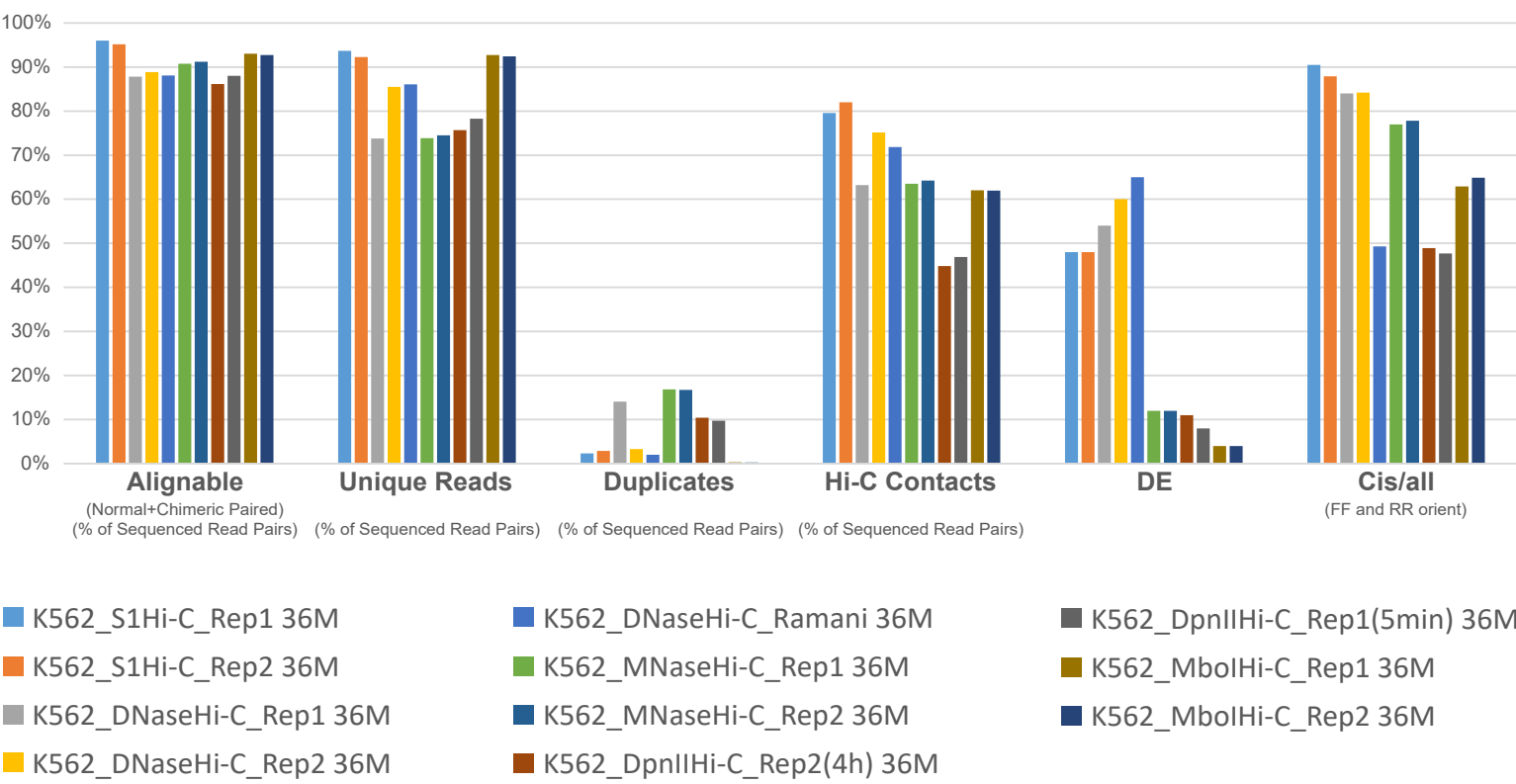
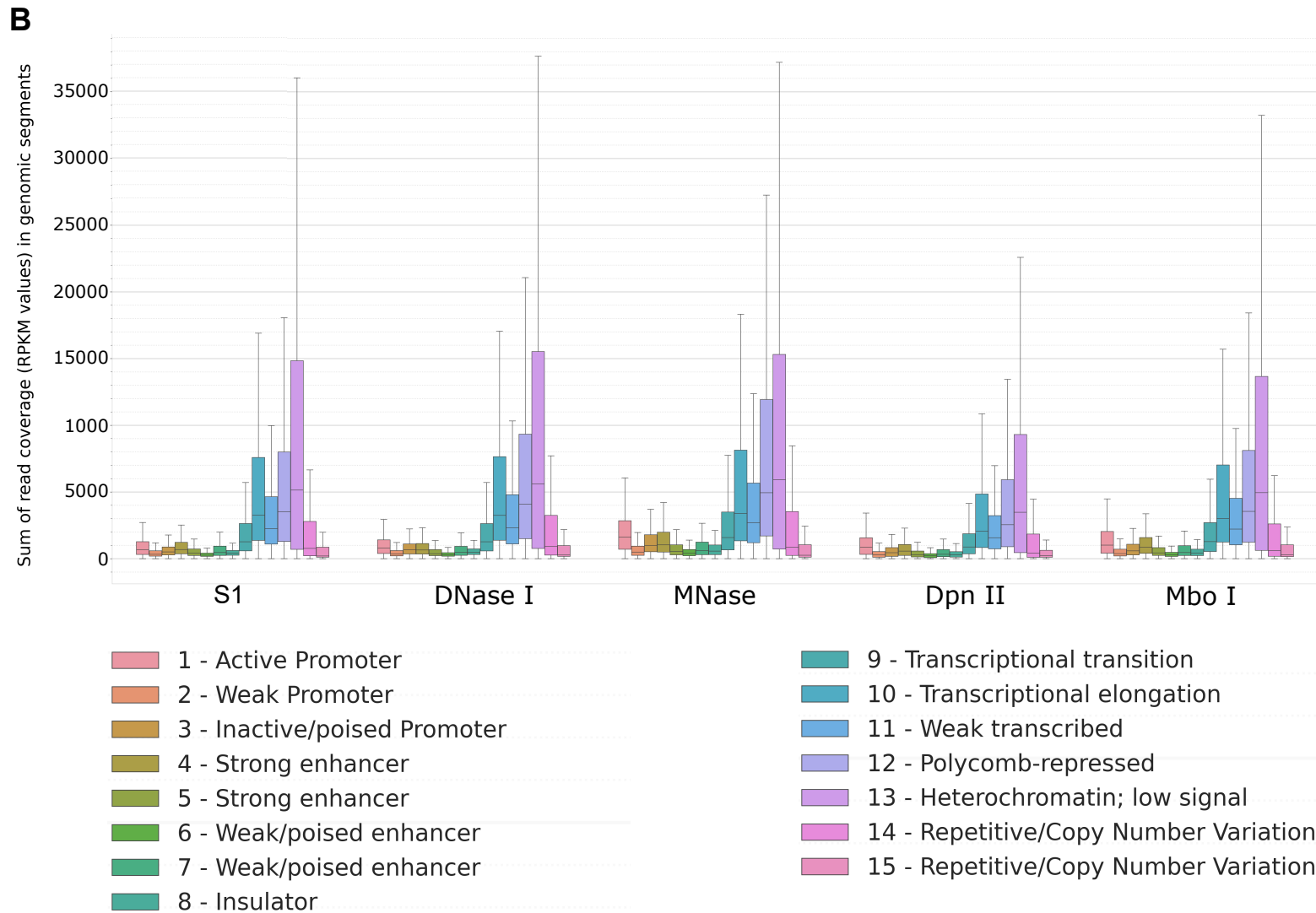
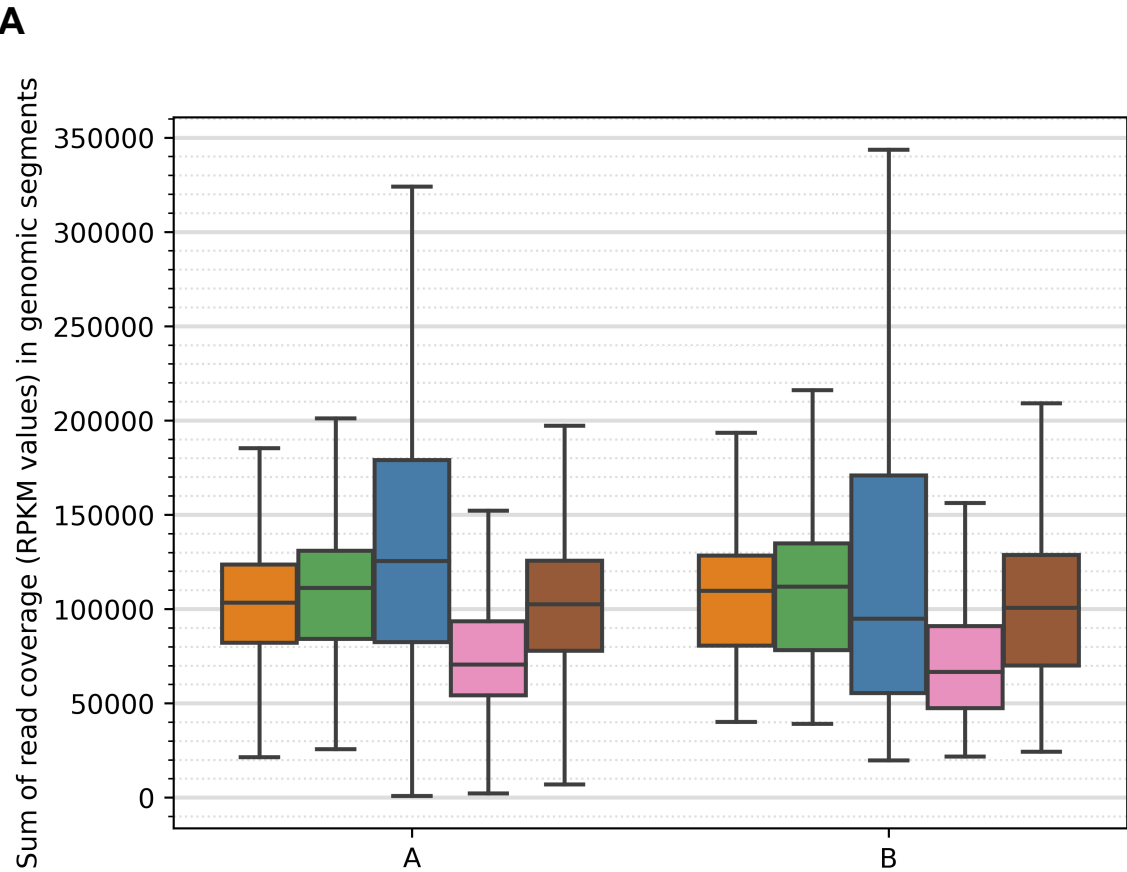


**Supplementary Figure 1.** Selected statistics of Hi-C data produced with different enzymes on K562 cells.



**Supplementary Figure 2.** Read coverage depth histograms showing distribution in annotated regions. (A) A/B compartments. (B) Chromatin state segmentation by Broad ChromHMM track.



**Supplementary Figure 3.** Schematic representation of S1 nuclease digestion. S1 nuclease introduces a double strand break at the sites (red arrowhead) resulting in blunt ends (A) or 3'-sticky ends (B). In the case of S1 nuclease makes blunt ends, we would expect C in -1 position of 50% forward reads and G in -1 position of 50% reverse reads (the indicates distance to the sequenced fragment end, i.e. +1 is a first nucleotide within sequenced fragment and -1 is a first letter in the flanking genomic sequence). This does not correspond to the obtained data. In the case of S1 nuclease makes 3'-sticky ends, they will be resected by S1 or during the next steps of library preparation. As a result, in -1 position of forward and reverse reads, we would find random nucleotides. This is concordant with the obtained data.

