

P014 MicroRNA-mediated translational repression is dependent upon the nuclear history of the message

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MicroRNAs (miRNAs) are non-coding RNAs that base-pair imperfectly to homologous regions in target mRNAs and negatively influence the synthesis of the corresponding proteins. Repression is mediated by a number of mechanisms, one of which is the direct inhibition of protein synthesis. Rather surprisingly, previous studies have suggested that two mutually exclusive mechanisms exist, one acting at the initiation phase of protein synthesis and the other at a post-initiation stage. Here we resolve this apparent dichotomy by demonstrating that the promoter used to transcribe the mRNA influences the type of miRNA-mediated translational repression. Transcripts derived from the SV40 promoter that contain let-7 target sites in their 3' UTRs are repressed at the initiation stage of translation, whereas virtually identical mRNAs derived from the TK promoter are repressed at a post-initiation step. Here we show that there is a miRNA-34c target site within the 3'UTR of *c-myc* mRNA and that promoter dependency is also true for this endogenous 3'UTR. Overall, these data establish a link between the nuclear history of an mRNA and the mechanism of miRNA-mediated translational regulation in the cytoplasm.