

Title: Dengue virus infection alters post-transcriptional modification of microRNAs in the mosquito vector *Aedes aegypti*

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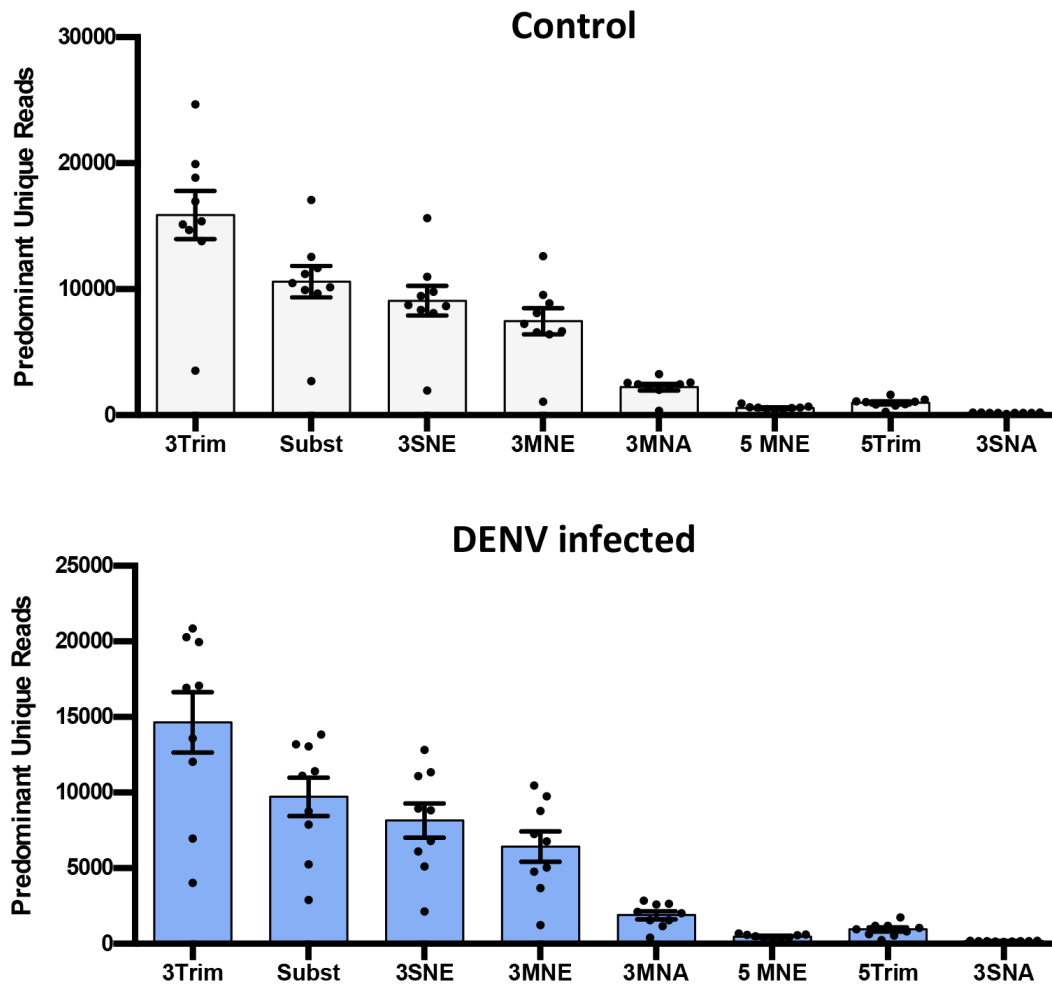


Figure S1. Different isomiR prevalence across DENV infected and non infected. Comparison of the proportion of unique reads for each type of isomiR for infected and non-infected mosquitoes (averaged across three time point and three biological replicates). Unique sequences with 3' modification were more abundant than 5' trimmed or extended sequences in all *Ae. aegypti* small RNA libraries. There were no considerable differences among all libraries (DenDf=124, P value= 0.07). 3SNE: 3' single nucleotide extension, 3MNE: 3' multiple nucleotide extension, 3Trim: 3' trimmed, 5MNE: 5' extension, 5Trim: 5' trimmed, Subst: nucleotide substitutions, 3SNA: 3' single nucleotide addition, 3MNA: 3' multiple nucleotide addition.

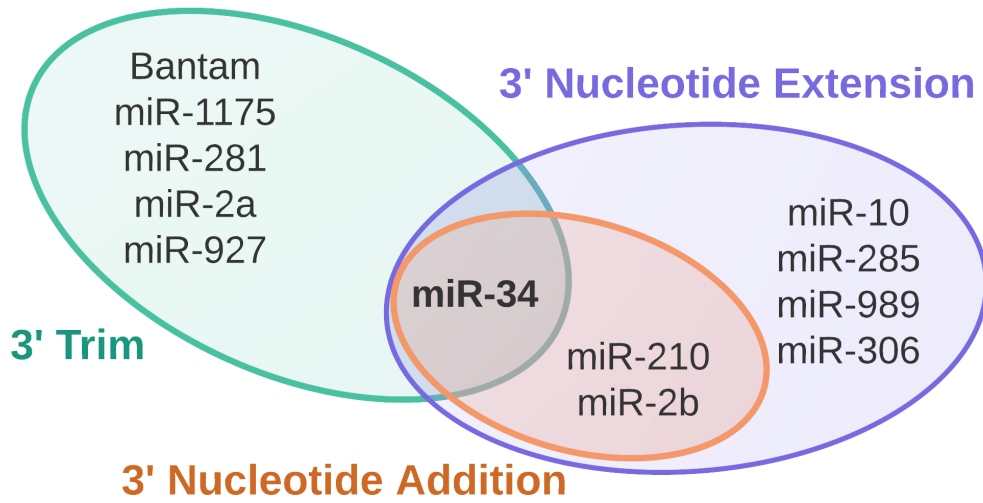


Figure S2. Venn diagram represent overlapped miRNAs with significant altered 3' isomiRs due to DENV infection. miR-34 is the only miRNA whose all 3' end modified isomiRs significantly altered by DENV infection ($P < 0.05$).



Figure S3. Schematic representation of two examples of arm-switching event. This figure displays schematically the area from which the most abundant isomiR read originates from within its precursor for both miRNAs (A) aae-mir-1000 and (B) aae-miR-305 in uninfected and DENV-infected treatments. Shifting of mature miRNA occurred in miR-1000 after infection and an arm-switching event happened in miR-305. The highly expressed miRNA was detected in 5p arm of the control group, which switched to 3p arm in infected mosquitoes (B).

A	Control day 2	B	Infected day 2
	AUGACU CUUGUGCGUGUGACAACGG CUAUUG 23908.0 0-0		ACU CUUGUGCGUGUGACAACGG CUAUUG 14493.0 0-
	.)))..)))))...))..))...))...))....		.)))))...))..))...))...))....
	CUUGUGCGUGUGACAACGG CUAU 5527.0 +		CUUGUGCGUGUGACAACGG CUAU 3267.0 +
	CUUGUGCGUGUGACAACGG CUAU 1910.0 +		CUUGUGCGUGUGACAACGG CUAU 907.0 +
	CUUGUGCGUGUGACAACGG CUAU 1481.0 +		CUUGUGCGUGUGACAACGG CUAU 735.0 +
	UUGUGCGUGUGACAACGG CUAU 994.0 +		CUUGUGCGUGUGACAACGG CU 468.0 +
	UUGUGCGUGUGACAACGG CUAU 476.0 +		UUGUGCGUGUGACAACGG CUAU 416.0 +
	CUUGUGCGUGUGACAACGG CUAU 448.0 +		CUUGUGCGUGUGACAACGG CUAU 254.0 +
	CUUGUGCGUGUGACAACGG CAAU 432.0 +		CUUGUGCGUGUGACAACGG CUAC 226.0 +
	CUUGUGCGUGUGACAACGG CU 379.0 +		CUUGUGCGUGUGACAACGG CUAU 217.0 +
	CUUGUGCGUGUGACAACGG CUAC 275.0 +		CUUGUGCGUGUGACAACGG CAAU 176.0 +
	CUUGUGCGUGUGACAACGG CUAU 266.0 +		UUGUGCGUGUGACAACGG CUAU 168.0 +
	CUUGUGCGUGUGACAACGG CUAUA 250.0 +		CUUGUGCGUGUGACAACGG CUAU 168.0 +
	UUGUGCGUGUGACAACGG CUAU 249.0 +		CUUGUGCGUGUGACAACGG CU 139.0 +
	CUUGUGCGUGUGACAACGG CUAU 234.0 +		CUUGUGCGUGUGACAACGG CUAUA 123.0 +
	CUUGUGCGUGUGACAACGG CU 221.0 +		UUGUGCGUGUGACAACGG CUAU 120.0 +
	CUUGUGCGUGUGACAACGG CUA 162.0 +		CUUGUGCGUGUGACAACGG CU 105.0 +
	CUUGUGCGUGUGACAACGG CUAU 160.0 +		CUUGUGCGUGUGACAACGG CC 92.0 +
	CUUGUGCGUGUGACAACGG AU 156.0 +		CUUGUGCGUGUGACAACGG CCAU 89.0 +
	CUUGUGCGUGUGACAACGG CUAUC 150.0 +		CUUGUGCGUGUGACAACGG CUAU 85.0 +
	CUUGUGCGUGUGACAACGG CU 121.0 +		CUUGUGCGUGUGACAACGG AU 81.0 +
	CUUGUGCGUGUGACAACGG CUAUG 119.0 +		CUUGUGCGUGUGACAACGG CUAUC 81.0 +
	CUUGUGCGUGUGACAACGG CUAUA 117.0 +		CUUGUGCGUGUGACAACGG CUA 80.0 +
	CUUGUGCGUGUGACAACGG CUAU 115.0 +		CUUGUGCGUGUGACAACGG CUA 78.0 +
	CUUGUGCGUGUGACAACGG CCAU 110.0 +		CUUGUGCGUGUGACAACGG CUAUG 78.0 +
	CUUGUGCGUGUGACAACGG AU 110.0 +		CUUGUGCGUGUGACAACGG CCAU 77.0 +
	CUUGUGCGUGUGACAACGG CAAU 104.0 +		CUUGUGCGUGUGACAACGG CUAU 72.0 +
	CUUGUGCGUGUGACAACGG CU 104.0 +		CUUGUGCGUGUGACAACGG C 70.0 +
	CUUGUGCGUGUGACAACGG CC 101.0 +		CUUGUGCGUGUGACAACGG CUAU 70.0 +
	CUUGUGCGUGUGACAACGG ACU 100.0 +		CUUGUGCGUGUGACAACGG ACU 67.0 +
	CUUGUGCGUGUGACAACGG CAAU 94.0 +		CUUGUGCGUGUGACAACGG AU 61.0 +
	CUUGUGCGUGUGACAACGG CUA 91.0 +		CUUGUGCGUGUGACAACGG CUAGU 60.0 +
	CUUGUGCGUGUGACAACGG CUAC 79.0 +		CUUGUGCGUGUGACAACGG CUAUA 58.0 +
	CUUGUGCGUGUGACAACGG UAU 79.0 +		CUUGUGCGUGUGACAACGG CUACU 57.0 +
	CUUGUGCGUGUGACAACGG CUAU 79.0 +		CUUGUGCGUGUGACAACGG UAU 55.0 +
	CUUGUGCGUGUGACAACGG CAUA 78.0 +		CUUGUGCGUGUGACAACGG GCU 55.0 +
	CUUGUGCGUGUGACAACGG CUA 76.0 +		CUUGUGCGUGUGACAACGG ACUAC 54.0 +
	CUUGUGCGUGUGACAACGG UUAU 75.0 +		CUUGUGCGUGUGACAACGG CUAUG 50.0 +
	CUUGUGCGUGUGACAACGG CUACU 75.0 +		CUUGUGCGUGUGACAACGG CUA 49.0 +
	CUUGUGCGUGUGACAACGG UAGCG 75.0 +		CUUGUGCGUGUGACAACGG CUAU 48.0 +
	CUUGUGCGUGUGACAACGG CU 74.0 +		CUUGUGCGUGUGACAACGG CAAU 47.0 +
	CUUGUGCGUGUGACAACGG CUAC 73.0 +		CUUGUGCGUGUGACAACGG CUAUAU 46.0 +
	UUGUGCGUGUGACAACGG CAAU 71.0 +		CUUGUGCGUGUGACAACGG CAAU 46.0 +
	CUUGUGCGUGUGACAACGG CUAU 70.0 +		CUUGUGCGUGUGACAACGG CUAC 45.0 +
	UUGUGCGUGUGACAACGG CUAU 70.0 +		CUUGUGCGUGUGACAACGG CCAU 45.0 +
	CUUGUGCGUGUGACAACGG CUAG 66.0 +		CUUGUGCGUGUGACAACGG CUAG 45.0 +
	CUUGUGCGUGUGACAACGG CUAC 66.0 +		CUUGUGCGUGUGACAACGG CUACU 45.0 +
	CUUGUGCGUGUGACAACGG GAUA 63.0 +		CUUGUGCGUGUGACAACGG 45.0 + M
	CUUGUGCGUGUGACAACGG CCAU 62.0 +		
	CUUGUGCGUGUGACAACGG CUAGU 62.0 +		
	UUGUGCGUGUGACAACGG CUAC 58.0 +		
	CUUGUGCGUGUGACAACGG CUA 57.0 +		
	CUUGUGCGUGUGACAACGG CUA 57.0 +		
	CUUGUGCGUGUGACAACGG CUA 56.0 +		
	CUUGUGCGUGUGACAACGG CAAU 55.0 +		
	CUUGUGCGUGUGACAACGG CUAUAU 54.0 +		
	UUGUGCGUGUGACAACGG CUAUA 53.0 +		
	CUUGUGCGUGUGACAACGG CCAU 52.0 +		
	UUGUGCGUGUGACAACGG CUAU 52.0 +		
	CUUGUGCGUGUGACAACGG C 50.0 +		
	CUUGUGCGUGUGACAACGG CUA 50.0 +		
	CUUGUGCGUGUGACAACGG CUAUG 49.0 +		
	CUUGUGCGUGUGACAACGG 49.0 + M Canonical miR-210		

Figure S4. Changes in the number of unique reads produced by miR-210 in infected and control groups. Highlighted in yellow are all those sequences which matched the exact miR-210 as annotated in miRBase. (A) IsomiRs expressed more highly than the canonical miR-210 in the control group. (B) The DENV-infected group exhibited a reduced number of unique reads.

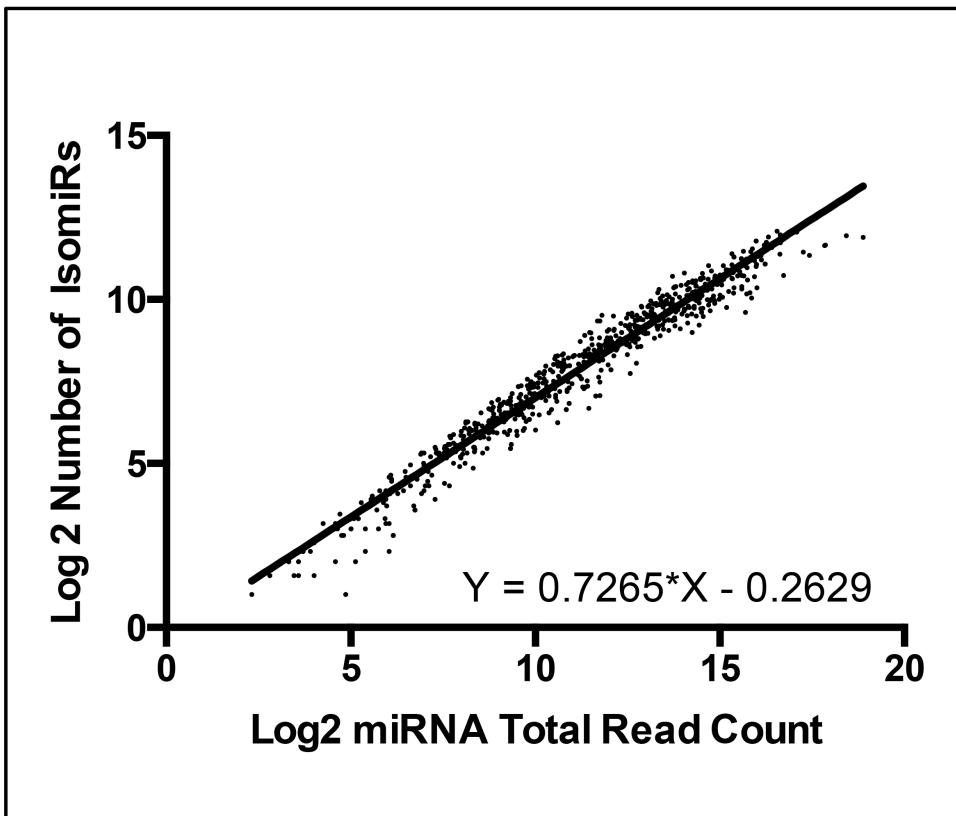


Figure S5. The linear relationship between miRNA expression and isomiR production. The graph depicts the relationship between the read count of miRNAs and the total number of unique reads or isomiRs produced by those miRNAs. For more highly expressed miRNAs, a greater number of unique reads were generated.