

**Figure S6.** *Comparison of differentially and non-differentially expressed genes within different TAD classes in the knockdowns.* (A) Count and proportion of DEG and non-DEG in the three knockdowns (BEAF-32 knockdown, Cp190 Chro double knockdown and BEAF-32 Dref double knockdown) within TADs that: are fully conserved; lose one or both borders; have slightly shifted borders in the knockdowns. (B) We group different TAD classes in two subgroups (blue and yellow) and performed a permutation test to investigate if DEG overlap with any of the class more than expected by chance and plot the corresponding proportion of DEG over non-DEG for each group together with the corresponding -log<sub>10</sub> p-values. (C) Examples of DEGs inside TADs that have: *(i)* both borders conserved, *(ii)* one border conserved or *(iii)* both borders are knockdown specific. From top to bottom we plot the insulation score, TAD borders in full dataset (grey are strong and yellow are weak), TAD borders recovered both in full and downsampled dataset (black are strong and yellow are weak) and contact map in WT cells. We also plot a mirror plot in the knockdowns and log<sub>2</sub> fold change between WT and knockdown. To compute the log<sub>2</sub>FC, we followed the steps and parameters recommended in diffHiC package (Lun and Smyth 2015). Briefly, we consider individual replicates and use edgeR package (Robinson et al. 2010) to compute the log<sub>2</sub>FC in 5 kb bins. On the last row, we plot the position of the non-differentially expressed (grey), upregulated (blue) and downregulated (red) genes.