A. Transient transfection assay

CR = Mouse CR1, CR2, CR3 and CR6

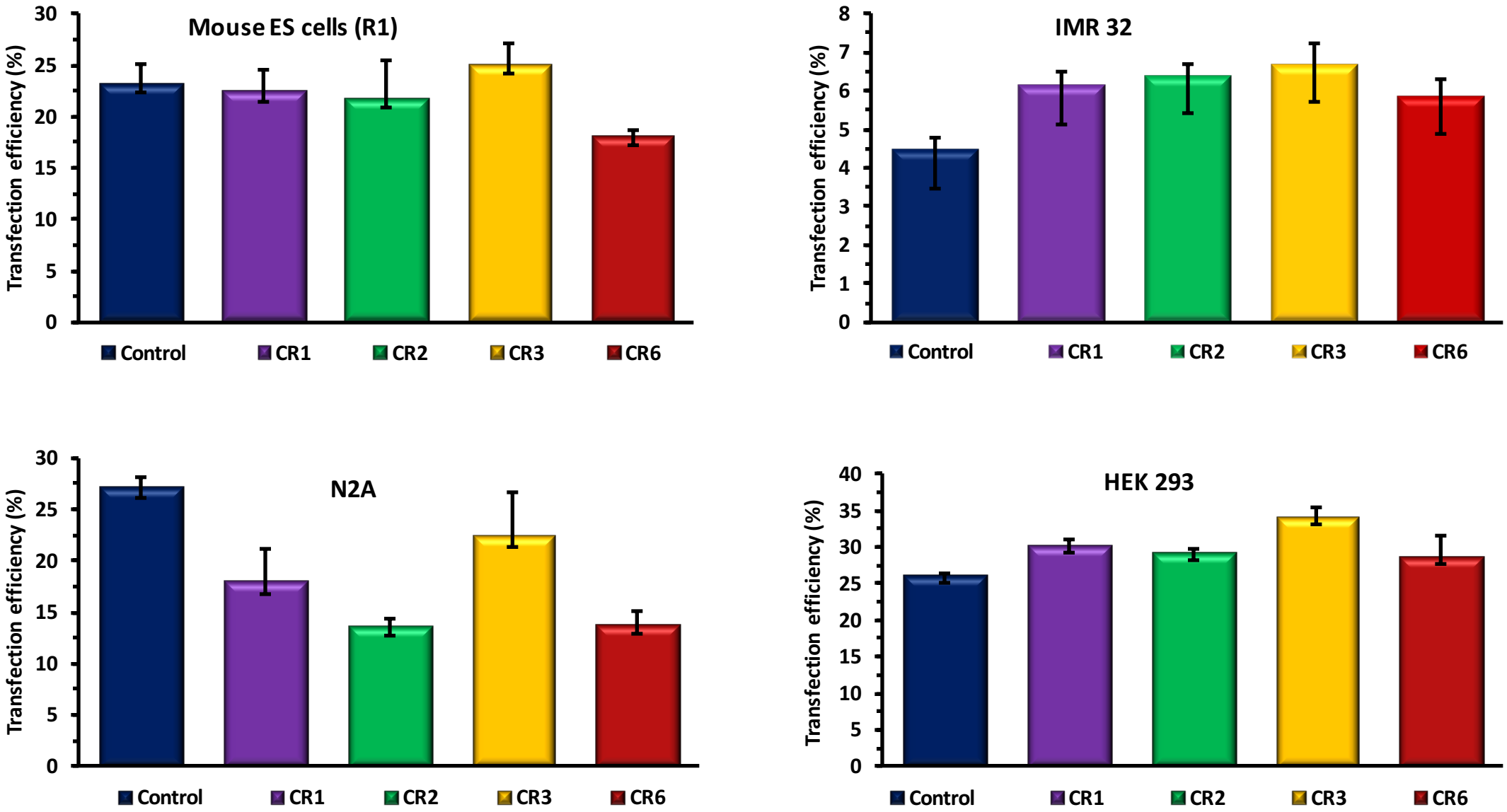
B. Colony formation assay

CR = Mouse CR1, CR2, CR3 and CR6

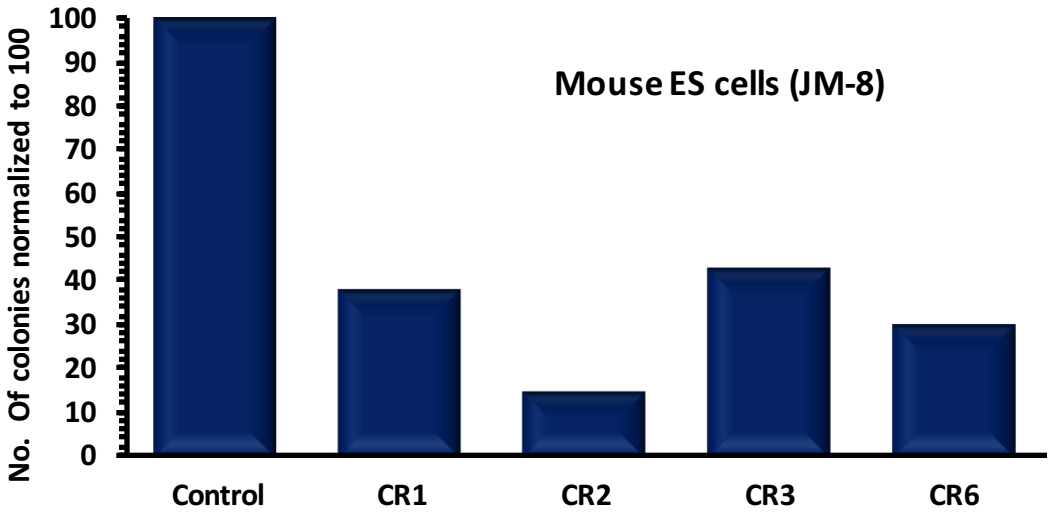
C. Reporter gene expression in zebrafish

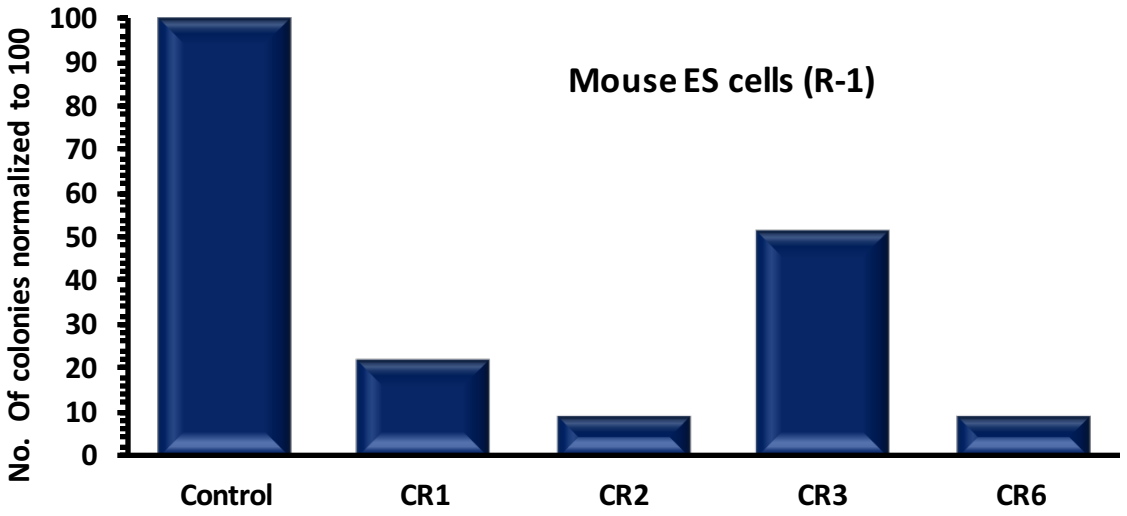
CR = Mouse and Zebrafish CR1, CR2, CR3 and CR6

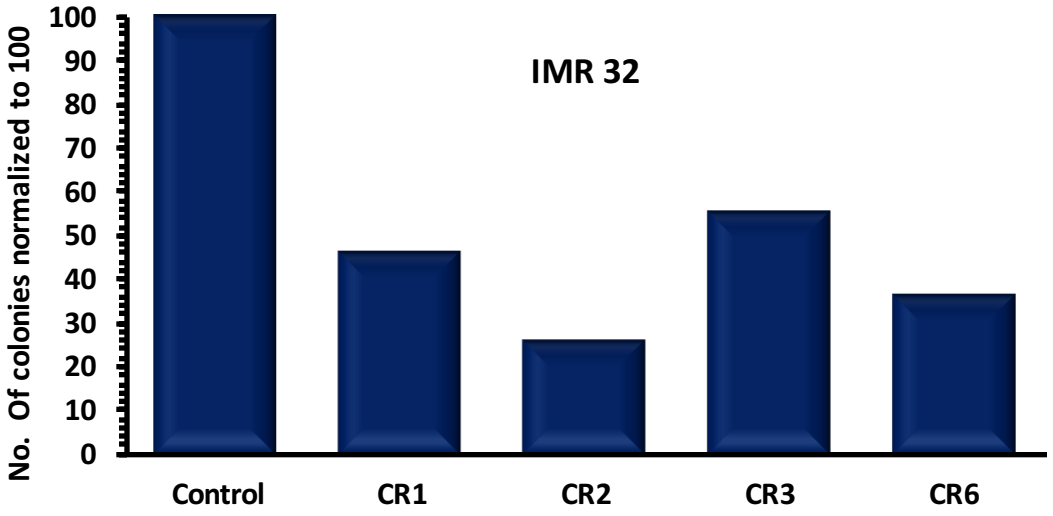
Supplementary figure 1. Different plasmid maps used in (A) transient transfection assay, (B) colony formation assay and (C) reporter gene expression assay in zebrafish.

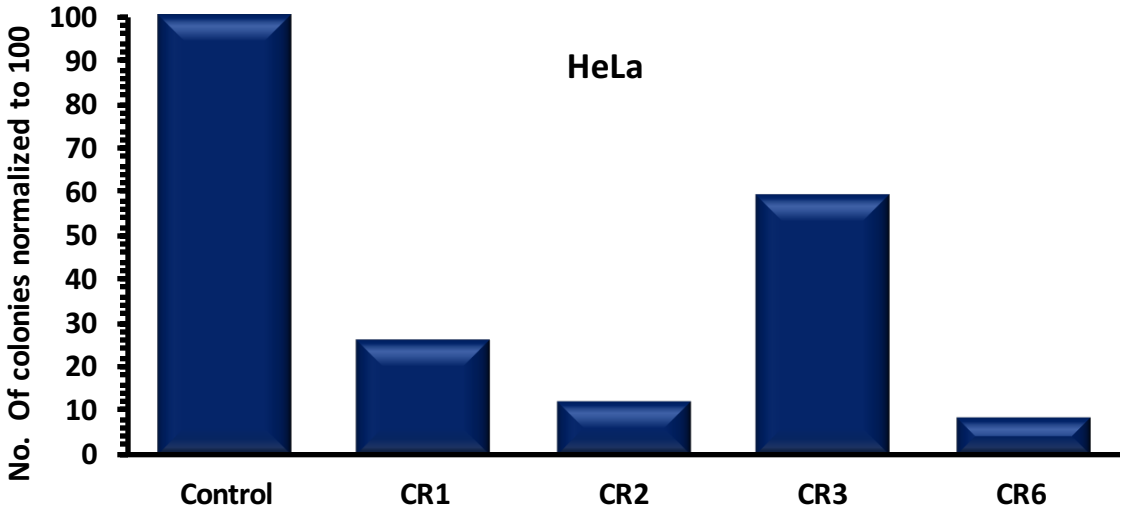


Supplementary figure 2. Transient transfection analysis using FACS: FACS data analysis from different cell lines (Mouse embryonic stem cells (R1), IMR32, N2A, HEK293T). X axis represents different plasmid constructs. Y axis represents percentage of GFP expression. Different CRs show cell line dependent activities.

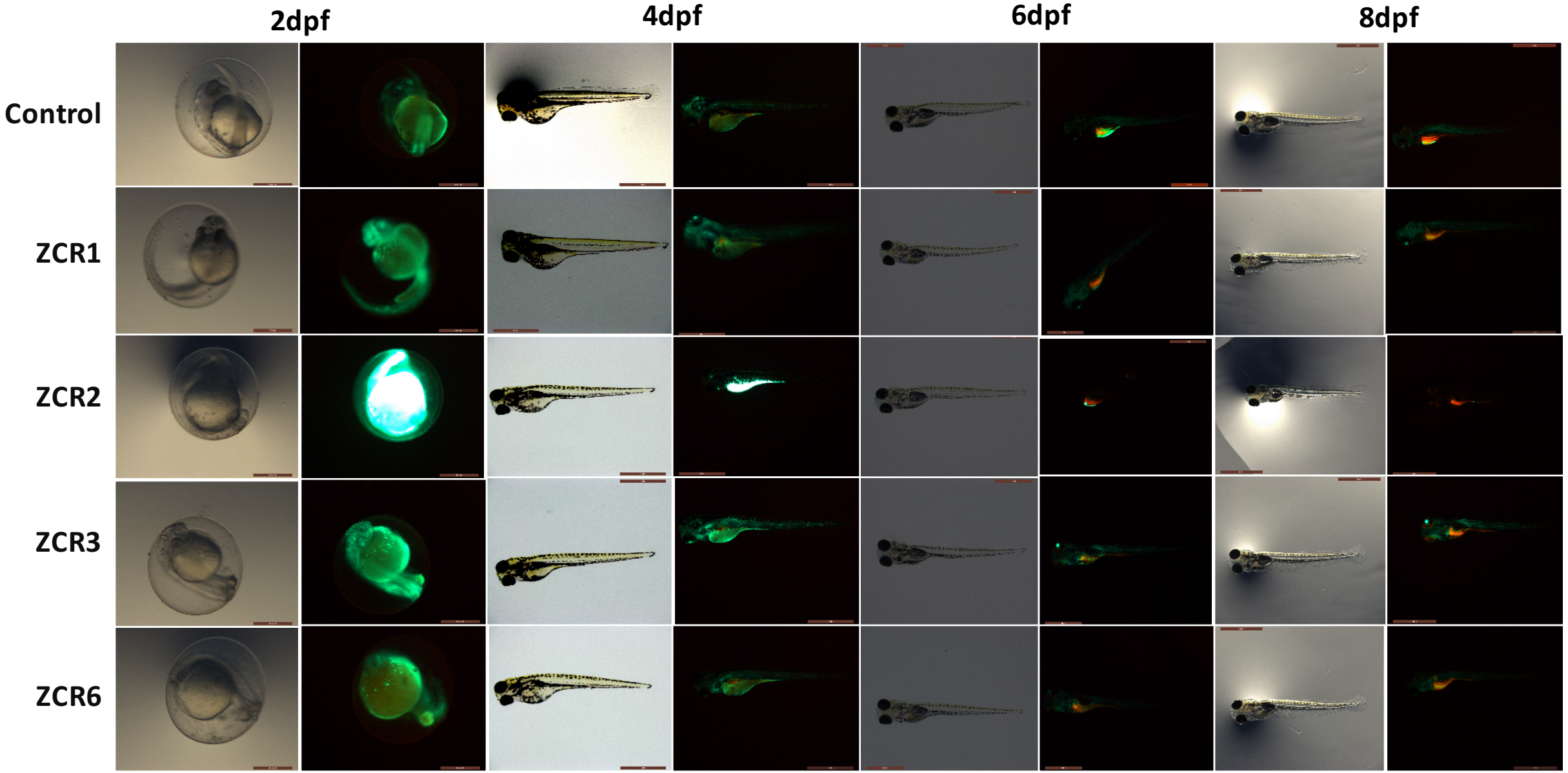




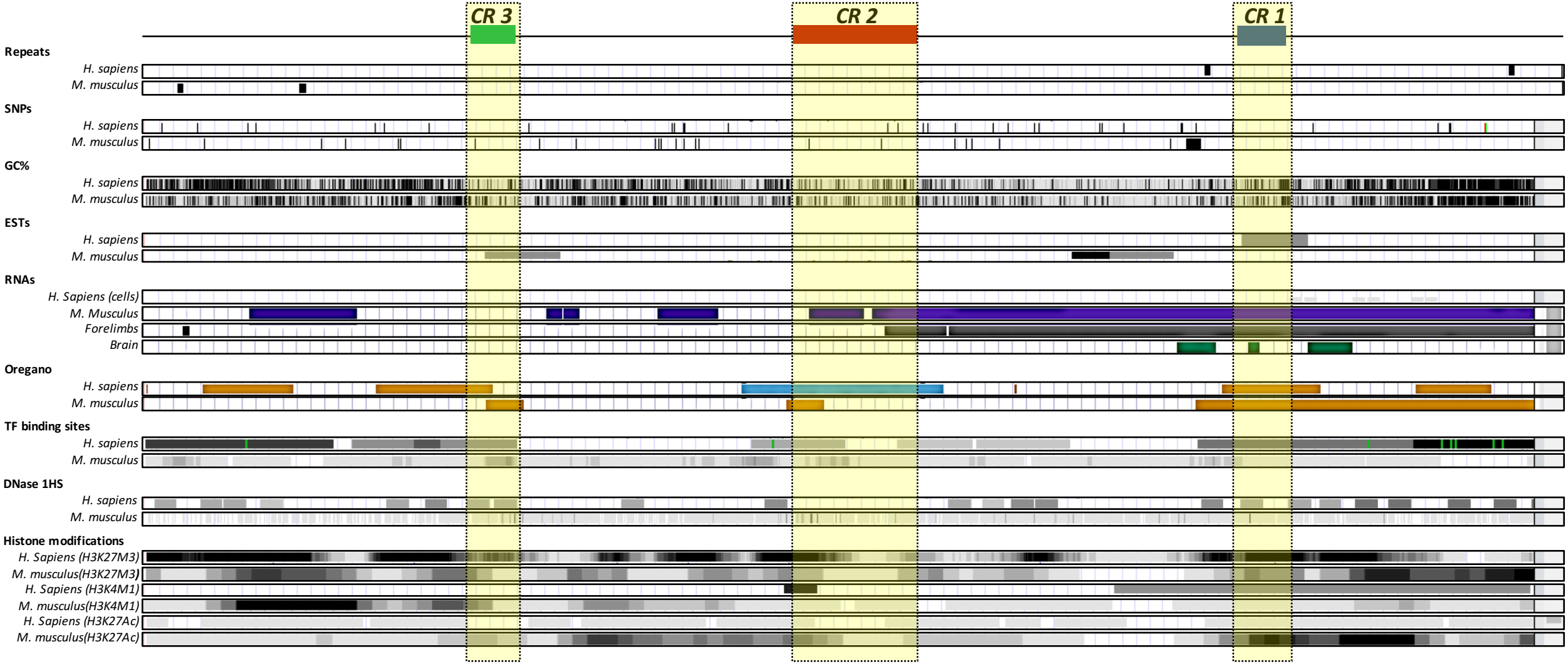




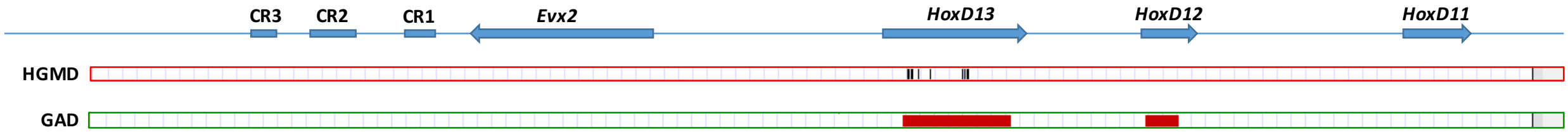
Supplementary figure 3. Colony formation assay: X axis represents different plasmid constructs and Y-axis total number of colonies formed normalized to 100. Data from two different cell lines, mouse embryonic stem cells (JM-8, R-1), IMR32, and HeLa suggest CRs work as repressors. CR2 and CR6 show strong repression activity as compared to CR1 and CR3.



Supplementary figure 4. Reporter assay in zebrafish : Embryos of different stages injected with zebrafish CR constructs are imaged (phase contrast and GFP). Same embryo is followed for for up to 8 dpf in each row. CR2 shows a high level of GFP at 2dpf which reduces drastically after 4dpf. CR1,3 & 6 show comparable GFP levels as in the case of control even after 8dpf.



Supplementary figure 5. Bioinformatics analysis of CRs: Repeats, SNPs and GC percentage show comparatively low distribution across different CRs in both human and mouse. Presence of ESTs and other RNAs from different tissues are seen from this region. Oregano (open regulatory annotation) predictions and transcription factor binding sites suggest association of this region with regulatory functions. Patterns of different epigenetic marks like DNase hypersensitive sites and histone modifications (H3K27Me3, H3K4Me3 and H3K27Ac), in both human and mouse show an overlap with CRs suggesting functionl relevance, although of unknown kind.



Supplementary figure 6. Bioinformatics analysis of mutations in CRs and associated genes in human: Data from different sources like human genome mutation database (HGMD) and genetic association studies of complex disease and disorders (GAD) suggest no known mutations in CRs. In the case of *HoxD13* and *HoxD12 (GAD),* however, show many mutations, which causes different complex genetic disorders during human development.