Atomic structures of kinetoplastid RNA editing sites

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Uridylate (U) insertion/deletion editing in trypanosomes corrects the coding sequence of most mitochondrial mRNAs. The expression of a dozen mitochondrial proteins requires this editing. Several hundred guide RNAs (gRNAs) direct RNA editing. Each gRNA has the sequence complement of a fragment of the final edited mRNA sequence. Our goal is to gain a rigorous description of this type of RNA editing to improve our understanding of its evolutionary basis. The gRNA has an anchor domain, a template domain, and a U-tail. The anchor domain binds its cognate mRNA. The template domain directs the editing reactions. The poly-U tail (i.e., U-tail) domain keeps the cleaved ends of the mRNA close to each other before religation. The U-tail binds the purine-rich unedited mRNA upstream of the editing site. We hypothesize that mismatches between the anchor domain and the mRNA will hinder mRNA editing activity. We predict that mismatches between the U-tail and the mRNA will have less dramatic impacts on mRNA editing. We also hypothesize that mismatches near the editing site can alter RNA editing efficiency. To test these ideas, we made variant gRNA:mRNA pairs and tested their function as editing substrates in vitro. We also relate their structures to editing efficiency.