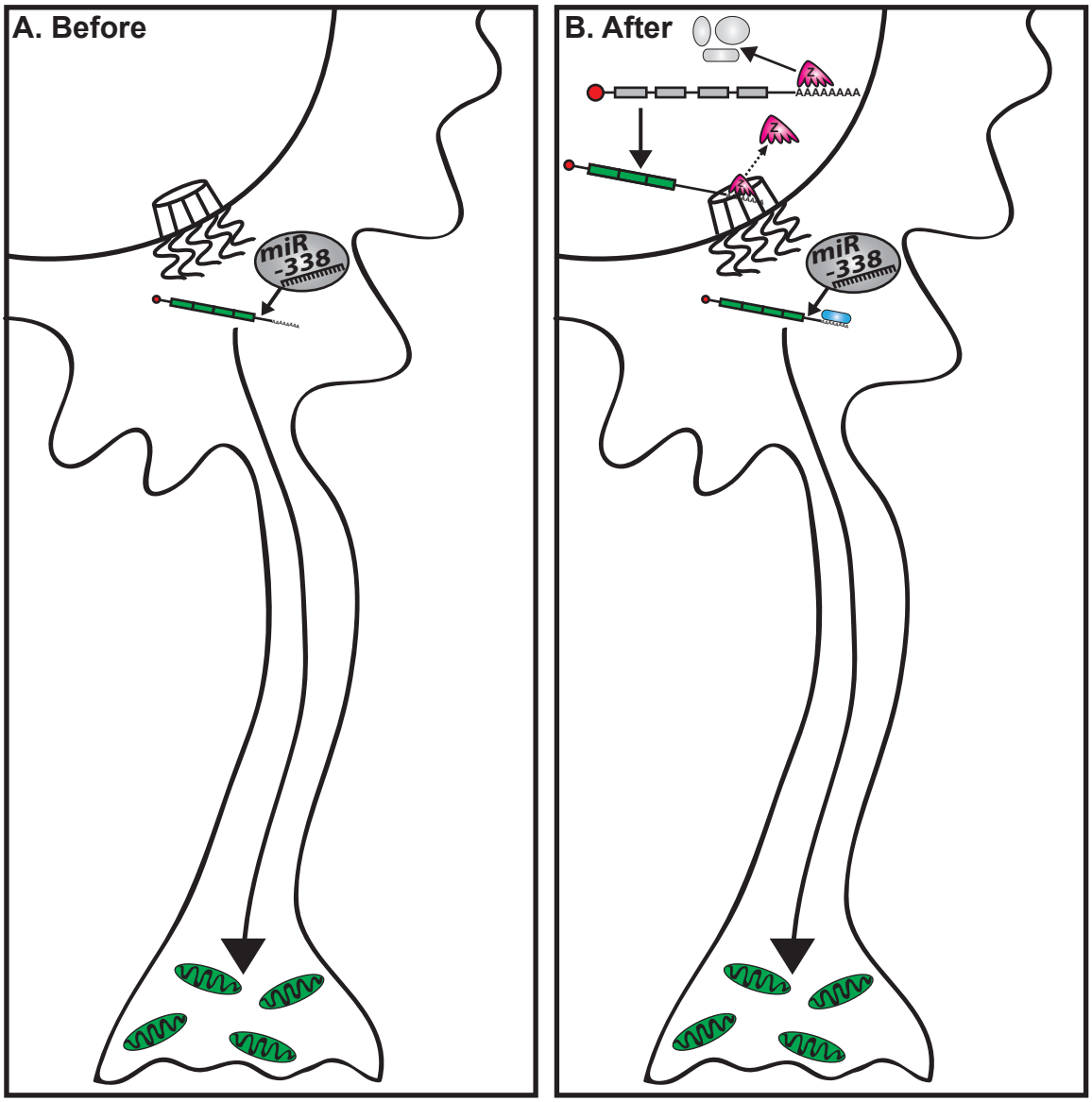

Figure 5.1. Proper *ATP5G1* regulation is critical for neuronal cell function. *A*) Previous studies demonstrate that in rat neurons, the *ATP5G1* 3'UTR is a target of *miR-338* and is trafficked to axonal synapses and locally translated there. Precise regulation of *ATP5G1* in rat neurons promotes axonal outgrowth and proper mitochondrial (green ovals) function. *B*) My work (detailed in Chapter 2) demonstrates that the novel poly(A) binding protein, ZC3H14 (pink, five-fingered shape), promotes and coordinates pre-mRNA processing events (processing factors represented by light grey shapes) critical for the production and export of mature *ATP5G1* mRNA. Loss of ZC3H14 results in improper pre-mRNA processing/export of *ATP5G1*, decreased cellular ATP levels and subsequent mitochondrial fragmentation. Understanding the factors and/or sequences that confer specificity on the *ATP5G1* transcript is a primary objective moving forward.

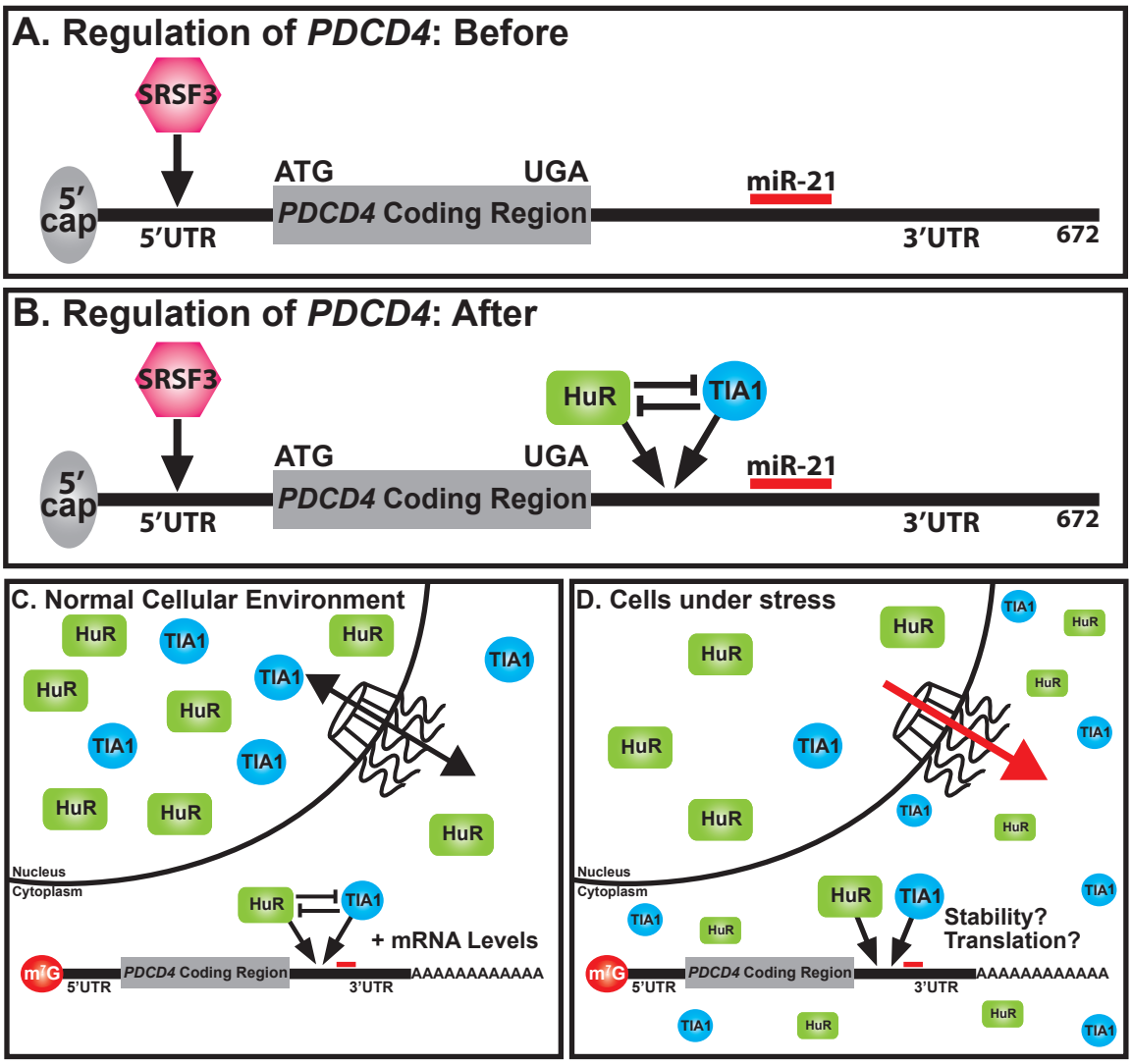

Figure 5.2 *PDCD4* is regulated by multiple post-transcriptional mechanisms. A) Previous studies have extensively characterized the *PDCD4* 3'UTR transcript as a target of the onco*miR-21* (red line). A more recent study demonstrated that the splicing factor SRSF3 (pink hexagon) also modulates *PDCD4* by repressing translation via an interaction with the 5'UTR. *B*) Our work (detailed in Chapter 4) reveals overlapping binding sites for the RNA binding proteins HuR and TIA1 (green rectangle and blue circle, respectively) within a U-rich region of the *PDCD4* 3'UTR, proximal to the well-defined *miR-21* binding site. Our work demonstrates that the overlapping binding sites for these two U-rich binding proteins result in a competitive mode of interaction for the *PDCD4* transcript. *C*) The steady-state localization of HuR and TIA1 is primarily nuclear, although both proteins shuttle in and out of the nucleus (bidirectional arrow). In an unstressed, normal cellular environment, HuR and TIA1 compete for binding to the *PDCD4* 3'UTR, an interaction that promotes the stability of the *PDCD4* transcript. *D*) In a stressful cellular environment, HuR and TIA1 undergo a shift in localization toward the cytoplasm (red arrow). Whether the interactions and functions of HuR and/or TIA1 are altered in these conditions is an important question moving forward.