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Regulation and Function of Kras Gene Expression by Rna Stability from the 5'utr in Kras Mrna.

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G-quadruplexes (G4s) are unique DNA and RNA secondary structures with key regulatory roles. In KRAS, G4s influence gene expression at both transcriptional and translational levels due to their presence in the promoter and untranslated regions (UTRs) of mRNA. Here, we reveal that human KRAS expression is governed by a dual regulatory mechanism involving both DNA G4 and RNA G-quadruplex (rG4) structures. Specifically, G4 elements in the KRAS promoter facilitate transcription factor recruitment, while rG4s in the 5'-untranslated region (5'UTR) of the mRNA modulate stability. ChIP-seq and RIP-seq analyses confirmed the presence of these structures in vivo. CRISPR/Cas9-mediated deletion of the 5'UTR rG4 region significantly increased KRAS mRNA levels, as did point mutations that destabilized rG4s. hnRNPA1, a protein that binds and unfolds rG4s, plays a crucial role in both mechanisms. Using biophysical approaches, we elucidate hnRNPA1's role in regulating KRAS expression. These findings highlight a dual regulatory mechanism: transcriptional control via promoter G4s and post-transcriptional regulation through 5'UTR rG4s and hnRNPA1.