

DIVERSITY OF RIBONUCLEIC ACID (RNA) VIRUS ENDOGENOUS VIRAL ELEMENTS (EVEs) IN INSECT GENETIC MATERIAL

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ABSTRACT

Many different RNA viruses infect insects, but the capacity to transmit to a single or numerous host species sets them apart. Through recipient transcription and replication, viral chromosomes may be incorporated into their host genes, resulting in the emergence of endogenous viral elements (EVEs). It has proven possible to find RNA virus EVEs in various of insect genomes with varying evolutionary paths, from extremely damaged genetic remnants to partial and full viral coding sections, in several different insects. Insect-virus contact has benefited much from research on these EVE, such as developing a novel kind of intuitive antiviral immunity. From a functional standpoint, RNA EVEs' effects on hosts and migratory viruses are still mostly unknown. However, new research shows that they are involved in a complicated arms race that affects the genetic path of these interdependent organisms. As additional insect genotypes and extrinsic viral are decoded, the variety of insect EVEs will continue to grow, making paleovirology an exciting study area for insects in the coming years.

Keywords—RNA viruses, EVEs, Insect genomes, Evolutionary pathway, Host genome.

INTRODUCTION

A viral genetic material or portion of a viral genetic material that is incorporated into the host chromosome is referred to as an endogenous viral elements (EVE). Transposable elements (Retroviridae) and caulimoviruses (Caulimoviridae) were the primary focus of initial EVE research (Navani et al., 2021). Going into the new millennium, findings of EVE generated from additional viral groups appeared, including those in insects (Ahmad et al., 2020, Chen & Xu, 2020), supplemented by larger-scale investigations of EVE inherited from numerous viral families in different eukaryotic genomes (Yang et al., 2017, El housse, Hadfi, Karmal, Ben-aazza, et al., 2021). A miRNA repository has been established, miR-Base (Rabi-zadeh et al., 2019), which contains the sequences of thousands of microRNAs, including several from insects. The identification of additional mi-RNAs has led to a greater knowledge of their production (Zuo et al., 2020). Non-canonical miRNA assembly routes have since been identified, for example, in contrast to the canonical process. A number of them include the creation of miRNAs from introns (known as mirtrons), ribonucleic RNAs, transfer RNAs, and endo-siRNAs (Chen et al., 2015). It is recommended miRNA synthesis in insects refer to certain other recent articles (Wang et al., 2017 and El housse, Hadfi, Karmal, EL Ibrahim, et al., 2021). Insect-borne wheat viruses presented a severe

danger to grain output in several maize nations from the mid-1950s through the 1980s (Jana et al., 2021). Recently, researchers in Shandong have discovered two new wheat viruses: SRBSDV and the RSMV (Rice Stripe Mosaic Virus). Relationships between EVEs and braconid wasps have developed over 74 million years, so much so that the line between the two creatures has been blurred.

Nudiviruses, a virus family that induces persistent infection in insects' hormonal imbalance, have been hypothesized to be EVEs ancestors (Urban et al., 2018). The discovery of nudivirus-like genes in the collected semi-structured genomes, verified by comprehensive sequence data and computational analysis, solidified the nudiviral origins of EVEs. In either a continuous or nearly continuous way, these wheat infections are transmitted by predatory insects or planthoppers. The translation of miRNA loci in the nuclei is the first step. A miRNA synthesis site may be obtained from a viral genome transcriptome, nucleotide sequences, or protein-coding sequences (Hannafon, 2021, Treviño-Villarreal et al., 2021). Rice viral infections can only be controlled in the field by fully comprehending the processes that allow viral transmission through insect vectors. As a consequence, the major parts of these miRNA-coding subunits are translated by RNA polymerase II and yield primary-miRNA transcripts that include one or more stem-loop configurations (pri-miRNA). When viruses infect

cells, the transcription of host protein-coding genetic makeup and microRNAs are altered to facilitate the virus's growth and replication. Viruses have acquired the ability to encapsulate miRNAs, which they exploit to dampen the host antiviral response (Müller et al., 2021, Shibata et al., 1990). Viruses have a distinct advantage in using miRNAs as weapons due to their small size, non-antigenic nature, and ability to influence host and own genomes. However, only infections with DNA sequences have been proven to synthesize miRNAs, which means that not all infections transmit miRNA. Due to the RNA genome's vulnerability to RNase III-type enzymes, the question of whether RNA viruses can encode for miRNAs is currently open (Iozzo et al., 2021). Structure-specific and non-structure-specific nrEVEs may persist and replicate in the host genome, as demonstrated in previous studies (Bernard & Wellberg, 2021). According to current research, exogenous nrEVEs may persist and replicate in the host genome. Viral resistance may be linked to nrEVEs. This can be done, for example, by expressing indigenous Bornavirus-like nucleoproteins, which have been discovered in numerous somatic mutations as well as in the following mortal cells (Rubenich et al., 2021). The Israeli acute paralytic viruses (IAPV, dicistrovirus) were discovered to have comparable performance in *Apis mellifera* that had a sequence derived from IAPV (Ibrahim et al., 2015). CRISPR-Cas, regulating the expression of nucleic acids and viral genes that were reprocessed and now play critical roles in host biology, has all emerged as a result of a continuous arms race between viruses and their hosts (Wu et al., 2020, Coffelt et al., 2015). However, until recently, scientists noticed that viral-derived sequences incorporated into the host genome had a significant influence on the mechanics of the space race and the biology of the host (Youn et al., 2012). As a result of this research, it is considered essential to contribute to an understanding of viruses and how host-virus interactions have affected eukaryotic organisms' development, especially via viral endogenization. Our goal is to summarize the variety of EVE that has already been discovered in insect chromosomes so far and compare it to the differences in the structure of exogenous insect viruses to supplement earlier studies on insect EVE (Powell & Huttenlocher, 2016, Puga et al., 2012). As a result of the various methodologies used to describe these two forms of EVE, we have successfully presented them individually: those derived from big dsDNA infections as well as those derived from other viruses.

Does viral infection alter the host's miRNA profile in any way?

First, Numerous studies have shown that infection alters the host's miRNA profile, with consequences ranging from subtle to severe, depending entirely on the host and virus combinations. Baculoviruses (Lämmermann et al., 2013, Mishalian et al., 2014), an ascovirus (Kow-anetz et al., 2010), a cytoplasmic polyhedrosis virus (Wislez et al., 2001), West Nile virus (WNV) (Ardi et al., 2007), chikungunya virus (Ma et al., 2013) and dengue virus (DENV) (Casbon et al., 2015) have been demonstrated to have different levels of host miRNA expression. As a result of a viral illness or the virus's modification of the host, transcriptomic and genomic amplicon techniques have shown alterations in gene expression. The Amsctamoorentomopoxvirus and other poxviruses have shown to degradation to host miRNAs by polyadenylation using a virus-encoded poly (A) polymerase (van der Windt et al., 2018). Although the polyadenylated host miRNAs are degraded due to this process, siRNAs are protected by 2'O-methylation and so are not affected by this mode of degradation. In addition to the many characteristics of mature snRNAs, these routes have various signatures: There are two distinct types of DNAs-derived RNAs: which are single-stranded DNAs and double-stranded DNAs (Quigley & Deryugina, 2012). Subverting the number of host miRNAs, which in certain circumstances act as therapeutic strategies, are one-way viruses evade the immune system. In the same way as Ran, a guanylyl imidodiphosphate, guanosine-5'-triphosphate, or guanosine triphosphate (GTP-binding) nuclear protein, is downregulated by *Bombyx mori* Nuclear Polyhedrosis (bmnpv-miR-1), the host defense is modulated by a similar method of reducing the miRNA population by inhibiting the expression of the transcription of Ran. The exportin-5-mediated small RNA transport mechanism relies heavily on this enzyme. The degradation of GTP by Ran supplies energy to exportin-5. Despite this, bmnpv-miR-1 was anticipated to have a peptide bond on the 3' untranslated region (UTR) of Ran mRNA, and luminescence and in vitro research in *B. mori* larvae confirmed this relationship (Najmeh et al., 2017, Shitara et al., 2011). Alternative snRNA biogenesis has been hypothesized in conjunction with the discoveries of virus- and EVE-generated snRNAs.

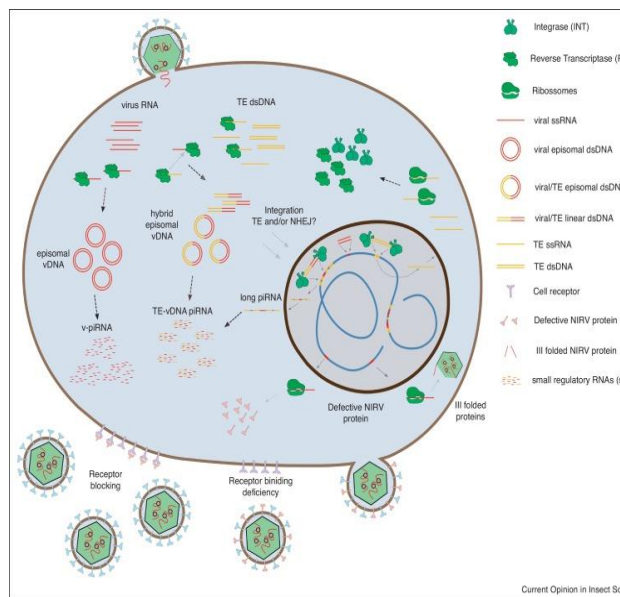


Fig.1. This review covers non-retroviral integrated RNA virus sequences's emerging processes and their influence on virus-host coevolution. Red rectangles represent viral genomes and non-retroviral integrated RNA virus sequences (NIRVS) single-strand RNA. Yellow squares are transposons' components, single-strand RNA. Adjacent squares and round particles are viral reverse transcription (red) and viral/retrotransposon non-homologous recombinants. A lengthy piRNA progenitor is made up of TEs (yellow) and non-retroviral integrated RNA virus sequences (NIRVS) (blue) (red). Pigment-inducible ribonucleic acid (piRNA) is formed from vDNA, virus/retrotransposon circular DNA hybrids, Nucleotide End Joining (NHEJ) The dark grey arrows show hypotheses with just observational evidence or stages that need to be examined.

snRNAs from endogenous viral sequences: discovery and function

Virus-encoded miRNAs: The template Virus-derived miRNAs (vmiRNAs) tend to be less abundant than siRNAs during a viral illness. Bugs with large viral proteins, such as ascoviruses (Shojaei et al., 2007), nudiviruses (Huang et al., 2017), and baculoviruses (Huang et al., 2017), contain miRNAs. When bmnv-miR-1 was overexpressed in Hela cells, the luciferase test revealed considerable suppression of Ran in comparison to the mutant Ran specified location (Wculek & Malanchi, 2015). In *B. mori* larvae and BmN cells, increased expression of the bmnv-miR-1 utilizing mimic decreased Ran mRNA and protein levels. Researchers found that bmnv-miR-1 reduced Ran activity, which resulted in lower transcription of host-derived miRNA expression (Shojaei et al., 2009). The matured vmiRNAs then direct the miRNA-Ago1 complex to identify and break the viral RNA (Figure 1). Many mi-RNAs from viral pathogens have indeed been found. In insect vectors, viral infection often triggers death (Antonio et al., 2015). While apoptotic cell death is often implicated in initiation and progression, certain viruses seem to harness it to their advantage (Shen et al., 2021). The rice ragged stunt virus (RRSV) pro-

motes mortality in specific locations of the brown leafhopper *Scirpophagalugens'* major salivary glands, and inhibiting mortality inhibits RRSV propagation (Sparmann & Bar-Sagi, 2004). RRSV probably undermines the embryonic apoptosis mechanism to promote its spread. Following transcription and replication in carrier cells, Rice gall dwarf virus (RGDV) particles also gathered around deteriorated mitochondria (Jin & Esteva, 2008). Thus, RGDV infection can lead to mortality in insect vector cells by depleting mitochondrial dysfunction. These miRNAs, bmolet-7, were considered as candidates for the host miRNome, including four *B. mori* miRNAs. Similarly, deoxy-ribonucleotide Ran depletion resulted in a significant intensification of host miRNAs (Di Maio et al., 2005). However, phagocytosis and death are kept low to minimize evident insect disease and sustain continuous viral propagation (Figure 1). These processes work together to maintain a thermodynamically stable equilibrium between viral abundance and virulence, enabling the virus to remain in insects. Insects manage the balance of apoptotic, phagocytosis, c-Jun N-terminal kinases (JNK), and siRNA systems in response to virus infection (Bekes et al., 2011).

RNA viruses

Recently, researchers detailed the various viral spread mechanisms (Strell et al., 2010, Singh et al., 2012). This article focuses on non-circulative, semi-persistent (NCSP) transmission regarding NCNP and C-type natriuretic peptide (CNP) transfer (Nathan, 2006). It is possible to acquire NCNP viruses from a fungal pathogen and to transmit them to a recipient species after a brief acquisition bandwidth utilization and an inoculated accessibility period (IAP) (Hazafa et al., 2021). Displacement is lost when the vector molts, and viral circulation (transit) through the carrier is not required for dissemination (Han et al., 2012). Most CNP viruses are phloem-specific, meaning they are obtained from and transmitted to the phloem by lengthy (minutes or hours) AAPs. As a result, they must circulate via their carriers for a lengthy period before being injected into the target species (Shaul & Fridlender, 2019). NCSP viruses have characteristics similar to NCNP and CNP viruses, such as phloem tropism and lengthy AAPs and IAPs. Their retention spans are longer than NCNP viruses' (hours to days), but they lose airborne transmission when the vector moults (Kwiatkowski, 2015). Previously, it was thought that RNA viruses could not produce miRNAs because their

genomes or replicative forms could be eliminated by complementary adsorption of microbe miRNAs and because most RNA viruses replicate in the cytoplasm, which lacks Droscha (Youn et al., 2008, Chung et al., 2013). Endogenous miRNAs can be generated from duplicated pre-miRNAs via RNA virus recombination without harming the virus genome (Rayes et al., 2015), and Droscha may not need to enter the nucleus if chronic inflammation causes Droscha to enter the cytoplasm. Several articles reported miRNAs encoded by several RNA viruses. A phage (HIV-1; discussed (Stark et al., 2005, Reiman et al., 2007) in produced the very first ribosome virus encoding miRNAs, but these have been questioned (Houghton et al., 2010) owing to low read counts of tiny RNAs identified in deep sequencing. The lack of miRNA commonality between *Cotesia* and *Microplitis* bracoviruses shows that these Polyhedra-Derived Virus (PDV) miRNAs were obtained separately or created after *Cotesia* and *Microplitis* diverged. It's worth noting that six PDV emiRNAs (including offerings that are compatible with an abundantly expressed insect miRNA) have miRbase mappings and are evolutionarily similar to miRNAs from the point (Mollinedo, 2019). In larvae, inhibiting *bmpv-miR-1* with LNA had a deleterious effect on BmNPV load. While *bmo-miR-8*, a putative cellular miRNA, was inhibited, the BmNPV load spiked, indicating the antiviral nature of host-miRNAs. The suppression of host antiviral miRNAs by *bmpv-miR-1* was shown to be essential for infection establishment in *B. mori* (Eruslanov, 2017, Yamanaka et al., 2007). Since Insect-Specific Viruses (ISVs) have mostly been found in all 4 phases of the mosquito life cycle, it appears that vertical transfer from females to their progeny is the most common method of EVEs propagation. There are two ways that EVEs and viral diseases maintain themselves in nature: by transovarial transmission, where the viruses infect vectors' germ cells processes, and through the transfer of the infections to mosquitoes' offspring. There is also a transocular process through which the virus infects the eggs as they travel through the oviduct (Nguyen et al., 2021). Neither the nudivirus nor the baculovirus genomes contain homologs. So far, the source of the new CvBV miRNAs is currently unexplained.

Conclusion and future research directions: The virus-insect co-evolutionary arms race might now be significantly impacted by the multiple interactions between RNA viruses and insects. NIRV-derived regulation influences host resistance and vector illustration competency. piRNA

regulates complementary viral replication, influencing host resistance and vector competency. The influence of non-retroviral integrated RNA virus sequences (NIRVS) on host_virus physiology in realistic insect virus environments has to be studied further. non-retroviral integrated RNA virus sequences (NIRVS) emerging is a regular occurrence, and our present understanding touches the surface of non-retroviral integrated RNA virus sequences (NIRVS) in insects. Too far, insects' EVE has viruses from three major dsDNA viral families, at minimum Fourteen of the 23 big RNA virus clades identified and four big ssDNA virus families. This variety is common in arachnids but rare in mammals. Many EVE is genetically linked to an existing endogenous virus, and several may be put in their own distinct family, which otherwise would have led to extinction. Also, new viruses discovered by large-scale genomics and proteomics will be used as bait in homology searches, substantially expanding the insects' EVE repertoire. The insect EVE environment seems to be very dynamic, and its research will likely add to our knowledge of insect-virus relationships in the coming years. It will be easier to detect multigene EVE originated from Poxviridae and Iridoviridae, which are widely distributed in insects, and to trace the history of big dsDNA viral selective breeding in hymenopteran and non-hymenopteran insects using novel EVE inspection processes. Like in the case of *The Aedes aegypti* mosquito it will be important to assess the percentage of EVE that affect host fitness and their potential roles. In wild vector mosquitoes, whether EVE-derived antiviral resistance influences the development of viral pathogens and if changes in this route alter vector competency are critical questions. Aside from genomic quantity and genome assembly quality, the EVE environment seems to be significantly different across insect species.

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