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Viral Micro RNA Transcriptomics (miRNAomics)

Shunmugiah V Ramesh*, Milind B Ratnaparkhe, Syed M Husain and Virender S Bhatia

CAR-Directorate of Soybean Research (ICAR-DSR), Indian Council of Agricultural Research (ICAR) Khandwa Road, Indore, Madhya Pradesh, India

Commentary

In an era of small RNA (sRNA) transcriptomics, microRNAs (miRNAs) require little introduction. miRNAs are small non-coding RNAs (sncRNAs) that play vital role in post transcriptional gene silencing (PTGS) in nucleotide sequence dependent manner either by cleaving target mRNA or by repressing cognate mRNA translation [1]. In plants, miRNAs have been implicated in regulating the expression of target mRNAs including transcriptional factors (TFs) [2]. Owing to its centrality in gene regulatory networks, miRNAs are ultimate small RNA (sRNA) effectors that control overall growth and development of an organism [3]. Furthermore, growing body of literature reveals that expression of miRNAs is a plant's adaptive response to biotic and abiotic stress [4]. In animals,carcinogen [Aristolochic Acid (AA)] induced genome wide impairment of miRNA mediatedgene regulation was observed. It thus implies the significance of sRNA mediated geneticcontrol in preventing carcinogenesis [5]. Among the plant derived stress responsive small RNAs (sRNAs), miRNAs with antiviral potential are reported in many instances [6-9]. Viruses, being obligate parasites, have developed counter-defence measures in the form of viral suppressors of RNA silencing (VSRs) that hinder host RNA based gene silencing mechanism [10]. In metazoan-virus interactions, pathogenic viruses deploy another mode of counter-defence strategy that involves expressing viral genome encoded miRNAs. These virus derived sRNAs are not only involved in modulating viral gene expression but host mRNAs are also selectively targeted for translational repression [11]. At the outset, animal virus encoded miRNAs were observed in B-cells infected with Epstein-Barr virus (EBV) [12]. Later on, miRNAs derived from animal viruses belonging to families, Herpesviruses, Polyomoviruses and Retroviruses were reported extensively [13]. The reason for existence of viral genome encoded miRNAs in animal infecting viruses could be assumed based on the observation that these miRNAs act by arresting the translation of cognate mRNA. This process of translational inhibition of mRNA involves time hence such a mode of gene expression control is advantageous for animal viruses where the transition from latent to lytic cycle is indispensable. Interestingly enough, viral derived miRNAs have been identified in plant-virus interactions only in very few instances. The compelling reason for this could be majority of the plant infecting viruses are RNA viruses which does not require to enter host nucleus- sub cellular location- where protein machinery necessary for miRNA biogenesis exists. In addition plant viruses do not rely on survival features like latency or persistent infection as observed in viruses infecting animals. Despite the rarity of plant virus derived miRNAs, here we argue that prevalence of viral genome encoded miRNAs is predicted even in plant-virus interactions. Firstly, RNA viruses have been demonstrated to enter plant nuclei. For example sRNAs derived from Turnip mosaic virus (TuMV) were found to enter *Arabidopsis* nucleus. Secondly, many instances of cross-kingdom sRNA interactions were known to occur in plant-virus interface. TuMV genomic loci responsible for encoding those sRNAs were identified, and were found to target host transcript HVA22D in *Arabidopsis* [14]. Similarly miRNA encoding potential of Potyvirus, Sugarcane streak mosaic virus (SCSMV) was also established. Analysis of SCSMV genome not only revealed secondary structural features capable of expressing precursor miRNAs but also host target genes for mature miRNAs were also identified. Pre-miRNA derived from 3' UTR of SCSMV genome was demonstrated to affect gene silencing activity directed against host mRNAs encoding proteins involved in plastidial isoprenoid biosynthesis pathway [15]. These instances of viral derived miRNAs acting upon host mRNAs are reminiscence of animal virus derived host miRNA analogs or miRNA mimics [16]. Host miRNA mimics are widely described in animal infecting viruses that shares target sites with host derived miRNAs thus viruses were able to reprogram host gene expression to its advantage. However, it is yet to be ascertained what advantage would be conferred to plant viral pathogens while expressing such host miRNA mimics or analogs.Furthermore, in an instance of plant-virus interactions (Hibiscus chlorotic ring spot virus–HCRSV) not only does the viral RNA have been shown to enter plant nucleus but also the miRNA encoding potential, and consequent miRNAs derived from its genome have also been shown [17]. More interestingly the viral derived miRNA (hcrsv-miR-H1-5p) has been identified to regulate viral replication [17]. This is a classic case of viral derived sRNAs regulating its own expression within host cell as found in many instances of animal infecting viruses [13]. Here again, further studies are required to identify the ultimate outcome of this mode of viral pathogenesis.

Thirdly, Geminiviruses are large group of plant pathogenic viruses that enters plant nuclei for viral genome replication and gene expression, thus are the potential candidates to search for sRNA encoding capability. A significant lead has been made in identifying precursor miRNA like sequences in the genomes of African cassava mosaic virus and East African cassava mosaic virus-Uganda. Further presence of hairpin like structures have also been validated [18]. Thus presence of miRNA coding potential and functional miRNAs in the genomes of one of the severely infecting plant viruses further emphasizes the indispensable role of small RNAs in plant virus interactions.

Finally it is anticipated that advent of next generation sequencing (NGS) based robust sequencing platforms would assist in deciphering very low copy number sRNAs but with a potential role in defining plant-virus interactions. Hence it is safe to conclude that viral genome encoded miRNAs are potential sRNA effectors that determine the outcome of plant-virus interactions. The knowledge gained in this arena of viral miRNAomics would help in devising novel disease control strategies against the infection of plant viruses.

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***Corresponding author:** Shunmugiah V Ramesh, CAR-Directorate of Soybean Research (ICAR-DSR),Indian Council of Agricultural Research (ICAR) Khandwa Road, Indore, Madhya Pradesh 452 001, India, Tel: 9993892302;E-mail: rameshsvbio@gmail.com

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