Supplementary Table 1. Comparison of approaches to discover RNA regulatory elements.

Strategy	Implementation	Advantages	Disadvantages	References
Full-length biological sequences	PCR or endogenous half-life measurements	Potential to capture regulatory RNA activity which require long-range interactions	Limited insight on the minimal regulatory element; multiple regulatory elements may be present per sequence whose effects can't be separated	Geisberg, 2014, Wolter, 2015 (3'LIFE)
Random oligonucleotide sequences	Custom synthesis	Unbiased sampling of potential regulatory sequences	Number of possible sequences grows exponentially for longer oligos, making it difficult/inefficient to assay longer regulatory elements	Rosenberg, 2015, Wissink, 2016
Targeted short biological sequences	Custom synthesis	Measuring activity of biological sequence fragments	Labor intensive curation, biased selection of sequences to assay (e.g., using sequence conservation level)	Oikonomou, 2014, Zhao 2014 (fast-UTR), Weingarten-Gabbay, 2016
Randomly fragmented biological sequences	PCR followed by sonication, or pre-built high-throughput sequencing libraries can also be used	Coverage by many partially overlapping random fragments yields high nucleotide resolution of regulatory element position	High nucleotide resolution depends on sufficient depth of sequencing (100X)	**Current study (RESA)**

Supplementary Table 2. Summary of sequencing results.

Condition	Replicate	Experiment	Total read pairs	Aligned read pairs		
				WT	C to T converted	G to A converted
Library Input	1	RESA	3530868	2928926	NA	NA
Early	1	RESA	3494047	2946878	NA	NA
Early	2	RESA	4766081	4020944	NA	NA
Late	1	RESA	5895953	4975343	NA	NA
Late	2	RESA	8845108	7477684	NA	NA
Late	3	RESA	3958477	3346324	NA	NA
430LNA	1	RESA	9489219	8013334	NA	NA
430LNA	2	RESA	8640935	7325241	NA	NA
430LNA	3	RESA	11840412	10020842	NA	NA
Early	1	RESA-Bisulfite	13487785	36351	2295038	7906741
Early	2	RESA-Bisulfite	11984468	31996	2195578	6866070
Early	3	RESA-Bisulfite	14991744	42034	2733234	8616533
Late	1	RESA-Bisulfite	4166676	11298	724906	2426895
Late	2	RESA-Bisulfite	7302088	19730	1243021	4278012
Late	3	RESA-Bisulfite	7412900	19946	1250178	4355579
Ago2	1	RESA-CLIP	61467344	47754369	NA	NA
CLIP Input	1	CLIP-Input	64900157	52860980	NA	NA

Each entry lists an independent biological sample. Total read pairs are reported, where each pair equals two sequencing reads (read 1 and read 2). Alignment count is with respect to concordantly aligned read pairs. For bisulfite-converted reads, alignment totals are reported separately for the two different converted genomes.

Supplementary Table 3. Summary of miR-430 target sequences across the UTR library.

	Within RESA destabilized region					
	miR-430 dependent	Non miR-430 dependent	Low confidence region	Poly-morphic seed	Low Seq coverage	No destabilization detected
8-mers	13	0	1	0	0	0 (0%)
7-mers	38	2	1	0	2	1 (2%)
6-mers	93	9	22	2	8	25 (16%)
Offset 6-mers	40	5	25	7	15	49 (35%)

miR-430 target seed sequences (8-mer, 7-mer, 6-mer and offset 6-mer matches) are enumerated across the 3'UTRs using the Zv9 reference genome sequence. For each category, a seed may fall within a RESA destabilized region (assigned to the miR-430 dependent, non miR-430 dependent, or low-confidence destabilized categories). Otherwise, a seed sequence may have nucleotide polymorphisms compared to the reference genome (affecting target complementarity) or low sequencing read coverage (<100X at early stage).