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REVIEW ARTICLES

Role of siRNAs and miRNAs in the Processes of RNA-Mediated Gene Silencing during Viral Infections[1]

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Abstract—Phenomenon of RNA-induced gene silencing is a highly conservative mechanism among eukaryotic organisms. Several classes of small RNAs (siRNAs and miRNAs) 21–25 nt in length, which play a significant role in the processes of development of an organism, occurred important components of antiviral defence in animals and plants. This review shortly describes the main stages of gene silencing mechanism, features of antiviral RNA silencing in plants, invertebrates, mammals, ways of suppression of RNA-interference by viruses, as well as possible approaches of utilization of abovementioned phenomenon for struggling against viral infections.

Key words: gene silencing, interference, transformation, antiviral, siRNAs, miRNAs.

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Abbreviations:
PTGS—posttranscriptional gene silencing
dsRNA—double stranded RNA
nt—nucleotide
siRNA—small interfering RNA
miRNA—micro RNA
RISC—RNA-induced silencing complex
RdRP—RNA-dependent RNA polymerase
TMV—tobacco mosaic virus
VIGS—virus induced gene silencing
CP—coat protein
TEV—tobacco etch virus
VSV—vesicular stomatitis virus
PFV-1—primate foamy virus 1
GFP—green fluorescent protein
EBV—Epstein-Barr virus
PVY—potato virus Y
PVX—potato virus X
ORSV—Odontoglossum rings pot virus
HIV—Human immunodeficiency virus
HBV—Hepatitis B virus
HCV—Hepatitis C virus
SARS-CoV—Severe Acute Respiratory Syndrome–Coronavirus
CMV—Cucumber mosaic virus
ZYMV—Zucchini mosaic virus
WMV-2—Watermelon mosaic virus-2
TSWV—Tomato wilt spot virus
TCSV—Tomato chlorotic spot virus
PRSV—Peanut ring spot virus

[1] The article is published in the original.

INTRODUCTION

In 1990 in order to enhance violet color of petunia flowers two independent groups of scientists additionally expressed an enzyme synthase that takes part in synthesis of pigment in plants. Hence, instead of awaited color obtained flowers occurred absolutely white [1, 2]. This phenomenon obtained the name of "cosuppression", according to the fact that transcription of both transgene and endogenous sequence was blocked.

Approximately at the same time molecular mechanisms of similar phenomenon were studied at the model of *Caenorhabditis elegans* [3–5]. In *Caenorhabditis elegans* Ambros et al. in 1993 found small RNA 22 nt in length—miRNA *lin-4*. It was shown that mutations in the nucleotide sequence *lin-4* inhibited the process of animals' development in the same way, as mutations in the protein-encoding gene *lin-14*. Taking into account the fact that RNA *lin-4* could bind to the transcript of *lin-14* in a complementary way, there appeared an idea that *lin-4* regulates RNA of *lin-14* using RNA-RNA interaction with untranslatable 3'-end of the latest [6].

Further investigations brought to conclusions that "*lin-4* is a representative of the side class of regulatory genes that code for antisense RNA-products" [6] and are called the class of ryboregulators. miRNA *lin-4* was found in 3 years after first data about RNA silencing in plants [7] and in 2 years before recovery of RNA-interference in nematodes. In 2006 miRNA database

Classes of small regulatory RNAs that are expressed in different organisms

Class of small RNAs	Organism	Characteristics
(miRNA)*	Plants Drotophila Nematodies Mammals Human	Class of small RNAs 19–25 nt in length that are coded by the genomes of the majority of studied multicellular organisms, as well as viruses. Cause block of transcription or translation of cellular or viral genes. Functions—participate in ontogenesis, protective function
Small interfering RNAs (siRNAs) –SiRNAs*	Plants Drotophila Nematodies Mammals Human	Class of dsRNAs 21–22 nt in length that originate from long molecules of dsRNA. SiRNAs cause suppression of genes activity by cleavage of RNA with complementary nucleotide sequences or by regulation of modification of complementary sequence of DNA. Main function-protection.
–ta-si RNAs	Plants Others – ?	Class of small RNAs that are expressed from non-coding gene regions and cause cleavage of specific RNAs. From one gene Tas several ta-si RNAs are formed, which express different classes of genes.
–nat-si RNAs	Plants Others – ?	Class of small RNAs that are formed form partially complementary transcripts of gene SROS that is expressed in a response to salt stress.
–ra-si RNAs	Plants Others – ?	Class of small RNAs 24 nt in length—regulators of DNA and histone methylation in certain retroelements and transposons.
Small noncodlng RNAs (tncRNAs)	Nematodes Others – ?	Class of small RNAs 20–22 nt in length. Evolutionary non-conservative. Formed without loop formation. Function is unknown.
Small modelling RNAs (smRNAs)	Mammals Others – ?	Class of small dsRNAs. Regulate expression of neuron-specific genes only in mature neurons.
PIWI-RNAs (pi RNAs)	Drosophila Mammals Others - ?	Class of small RNAs that are expressed from different genome regions. Formed without loop formation. 5' and 3'-ends are modified. Function—control of transposons.

*Main classes of small RNAs.

already included 1650 miRNA genes, including 227 human and 21 of viral origin [8].

RNA-interference was also found in human cells [16], and in 2002 the link between this mechanism and appearance of tumors was shown [17].

Till the end of 2002 the process of gene silencing was studied in the wide spectrum of eukaryotes and got the name of posttranscriptional gene silencing (PTGS), cosuppression [18] and RNA-induced plant resistance to viruses [19], RNA-interference in animals [20], quelling in fungi and algae [21]. All mentioned processes have the same basic mechanism but different goals of action.

Today the mostly studied and described classes of small regulatory RNAs are siRNAs and miRNAs. Hence now subclasses of siRNAs (tasi-RNAs, ra-si RNAs, nat-si RNAs) [22] and even separate classes of small RNAs, such as tnc RNAs and pi RNAs exist (table).

Mechanism of action. The process of gene silencing has mechanism of action that is similar for the organisms of different taxonomic groups: plants, animals, human.

In the basis of the process lies formation of siRNAs and miRNAs from dsRNA that was formed from endogenous transcripts or exogenous dsRNA (Fig. 2). PTGS with formation of siRNAs is carried out in cytoplasm, while the process of miRNA biogenesis as well has the stages in nucleus [23].

Formation of siRNAs. Mechanism of PTGS includes such stages as initiation and establishment of the process of silencing, as well spreading of signal [24]. At the stage of initiation the key role is played by the formation of dsRNA. Such RNA can be synthesized by viral replicate apparatus; cell RNA-dependent RNA polymerase present in plant cells, or from RNA-loop formed from two-side directed transgene or as a result of antisense strategy of cloning. dsRNA is recognized and cleaved by the protein Dicer that is a member of the IIIrd class of protein family of RNAse III and includes N-tail DEXH domain, RNA helicase/ATPase domain, two RNAse III domains—endoND and dsRNA-binding domain (dsRBD). The majority of Dicer proteins include RNA-binding PAZ domain [25].

The quantity of Dicer genes varies in different organisms. For instance, the cells of *C. elegans* code only 1 Dicer protein [26, 27]. The cells of *Neurospora crassa* code two Dicers that are multifunctional [28], while both of Dicer proteins in *D. melanogaster* (Dcr1 and Dcr2) have certain functions. Genome of *A. thaliana* codes for 4 Dicer like proteins (DCL): DCL1 participates in processing of miRNAs precursors [29, 30], DCL2 and DCL4 are necessary for cleavage of virus-specific dsRNAs [31, 32], and DCL3 dices dsRNA of exogenous origin [33].

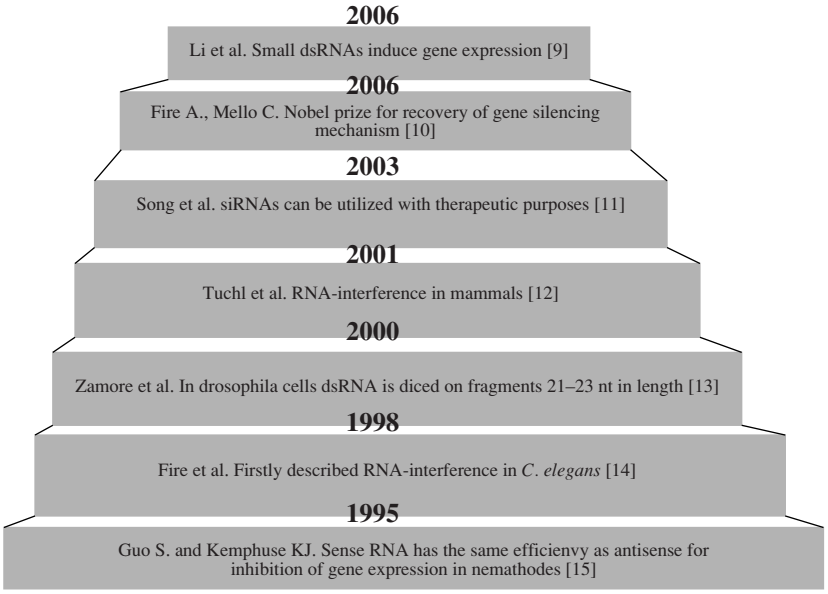

Fig. 1. Historical steps in the field of RNA-interference.

Basing on the structural and biochemical comparison of RNAse III enzyme of *Aquifex aeolicus*, residues of catalytic domains of RNAse III of *E. coli* and human Dicer [34], it is assumed that molecules of Dicer have one identical center of processing of RNA, which when being activated is able to cleave one from the strands of dsRNA (Fig. 3).

The first domain of RNAse Dicer cleaves one chain of dsRNA that has 3'-hydroxyl group approximately at 21 nt from the end of RNA. In combining with PAZ-domain it probably is responsible for determining of distance from the end of RNA to the site of cleavage [36]. PAZ-domain also takes part in recognizing of RNA-substrate [37–39]. The cleavage of the other chain of dsRNA by RIIIb domain in 21–24 nt from the place of dicing by the domain RIIIa is carried out in the same way. As a result it causes formation of products with typical at 3'-overhangs of dsRNA—small interfering RNAs (siRNAs) [33].

The next step is phase of establishment of RNA silencing, which starts from the moment when siRNAs formed by Dicer, bind to the complex of proteins—RNA-induced silencing complex (RISC). While binding to siRNAs RISC is transformed from non-active to functional form and causes unwinding of siRNAs, their binding to RNA with complementary sequence and cleavage of the latest.

One of the main components of protein complex belongs to the family of proteins Argonaute and has the name AGO. AGO is the protein with molecular weight of about 130 kDa and includes such domains as PAZ and PIWI [40]. For today three main classes of AGO proteins are described according to their aminoacid sequences: subfamily Argonaute, subfamily Piwi and *C. elegans*—specific subfamily [41]. In *A. thaliana* 10 proteins AGO were found [42], while in *D. melanogaster* there are 5 of them, in human—8. In *A. thaliana* protein AGO1 and closely related protein AGO10 (also known as PINHEAD/ZWILLW (PNH/ZLL)) necessary for development of plant organs with help of miRNA formation [43, 44]. Mutants *ago1* have defects of apical meristems and meristem tissue of the root, similar to those observed in *pnh* (*ago10*) mutants. It was established that in *ago1* mutants AGO10 can change AGO1 in miRNA-induced regulation of determinant of leaves polarity PHABULOSA (PHB) [44].

The central domain of protein AGO PAZ is formed by 5–6 β-strands, which on one side have α-helices [45]. PAZ-domain of AGO protein is an RNA-binding factor that specifically recognizes 3'-overhangs of siRNAs. Helicase that also is in the content of RISC causes unwinding of siRNA thus that only one chain is left bound with complex RISC [46].

X-ray analysis data of the domain PIWI of archebacterial protein AGO showed proper similarity to the proteins of RNAse H family [47]. PIWI domain recognizes 5'-phosphate residues of siRNAs, similar to how RNAse H recognizes the chain of RNA in RNA/DNA duplexes, and PIWI is able to cleave RNA in RNA/siRNAs complexes.

Thus, after only one chain of siRNA is left bound to the complex RISC, it binds complementary to the sequence of RNA, and domain PIWI of AGO protein dices RNA approximately in the middle of fragment to which siRNA is bound. Specificity of siRNA-RNA interaction is high, and often miscomplementarity even in one nucleotide can strongly inhibit the process of silencing [49]. Activation of RNA silencing firstly is held at the level of one cell, and further is expanded around the area of initiation that includes about 10–15 neigh-

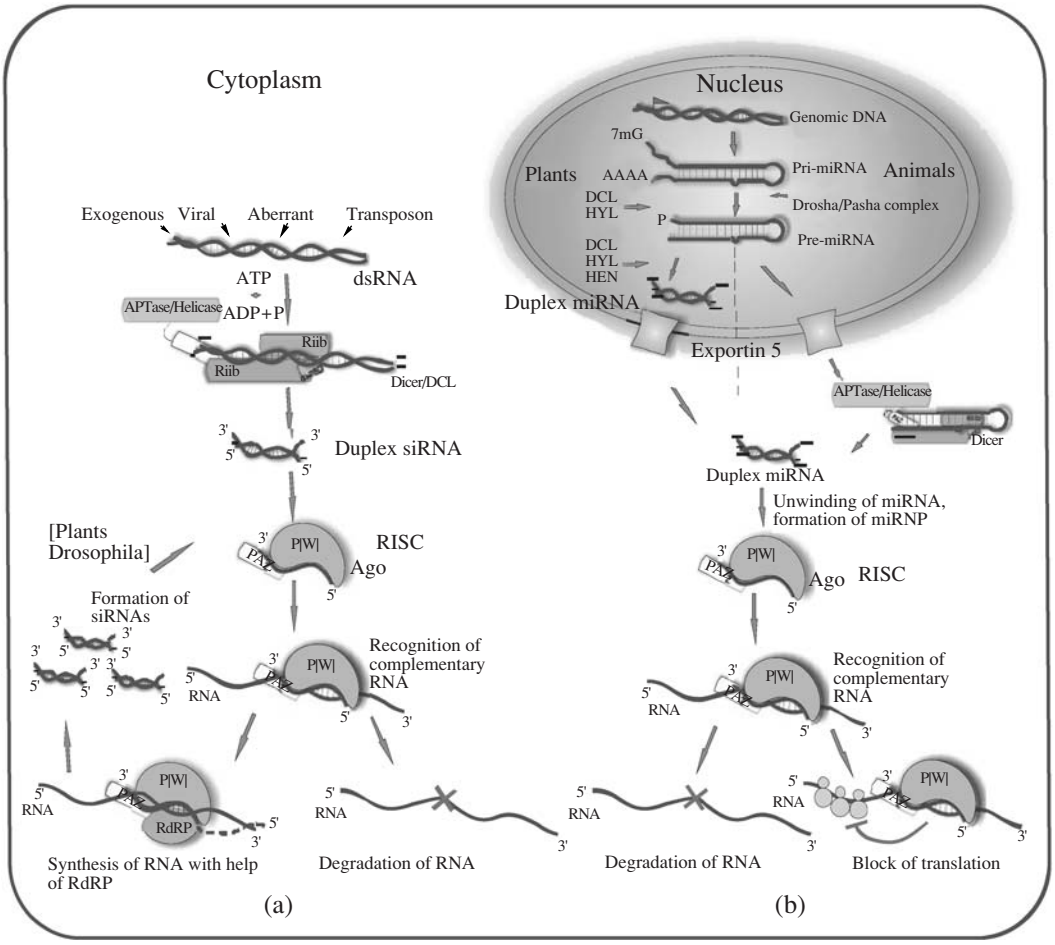

Fig. 2. Mechanisms of gene silencing based on formation of siRNAs (a) and miRNAs (b).

bour cells. Primary siRNAs diffuse from these cells to others causing synthesis of so called secondary small RNAs (Fig. 2). These secondary RNAs are able to move into the neighbour cells and cause systemic silencing using further amplification [49].

In animal cells presence of dsRNAs not always causes activation of mechanism of gene silencing, as it was shown for the plants. In animal cells appearance of dsRNA as a rule initiates a mechanism of non-specific gene knock down and cell death [50]. Such generalized reaction can be caused by activation of RNAses [51] or interferon synthesis [52].

miRNAs biogenesis. miRNAs, found in the genome of plants, animals and human, according to their location can be divided into the following categories:

(1) Exonic miRNAs (for instance, miR-21) [53], miR-155 [54], claster miR-23a-27a-24-2 [55]).

(2) Intronic miRNAs (for instance, miR-15a-16-1 claster in non-coding region of gene DLEU2 of mammals [55]).

Additionally there is a group of miRNAs mixed by their origin. Their sequence in genome is located both in the region of exon and intron. One of the examples is miRNAs of human—has-mir-20a, that according to miRBase origins from exon 2, as well as from introns 5 and 8 of transcripts C13orf25 [56].

The first stage of formation of miRNAs in the nucleus is transcription of miRNA with help of RNA-polymerase II and formation of primary transcript, which has a view of loop and contains approximately 70 nt—pri miRNA. In plants the long primary transcript is cleaved by the enzyme DCL1 [57] in order to form the loop that has 3'-overhangs—pre miRNA, which later again is cleaved by DCL1 and forms miRNAs. Maturation of such RNA-duplexes requires interaction between DCL1 and protein HYL1, necessary for interaction with RNA [58]. Each of the chains of duplex on 2-hydroxyl group of 3'-end ribose undergoes methylation by methylase HEN. After necessary modifications duplexes are transported to the cytoplasm with help of transport protein HASTY (HST) [59].

In animals pri-miRNA is cut by the proteins Drosha (*D. melanogaster*) and Pasha (mammals, human), forming pre-miRNA. Pre-miRNA is transported to cytoplasm by exportin-5 [60]. In cytoplasm pre-

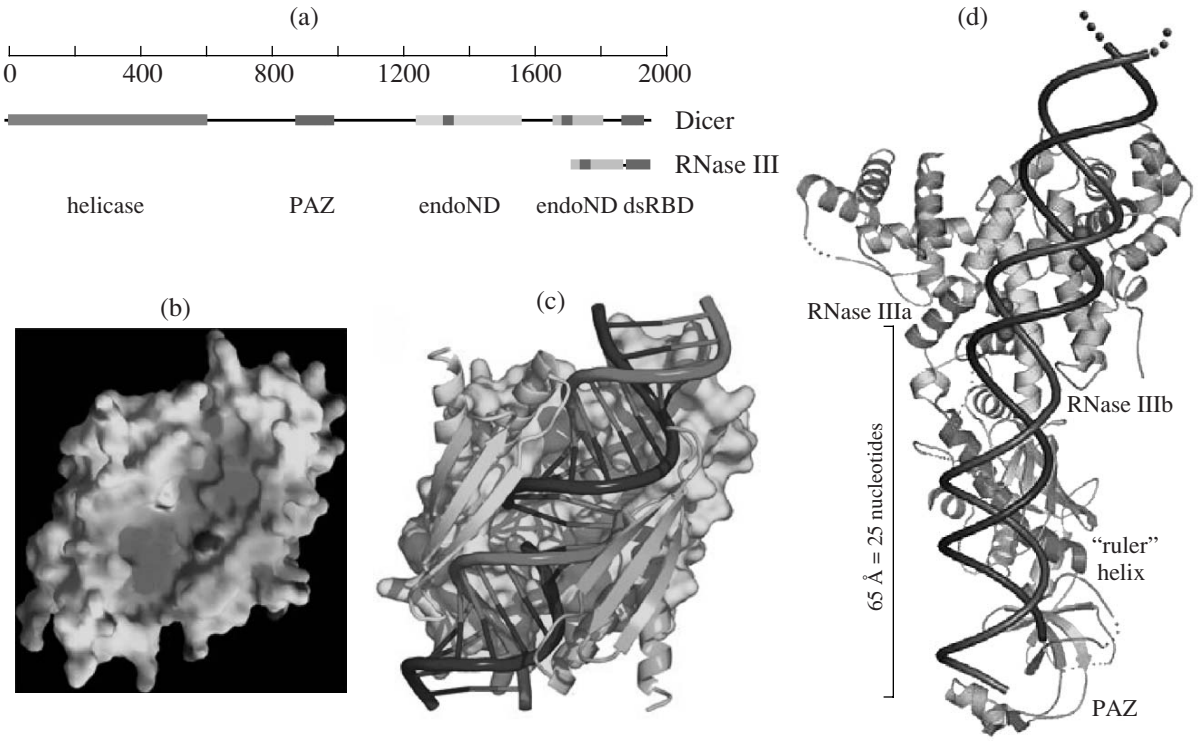

Fig. 3. Features of the structures of RNAse III and Dicer [35, 36]. (a) Structure of domains of RNAse III of *Aquifex aeolicus* (Aa-RNase III, SWISS-PROT O67082) and Dicer of *Homo sapiens* (Hs-Dicer, SWISS-PROT Q9UPY3). The scale specifies the length of polypeptide chain. (b) Image of endoND dimmer surface (c) Schematic image of complex of Aa-RNAse III with dsRNA. (d) Formation of complex of dsRNA with Dicer (RNAse IIIa and RNAse IIIb reflect domains endoND).

miRNA is recognized and diced by Dicer with further formation of miRNAs [61]. Both in plant and animal cells duplexes miRNAs bind RISC forming ribonucleoprotein complex miRNP [62]. Similarly to the process of gene silencing with siRNAs, the unwinding of duplex and complementary binding to RNA-target occur. Animal miRNAs bind to several, probably partially complementary fragments at 3'- and 5'-ends of RNA and block the process of translation, while plant miRNAs mostly bind to specific RNAs of protein-coding sequences and cause their cleavage [63]. 5'-fragment of RNA, which is formed after cleavage of the latest, undergoes degradation in exosomes—P-bodies [64], and 3'-end of RNA is destructed by exonuclease XRN4 [65].

Antiviral gene silencing in plants. First assumptions that RNA silencing is an effective protective mechanism against viral infections in plants occurred with the recovery of the fact that plant viruses initiate the process of silencing of endogenous RNAs regarding the presence of homologous sequences. For example RNA of transgene of phytoene desaturase [66] underwent a process of gene silencing while replication of tobacco mosaic virus (TMV), which had the sequence of plant gene in its genome [67]. It caused formation of new term in plant virology as "Virus-induced gene silencing" (VIGS). Phenomenon of recovery later demonstrated that plant viruses undergo gene silencing: transgenic plants, which were transformed by the coat protein (CP) of Tobacco etch virus (TEV) and infected by this virus, showed symptoms on inoculated leaves. Hence, new leaves on tobacco plants already were free from the symptoms of viral infection, and plants became resistant to super-infection by TEV [68]. This resistance was associated with complete degradation of both RNA of CP and RNA of transgene. But the real proof that gene silencing is an important mechanism of plants protection against viruses became recovery that siRNAs accumulate in plants in high quantity during infection.

Antiviral gene silencing in invertebrates. Insects. The process of gene silencing was described also for different species of arthropods, including drosophilas [70] and mosquitoes [71]. First observations of this phenomenon in insects date 2002—in *Drosophila* S2 cells, infected by Flock House virus from the family Nodaviridae. Li et al. observed accumulation of siRNAs in the infected cells, as well as enhanced accumulation of virus in the cells with mutations in gene *ago2* [72].

Virus-induced gene silencing was observed for silk worm *Bombyx mori*, in which translation of transcription factor Broad-Complex (BR-C) was inhibited by the recombinant alphavirus Sindbis that expressed RNA antisense to BR-C [73]. Roignant et al. [74] proved that in organism of *Drosophila* there is no prop-

agation of the process of silencing, and this mechanism is limited to the cells where it occurred. RNA silencing directed against endogenous and exogenous nucleotide sequences is very similar to the one that acts against exogenous pathogens. However the presence of mechanism of gene silencing of viral sequences is not still shown for insects.

Nematodes. On the contrary to *Drosophila* the process of gene silencing in nematodes is mobile and can be spread over the whole organism [75]. Fire et al. showed that injections of dsRNAs into the body and germ glands of young specimen of *C. elegans* cause gene-specific interference in somatic tissues [76]. Genome *C. elegans* includes 2 genes RdRP, *ego-1* and *rrf-1*, necessary for RNA silencing in embryos and somatic tissues [77, 78]. Recently it was shown that the majority of siRNAs formed under the process of gene silencing in nematodes included the secondary siRNAs—i.e. thus, which were created from dsRNAs synthesized after the first round of silencing [79]. In nematodes RNA silencing plays a very important role while protection of genome from transposons [80], hence the question whether this mechanism is used as antiviral defense is left open. Thus, it was shown that replication of Vesicular stomatitis virus (VSV) was enhanced in nematodes, mutant in complex *rde-4-rde-1*. As well it was noted that development of the disease is increased in nematodes that had mutations in genes *rrf-3* and *eri-1*-two negative regulators of interference. Lu et al. showed inability of Flock house virus to replicate in *C. elegans* species that had integrated transgene coding for full-length RNA of virus [81]. Antiviral response used the activity of RdRP and could be blocked by viral protein B2 [82].

Plant species	Quantity of genes coding for miRNAs
*Arabidopsis thaliana**	117
*Oryza sativa**	178
*Populus thrichocarpa**	213
Zea mays	97
Sorghum bicolor	72
Glycine max	22
Medicago truncatula	16
Saccharum officinarum	16

Quantity of genes that code for miRNAs in different plant species [69].
* Plants with completely sequenced genome.

Antiviral gene silencing in mammals. Tusch et al. tried to identify siRNAs in animal cells infected with different viruses [83]. They found neither viral RNAs, nor small endogenous RNAs obtained from transposon elements. It caused the assumption that comparing to plants, insects and nematodes, transposons of mammals do not undergo the suppression with help of siRNAs. Hence they identified small loop RNAs that could initiate RNA-interference.

Lecellier et al. first demonstrated that miRNA of mammals *mir-32* terminates the accumulation of primate foamy virus (PFV-1) in human cells [84]. It was shown that cell lines that express viral protein Tas that interferes with mechanism of RNA silencing, accumulate high quantity of virus. Mutations in nucleotide sequence of abovementioned viral protein caused loss of virus an ability to replicate and accumulate in cells. It was proved that Tas is a non-specific blocker of gene silencing and that cells that do not express this suppressor have increased activity of miRNA *mir32*. These investigations proved antiviral function of miRNA as well as demonstrate suppression activity of viral protein.

As a result of carried out research miRNAs of human that are expressed as a response to the infection caused by influenza virus were recovered. They participate in blocking of genes critical for pathogenesis and tropism of influenza virus of type A/H5N1. Two miRNAs of human *mir-507* and *mir-136* have sites of binding to the genes of viral polymerase and hemagglutinin [85].The additional proof that miRNAs act as antiviral agents is the fact that *mir-136* is expressed only in lungs [86]. An interesting fact is that miRNAs to the polymerase of murine strain were absent in the genome of chicken, hence the large quantity of miRNAs of human (160 from 336 human miRNAs) have homologs in avian genome [87].

Suppression of gene silencing by viruses. Taking into consideration the fact that the majority of living organisms use gene silencing as an effective measure of protection with viral infections, it is possible to assume that virus couldn't replicate effectively. Hence, in response to protective reactions of organism, viruses use mechanisms that will permit them to overcome gene silencing. Mostly it is reached by synthesis of viral proteins, which are able to block certain stages of gene silencing process. Observation over the symptoms caused in plant by one virus or several non-related viruses brought understanding of features of suppression of gene silencing. Potyvirus Potato virus Y (PVY) significantly enhances replication of potato virus X (PVX) in mixed infection. This fact specifies that PVY has mechanism of suppression of protective reaction of the host. For today it is already known that the protein that is in charge of this effect is potyviral helper component protein kinase (HC-Pro) that was able to cause suppression of reporter gene of green fluorescent protein (GFP) in transgenic plants [88]. Further investigations showed that phenomenon of inhibition or suppression of gene silencing is a common feature for the majority plant viruses [89]. Proteins, which are in charge of this process in different viruses are absolutely different in their aminoacid sequence and structure, and are coded both by DNA and RNA viruses [90]. Probably it is connected to the presence of large amount of targets for these proteins. The mostly studied viral suppressor of gene silencing in plants is protein p19 that is expressed by representatives of genus *Tombusvirus*.

As the result of investigations it was shown that protein p19 of Odontoglossum ringspot virus (ORSV) was able to bind only to dsRNAs 21 bp in length with 3'-overhangs, i.e. such small RNAs that have all characteristics of siRNAs. Moreover, p19 of Tomato bushy stunt virus close-related to ORSV coimmunoprecipitated with siRNAs [91]. X-ray data of protein p19 determine that tombusviral suppressor identifies duplex of RNA independently of their nucleotide sequence and acts on the principle of claws that "seize" siRNA [92]. Thus, siRNAs are not unwound and are not bound to RISC. Approximately the same way acts suppressor of gene silencing B2-protein of Flock house virus, seizing and blocking of molecules of dsRNAs that are formed while replication of viral RNA [93]. Proteins NS1 of influenza virus and E3L of vaccinia virus are also suppressors of gene silencing and act by binding of dsRNAs [94].

RNA-interference as method of antiviral protection. Process of RNA-interference or gene silencing can be effectively used for suppression of replication of viruses by inhibition of viral or host genes necessary for replication of virus. Suppression of such viral genes, as viral polymerase, regulators of transcription of viral genes or inhibition of viral genes, which are active at the early stages of viral infection, is very perspective in antiviral therapy. For today investigations *in vitro* show efficiency of RNA-interference in suppression of different viruses, nevertheless what kind of nucleic acid it has.

For today an active search of different ways of obtaining of transgenic plants resistant to viruses is carried out. Thus RNA-induced resistance of potato plants to PVY by transformation of plants with gene of viral replicase *NIb* was obtained [95]. Plants of *Nicotiana benthamiana* showed high level of resistance to plum pox virus (PPV) after being transformed with *NIb* gene [96]. Transgenic clone of European plum was highly resistant to plum pox as a result of transformation with coat protein gene of PPV [97]. RNA silencing of sequence P1/HC-Pro in transgenic plants of plum caused resistance to plum pox [98].

For today approaches as for utilization of mechanism of RNA-interference for antiviral therapy directed against the most important infectious viral diseases of human are worked out. Such are Human immunodeficiency virus (HIV), Hepatitis B virus (HBV), Hepatitis C virus (HCV) and influenza virus. Jacque et al. showed siRNA-based inhibition of early and late stages in replication of HIV that made synthesis of DNA from RNA impossible. By now exist several viral sequences-targets that are attacked by specific to them siRNAs: *Gag* [99] and *Env* [100], gene of reverse transcriptase *Pol* [99], genes coding for regulatory proteins—*Tat, Rev, Nef* and *Vif* [101].

Several fragments of genome of HCV, including 5'UTR and coding regions *Core, NS3, NS4B* and *NS5B* are sensitive to siRNAs [102]. Therapeutic potential of mechanism of gene silencing was further studied *in vivo*.

Wu et al. [103] showed effectiveness of siRNAs against influenza virus. siRNAs specifically suppressed conservative regions of viral genes of nucleocapsid and polymerase. It was shown that activity of virus was significantly decreased both in vitro, and in vivo.

Utilization of process of gene silencing for protection against viral infections was shown also for DNA-viruses. In particular, for HBV several sites of the genome are used as targets for abovementioned mechanism [104]. Process of RNA-induced antiviral gene silencing is actively tested for coronaviruses because of absence of effective treatment measures and vaccines. Investigations in vitro and in vivo showed effectiveness of using of synthetic small RNAs in order to suppress 3'UTR, genes of structural and non-structural proteins of coronavirus causing severe acute respiratory syndrome (SARS-CoV) [105]. Significant inhibition of development of viral infection was observed after transformation with utilization of highly conserved regions of viral genome. Last results showed that region that is conserved among flaviviruses caused silencing of both Japanese encephalitis virus and West Nile virus [106].

CONCLUSIONS

The phenomenon of RNA silencing is a highly conserved mechanism in the representatives of animal and plant world and plays a significant role in the processes of development of organism and antiviral defence. In the basis of this mechanism lies recognition of exogenous or endogenous dsRNAs by complexes of cell proteins and their cleavage into siRNAs or miRNAs. One of the chains from these duplexes binds in complementary manner to RNA, and proteins of RISC complex cleave this target RNA.

The process of RNA-interference or gene silencing can be effectively used for suppression of replication of viruses using inhibition of viral or host genes necessary for viral replication. For today approaches as for utilization of gene silencing for antiviral therapy already are worked out. They are directed against the most important viruses causing serious human diseases. This phenomenon can be initiated while using siRNAs in vitro and in vivo, by expression of RNA from transgene. RNA silencing is actively used for obtaining of transgenic plants resistant to pathogens of viral etiology, as well as showed perspectives in using for struggle with viral infections of human and animal.

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