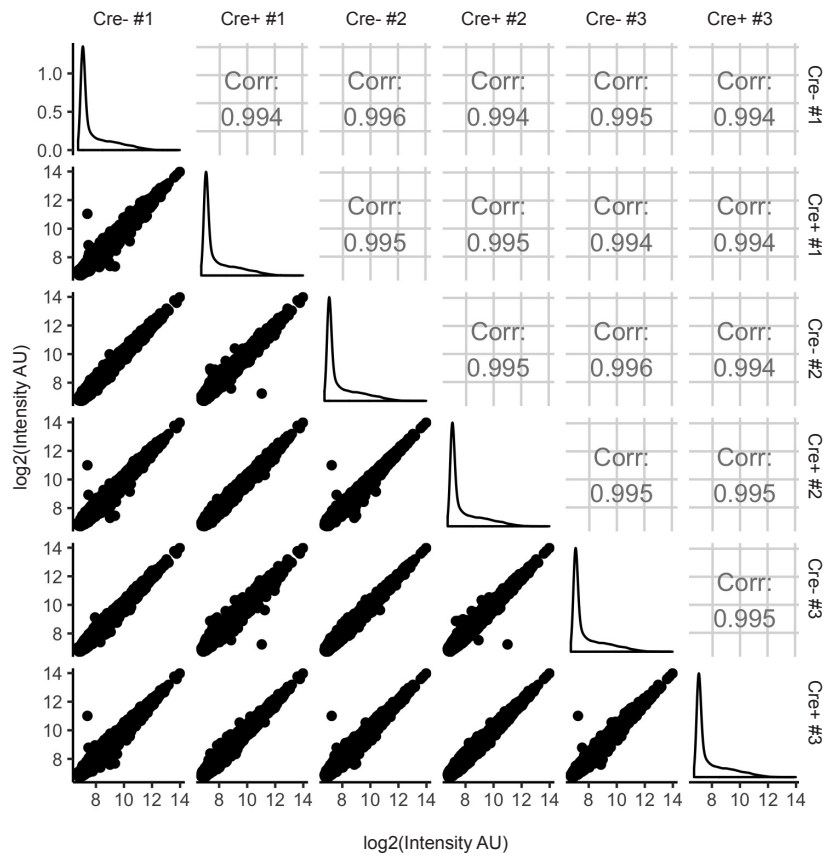


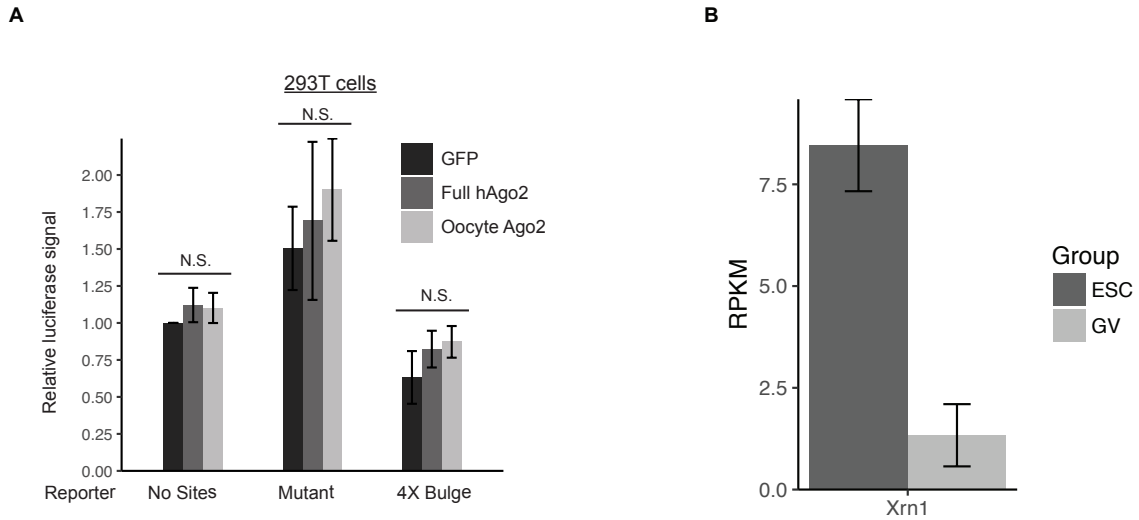
**Figure S2 – Characterization of Oocyte-specific Ago2 isoform. Related to Figure 2.**

A) qRT-PCR with primers spanning exons in full length or oocyte specific AGO2. Data is  $\Delta$ Ct in embryonic stem cells and GV oocytes relative to primers spanning exon 13/14. Embryonic stem cell N=2, oocyte N=3. ND = Not detected. Asterisks (\*) represent significantly different data from the corresponding ‘ESC’ control data (Student’s T-test,  $p < 0.05$ ). Luciferase assays in (B) Xenopus GV oocytes or (C) mouse GV oocytes following injection of miR-15a mimic, reporter lacking target sites, plus and minus wild-type AGO2 mRNA. N=10 for B, N=2 for C. D) RT-qPCR for Renilla 4x Bulge and Firefly in either control (WT or LSL-GFP-myc-hAgo2/+; Zp3-Cre-) or AGO2 overexpressing (injected with AGO2 mRNA or LSL-GFP-myc-hAGO2/+; Zp3-Cre+) mouse GV oocytes along with miR-15a mimic. Dots represent biological replicates. N=4. All error bars represent standard deviation. N.S. = not significant.



**Figure S3 – Correlations between arrays. Related to Figure 3.**

A) Log2 quantile normalized intensity values between replicates of LSL-GFP-myc-hAGO2/LSL-GFP-myc-hAGO2; Zp3-Cre+ and Zp3-Cre- mouse GV oocytes injected with miR-15a mimic.



**Figure S4 – Evaluation of additional potential mechanisms that impact miRNA activity. Related to Figure 4.**  
 A) Luciferase assay in HEK-293T cells transfected with psiCHECK2, a vector containing Firefly luciferase and Renilla luciferase with either no let-7 sites, mutated sites, or 4X Bulge sites in the 3' UTR for Renilla luciferase. psiCHECK2 was co-transfected with either GFP, full length hAGO2, or truncated oocyte AGO2. Luciferase data is a ratio of Renilla signal over Firefly signal. Full and truncated AGO2 is not significantly different from GFP control in all cases. All error bars represent standard deviation. N.S. = not significant. B) RNA-Seq expression of Xrn1 in mouse embryonic stem cells and mouse GV oocytes.

Let7Perfect Sense	TCGAATAAACTATACAACCTACTACCTCC
Let7Perfect Anti	GGCCGGAGGTAGTAGGTTGTATAGTTTAT
Let7Bulge Sense1	TCGAATAAACTATACACATACTACCTCCGATACTATACACATACTA CCTCACGCGT
Let7Bulge Sense2	ACTATACACATACTACCTCTCACACTATACACATACTACCTCC
Let7Bulge Anti1	GGCCGGAGGTAGTATGTGTATAGTGTGAGAGGTAGTATGTGTATA GTACGCGT
Let7Bulge Anti2	GAGGTAGTATGTGTATAGTATCGGAGGTAGTATGTGTATAGTTTAT
Let7Mutant Sense1	TCGAATAAACTATACACATAATCCATCCGATACTATACACATAATC CATCACGCGT
Let7Mutant Sense2	ACTATACACATAATCCATCTCACACTATACACATAATCCATCC
Let7Mutant Anti1	GGCCGGATGGATTATGTGTATAGTGTGAGATGGATTATGTGTATAG TACGCGT
Let7Mutant Anti2	GATGGATTATGTGTATAGTATCGGATGGATTATGTGTATAGTTTAT
miR15Perfect Sense	TCGAATAACACAAACCATTATGTGCTGCTAC
miR15Perfect Anti	GGCCGTAGCAGCACATAATGGTTTGTGTTAT
miR15Bulge Sense1	TCGAATAAcacaaacctCAgtgctgctaCGATcacaaacctCAgtgctgctaACGCGT
miR15Bulge Sense2	cacaaacctCAgtgctgctaTCACcacaaacctCAgtgctgctaC
miR15Bulge Anti1	GGCCGTAGCAGCACTGATGGTTTGTGGTGATAGCAGCACTGATGGT TTGTGACGCGT
miR15Bulge Anti2	TAGCAGCACTGATGGTTTGTGATCGTAGCAGCACTGATGGTTTGTG TTAT
miR15Mutant Sense1	TCGAATAACACAAACCATCAGTTCGGATACGATCACAAACCATCA GTTCCGATAACGCGT
miR15Mutant Sense2	CACAAACCATCAGTTCGGATATCACCACAAACCATCAGTTCGGATA C
miR15Mutant Anti1	GGCCGTATCCGAACTGATGGTTTGTGGTGATATCCGAACTGATGGT TTGTGACGCGT
miR15Mutant Anti2	TATCCGAACTGATGGTTTGTGATCGTATCCGAACTGATGGTTTGTG TTAT

Rosa26 Ago2 common genotyping	CCAAAGTCGCTCTGAGTTGTTATC
Rosa26 Ago2 WT RVS genotyping	GAGCGGGAGAAAATGGATATG
Rosa26 Ago2 MUT RVS genotyping	CGGGCCATTTACCGTAAG
Cre genotyping FWD genotyping	tggcgcatggtgcaagt
Cre genotyping RVS genotyping	cggctgaaccagcttttc
Il2 genotyping FWD genotyping	ctagccacagaattgaaagatct
Il2 genotyping RVS genotyping	gtagtggaattctagcatcatcc
RPL7 qPCR FWD	gattgtggagccatacattgca
RPL7 qPCR RVS	tgccgtagcctcgttct
mouse human Ago2 qPCR FWD	ctcacctggtggccttc
mouse human Ago2 qPCR RVS	agaggtatggcttcctcagc
Oocyte Exon 1 - Exon 2	AGAATCCTTCCTGCCTTCCTTC
Oocyte Exon 1 - Exon 2	TTGAAGGCATATCCTGGGATGG
WT Exon 2 - Exon 3	GGACATCAAACCTGAGAAATGCC
WT Exon 2 - Exon 3	TCCATCAAACACTGGCTTCC
Oocyte Exon 3 - Exon 4	TACACAGCAATGCCCCTTCC
Oocyte Exon 3 - Exon 4	CAGTTCATGCTTCTGCTCTTGC
WT Exon 1 - Exon 2	GCAACGCCACCATGTACTC
WT Exon 1 - Exon 2	TTGAAGGCATATCCTGGGATGG
WT Exon 3 - Exon 4	AGCCAGTGTTTGATGGAAGG
WT Exon 3 - Exon 4	ATGCGATCTTTGCCTTCTCC
WT Exon 8 - Exon 9	cagacaatcagacctcaacctg
WT Exon 8 - Exon 9	cacttcgcatcagtttgctg

WT Exon 13 - Exon 14	acagaccctatccaatctctgc
WT Exon 13 - Exon 14	atgacagggtgctggaacac
Renilla qPCR FWD	ACGCAAACGCATGATCACTG
Renilla qPCR RVS	GCAGAAAAATCACGGCGTTC
Firefly qPCR FWD	CGTGCCAGAGTCTTTCGACA
Firefly qPCR RVS	ACAGGCGGTGCGATGAG

**Table S1: Oligonucleotides used in this study. Related to STAR Methods.**