**Library Preparation and Sequencing**
miRNA sequencing library was prepared using the QIASeq™ miRNA Library Kit (Qiagen, Hilden, Germany). Total RNA was used as the starting material. A preadenylated DNA adapter was ligated to the 3’ ends of miRNAs, followed by ligation of an RNA adapter to the 5’ end. A reverse-transcription primer containing an integrated Unique Molecular Index (UMI) was used to convert the 3’/5’ ligated miRNAs into cDNA. After cDNA cleanup, indexed sequencing libraries were generated via sample indexing during library amplification, followed by library cleanup. Libraries were sequenced on a NextSeq 500 (Illumina, San Diego, CA) with a 1x75 bp read length and an average sequencing depth of ~10M reads/sample.

**Data Analysis**
The demultiplexed raw reads were uploaded to GeneGlobe Data Analysis Center (Qiagen) at [https://www.qiagen.com/us/resources/geneglobe/](https://www.qiagen.com/us/resources/geneglobe/), for quality control, alignment and expression quantification. Briefly, 3’ adapter and low quality bases are trimmed off from reads first using cutadapt (version 1.13) with default settings, then reads with less than 16bp insert sequences or with less than 10bp UMI sequences are discarded. The remaining reads were collapsed to UMI counts and aligned to miRBase (release v21) mature and hairpin databases sequentially using Bowtie v1.2 (Langmead et al., 2009). The UMI counts of each miRNA molecule are counted and the expression of miRNAs are normalized based on total UMI counts for each sample.

**References**