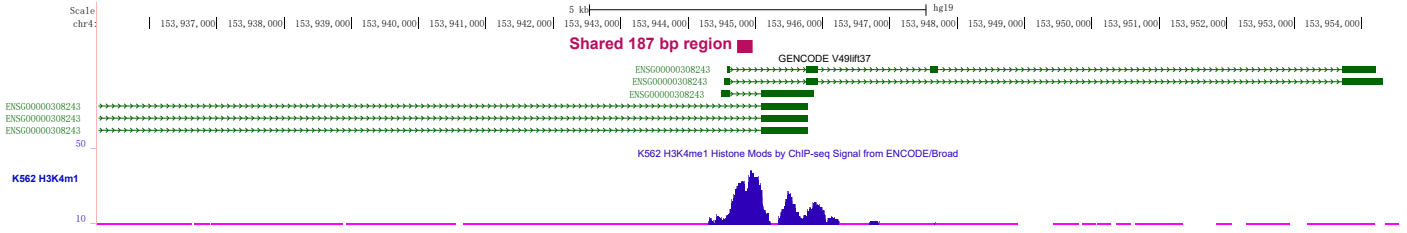
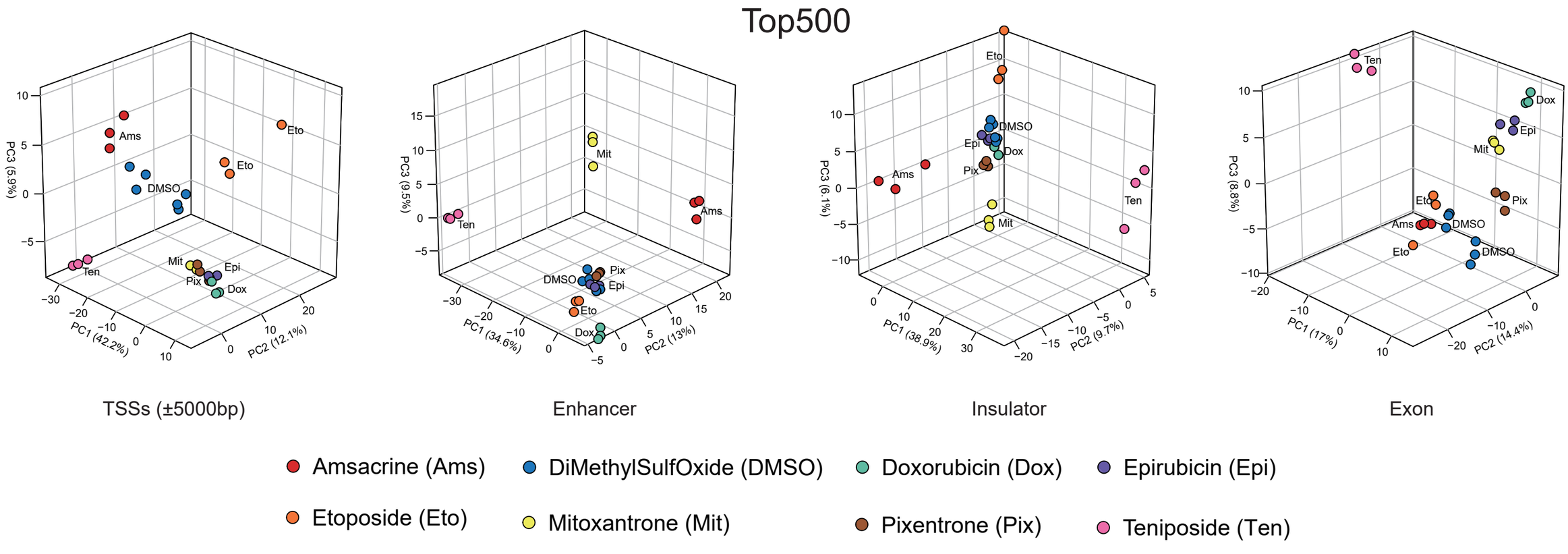
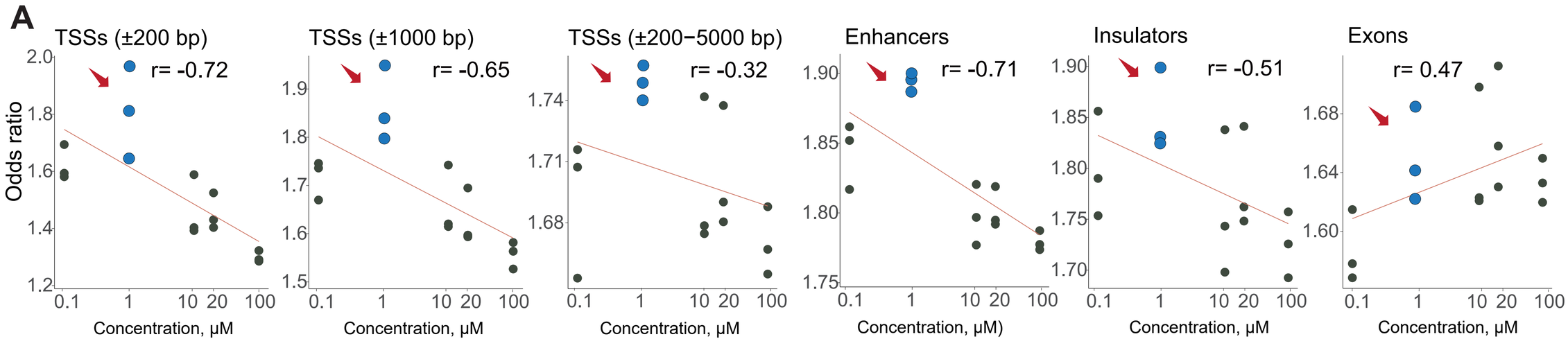
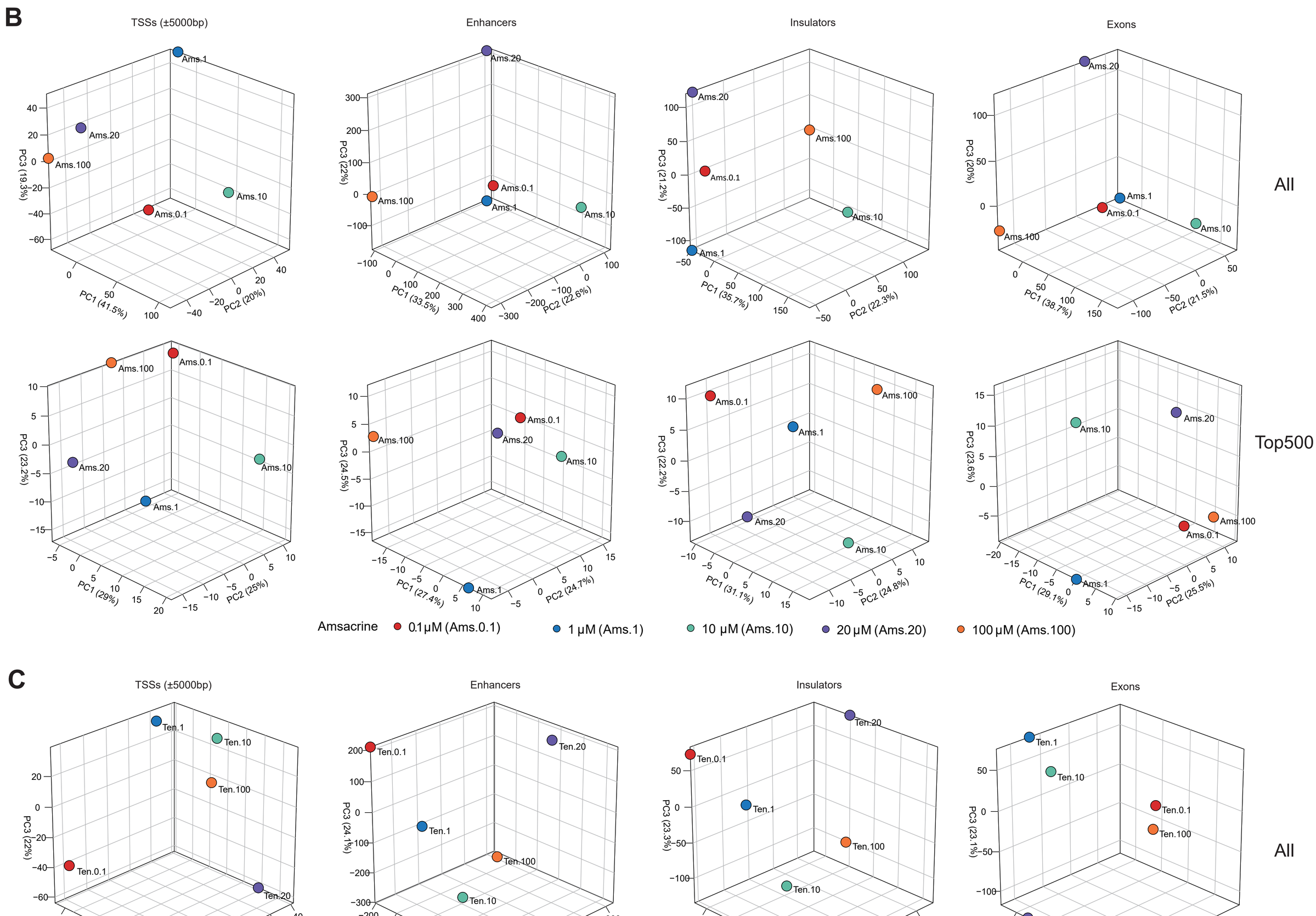


Supplementary Figure 1. Genomic context of the TOP2 cleavage region shared by all the 7 drugs. GENCODE gene annotations and ChIPseq signal for the H3K4m1 histone modification obtained by ENCODE/Broad Institute from the K562 cell line are shown from the UCSC Genome Browser.

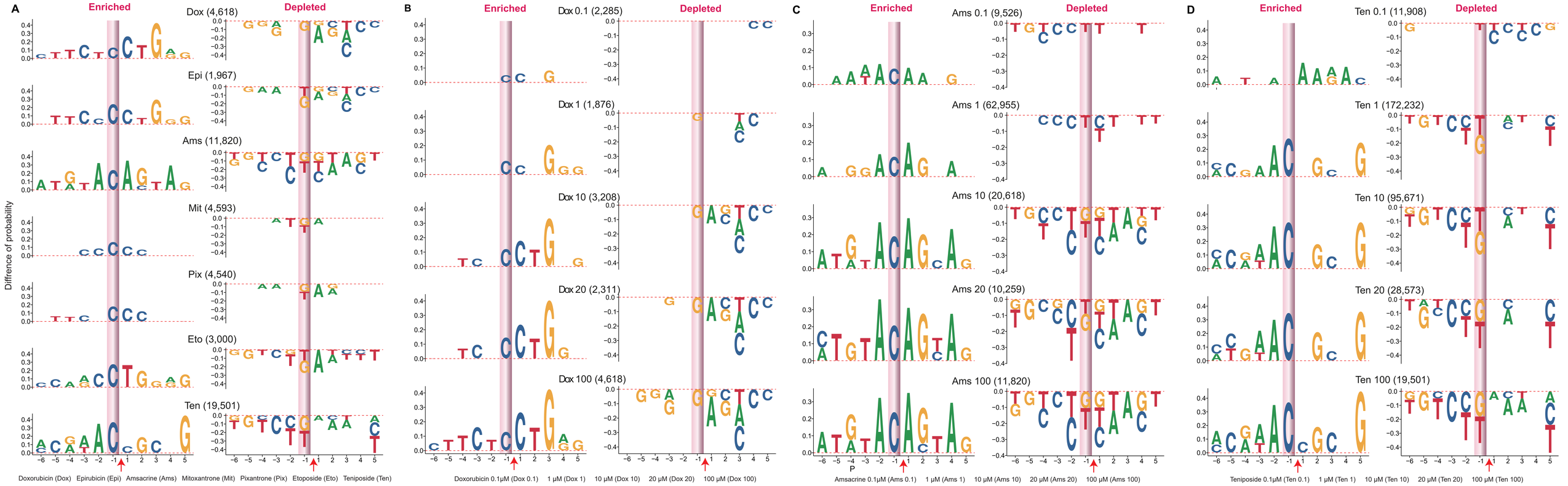


Supplementary Figure 2. The differences in the genomic profiles among different poisons are also evident at the level of all SSBs. The PCA results for each poison and each type of the genomic elements. The PCA is based on the normalized counts (LPKM-SSB, Materials and Methods) of all SSBs mapping to the top 500 elements that are most variable among all the drugs.

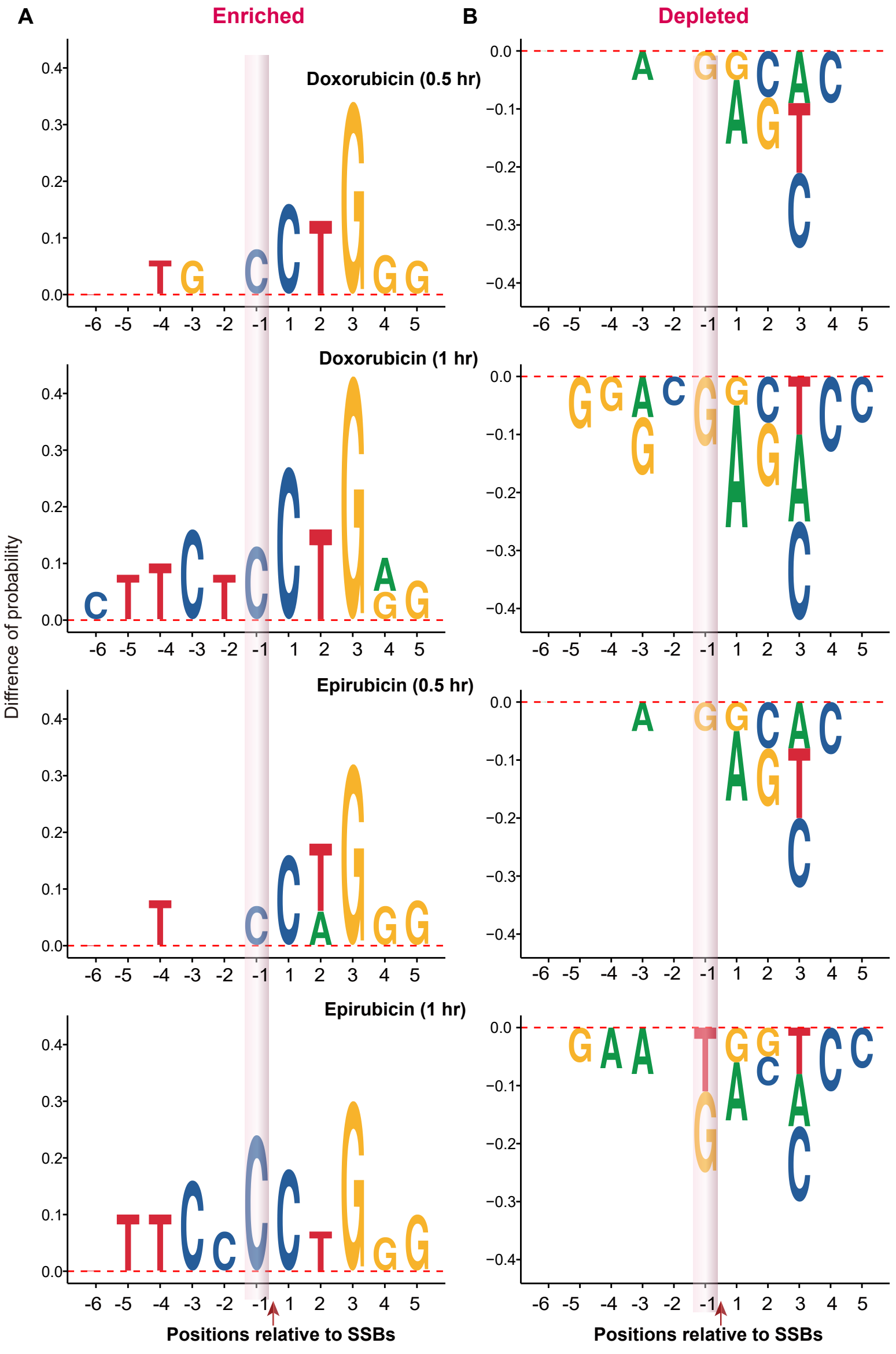




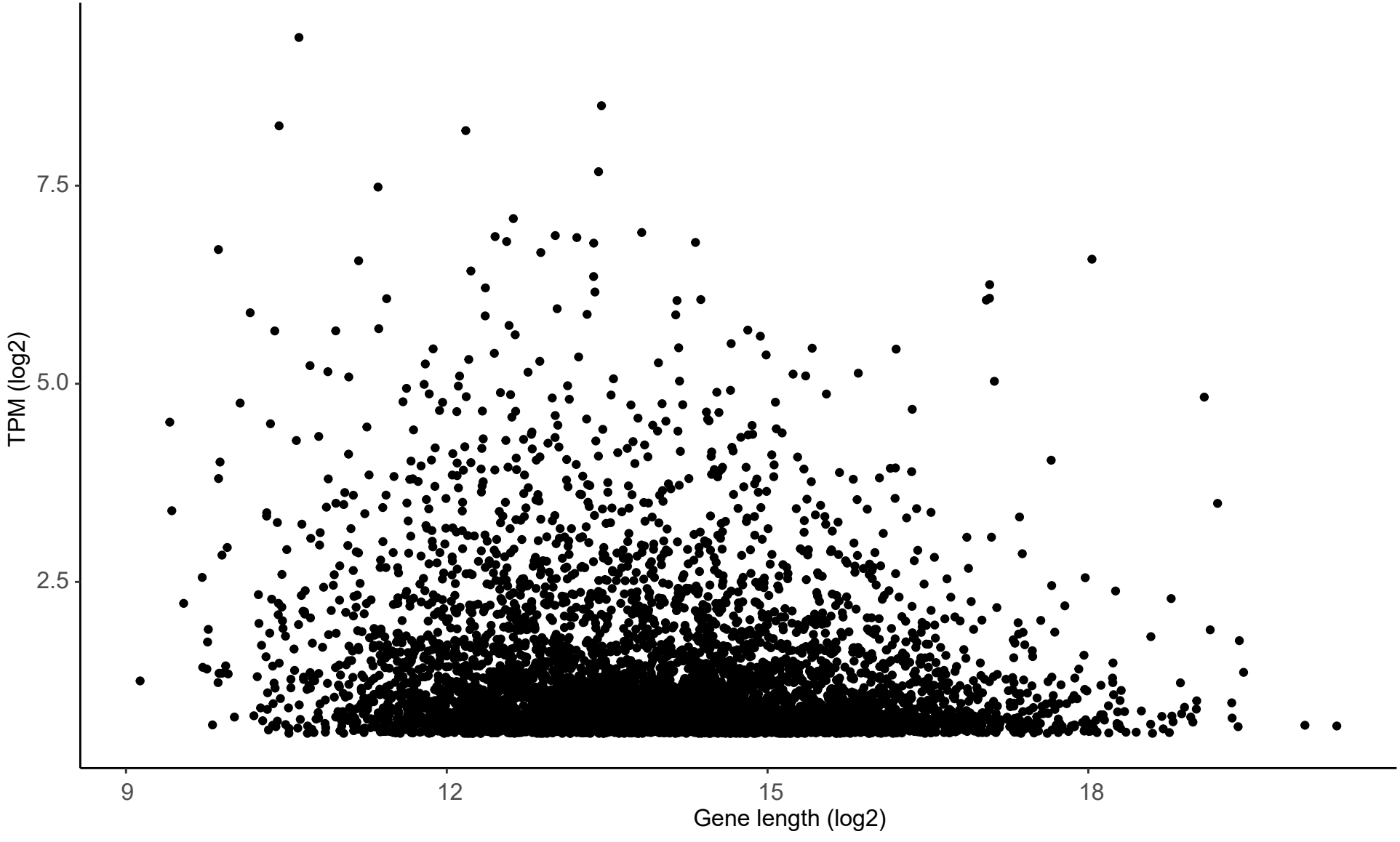
Supplementary Figure 3. Concentration-dependency of the TOP2 cleavage sites of doxorubicin, amsacrine and teniposide. (A) All SSBs plotted vs doxorubicin concentration in each type of the genomic elements. The concentrations are plotted on the $\log_2$ scale. Note that each of the 3 replicates was scored separately. (B, C) The PCA results for each concentration and each type of the genomic elements. The PCA is based on the normalized counts (LPKM-SSB, Materials and Methods) of the TOP2 cleavage sites mapping to all elements annotated in the genome or only the top 500 elements that are most variable among all the concentrations of amsacrine (B) or teniposide (C).



Supplementary Figure 4. The local sequence preference of the different poisons. The local nucleotide preference for all drugs (A) and the different concentrations of doxorubicin (B), amsacrine (C) and teniposide (D) are shown as the enriched and depleted nucleotides for each genomic position around the TOP2 cleavage (the red arrow at the bottom) relative to DMSO. The position identified by SSiNGLe is represented as "−1". The numbers in the parentheses show the numbers of the single-nucleotide hotspots of TOP2 cleavage used to calculate each local sequence preference signature.



Supplementary Figure 5. Effect of the treatment time on the local sequence preference.
The nucleotides either enriched (A) or depleted (B) in the doxorubicin and epirubicin treatments compared to the DMSO control at each genomic position around the TOP2 cleavage sites (indicated by the red arrows at the bottom) are shown for the 2 different treatment durations: 0.5 and 1 hr. The position identified by SSiNGLe is represented as “-1”. The concentrations of doxorubicin and epirubicin were respectively 100 μM and 20 μM.



Supplementary Figure 6. The expression levels of genes are not correlated with their length. The expression level (TPM) of each gene is plotted against its length (exons+introns). Both values are in the log2 scale.