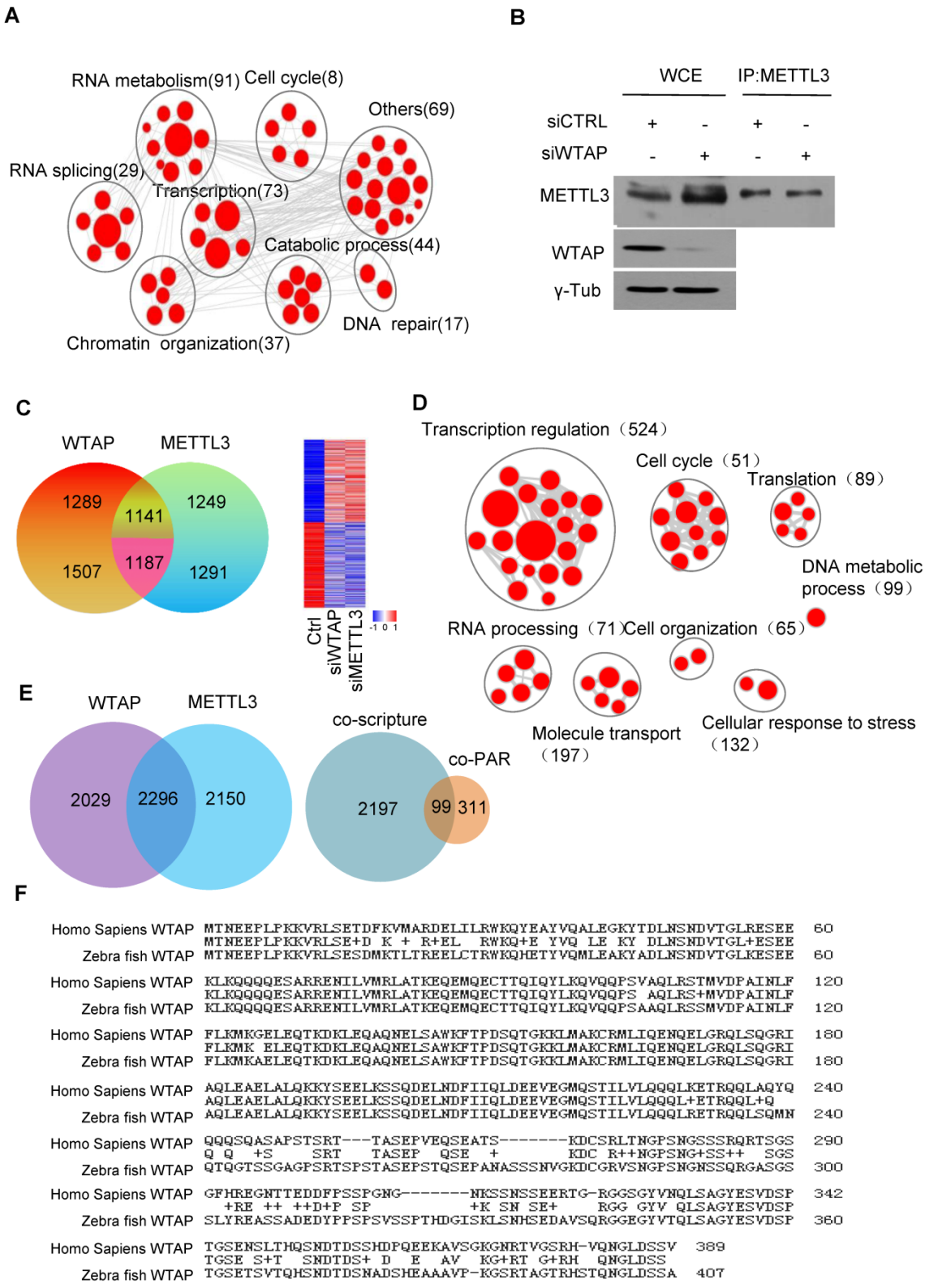

Supplementary information, Figure S5 (Related to Figure 3) METTL3 and WTAP influence gene expression and alternative splicing **(A)** The 410 genes identified in both METTL3 and WTAP PAR-CLIPs were analyzed by GO analysis and an

enrichment map was constructed by Cytoscape (parameters: $p < 0.05$, overlap cutoff > 0.5). **(B)** Western blots showing the immunoprecipitation efficiency related to Figure 3F**. (C)** Venn diagram of the overlapping genes showing differential expression in WTAP and METTL3 knockdown cells. The top value indicates the up-regulated genes while the bottom value indicates the down-regulated genes. Expression profiles of the 2328 overlapping genes (1141 up-regulated; 1187 down-regulated) in the Venn diagram (left) assessed by Heatmap plot generated by R package (right). The colors correspond to log values of genes RPKM in control, WTAP-deficient and METTL3-deficient cells. **(D)** Go analysis of DEGs from WTAP and METTL3 deficient cells visualized in an enrichment map created by Cytoscape (parameters: $p < 0.05$, overlap cutoff > 0.5). **(E)** Both METTL3 and WTAP knockdown resulted in a pronounced variation in isoform number with about half of the variations (2296) present in both WTAP and METTL3 deficient cells (Left). When comparing the 2296 genes with isoform number variation to the 410 bound mRNA species that were present in both WTAP- and METTL3-deficient cells, 99 genes also contained binding clusters for both proteins (Right).(F) Alignment of human WTAP and zebra fish WTAP demonstrated 81% identity.