A comprehensive overview of miRNA-like RNAs in RNA viruses

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Current state in RNA viruses

Currently there are roughly 500 mature miRNA sequences distributed to 30 different viruses uploaded in the miRBase database [1]. From these 500 sequences only 18 sequences are distributed to three RNA viruses: bovine leukemia virus, bovine foamy virus and HIV1.

However, none of the 18 sequences are validated with a high confidence. Most of them are not associated with a function within the host cell. Therefore, more studies related to function analysis are needed.

miRNAs in DNA viruses

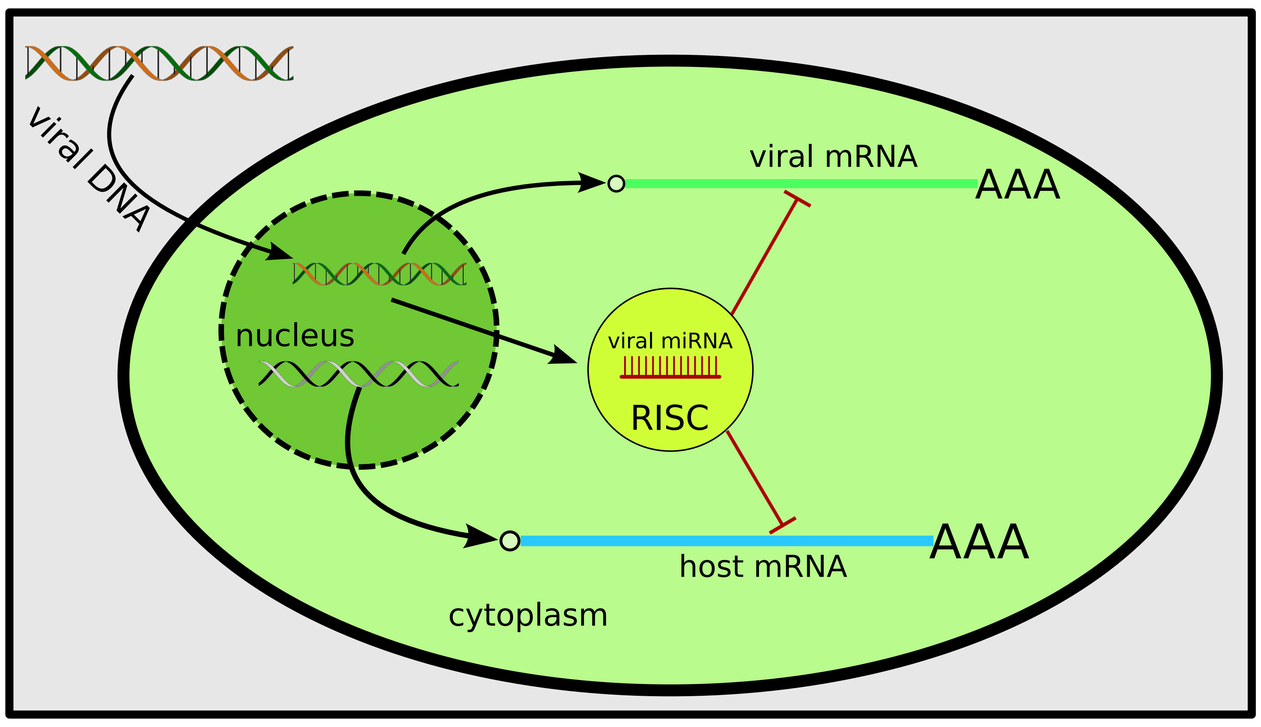

Figure 1: DNA viruses are able to inject their genome into the nucleus of the host cell. From there, viral mRNA and viral miRNA are processed using the mechanisms and proteins of the host. The matured viral miRNA inhibits both viral and host mRNA. These inhibitions are known to interact with the immune system of the host cell, suppress the viral replication and regulate viral and host genes. Figure adapted from [2].

RNA viruses and miRNAs

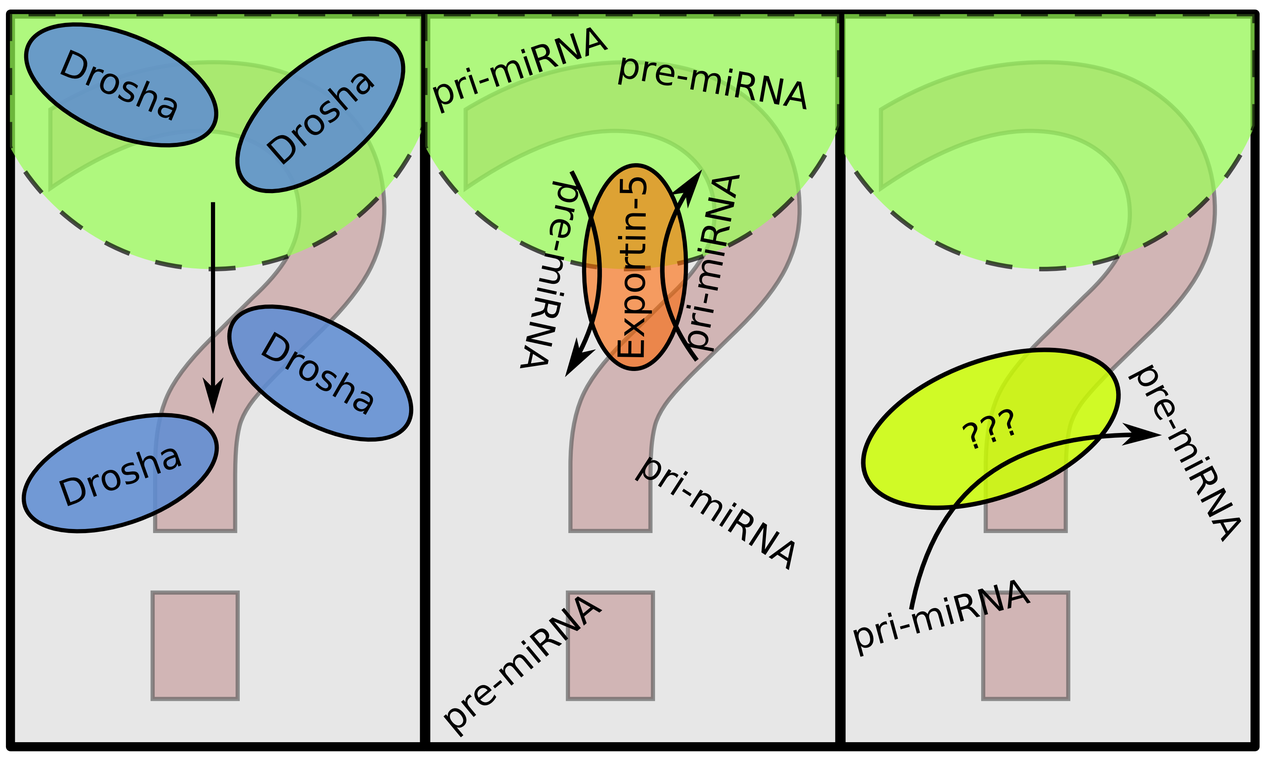

Figure 2: RNA viruses are shown to be able to induce pri-miRNAs in the host cell that are processed to mature miRNA [3]. However, there is no complete understanding how the pri-miRNA is processed to the precursor miRNA, as the genome of RNA viruses is not injected into the nucleus of the host. There are different hypotheses that have to be validated.

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Finding novel candidates

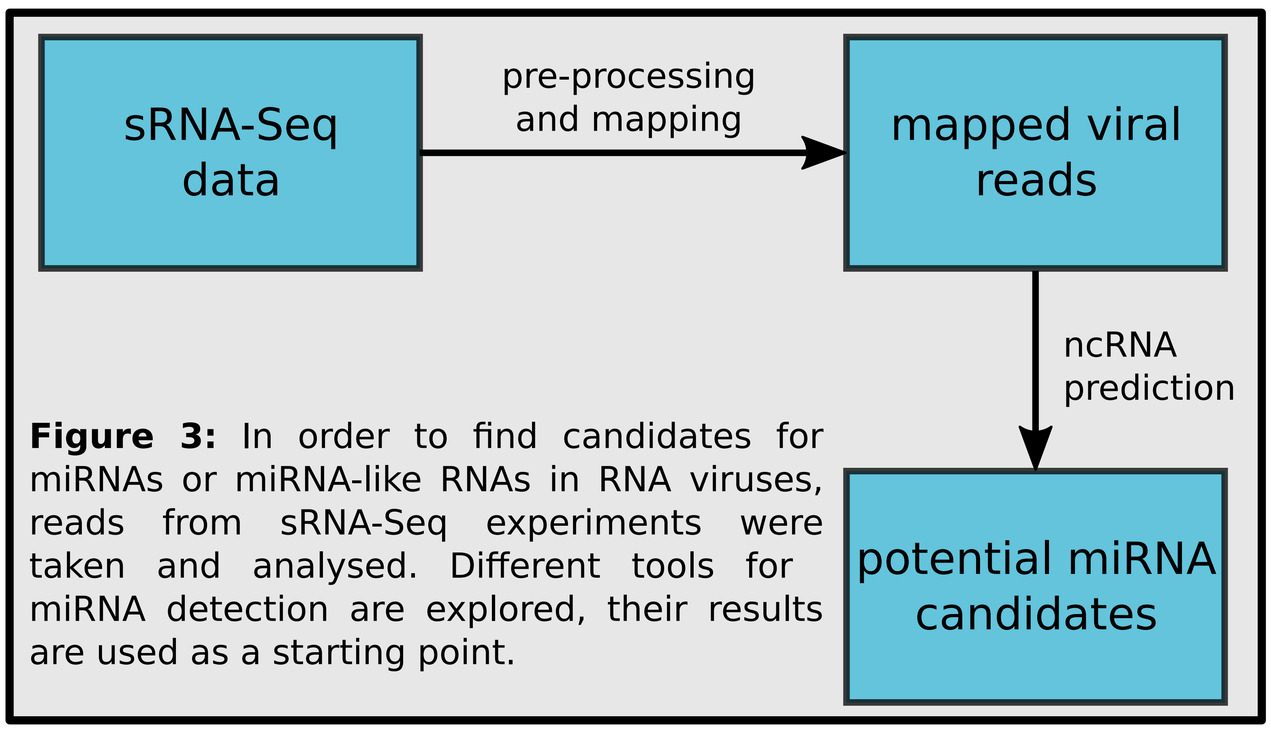

Figure 3: In order to find candidates for miRNAs or miRNA-like RNAs in RNA viruses, reads from sRNA-Seq experiments were taken and analysed. Different tools for miRNA detection are explored, their results are used as a starting point.

Prediction tools and first results

Table 1: Overview of tested miRNA and small ncRNA prediction tools divided by sequence-based and alignment-based analysis. Sequence-based methods usually use machine-learning techniques, whereas alignment-based methods require reference genomes or annotation files.

Tool	Method	Results
HHMMiR	sequence	√
miReader	sequence	x
novoMIR	sequence	x
RNA-Code	sequence	x
Triplet-SVM	sequence	x
BlockClust	alignment	√
CoRAL	alignment	x
miRDeep2	alignment	√
miRspring	alignment	x

Conclusion

Several miRNAs encoded by DNA viruses are described. They are known to regulate both viral and host genes.
First studies indicate RNA viruses being capable of transferring pri-miRNA into the host cell which are processed to mature miRNAs. However, the first processing step that results in pre-miRNA is not understood yet.
We will develop a virus-specific prediction tool leading to the identification of potential (pre-)miRNA candidates in RNA viruses. For this, we aim to adapt known approaches from eukaryotic miRNA prediction tools, e.g. considering conserved regions in multiple alignments (sequence and structure), calculating minimum free energy structures and using machine learning methods for improved predictions.

References:

[1] Ana Kozomara, Sam Griffiths-Jones;
miRBase: annotating high confidence microRNAs using deep sequencing data.
Nucleic Acids Res 2014; 42 (D1): D68-D73.

[2] Isaac W Boss, Rolf Renne;
Viral miRNAs: tools for immune evasion
Current Opinion in Microbiology, Volume 13, Issue 4

[3] Harald Rouha, Caroline Thurner, Christian Mandl;
Functional microRNA generated from a cytoplasmic RNA virus
Nucleic Acid Res 2010; Volume 38, No. 22