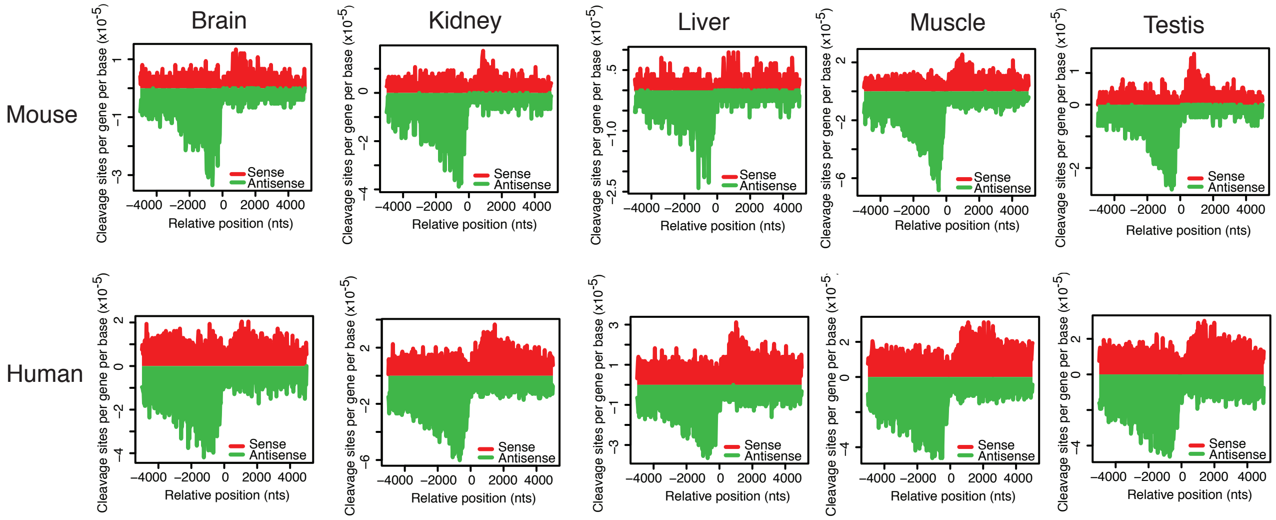

**Supplementary Figure 2. The cleavage bias near gene TSS is conserved in various tissues in mouse and human.** To determine if the bias found in mouse ES cells can be observed in other mouse tissues or another mammalian species, we examined published 3'-end sequencing data. Panels display metagene plots of sense (red) or antisense (green) unique cleavage sites flanking coding gene TSS. The number of unique cleavage sites in each 25 bp bin across 5 kb upstream and downstream of the TSS is plotted and unique cleavage sites within 5 kb of annotated 3'-ends were removed. In all tissues of human and mouse, we observed more upstream antisense cleavage and a promoter proximal antisense peak. Despite different sets of genes being expressed across various tissues and analyzing 3'-end sequencing data generated from another mammalian species, the pattern is consistent with the biased distribution of PAS and U1 sites that is generally encoded in gene sequences.