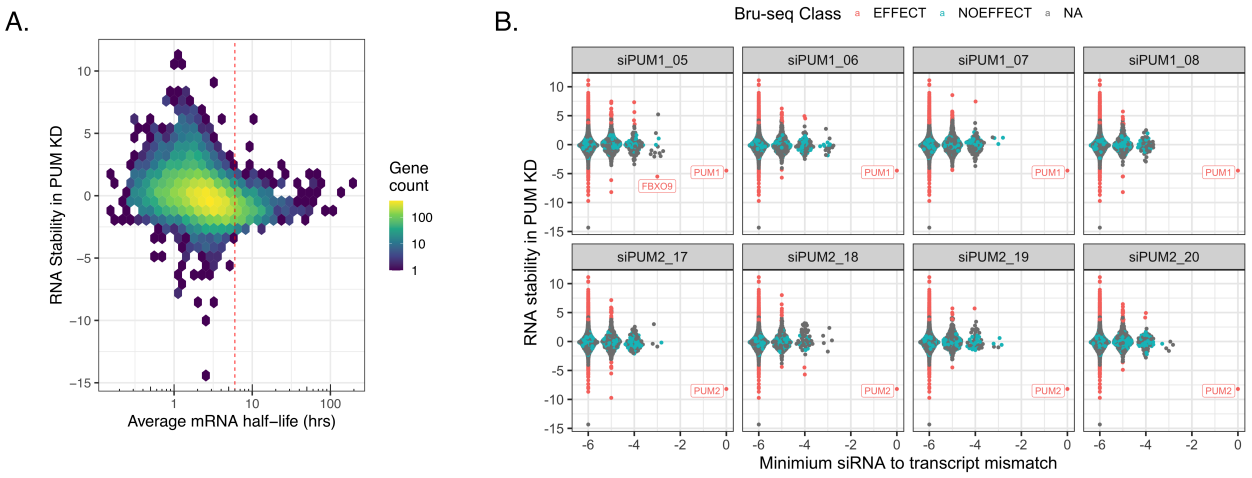

Figure S1: Relationship between PUM-mediated decay and potential confounders. **A)** Relationship between PUM-mediated decay and previously measured mRNA half-lives. mRNA half-lives for HEK293 cells determined using metabolically labeled RNA were obtained from Lugowski et al. [41] using publicly available data at GEO accession number GSE99517. Half-lives calculated using six time-points were averaged over two biological replicates. The red dotted line indicates the six hour time point used in this study. A slight trend is apparent of PUM-destabilized transcripts tending to be those with shorter half-lives, which is to be expected for a set of genes that by definition are actively degraded. In addition, we compared the Bohn et al. [31] RNA abundance data to the Lugowski et al. [41] stability data to determine the fraction of genes that had half-lives shorter than 30 minutes in transcripts previously identified as PUM-degraded, PUM-stabilized, and undetermined using steady-state RNA abundance measurements. Of the genes present in both datasets, we found that the fraction of genes with short half-lives (< 30 minutes) was nearly identical between PUM-stabilized ($5/237 = 0.021$), PUM-degraded ($12/504 = 0.024$) and undetermined ($228/10804 = 0.021$) groups indicating that there is no notable bias in any of these groups towards mRNA half-lives shorter than our initial labeling time. **B)** Relationship between potential off-target siRNA sites and RNA stability in PUM KD. For each siRNA used to knockdown PUM1 and PUM2 in this study the closest match up to five mismatches was determined for each full-length transcript isoform. The minimum number of mismatches over all isoforms was plotted for each gene. Genes for which no match could be found of five mismatches or less are lumped together in the -6 category. Only matches lacking insertions or deletions were considered.