



Supplemental Figure S6. SE-associated orthologous genes in vertebrates. (A-D) Venn diagrams show the number of orthologous genes associated with typical enhancers and SEs from zebrafish (green), mouse (blue) and human (purple) in pluripotent state (A), heart (B), intestine (C) and testis (D). Following the same color designation, color-coded tables show the percentage of intersection and difference for each species. The observed differences in overlap between typical enhancers and SEs in the three species and in all cells and tissues analyzed are significant (p -values $< 2.2 \times 10^{-16}$) based on G-tests of independence. (E) H3K27ac ChIP-seq profiles at the *irf2bpl*/*Irf2bpl*/*IRF2BPL* loci in zebrafish, mouse and human pluripotent state (raw H3K27ac tag counts represented on the y-axis). Gene positions are noted along the x-axis. Typical enhancers and SEs are denoted by grey and red bars, respectively. (F) H3K27ac ChIP-seq profiles at the *nkx2.5*/*Nkx2-5*/*NKX2-5* loci in zebrafish, mouse and human heart as shown in (E). (G) H3K27ac ChIP-seq profiles at the *rassf1*/*Rassf1*/*RASSF1* loci in zebrafish, mouse and human intestine as shown in (E). (H) H3K27ac ChIP-seq profiles at the *daxx*/*Daxx* loci in zebrafish and mouse testis as shown in (E). (I) Box plots depicting average sequence conservation of SEs with conserved and non-conserved association to orthologs in the indicated zebrafish, mouse and human cells and tissues. The y-axis shows sequence conservation calculated by PhastCons. The box bounds the interquartile range divided by the median and the notch approximates a 95% confidence interval for the median. Observed significant differences in conservation between SE categories are denoted with an asterisk (p -value $\leq 5.7 \times 10^{-3}$) based on Wilcoxon rank-sum analyses.