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RAKHMETULLINA AIZHAN KAZIEVNA

Characteristics of miRNAs binding with mRNAs of transcription factor genes of agricultural plants

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Scientific advisor:
Ivashchenko A. T.,
doctor of biological sciences,
professor
Foreign scientific advisor:
Piotr Zielenkiewicz,
PhD, professor

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NOTATIONS AND ABBREVIATIONS

5'UTR – the 5′-untranslated region
3'UTR – the 3′-untranslated region
A. thaliana – Arabidopsis thaliana
O. sativa – Orysa sativa
T. aestivum – Triticum aestivum
Z. mays – Zea mays
TCP - teosinte branched, CYCLOIDEA, and the PROLIFERATING CELL FACTORS
HSF - heat stress transcription factor
MYB – myeloblastosis family of transcription factors
GRAS – GIBBERELLIC-ACID INSENSITIVE, REPRESSOR of GAI and SCARECROW
ERF – ethylene responsive factor
C2H2 - Cysteine and Histidine residues in their secondary structures, such as Cys2/His2-type
GenBank – database of annotated nucleotide sequences of DNA, RNA and amino acid sequences of proteins
CDS – the coding sequence
cDNA - complementary deoxyribonucleic acid
dsRNA - double-stranded ribonucleic acid
eFP - electronic fluorescent pictograph
miRNA– mRNA-inhibitory RNA
MIRNA gene - the corresponding genes encoding miRNAs
miRBase – miRNA nucleotide sequence database
mRNA – messenger RNA
nt - nucleotide
NCBI – National Center for Biotechnology Information
NGS - next generation sequencing
pre-miRNA – precursor miRNA
pri-miRNA – primary miRNA
PUBMED – Biochemical Literature Citation and Abstracts
RACE - Rapid Amplification of cDNA Ends
RISC – RNA-induced silencing complex
sRNA – small RNA
TF – transcription factor
ex-miRNA – exogenous miRNA
xe-miRNA - exogenous miRNA

INTRODUCTION

General description of the research.

This thesis is devoted to the determination of the quantitative characteristics of the interaction of miRNAs with mRNAs of genes of transcription factors (TF) of agricultural plants.

Significance of the research.

TF play a key role in the regulation of the expression of many genes and, in general, the entire eukaryotic genome [1]. Currently, there is an important problem of controlling the expression of transcription factors in order to increase the productivity of plants by changing their growth, development, and increasing resistance to biotic and abiotic environmental factors [2, 3]. Most types of agricultural plants contain more than 50 families of transcription factors and it is necessary to choose the most important ones in the functioning of plants.

According to the Food and Agriculture Organization of the United Nations (FAO), the most used grain crops in the world are rice, corn and wheat, so these types of plants are chosen as objects of our research. We used Arabidopsis as the most well-studied plant type.

Recently, miRNA (mRNA-inhibitory RNA) effect on TF expression has been discovered, which opens up new possibilities for regulating their synthesis [4]. The miRNAs can interact with mRNA of TF genes with different efficiencies, defining a wide range from weak suppression of expression to complete repression of protein synthesis or mRNA degradation [5]. Solving the problem of establishing the interaction of miRNA with mRNA target genes is complicated by the determination of miRNA target genes and the establishment of quantitative characteristics of the interaction of these molecules. Existing programs for predicting target genes and miRNA binding sites in their mRNAs are imperfect and find many false-positive target genes and miRNA sites. This reason significantly inhibits the establishment of miRNA associations and their target genes in plants and animals.

Despite the constant increase in the detected miRNAs in plant genomes, it is not always possible to credibly identify their specific target genes. Data on changes in the concentration of miRNA in cells at different stages of ontogenesis and under various influences are rapidly increasing, which confirms their important role in plant functioning. The use of miRNAs as modifiers of gene expression regulation is promising, however, it is necessary to accurately identify the target genes and avoid side effects. The MirTarget program used in the work can solve this problem and therefore the goal and research tasks set in the dissertation can be solved. The establishment of miRNA associations and their target genes will enhance the efficiency of plant genetic engineering.

Objects of the research: miRNA and TF genes of fully sequenced plant genomes of *A. thaliana, O. sativa, Z. mays* and *T. aestivum;* human genes as plant miRNA targets

Subject of the study: Quantitative characteristics of the interaction of miRNA with mRNA of TF genes of *A. thaliana, O. sativa, Z. mays* and *T. aestivum*

The purpose of the research:

To study the quantitative characteristics of the interaction of miRNA with mRNA of TF genes of *A. thaliana, O. sativa, Z. mays* and *T. aestivum* and to identify the most effective associations of miRNA and target genes.

The main tasks of the research:

1. Create databases of TF genes of the TCP, HSF, MYB, GRAS, ERF, C2H2 families and miRNA of *A. thaliana, O. sativa, Z. mays* and *T. aestivum*.
2. To determine the characteristics of interaction miRNA with mRNA of the TCP TF genes of *A. thaliana, O. sativa, Z. mays* and *T. aestivum*
3. To determine the characteristics of interaction miRNA with mRNA of the HSF TF genes of *O. sativa, T. aestivum, Z. mays* and *A. thaliana*
4. To determine the characteristics of interaction miRNA with mRNA of the MYB TF genes of *O. sativa, T. aestivum, Z. mays* and *A. thaliana*
5. To determine the characteristics of interaction miRNA with mRNA of the GRAS TF genes of *T. aestivum, O. sativa, Z. mays* and *A. thaliana*
6. To determine the characteristics of interaction miRNA with mRNA of the ERF TF genes of *T. aestivum, O. sativa, Z. mays* and *A. thaliana*
7. To determine the characteristics of interaction miRNA with mRNA of the C2H2 TF genes of *O. sativa, Z. mays* and *A. thaliana*
8. To determine characteristics of interaction rice, maize and wheat miRNAs with the mRNA of human genes.

The scientific novelty of the research.

The novelty of the study is the following: 1. The groups of target genes for miRNAs among TF families TCP, HSF, MYB, GRAS, ERF, C2H2 of the *A. thaliana, O. sativa, Z. mays* and *T. aestivum* have been predicted for the first time; 2. For the first time binding sites of some miRNAs were identified in mRNAs of the target genes of different plants, that are conservative and encode conservative oligopeptides; 3. For the first time, it was revealed that some miRNAs can have more than one target gene and mRNAs of some target genes contain binding sites for two or more different miRNAs; 4. The binding sites of some miRNAs in CDS mRNA of plant TF genes can encode different oligopeptides depending on the reading frame; 5. For the first time, the binding sites of miRNAs of rice, maize and wheat with mRNA genes involved in various human diseases have been established.

The theoretical significance of the research. Quantitative characteristics of the interaction of miRNA with mRNA of many plant TF genes have been established, which make it possible to evaluate the interactions of these molecules. Fully complementary interactions of nucleotides of some miRNAs with mRNA of plant TF genes were revealed, which indicates the efficient binding of these miRNAs to mRNAs. The revealed interactions of plant miRNA with TF mRNA contribute to understanding the effect of miRNA on many physiological processes

in plants and make it possible to purposefully use miRNA in genetic modification of plants. The predicted interactions of plant miRNAs with human mRNA genes make it possible to recommend some miRNAs as regulators of human gene expression.

The practical significance of the research. The establishment of plant miRNA associations and their target genes TFs of the TCP, MYB, GRAS, ERF, C2H2 families reduces the time and material costs of searching for connections between miRNAs and target genes of agricultural plants, compared to finding associations of miRNAs with mRNAs experimentally. The revealed associations of miRNA and TF target genes in the studied plants allow targeted modification to improve many useful properties of various species of plants. MirTarget program has been successfully used to find miRNA binding sites in mRNAs of plant and human genes, and to quantify the interaction of miRNA with mRNA target genes. The identified plant miRNAs can influence human genes and be used in medicine as biologically active compounds, since they easily penetrate the human body. The copyright certificate “MirTarSeq” No. 15600 dated March 2, 2021 was received.

The main provisions for the defence:

Some genes out of the total number of 2403 genes of TCP, HSF, MYB, GRAS, ERF, C2H2 TF of *A. thaliana, O. sativa, Z. mays* and *T. aestivum* families can be miRNA targets of these organisms.

The results of studies of the influence of plant miRNAs on mRNA of TF genes of TCP, HSF, MYB, GRAS, ERF, C2H2 families of *A. thaliana, O. sativa, Z. mays* and *T. aestivum* showed that the many studied miRNAs can influence plant growth and development.

The miRNA binding sites in the mRNA of the studied genes of TCP, HSF, MYB, GRAS, ERF, C2H2 TF are located in the 5'UTR, CDS, and 3'UTR.

Different quantitative characteristics of the interaction between miRNA and mRNA of the studied TF genes of the TCP, HSF, MYB, GRAS, ERF, C2H2 families indicate the effectiveness of the influence of miRNA on a number of genes of these TF families.

Most of the studied miRNAs of *O. sativa, T. aestivum, Z. mays*, which are actively involved in plant growth and development can affect mRNA translation of human genes.

The relationship of the research study with the scientific project.

The dissertation work was carried out within the framework of the project "Development of test-systems for early diagnosis of cardiovascular, oncological and neurodegenerative diseases based on miRNA associations and their target genes" № AP05132460 of the Ministry of education and science of the Republic of Kazakhstan (2018-2020).

Research approbation. The main results and observations are presented and discussed at international conferences and symposiums:

- at the VII international scientific conference "Prospects for the development of biology, medicine and pharmacy" (Shymkent, Kazakhstan, 2018);

- at the international congress "Biotechology: state of the art and perspectives" (Moscow, Russia, 2019);

- at the fifth international conference "Plant genetics, genomics, bioinformatics and biotechnology" (Novosibirsk, Russia, 2019);

- at the VI international scientific conference of students and young scientists "Farabi alemi" (Almaty, Kazakhstan, 2019);

- at the 9th Moscow Conference on Computational Molecular Biology MCCMB'19 (Moscow, Russia, 2019).

- at the fifth international scientific conference "Current challenges in plant genetics, genomics, bioinformatics, and biotechnology" (Novosibirsk, Russia, 2019);

- at the international scientific conference of young scientists «Fundamental research and innovations in molecular biology, biotechnology, biochemistry» dedicated to the 80th anniversary of academician Murat Aitkhozhin (Almaty, Kazakhstan, 2019);

- at the international scientific and practical conference "The synergy of science and practice in the context of innovative breakthroughs in the development of economy and society: national and international aspects" (St. Petersburg, Russia, 2019);

- at the VII international scientific and practical conference "Biotechnology: science and practice" (Sevastopol, Russia, 2019);

- at the twelfth international multiconference "Bioinformatics of genome regulation and structure/systems biology" (Novosibirsk, Russia, 2020).

Publications.

The main content of the thesis is reflected in 16 printed works, including 2 articles in the international journal with the Impact Factor quoted in Scopus; 3 articles from the list of the Committee for Quality Assurance in Education; 11 abstracts in materials of international conferences.

Dissertation structure. This dissertation is written in 164 pages, and contains notations and abbreviations, introduction, literature review, materials and methods, results and discussions, conclusions, references and appendices from 422 sources, contains 32 tables, and 17 figures.

1 LITERATURE REVIEW

1.1 The Function of miRNAs in Plants

Regulation of gene expression at the post-transcriptional level is a well-known function of miRNAs which has been extensively studied in plants [6]. These 19–24 nucleotides (nt) small non-coding RNAs are generated with the assistance of precursors with special stem-loop structures and regulate the translation of target gene mRNA by binding the target mRNA according to sequence complementarity [7]. It has been established within the previous research that plant miRNAs have been recognized as key regulators of a variety of plant developmental and physiological processes, including genome integrity maintenance, development of root, stem, leaf, and flower organ, metabolism, and adaptive responses toward environmental stresses [8-16]. Also, among the miRNAs known to be involved in plant development, some are highly conserved in the plant kingdom, while others are more unique in certain plant species [17-20]. The degree of the conservation of a miRNA is an indicator of the “age” in evolution time and is connected to its expression patterns and functions [18, p. 434]. Plants are an essential part of the ecosystem and may be utilized by people as medicine and food. Such abiotic stresses as drought, soil toxicity, climate change, and biotic threats like insects, herbivores, and microbial pathogens pose thereaten plant productivity. An increase in demand for plants and plant products is attributable to the growth in the human population. This growing demand justifies the increase in crop yields. One way to achieve this aim is to reduce the yield penalties by designing and adopting environmentally friendly crop protection measures. Molecular biology development revealed that miRNAs are involved in the regulation of essential plant metabolic processes at the post-transcriptional level [21-23]. These miRNAs can fulfill the function of improving plant productivity. The miRNAs as important regulators of gene expression and their action modes have been increasingly studied [24-28]. Most plant miRNAs have demonstrated the ability to regulate gene expression mainly at the post-transcriptional level through a high stringency of complementarity [27, p. 3]. Perfect binding of a miRNA to the corresponding target mRNA is considered to cause the degradation of the target mRNA, while imperfect pairing to the target mRNA results in translational repression [29]. The miRNAs of diverse lengths can be generated from different genes, and miRNAs that are heterogeneous in length from the same MIRNA gene (the corresponding genes encoding miRNAs) [30]. The first and critical step to elucidate miRNAs functions is their identification, and miRNAs have been primarily discovered by direct cloning and sequencing, genetic screening, and bioinformatic predictions [31]. Food demands of the increasing world population caused the efforts to be focused on sustainable food production through the improvement of crop plants.

The primary source of food consumed by more than half of the world's population is rice. The variety of environmental stresses, including cold, salt, drought, heat, and nutrient deficiency, is the factor that induces limitation of

growth and yield of the rice. In 2004, 20 miRNAs were first identified in rice from a rice cDNA (complementary DNA) library, and it was established that their predicted potential target genes participate in disease resistance, transcription, metabolism [32]. The following year another study identified 35 rice miRNAs, of which 14 were novel and involved in diverse physiological processes in rice [33-36]. Today, many rice miRNAs have been identified with 738 miRNAs sequences present in miRBase version 21 (http://www.mirbase.org). Drought [37], cold [38, 39], salinity [40, 41], aluminium [42], heavy metal [43], cadmium [44], arsenite [45], low and high dose rate γ-ray [46] triggers significant changes in expression of miRNAs in rice. Drought conditions reveal high expression of miR393, which targets two rice auxin receptor gene homologs [47]. The reduction of tolerance to drought is the result of its overexpression [48]. Two new phenotypes: high tillering and early flowering, which are beneficial for productivity, are shown as the result of the miR393-overexpressing in plants [49]. Several cold-stress-responsive miRNAs (miR167, miR319, miR812q, and miR1425) were identified within other studies that investigated extreme temperatures (cold or heat) [50]. These miRNAs play an important part in modulating the expression of their target genes to respond to cold conditions [50]. Cold tolerance can be enhanced by miR319 overexpression [39, p. 2212]. A high-temperature-responsive miRNA that modulates the expression of L-ascorbate oxidase in response to the heat stress and adaptation of rice has been reported as miR397 [50, 51]. In addition, it was reported that the improvement of yield due to increasing grain size and promoting panicle branching is the result of the overexpression of miR397 and the downregulation of the corresponding target gene [52]. Enhanced disease resistance to the fungal pathogen *Magnaporthe oryzae*, the cause of rice blast disease, has been revealed to be the result of the overexpression of the miR7695 [53]. The miR820 has been reported to influence salt, high temperature, and drought stress responses [54]. The miR396d and its target, the growth regulatory factor gene, have been identified to be involved in floral organogenesis. The miR156 was reported to negatively control the number of panicle branches and grain yield [55]. The miR397 causes increased grain size, more rice panicle branching, and higher grain productivity. The expression of the laccase gene was down-regulated due to the performance of this miRNA, which successively impacted the sensitivity of plants to brassinosteroids, thereby causing the growth in the yields [52, p. 850]. The miRNAs involved in the progression of plant growth and development are differentially expressed within abiotic stress responses. The role of miRNAs in regulating rice yield is implied in these observations. The miRNA-based genetic modification technology can be a promising solution to food security due to developing superior crop cultivars with enhanced biotic and abiotic stress tolerance and increased biomass yields [56].

Maize is the most important food crop worldwide, used for food, feed, and forage and as a source of ethanol for fuel production. Along with being used in various industrial branches, maize has taken part in research as a model plant [57]. The maize crop development and adaptation to the abiotic stress responses have been the scope of extensive research to gain better continuous yield. The growth

and development of the plant are influenced by a great number of environmental stresses, including salt, light, thermal, radiation, drought, and oxidative stress, which, in its turn, result in halting the crop yield [58]. In recent years few attempts have been made for developing stress tolerance in this crop [59].

Five miRNAs, including miR156, miR160, miR166, miR167, miR169 families involved in maize development, growth, and responses to biotic stress, were first outlined and characterized their potential target genes [60]. The 325 miRNAs of maize playing a crucial role in growth, development, and plant responses to biotic and abiotic stresses are listed in the miRBase database. Plant TF family, involved in development and stress regulation, has been shown to be negatively regulated by miR164 [61]. Furthermore, such miRNAs as miR156a, miR160a, miR164e, miR164a, miR167d, miR168, miR169a, miR393a, miR397b, miR408b, miR528a belonging to 20 families, including 11 novel miRNA families, were established and characterized to take part in maize endosperm development [62]. Three maize miRNAs, miR528a, miR167a, and miR160b, were identified and characterized as playing an essential role in ear germination, development, and physiology, providing a greater understanding of molecular mechanisms involved in the plant [63]. Lately, 124 conserved maize miRNAs and 68 novel maize miRNAs were identified to be related to drought stress resistance. They take an important part in regulating genes incorporated in the drought stress response [64]. The aberrant expressions of miRNAs, especially related to abiotic stress, are highly important in developing drought-tolerant and genetically improved plants. The previous experience has proved the need to study the new targets to develop agriculturally important crop varieties as being extremely important.

Nutritional qualities and massive contribution toward food security are the factors that make wheat one of the most important cereal crops worldwide. Great endeavor has been made to study miRNAs in wheat with the assistance of sequencing leading to the discovery of 58 wheat miRNAs comprising 43 miRNA families, 20 of these families were conserved (miR156, miR157, miR159, miR160, miR164, miR165, miR166, miR167, miR168, miR169, miR170, miR171, miR172, miR319, miR390, miR393, miR396, miR397, miR399, and miR408) and 23 were novel (miR501, miR502, miR503, miR504, miR505 miR506, miR510, miR514, and miR516) [65]. They have been predicted to target genes participating in wheat development and various physiological processes [65, p. 9]. Sixty-two conserved miRNAs, belonging to 30 miRNA families and several new miRNAs were found in wheat by EST analysis, and their predicted potential target genes are known to be involved in various biological processes among which there is development (miR397, miR437), disease resistance (miR1436, miR1439, miR5067, miR5205), abiotic stress response (miR395d, miR1435), ion transportation (miR5181, miR5175), metabolic pathways (miR774, miR1126), and signal transduction (miR530, miR5175) [66]. New abiotic stress-responsive miRNAs comprising miR1122, miR1117, miR1134 and miR113, miR5653, miR855, miR819k, miR3708, and miR5156 were detected in wheat [67]. These miRNAs are involved

in regulating corresponding target genes that engaged in growth, metabolism, and stress responses [68].

The staff of ENU have carried out several works devoted to the study of plant miRNAs in Kazakhstan, in which RNA silencing in plants has been studied [69-72]. The above review of studies of miRNAs in rice, maize, and wheat indicates that the role of miRNAs in the growth and development of important food crops is investigated poorly. In most cases, the involvement of miRNAs in various biological processes has been described, but it has not been established which genes are the targets for these miRNAs. It is essential to solving this problem since it is necessary to know which miRNAs interact with target genes to carry out genetic-engineering manipulations.

1.1.1 Biogenesis of plant miRNAs

Gene expression of a variety of protein-coding genes at the posttranscriptional level is regulated by miRNAs [73, 74]. At the first stage, they are transcribed as primary miRNAs with a few hundred nucleotides. The mature miRNA sequences, which consist of only 19-24 nt are formed after several processing steps [75, 76]. The most important for recognizing the transcript of target protein-coding genes in animals is the seed sequence (second to seventh nucleotides of the mature sequence). The entire mature sequence is used for recognizing the transcript with near-perfect base pairings in plants [77].

Plant miRNAs are endogenous 19-24 nt small RNAs, which can fulfill functions of regulation of development, metabolism and respond to biotic and abiotic stresses [78]. Thousands of miRNAs have been found in plants since the lin-4 miRNA was first discovered in the nematode Caenorhabditis elegans in 1993. Regulatory roles performed by miRNAs in many biological processes have been uncovered. Such miRNAs as miR156, miR159, miR164, and miR171 were first described in *A. thaliana* by isolating, cloning, and sequencing small RNA populations [79, 80].

The miRNAs are processed from mRNA precursors that are transcribed by RNA polymerase II (Pol II) from MIRNA genes (the corresponding genes encoding miRNAs). Most plant species contain more than 100 MIRNA genes in their genome [81-84]. MIRNA genes generally do not overlap with other genes and are widely distributed in the genome, even though miRNAs are encoded in introns (termed “mirtrons”), in exons of protein-coding genes, and miRNAs transcribed from transposable elements have also been described in plants [85]. MIRNA genes and their RNA products group families on the base of nucleotide sequence similarity of the mature miRNA. These sequences are very akin within a family (at least about 85% identical), even though the sequences of the MIRNA gene and that of the pri- and pre-miRNA outside the mature miRNA sequence can be highly variable [85, p. 233]. Multigene families typically encode the miRNAs, and several miRNA genes can exist for the same mature miRNA [86, 87]. Transcription of the initial non-protein-coding RNA from a MIRNA gene, termed the primary miRNA (pri-miRNA) transcript, by Pol II identifies the nascent transcript for modification.

Pri-miRNA modification includes the addition of a 7-methylguanosine capping structure at the 5’ terminus (5’ cap) and a polyadenylated tail (poly(A) tail) at the 3’ terminus of the transcript [88-91]. All pri-miRNAs are presented by a region of sequence partial self-complementarity, enabling the transcript to fold back onto itself to form a stem-loop structured, imperfectly double-stranded RNA (dsRNA). The pri-miRNA is cleaved by a complex of the endonuclease DICERLIKE 1 (DCL1), the RNA binding protein HYPONASTIC LEAVES 1 (HYL1), and the zinc-finger protein SERRATE (SE) into a miRNA precursor that includes only the hairpin (called a pre-miRNA). When the hairpin pre-miRNA is cleaved for the second time by the DCL1/HYL1/SE complex, a 19–24 bp miRNA duplex is produced. DCL1 processes most plant pre-miRNAs to generate 21 nt mature miRNAs, but DCLs 2–4 can also be involved to generate diverse lengths [92]. Such miRNA heterogeneity varies the miRNA pools and tends to raise their regulatory potential. The 3’ ends of both miRNAs in the duplex are methylated by HUA ENHANCER 1 (HEN1), enhancing their stability [93-95]. When the duplex strands are detached from one another, the now single-stranded sRNA must be readily distinguished from other RNA species of a similar size, such as mRNA degradation products. Therefore, HEN1-directed methylation of plant sRNAs ensures that the mature sRNA is not cleared from the plant cell prior to being loaded by an RNA silencing effector complex [96].

The current nomenclature calls for the mature miRNA derived from the 5’ end of the hairpin to be called the “5p” and the miRNA derived from the 3’ end of the hairpin the ‘3p’. Gene silencing is promoted when one strand of the miRNA-5p/miRNA-3p duplex is loaded onto ARGONAUTE1 (AGO1) to establish the RNA-induced silencing complex (RISC), which recognizes target mRNAs by their complementarity with the miRNA. mRNA degradation and/or translational repression is caused by the interaction of the RISC complex with the target mRNA [97-101].

Mature miRNAs in databases are presented in the form of zma-miR-156, with the first three letters referring to the species of origin (here, *Z. mays*). In that case, zma-MIR-156 would express the corresponding gene or a precursor sequence. Closely related mature sequences may be denoted by lettered suffixes, zma-miR-156a and zma-miR-156b would have been expressed from the precursor sequences zma-MIR-156a and zma-MIR-156b, respectively.

It has been revealed with the application of genomics resources and bioinformatics tools that miRNAs show impressively different taxonomic distributions. Some miRNAs exist in all land plants, from bryophytes to flowering plants, whereas many others have been revealed only in a single species [102-106]. Many miRNAs have been uncovered to be evolutionarily conserved across all major lineages of plants, including gymnosperms, mosses, monocots, and eudicots [107]. The conservation and diversification of miRNAs during plant kingdom evolution form the basis for two miRNA family classes: highly expressed, evolutionarily conserved miRNAs, and non-conserved miRNAs, miRNAs only found in a smaller and usually more closely related group of plant species or

triggered under particular conditions [108]. The ancient miRNAs are often highly expressed and evolutionarily conserved, whereas the young miRNAs are expressed at comparatively low levels or only induced under specific conditions and generally exist only in few species, as a result being evolutionarily non-conserved [108, p. 1]. The miRNAs limited to single species or even populations and do definitely not exist in the sister species might be assumed to have been originated quite recently, after the lineage that led to the sister species had branched-off. The miRNAs identified in distantly related plants may have existed in the stem group of the respective lineages. Therefore, their origins are dated back to the early evolution of land plants. Eight of the 16 miRNAs originally cloned from *A. thaliana* have been perfectly conserved across the length of the mature miRNA sequence in rice by the Bartel group [78, p. 1621]. Absolute conservation at the miRNA level in dicot- and monocotyledonous was the factor that miRNAs may play a vital role in plant survival. miRNA-directed gene expression regulation has now shown its ability to assist in providing all aspects of vegetative and reproductive development in plants [109-112].

1.1.2 miRNA target prediction

Within the past ten years, thousands of miRNAs in plants have been identified with the use of computational strategies and experimental methods. Plant miRNAs exhibit a high degree of sequence complementarity to their target mRNAs, and among the early computational approaches, homolog-based comparative genomic strategies predominated and conserved miRNAs were identified in cotton [113], switchgrass [114], wheat [66, p. 3796], potato [115], and others. The early experimental methods involved direct cloning and approaches based on genetic screening to detect miRNAs in plants and conduct their functional analysis [19, p. 3]. Sanger sequencing and analysis were used after direct cloning. The development of next-generation deep sequencing was the factor that evolved this technology into a powerful tool improving the processes of miRNA discovery and target identification in plants [116, 117]. Northern blotting or real-time PCR-based assays are utilized to validate the expression of the miRNAs under identification [118-120]. Furthermore, miRNA target identification at the protein level can be conducted using techniques focused on the chromatography of proteins, mass spectrometry analysis, Western blotting, protein foot printing.

Databases containing searchable information on the miRNAs are being developed due to the identification of miRNAs. The miRBase is the tool that is the most useful to research miRNA. The miRBase database, being a prominent register of all identified mature miRNAs, also enables to detection of their precursor sequences, primary evidence of existence, and other information [121]. A great amount of information for plant miRNAs, including the miRNA and their targets, secondary structure, expression profiling, and genome browser, is contained in the Plant MicroRNA Database [122].

The miRNAs are important regulatory molecules. One of the main reasons why the functions of the majority of miRNAs targets remain unknown is a lack of

knowledge in this sphere of studies, even though the increasing cases of evidence have demonstrated that miRNAs play important roles in plant growth and development. The critical step for defining the regulatory miRNA role in the complex networks that regulate biological processes is identifying and validating the interactions between miRNAs and their targets.

A wide number of potential target sites may be present for any miRNA. Knowledge of miRNA targets allows recognizing their role in the cell. The miRNA molecules downregulate gene expression by sequence-specific hybridization to target mRNAs [123, 124]. Effective plant miRNA binding usually requires a perfect complementarity with the target sequence. This phenomenon makes the designation of a potential miRNA: target pair easier with higher specificity than in the case of animal miRNA molecules [125]. Due to high expenses and a long period of time that should be spent on the experimental validation of every potential miRNA target in the laboratory, this approach is not feasible. A more reasonable approach to predict the potential targets of miRNAs is a computational one. Implementation of this method can simplify the miRNA's potential targets prediction procedure because it allows at the stage of an initial selection to reduce the number of target sites to be experimentally validated. The number of tools for computational analysis is constantly increasing; each of them maintains a different strategy to perform potential miRNA target prediction. A large number of Watson-Crick base pairings with the target mRNA are required to use most of these approaches. In addition, the accuracy of prediction is increased because these algorithms take into account other features, among which binding free energy, evolutionary conservation, local AU content, and target-site accessibility [126-128].

Many of the target genes of plant miRNAs are predicted using bioinformatics tools, with subsequent experimental validation [129-131]. While the expression levels of the target mRNAs can be monitored by real-time PCR, the target cutting site can be mapped by 5′-RACE. Recently, the technique of degradome sequencing was developed, which is a modified version of 5′-RACE using a high-throughput, deep sequencing method [132]. The degradome sequencing approach also gives information on the relative abundance of cleaved targets [129, p. 14758].

The advantages of performing computational methods for identifying miRNAs in plants lay in its rapidness, lower expenses, and relatively easy comparison with experimental procedures. In plants, miRNA targets can be identified through perfect or near-perfect base pair complementarity between miRNAs and mRNA sequences [133, 134]. Bioinformatic tools for miRNA target prediction include the Target-align algorithm, which first calculates a score for a specific miRNA and its potential targets. Then, the specific criteria are used to identify potential plant miRNA targets. The program uses maximum mismatches and maximum consecutive mismatches between miRNAs and their targets [135]. Users can adjust almost all of the parameters in this alignment tool. Target-align can identify multi-target sites as well the potential for non-cleaved target sites by

changing the default settings. TAPIR is another plant miRNA target prediction web service that offers a designation of target sequences by two different algorithm modes, fast or precise (much slower) [136, 137]. The latter also allows predicting miRNA/mRNA duplexes with a large bulge in a cleavage site that inhibits the miRNA activity [136, p. 1566]. The user must provide the miRNA and mRNA sequences in a FASTA file as inputs. Features that are evaluated during TAPIR target predictions include “seed” region matching (the “seed” region describes the 2–8 nt at the 5’ end of molecule), free energy, and the number of mismatches, gaps, as well as G:U pairs. TAPIR method is also available as a stand-alone tool for Linux operating systems. The psRNATarget is dedicated to predicting targets for small RNAs of plants, including miRNAs [138]. Because of built-in databases, this online tool enables the user to find targets by providing only the sRNA sequences from the species of interest or by providing only the set of potential target sequences that will be used for all published miRNA molecules from a given species. If these options do not fulfill the user’s need, there is also the possibility to provide custom sRNA and target sequences for analysis. During the miRNA target evaluation, psRNATarget focuses on several features, including “seed” region matching (the “seed” region describes the 2–8 nt at the 5’end of molecule), complementary matching, target-site accessibility, and target-site abundance [138, p. 155]. The presented tool also proposes a mechanism of miRNA action for each of the predicted targets, either “Cleavage” or “Translation Inhibition.” pTAREF uses a machine-learning algorithm that predicts RNA:miRNA interactions based on alignment penalty, target:miRNA binding thermodynamic, and plant-specific flanking region dinucleotide density profile variation in a position-specific manner with respect to the possible target site [139]. FindmiRNA, a resource of predicted miRNA and precursor candidates for the Arabidopsis Genome. FindmiRNA algorithm is used for predicting potential miRNAs in a given set of candidate precursor sequences that have corresponding target sites in the transcriptome. Generally, the algorithm is based on the complementarity existing between plant miRNAs and their mRNA targets to identify initial putative miRNA. Then the software analyzes the candidate miRNA precursor sequence with regard to forming a stem-loop structure [140]. miRTarBase is a database for experimentally validated microRNA-target interaction database [141, 142]. RNA22, a pattern-based approach for the discovery of miRNA binding sites and their corresponding miRNA/mRNA complexes. Rna22 has high sensitivity and can be applied to the analysis of any genome without requiring genome-specific retraining. Rna22 is a target prediction algorithm that is based on a search for patterns that are statistically significant miRNA motifs created after a sequence analysis of known mature miRNAs [143]. It first searches for reverse complement sites of patterns within mRNA of interest and determines sites with many patterns aligned (so-called ‘hot spots’). The next step is the identification of miRNAs that are likely to bind to these sites. This approach also allows to identifying sites targeted by yet-undiscovered miRNAs. The minimum number of base pairs between miRNA and mRNA, the maximum number of unpaired bases, and the free energy cutoff are

user-defined parameters [143, p. 1204]. RNAhybrid finds the energetically most favorable hybridizations of a small RNA to a large RNA. Intramolecular hybridizations, that is, base pairings between target nucleotides or between miRNA nucleotides, are not allowed. The program predicts optimal and additional suboptimal, nonoverlapping hits, either up to user-defined number or with free energies up to a user-defined energy or p-value threshold. For large targets, the time complexity of the algorithm is linear in the target length, allowing many long targets to be searched in a short time [144].

1.1.3 Plant transcription factors

Many genes targeted by miRNAs encode TFs. These TFs control important developmental processes such as cell division, expansion, differentiation, specification of organ identities, phase transition, and nutrition homeostasis [145]. TFs, also known as *trans*-acting factors, are a class of regulatory proteins that can activate or suppress the transcription of target genes by interacting with *cis*-acting elements in the promoter region of the genes [146]. As a result of recent studies, it has been discovered that TFs and miRNAs regulate gene expression not isolated but more in an interactive, cooperative manner. TFs regulate the transcription initiation of their target genes, including miRNA transcripts on the transcriptional level. At the same time, miRNAs can regulate their targets, which can also be TFs, post-transcriptionally [147].

Plant growth and development are a reflection of gene expression. To ensure proper growth and development in plant, appropriate timing and pattern of gene expression and production of proteins are required [148, 149]. The key regulators determine how gene expression includes miRNAs and TFs; thus, they influence plant physiology and phenotype [150-153].

TCP TF contains a TCP domain, which codes a motif that is predicted to form a basic helix-loop-helix structure known for distinct DNA-binding domains [154-157]. This domain was initially identified in four proteins encoded by apparently unrelated genes, from which the name ‘TCP’ was derived: teosinte branched1 (tb1) from maize, CYCLOIDEA (CYC) from snapdragon, and the PROLIFERATING CELL FACTORS 1 and 2 (PCF1 and PCF2) from rice [158]. According to the plant transcription factor database, 4187 genes of different plant species are included in the TCP family. TCP transcription factors are found in many plant species. They participate in various aspects of plant growth and development, among which branching, flower development, female and male gamete development, leaf development, and senescence [159-164]. The TCP family genes participate in apical domination [165], regulation of bilateral color symmetry [166] and cell cycle control [167]. The involvement of TCP to promote leaf development by cell division, growth, and differentiation has been unraveled due to previous findings [168-172]. As it was revealed in another functional analysis, a slight increase in the leaves size was attributed to the loss-of-function of miR319, which was regulating TCP genes [159, p. 1992]. In tomatoes, overexpression of miR319 resulted in the formation of a giant tomato leaf [173]. The TCP genes

affect leaf size, shape, and curvature and control the pace of leaf senescence in plants [155, p. 3; 159, p. 1996]. The secondary cell wall in plants is composed mainly of lignin, cellulose, and hemicellulose. TCP TF was considered to activate secondary cell wall biosynthesis in *A. thaliana* [174-176]. Silencing of TCP genes by miR319a overexpression, increased cell wall lignification, and the enhanced secondary cell wall thickening [177]. Anther dehiscence, essential for plant fertilization, is conducted due to the optimal shear force produced by secondary cell wall thickening [178]. TCP TFs in plants control flowering time [179, 180]. Overexpressing miR319 in *A. thaliana* mutants delayed the flowering phenotype in long-day conditions [181, 182]. The late-flowering phenotype was observed due to loss-of-function, where miR319 had targeted TCP4 [182, p. 373]. The TCP family genes also participate in auxin and jasmonic acid signaling [183, 184], development of male and female gametophyte [185], mitochondrial biogenesis [186, 187], and interaction with the circadian clock [188].

Unfavorable environmental conditions are the factor to which plants are constantly subjected. An interrelation between miRNA-regulated TCP genes and plant response to abiotic stresses has been discovered by several researchers [189, 190]. The miR319 positively regulates cold tolerance in rice. Repression of the expression of two TCP genes in rice led to increased cold tolerance of rice seedlings after chilling acclimation [38, p. 41]. Another potential rice target genes of miR319, showed obvious cold-induced expression, and this induction pattern was markedly inhibited in miR319-overexpressing plants [38, p. 42-44].

The large size of the MYB family in plants indicates their importance in the control of plant-specific processes. The roles of MYB TFs in plants are described in a tremendous amount of works [191, 192]. MYB participates in the growth and development of different plant species, e.g., in *Glycine max*, they are involved in flower color development and in signal transduction pathways in *A. thaliana, O. sativa* [193-196]. In *A. thaliana* and *Medicago truncatula* they regulate the biosynthesis of secondary metabolites [197-200]. Loss-of-function of miR858 plants led to robust growth and early flowering [201]. MYB TF was able to activate miR399, which is a response to phosphate starvation in Arabidopsis [202, 203]. In maize, miR159d, which targeted MYB TF was significantly downregulated in the leaves during senescence, while in another inbred line, miR159d was upregulated [204]. The miR447a and miR5255 might play a significant role in root and fiber development under drought and salinity stresses by regulating MYB TF in cotton [205]. Two miRNAs in cotton, miR828 and miR858, targeted MYB2, which is responsible for fiber development, was the similar study object [206]. A study had been carried out to functionally characterized miR858a in Arabidopsis. The downregulation of several MYB TFs involved in the flavonoid biosynthesis pathway was caused by overexpression of miR858a in Arabidopsis, consequently, the flavonoid production was reduced. On the opposite, plant growth reduction and delayed flowering were the results of the knockdown of miR858a [201, p. 955]. In cotton, MYB TF was found to be upregulated in response to high temperatures. Like the previous study [206, p. 2],

MYB TF was targeted by miR828a and miR858 [207]. This finding suggested that MYB TF and miR828 and miR858 might have a dual role in cotton during fiber development and adaptation against high temperature.

Plant growth and development are vulnerable to environmental stresses, which negatively impact the molecular functions of plants [208]. Among the abiotic factors, increased temperature due to global warming is a critical parameter in limiting biological processes and yields in plants [209-212]. Transiently increased temperature resulted in male sterility in wheat, rice, and maize [213-215]. Among the consequences of exposure to high-temperature stress there are protein denaturation, lipid peroxidation elevation, membrane fluidity disturbance, and reactive oxygen species generation [216-219]. These changes disrupt normal physiological processes, and these disturbances may even lead to plant death.

The enhancement of crop productivity influenced by diverse abiotic stresses remains the major objective for agronomic research [220]. Heat stress, being one of the major abiotic stresses, has an independent mode of action on plant cells' physiology and metabolism and negatively affects the growth and development of plants, which may lead to catastrophic loss of crop productivity and result in widespread famine [221]. The distribution and productivity of agriculturally important plants worldwide experience adverse effects because of the heat stress that influences plant processes like germination, growth, development, reproduction, and yield [222]. One of the key regulators in plant abotic stress response is heat shock TF. Plants contain multiple genes coding for HSFs [223]. Comprehensive identification of HSF TFs from different plant species has been accomplished recently. For example, HSF in tomatoes plays an important role in response to high temperatures[224]. Tomato HSF TF contributes to fruit set under heat stress conditions [225]. In Arabidopsis, the expression level of HSF rose at the stages of embryogenesis and seed maturation [226]. In rice, HSF TF are related to cadmium tolerance [227], and contribute to embryogenesis in sunflowers [228]. The miR160 modulates plant development and heat shock protein gene expression to mediate heat tolerance in Arabidopsis [229]. Heat-responsive miRNAs in switchgrass have also been reported [230].

Recent studies have been conducted to find out more data on the ERF. Being involved in different stress responses, ERFs could act both as activators or repressors of gene expression [231]. Such species as Arabidopsis, tobacco, tomato, soybean, rice, and hot pepper have shown various ERFs [232]. Both growth and productivity of plants are influenced by cold stress. Plants have adopted alteration in gene expression patterns in response to cold stress. The cold-inducible gene products may directly fight against cold or be a TF that activates other upstream genes [233, 234]. Tomato ERF was involved in salt tolerance in transgenic rice via activation of cold-related genes. During heat stress, ERF requires HSF TFs as a coactivator to confer heat stress tolerance.

The miRNAs post-transcriptionally regulated genes encoding ERFs. The miR156 and miR172 are proved to mediate ERF regulation under salt stress in radish [235]. Many key functions, including development, abiotic and biotic stress

responses, can be regulated by ERF TF. Therefore, clarifying the mechanisms underlying the transmission of stress signals is important to manipulate ERF regulation to improve crop stress resistance.

The GRAS family of plant proteins regulates many aspects of growth and development processes, including gibberellin signal transduction, axillary meristem initiation, shoot meristem maintenance, root radial patterning, and responses to the biotic and abiotic environment [236-241]. According to the previous studies, some GRAS genes are discovered to be regulated by miR171. The miR171-GRAS regulatory network assists various physiological processes, including shoot meristem maintenance, axillary bud formation, flowering time, chlorophyll biosynthesis and trichome distribution. In *Lilium longiflorum*, a GRAS protein was found to be involved in microsporogenesis [242]. It was reported that miRNA171 was involved in the regulation of shoot branching by regulating the transcription of GRAS genes [243]. This mechanism is identified in many species, for instance, *A. thaliana* [243, p. 795], rice [244], and grapevine [245]. Multiple agronomical traits are affected by overexpression of the miR171 target gene due to modulating gibberellin and auxin signaling, highlighting the role of hormone crosstalk in tomato development [246]. In Arabidopsis, GRF genes are regulated by the miR396 [247-252]. In young leaves, GRF activity is restricted to the proximal proliferative zone of the leaf because miR396b is expressed in the distal part and antagonizes GRF expression [253-255]. In adult leaves, miR396b expression spreads and restricts GRF activity in the entire organ [256]. Plants overexpressing the miRNA-insensitive GRF5 or a miRNA-resistant variant of GRF3 have larger leaves than the wild type, while leaves of plants overexpressing miR396b are smaller [256, p-4]. Such abiotic stresses as cold, salinity and drought, pose a threat to global agriculture because they prevent crop plants from reaching their full genetic potential and causing yield loss [257]. Abiotic stresses limit plant performance by reducing plant growth, development, and yield. One critical component of plant stress response mechanisms is the transcriptional regulation of plant genes through the action of plant transcription factors in response to environmental stresses. TFs containing zinc finger-binding domains are among those transcriptional regulators extensively involved in plant stress responses. C2H2 zinc finger proteins form a relatively large family of transcriptional regulators in plants [258]. The ability of C2H2 zinc finger proteins to regulate genes involved in plant growth and development under normal growth conditions has been revealed in recent studies and the genes involved in plant stress responses [258, p. 5]. C2H2 zinc finger proteins participate in plant response to such adverse stresses as low temperatures, salt, drought, oxidative stress, excessive light, and silique shattering [259-262]. These C2H2 proteins regulate the expression of stress-responsive genes and act as part of stress response networks. Worldwide crop production faces the problem of salt stress [263, 264]. Many C2H2-type TFs act as transcriptional activators or repressors to regulate plant responses to salt stress [265]. Ionic, osmotic, and oxidative stress to plants are generated as a result of salt stress [266, 267]. C2H2-type zinc finger proteins

participate in salt tolerance by influencing salt-regulated genes [268-271]. Salinity, cold, and drought stress are abiotic stresses that induce osmotic stress [272]. In plants, osmotic stress can cause for physiological drought, ion imbalance, oxidative damage, and growth inhibition [233, p. 784]. The ability of plants to resist osmotic stress is related to their ability to alter osmotic pressure and increase the biosynthesis of osmotic regulators [273]. The C2H2 zinc finger proteins are involved in regulating the osmotic stress pathway in Arabidopsis [274-276].

Serious damage can be caused to plants by a cold snap, which can lead to plant loss when severe [277, 278]. A possible solution to the problem of cold stress injury is to understand comprehensively the mechanism underlying cold damage in plants [279-282]. C2H2 zinc finger proteins enhance cold resistance due to direct regulation of downstream cold-related genes in Arabidopsis [283], sweet potato [284], banana [285]. One more important factor limiting plant growth globally is drought, which provokes adverse reactions such as osmotic imbalance, membrane system damage, and decreased respiratory and photosynthetic rates. Along with preventing plant growth and metabolism at various stages, drought impacts crop quality and yields [286-288]. C2H2 zinc finger proteins enhance plant drought resistance by increasing the levels of osmotic adjustment substances [289-292].

The study of miRNAs and their targets has become a plant research focus over the last few decades. Newly developed relations between various miRNAs and TFs, will allow plant scientists to develop plants with desired phenotypes and stress tolerance ability against particular stress. The plants with stress tolerance will supply food production security for the continuously increasing world population. We have reviewed the regulatory relationships between miRNAs and various families of TFs like TCP, MYB, HSF, GRAS, ERF, C2H2 from different plant species. The studied interactions between various miRNAs and above mentioned TFs have important roles during drought tolerance, signal transduction and biosynthesis of secondary metabolites, floral development and nodule formation, leaf development, multiple stress tolerances, lateral root growth, and plant transition from juvenile to adult, respectively. The miRNAs and TFs, as major gene regulators, define the phenotype, physiology, and response to a number of environmental stresses. Most studies that we have cited above were to investigate the effect of miRNAs on gene expression and physiological processes. Nevertheless, the connection between miRNAs and their target genes was not certainly revealed. The effect of miRNAs on the expression of the TF family genes, which play an important role in plant development and growth, is poorly studied. The aim of our work was to set the study of quantitative characteristics of interactions between miRNAs and mRNAs of the TCP, MYB, HSF, GRAS, ERF, C2H2 TF genes using bioinformatic approaches.

1.2 Cross-kingdom regulation by plant miRNAs

For humans, plant and animal miRNAs are exogenous (ex-miRNA or xe-miRNA) and do not have distinctive features among themselves. Therefore, they will be considered the general variety of endogenous miRNAs source for a human

body, which means that all human genes can be their potential targets [293, 294]. The effect of ex-miR on human target genes and the consequences of this effect will depend on their concentration and the duration of their presence in the cells. Many studies have shown that miRNAs that enter the gastrointestinal tract with food (dietary miRNA) are then found in various tissues [295-305].

In 2012, plant-derived miRNAs are reported to be present in the serum of human or herbivorous mammals and regulate the gene expression of particular targets at the post-transcriptional level [303, p. 108]. A few years later, a honeysuckle miRNA, miR2911, was revealed to be absorbed through the gastrointestinal tracts of mice infected with influenza A virus upon ingestion of a honeysuckle decoction and travel via the bloodstream to the lungs where it directly targets influenza A virus [306]. Due to the results of this research, the initial evidence that plant miRNAs may have the ability to be transmitted from plants to mammals through the gastrointestinal tract has been provided. Thus, plant miRNAs are able to regulate their endogenous targets in a cross-kingdom manner and affect the cellular systems of their recipients. The novel ability of plant miRNAs to regulate target genes in different organisms may lead to the complete transformation in our current knowledge and, therefore, new opportunities for novel therapies through plant-based diets are possible to be identified [307].

The gastrointestinal tract is the way through which the plant miRNAs can enter the human body. Then the miRNAs spread with blood in combination with proteins or as part of exosomes [308-312]. According to the previous findings, food storage, processing and cooking do not reduce the miRNA content in plants. This factor might be crucial in understanding the reason for the abundance of miRNAs in food products. Although plant miRNAs can survive all food processing stages, they still tend to be degraded in the mammalian circulation system due to endonuclease activity, especially in the spleen and liver [313]. A simulated human digestion system was utilized in the study to investigate this topic further. Significant bioavailability of miR166, miR167, and miR168 (from rice and soybean) after early-stage digestion for 75 min was depicted in the issue of the research [314]. It has been suggested that plant miRNAs are packaged into microvesicles or exosomes before being absorbed via intestinal epithelial cells. Due to acting as barriers despite all the protective mechanisms of plant miRNAs, the microvesicles or exosomes are the way of further protection from miRNA degradation. Furthermore, miRNAs can be transported by several types of carriers, among which there are apoptotic bodies and edible plant-derived exosome-like nanoparticles [315]. After packaging, miRNAs are released into the circulation and subsequently carried to various tissues and organs where the regulation of the expression of target genes is provided [316]. Moreover, the AGO2 protein, presenting in exosomes, can be utilized by plant miRNAs to form a RISC, thereby facilitating binding to target genes [303, p. 120]. The attractiveness of the topic of cross-kingdom regulation of miRNAs relates to the fact that they are ingested with food [317, 318]. A digestive tract is a place where plant miRNAs can be stored. They can penetrate into the circulatory system and regulate protein synthesis on

mRNA [319-321]. For example, most zma-miRNAs were found in the heart, brain, mammary gland, lung, liver, kidney, and serum exosomes of the pig as the result of the consumption of fresh maize [315, p. 2].

In different human organs, the concentration of plant miRNAs can vary, and their amount can be compared to en-miR. Minor concentrations of plant miRNAs have been found in humans and animals as a result of some studies [322]. After entering the recipient's organism, plant miRNAs lead to reproducible changes in some properties and physiological processes [323-325]. The ex-miR involved in the regulation of recipient gene expression may cause disease [326-330]. Plant miRNAs were assumed to circulate in the blood throughout the body in the absence of features that restrict their entry into any cell [331]. This assumption is based on the diversity of the nucleotide composition of hsa-miRNAs, some of which overlap with diverse pl-miRNAs [332, 333].

The transfer of ex-miRNAs to animal objects has been studied [334, 335]. The stomachs, intestines, serum, and feces of mice were the locations where the most enriched miR172 in cabbage was identified [317, p. 6]. As the results of the study, it was found out that absorbed miRNAs can participate in metabolism in a similar way to endogenous miRNAs and the concentration of miRNAs can remain stable for several days under the condition of continuous feeding [313, p. 383]. After consumption of 2.5 L of watermelon juice and 2.5 kg of mixed fruits, the miR156a, miR157a, miR162a, miR166a, miR167a, miR168a, miR172a, miR390a, miR528, and miR894 were found in the human plasma of volunteers [298, p. 506]. When pigs had been fed with corn for 7 days, the miR164a-5p, miR166a-3p, miR167e-5p, miR168a-5p, miR319a-3p and miR408a-3p were detected in porcine tissues and serum [315, p. 2]. Studies in the interaction between the miRNAs of plants, ingested for food ex-miR and the regulation of vital processes in humans and animals have been actively carried out recently [336-338]. Ex-miRs participation in the regulation of cellular function in healthy cells and their acting as important mediators in the development of animal diseases have been presumed [339-341]. Furthermore, they can serve as evolutionary linkers between different species, and both intra- and interspecies signal transmission is possible to be provided by ex-miRs [342-346]. Treatment of human diseases using ex-miR has become possible due to the ability of plant miRNAs to regulate target genes in humans and animals [347, 348]. Based on the available data, it has been suggested that the beneficial properties of medicinal plants can be provided due to the contribution of such xe-miRs [349], and cross-reference of species between kingdoms of living organisms is performed by ex-miRs taking part in many mechanisms associated with the occurrence and pathogenesis of various diseases [350-353].

Although the range of miRNAs in each plant species varies, each of them contains identical key miRNAs specifying plant growth and development regulation [354-365]. Recently, the effect of exogenous miRNAs on mRNA of human genes has been predicted due to the possibility of using bioinformatic approaches, which significantly save material and time expenditure for establishing

interactions of miRNA with mRNA [366-369]. Plant miRNA and animal miRNA binding sites, regardless of the origin of miRNAs, can be reliably identified with the implementation of the program for searching binding sites in target genes. Such a method allows predicting plant miRNA and human mRNA interaction [370]. The subject of our study was the possible interactions of plant miRNAs with human mRNA genes.

MATERIALS AND METHODS

2.1 Research materials

The object of the study was completely sequenced *A. thaliana, T. aestivum*, *Z. mays* and *O. sativa* genomes. The nucleotide sequences of the TCP, MYB, ERF, HSF, C2H2, GRAS genes, and other genomes of plant species (table 1) were obtained from Plant Transcription Factor Database v4.0 (http://planttfdb.cbi.pku.edu.cn/index.php). The nucleotide sequences of the mRNAs of 17 508 human genes were downloaded from GenBank (http://www.ncbi.nlm.nih.gov), the National Center for Biotechnology Information USA, NCBI. The GenBank flat-file format is one of the most commonly used formats used for nucleotide sequences. It contains all of the information associated with the sequence, as well as the sequence itself. The longest transcript was selected for each gene. The nucleotide sequences of *Homo sapiens*, *A. thaliana*, *T. aestivum*, *Z. mays*, and *O. sativa* miRNAs were taken from miRBase v.22 (http://www.mirbase.org/), which is a comprehensive and searchable miRNA database based on miRNA name, keyword, references, and annotation [121]. When creating a database of genes and interpreting the results obtained in work, the Sequence Manipulation Suite resource was used (https://www.bioinformatics.org/sms2/). The Sequence Manipulation Suite is a collection of over 30 JavaScript programs for analyzing and formatting nucleotide and amino acid sequences [371]. From the list of programs we used: Filter DNA/Protein - to remove spaces and numbers from nucleotide or amino acid sequences; GenBank to FASTA - to convert a DNA sequence from GenBank format to FASTA format.

The eFP (electronic fluorescent pictograph) browser was used to determine the expression patterns of the studied genes [372]. The eFP Browser is a tool that pictographically visualizes gene expression levels at different tissues for one of many datasets ranging across species. Where and when a gene is expressed – in developmental time or in response to environmental perturbations like drought or pathogens – can tell us a lot about the gene product's biology. If we don’t know the function of a gene, the information on where and when it is expressed can help suggest a function. A collection of eFP Browsers at the Bio-Analytic Resource for Plant Biology at (http://bar.utoronto.ca) provides easy access to 150 million expression measurements from arabidopsis, maize, rice, wheat and others. Approximately half of the measurements were made using Arabidopsis samples. Small pictographs are used to represent the experimental samples and contexts from which the expression data were generated, while a colour scale represents expression levels in different samples. To establish the involvement of predicted miRNA target genes of such agricultural crops as rice, wheat, and maize in the development of human diseases (with their abnormal expression), the DisGeNET (http://www.disgenet.org) program was used [373]. DisGeNET is one of the largest available collections of genes and variants involved in human diseases. DisGeNET integrates data from expert-curated repositories, catalogues, and the scientific literature.

To search for the predicted interactions between miRNA and mRNA, we used miRTarBase, the experimentally validated miRNA-target interactions database [141, p. 165; 142, p. 297]. As a database, miRTarBase has accumulated more than three hundred and sixty thousand miRNA-target interactions. Generally, the collected miRNA-target interactions are validated experimentally by reporter assay, western blot, microarray, and next-generation sequencing experiments. The miRTarBase provides the most updated collection by comparing with other similar, previously developed databases. When analyzing the amino acid sequences orthologous proteins, we used the database of the Kyoto encyclopedia of genes and genomes KEGG orthology (https: //www.génome.jp/kegg) [374].

Variability of amino acids and as well as nucleotide sequences was assessed with the WebLogo program (https://weblogo.berkeley.edu/logo.cgi) [375]. Aligned amino acid and nucleotide sequences of orthologous proteins and genes were used to study the evolutionary conservatism of the predicted miRNA binding sites in the mRNA of the studied genes. Logo charts were constructed to represent the results graphically. Logo charts are used to detect and analyze the conservatism of amino acids and nucleotide sequences of different types of organisms. According to the patterns of preservation or variability of sequences during evolution, a conclusion is made about their structural or functional significance. The Logo diagrams show the amino acid/nucleotide symbols in each position (on the abscissa axis), and the relative sizes of the symbols indicate their frequency in the studied sequences and are measured in bits (displayed on the ordinate axis). The list of species of organisms considered in the study of the conservatism of miRNA binding sites in orthologues is given in table 1.

Table 1 - The list of abbreviated names of plant species used in this work [383, p. 607-608]

Species name	Abbreviated names	Species name	Abbreviated names
1	2	3	4
Aegilops tauschii	*Ata*	*Oryza barthii*	*Oba*
Aethionema arabicum	*Aar*	*Oryza brachyantha*	*Obr*
Amborella trichopoda	*Atr*	*Oryza glaberrima*	*Ogl*
Ananas comosus	*Aco*	*Oryza glumaepatula*	*Ogu*
Arabidopsis halleri	*Aha*	*Oryza longistaminata*	*Olo*
Arabidopsis lyrata	*Aly*	*Oryza meridionalis*	*Ome*
Arabidopsis thaliana	*Ath*	*Oryza nivara*	*Oni*
Arabis alpina	*Aal*	*Oryza punctata*	*Opu*
Azadirachta indica	*Ain*	*Oryza rufipogon*	*Oru*
Boechera stricta	*Bst*	*Oryza sativa subsp. indica*	*Osai*
Brachypodium distachyon	*Bdi*	*Oryza sativa subsp. japonica*	*Osa.j*
Brachypodium stacei	*Bsa*	*Panicum hallii*	*Pha*
Brassica napus	*Bna*	*Panicum virgatum*	*Pvi*
Brassica oleracea	*Bol*	*Phalaenopsis equestris*	*Peq*
Brassica rapa	*Bra*	*Phoenix dactylifera*	*Pda*
Camelina sativa	*Csa*	*Phyllostachys heterocycla*	*Phe*

Continue of Table 1

1	2	3	4
Capsella grandiflora	*Cgr*	*Populus trichocarpa*	*Ptr*
Capsella rubella	*Cru*	*Raphanus raphanistrum*	*Rra*
Carica papaya	*Cpa*	*Raphanus sativus*	*Rsa*
Citrus clementina	*Ccl*	*Setaria italica*	*Sit*
Citrus sinensis	*Csi*	*Setaria viridis*	*Svi*
Dichanthelium oligosanthes	*Dol*	*Sisymbrium irio*	*Sir*
Elaeis guineensis	*Egu*	*Solanum lycopersicum*	*Sly*
Eragrostis tef	*Ete*	*Sorghum bicolor*	*Sbi*
Eucalyptus grandis	*Egr*	*Spirodela polyrhiza*	*Spo*
Eutrema salsugineum	*Esa*	*Tarenaya hassleriana*	*Tha*
Glycine max	*Gma*	*Thellungiella parvula*	*Tpa*
Gossypium arboreum	*Gar*	*Theobroma cacao*	*Tca*
Gossypium hirsutum	*Ghi*	*Triticum aestivum*	*Tae*
Gossypium raimondii	*Gra*	*Zea mays*	*Zma*
Hordeum vulgare	*Hvu*	*Zostera marina*	*Zmr*
Leersia perrieri	*Lpe*	*Zoysia matrella*	*Zmt*
Musa acuminata	*Mac*	*Zoysia japonica*	*Zja*
Oropetium thomaeum	*Oth*	*Zoysia pacifica*	*Zpa*

2.2 Research methods

2.2.1 MirTarget program for predicting miRNA binding sites with mRNA target genes

The miRNA binding sites in mRNAs of the target genes were predicted with the MirTarget program (Certificate of the Republic of Kazakhstan on carrying information to the State Register of Rights to Objects Protected by Copyright No. 6598 dated November 22, 2019) [376]. MirTarget is developed using the Java programming language. This program estimates the following quantitative characteristics of miRNA binding: (1) the beginning of the miRNA binding sites in mRNA; (2) the position of these sites in the 5’-untranslated region (5’UTR), in the protein coding sequence (CDS), and in the 3’-untranslated region (3’UTR) of mRNA; (3) free energy of miRNA interaction with mRNA (ΔG, kJ/mol); (4) nucleotide interaction schemes between miRNA and mRNA. Throughout the whole length of the binding site in mRNA, the formation of only one single nucleotide bulge is admitted. The calculated characteristics of interactions between miRNA and mRNA are shown for their concentration ratio 1:1. If the concentration ratio changes, the portion of miRNA and mRNA complexes will change significantly, according to the kinetic equation for the inhibitor–target system. ΔG/ΔGm (%) was calculated for each binding site, where ΔGm corresponds to the free energy of miRNA binding to the fully complementary nucleotide sequence. Intramolecular interactions within mRNA, which involve the miRNA binding sites, are always weaker than that between miRNA and mRNA in the binding site.

The positions of binding sites are shown from the first nucleotide 5'UTR of mRNA. Not only bonds between adenine (A) and uracil (U), and guanine (G) and cytosine (C) but also interactions between A and C, and G and U via a single hydrogen bond are considered. Distances between A and C (1.04 nm), G and U (1.02 nm) were similar to those between G and C, and A and U (1.03 nm) [377-379]. Therefore, the pairs G-C, A-U, G-U, and A-C promote the formation of the double-stranded structure of RNA without disrupting stacking interactions [380]. The number of hydrogen bonds in the G–C, A–U, G–U, and A–C interactions was 3, 2, 1, and 1, respectively. The value of the free energy of the hydrogen bond varies in the range from -0.7 to -1.6 kcal/mol. In the MirTarget program, the free energy of interaction of nucleotides due to hydrogen bonds was considered equal to 6.368 kJ/mol and 4.246 kJ/mol for G-C, A-U pairs, and 2.123 kJ/mol for G-U and A-C pairs, respectively.

The families of miRNAs differ from each other by 2-3 nucleotides, which corresponds to 15% of the differences in their nucleotides. Therefore, to avoid taking into account false-positive binding sites and low-specific interactions of miRNA and mRNA nucleotides, binding sites with ΔG/ΔGm 88% and above were selected. For miRNA 19 nucleotides (nt) in length, the minimum allowable value of ΔG/ΔGm was 94%, 20 nt – 92%, 21 nt – 91%, 22 nt – 90%, 23 nt – 89%, 24 nt – 88%. The MirTarget differs from other programs aimed at the finding of miRNA binding sites in mRNAs of plant genes by the following features: (1) it takes into account the interaction of miRNA with mRNA throughout the whole miRNA sequence; (2) it takes into account noncanonic pairs, G–U and A–C; (3) it calculates free energy of the miRNA-mRNA interaction.

2.2.2 MirTarSeq program for building oligopeptides encoded by miRNA binding sites

The MirTarSeq program (The copyright certificate "MirTarSeq" No. 15600 dated March 2, 2021) was used to search for oligopeptides encoded by the nucleotide sequences of miRNA binding in CDS of mRNA genes. For further analysis of evolutionary conservatism, the program includes 15 additional nucleotides in the results, located to the left and right of the interaction site. This program performs analysis in the presence of files with schemes of the interaction of miRNA with mRNA obtained as a result of the search for binding sites by the miRTarget program (interaction schemes are saved in a separate file with the scheme.mres extension) and files with genes in the gene format. When analyzing the data on MirTarSeq, the result is presented in the form of a table with the following information for each binding site: mRNA of the target gene, miRNA, beginning of the binding site (nt), ΔG value (kJ/mol), ratio ΔG/ΔGm (%), miRNA length, a nucleotide sequence of the site, a nucleotide sequence of the binding site with nucleotides flanking it on the left and right, oligopeptide encoded by the binding site and additional nucleotides, as well as oligopeptides encoded only by the miRNA binding site, translated in three reading frames. Due to this, we can study evolutionary conservatism, variability, that is, the analysis of changes in

nucleotide sequences in the process of evolution. We can study evolutionary conservatism, variability, that is, the analysis of changes in nucleotide sequences in the process of evolution. Orthologous sequences are evidence that certain sequences can be maintained by evolution despite the process of speciation. Since information about the amino acid sequence in proteins is normally passed from parents to offspring, conserved sequences in proteins indicate the presence of a conservative gene. The obtained data on plant genes can be used to develop a strategy for creating transgenic plants with increased productivity. The created MirTarSeq program allows to significantly reduce the number of commonly used steps in finding oligopeptides encoded by miRNAs binding sites.

2.2.3 Comparative characteristics of programs for searching miRNA binding sites with mRNA target genes

In order to substantiate the choise of the MirTarget program, we compared the known programs for searching for miRNA binding sites with mRNA. To compare and demonstrate the effectiveness of our program over other programs, we used TAPIR (http://bioinformatics.psb.ugent.be/webtools/tapir) [136, p. 1567], psRNATarget (http://plantgrn.noble.org/psRNATarget/) [138, p. 156], and RNA 22 (https://cm.jefferson.edu/rna22/Interactive/) [143, p. 1204]. The following examples of search for binding sites by the MirTarget program and other programs show the great advantage of the MirTarget program.

As a result of the comparative characteristics of the programs for searching for miRNA binding sites, the ath-miR5658-5p binding sites in the mRNA of the GSBRNA2T00009950001, AT1G53230.1 genes were studied. The TAPIR, psRNATarget, RNA 22 programs did not provide information on the interaction ath-miR5658-5p with mRNA of the GSBRNA2T00009950001 gene at site 610. Moreover, TAPIR did not detect a single ath-miR5658-5p binding site in the mRNA of the *Brassica napus* gene. The psRNATarget and RNA 22 programs found one binding site starting at positions 886 to 906 nt. The interaction schemes show that the psRNATarget and RNA 22 programs do not take into account noncanonical interactions between nucleotides. In this case, only 17 out of 21 miRNA nucleotides interact with mRNA of the GSBRNA2T00009950001 gene, whereas during the interaction of ath-miR5658-5p with GSBRNA2T00009950001 at position 610, the entire nucleotide sequence of miRNA interacts with mRNA (21 nt). Therefore, the probability of the ath-miR5658-5p interaction with the mRNA of the GSBRNA2T00009950001 gene at position 886 is lower than at position 610.

As a result of the search for the ath-miR5658-5p target genes, all compared programs revealed one binding site for the *A. thaliana* AT1G53230.1 gene. When considering the interaction schemes, it can be seen that the programs TAPIR, psRNATarget, and RNA 22 identified binding sites at positions 1242, 1239, and 1242, respectively. In all three cases, only 18 out of 21 nucleotides interact. The interaction scheme of the binding site detected by the MirTarget program at position 1236 of mRNA indicates the formation of hydrogen bonds between 21 nt ath-miR5658-5p and mRNA of the AT1G53230 gene, taking into account three

non-canonical pairs, which also indicates that the interaction energy of the studied miRNA-mRNA pair is higher at the site with the 1236 nt position in the AT1G53230 mRNA.

A comparative analysis of the four prediction programs for miRNA binding sites shows that the TAPIR, psRNATarget, and RNA 22 programs do not detect all binding sites, since they do not take into account noncanonical nucleotide pairs. TAPIR and RNA 22 showed the same results in both cases because it is possible that the same algorithms for finding miRNA binding sites are used. Since the psRNATarget and RNA 22 programs did not find more efficient binding sites at positions 610 and 1236 with the interaction of all miRNA nucleotides identified by the MirTarget program in the examples we have considered, during experiments this can lead to an off-target effect, which therefore can lead to unexpected effects that may be harmful.

Table 2 - Comparative characteristics of programs for searching miRNA binding sites with mRNA target genes [the material obtained in this study by Rakhmetullina A.K]

Gene: GSBRNA2T00009950001 (610; CDS; -87; 85; 21)		
miRNA	Programs	Schemes
ath-miR5658-5p	MirTarget	5'-**C**UUCA**C**CA**C**CA**C**CA**C**CA**C**CA**C**-3' |||||||||||||||||||| 3'-**A**AAGU**A**GU**A**GU**A**GU**A**GU**A**GU**A**-5'
	TAPIR	No binding site found
	psRNATarget	No binding site found 21 AAAGUAGUAGUAGUAGUAGUA 1 ::: ::: :::::: ::::: 886 UUUGAUCCUCAUCACCAUCAG 906
	RNA 22	No results found TTTGATCCTCATCACCATCAG 886 ||| ||| |||||| ||||| AAAGTAGTAGTAGTAGTAGTA
Gene: AT1G53230.1 (1236; CDS; -96; 94; 21)		
ath-miR5658-5p	MirTarget	5'-**CC**UCA**C**CAUCAUCAUCAUCAU-3' ||||||||||||||||||| 3'-**AA**AGU**A**GUAGUAGUAGUAGUA-5'
	TAPIR	AAAGUAGUAGUAGUAGUAGUA ..|||||||||||||||||. CAUCAUCAUCAUCAUCAUCAG 1242
	psRNATarget	21 AAAGUAGUAGUAGUAGUAGUA 1 ::::::::::::::::::: 1239 CACCAUCAUCAUCAUCAUCAU 1259
	RNA 22	CATCATCATCATCATCATCAG ||||||||||||||||||| AAAGTAGTAGTAGTAGTAGTA 1242

RESULTS AND DISCUSSION

3.1. Creation of databases of TCP, HSF, MYB, GRAS, ERF, C2H2 TF genes and miRNA of *A. thaliana, O. sativa, Z. mays,* and *T. aestivum*.

In the format available for the MirTarget program, the following databases were created: for genes of the TCP, HSF, MYB, GRAS, ERF, C2H2 TF families, consisting of 442 genes of *A. thaliana*, 474 genes of *O. sativa*, 653 genes of *Z. mays* and 834 genes of *T. aestivum*; for 428, 738, 325, and 125 miRNAs of *A. thaliana, O. sativa, Z. mays*, and *T. aestivum* (Appendix B, Table B1-B6).

We chose miRNAs in *A.thaliana* for our analyses for the following reasons. A miRNA family often shares similar nucleotide sequences among different plant species. Arabidopsis is a model organism [381, 382], and compared with other plants, and it has more data and annotations.

To predict binding sites with the MirTarget program, separate text files with their nucleotide sequences and specific parameters were created for each studied gene and miRNA. The binding site prediction programs only work with the textual format of the data presented in the files with the mir and gene extensions.

Table 3 - The number of genes in the families of TF and miRNAs of *O. sativa, T. aestivum, Z. mays* and *A.thaliana* [the material obtained in this study by Rakhmetullina A.K. based on PlantTFDB and miRbase data]

TF family	*Ath*	*Osa j*	*Zma*	*Tae*
TCP	27 *genes*	22 *genes*	46 *genes*	28 *genes*
MYB	144 *genes*	124 *genes*	169 *genes*	258 *genes*
HSF	24 *genes*	25 *genes*	28 *genes*	51 *genes*
GRAS	37 *genes*	60 *genes*	86 *genes*	117 *genes*
ERF	123 *genes*	138 *genes*	186 *genes*	169 *genes*
C2H2	87 *genes*	105 *genes*	138 *genes*	211 *genes*
miRNA	428	738	325	125

3.2 Characteristics of interaction miRNA with mRNA of the TCP TF genes of *A.thaliana, O. sativa, Z. mays,* and *T. aestivum*

3.2.1 Characteristics of interaction miRNA with mRNA of the TCP family genes of *A. thaliana*

The analysis of interactions of 428 miRNAs with mRNAs of 27 TCP family genes of *A. thaliana* revealed only 11 target genes for the miR5658-5p, miR5021-5p, miR319c-3p, miR1886.2-5p, miR172d-5p (Table 4). The mRNAs of the AT3G02150.1, AT1G53230, AT1G69690.1, and AT2G31070 genes carried binding sites for the miR5021-5p and miR5658-5p. The mRNAs of the AT1G30210, AT4G18390, AT2G45680.1, AT5G41030.1, AT2G31070.1, AT3G15030.1, and AT5G08330 genes carried binding sites for only one miRNA. The miRNA binding sites were located in the 5'UTR and CDS regions of miRNAs of the TCP family genes of *A. thaliana* [383].

Table 4 - Characteristics of interaction miRNA with mRNAs of the TCP family TF-target genes of *A. thaliana* [383, p. 612]

Gene	miRNA	Start of site, nt	mRNA region	ΔG, kJ/mol	ΔG/ΔGm, %	Length, nt
AT2G45680.1	miR172d-5p	114	CDS	-93	88	21
AT5G41030.1	miR1886.2-5p	199	CDS	-91	88	21
AT2G31070.1	miR319c-3p	1380	CDS	-100	89	21
AT3G15030.1	miR319c-3p	1620	CDS	-100	89	21
AT1G30210.1	miR5021-5p	1241	CDS	-93	96	20
AT1G30210.2	miR5021-5p	1114	CDS	-93	96	20
AT1G53230.1	miR5021-5p	91,94	5'UTR	-91,-96	93,98	20
AT1G69690.1	miR5021-5p	945	CDS	-91	93	20
AT2G31070.1	miR5021-5p	52	5'UTR	-89	91	20
AT3G02150.1	miR5021-5p	697	CDS	-89	91	20
AT5G08330.1	miR5021-5p	359-370(5)	5'UTR	-89÷-91	91÷93	20
AT1G53230.1	miR5658-5p	1236	CDS	-96	94	21
AT1G69690.1	miR5658-5p	415-422(3)	5'UTR	-93÷-100	92÷98	21
AT2G31070.1	miR5658-5p	1287	CDS	-91	90	21
AT3G02150.1	miR5658-5p	972,1183	CDS	-91	90	21
AT4G18390.1	miR5658-5p	1215-1224(3)	CDS	-91÷-98	90÷96	21

The characteristics of interactions of the ath-miR5021-5p with mRNAs of the TCP family genes that may bind with the ΔG/ΔGm value of 91%-96% are shown in Table 5.

Table 5 - Characteristics of the interaction ath-miR5021-5p with the CDS mRNAs of the TCP genes of plants [383, p. 613]

Species	Gene	Start of site, nt	ΔG, kJ/mol	ΔG/ΔGm, %
1	2	3	4	5
Aly	473241	808	-93	96
Aly	476101	511	-91	93
Sir	676708942	877	-89	91
Aha	Araha.15691s0008.1.p	508	-91	93
Aha	Araha.6346s0001.1.p	829	-93	96
Ath	AT1G30210.1	1241	-93	96
Ath	AT1G69690.1	945	-91	93
Ath	AT3G02150.2	697	-89	91
Cgr	Cagra.13056s0010.1.p	508	-91	93
Cru	Carubv10011113m	832	-93	96
Cru	Carubv10020637m	508	-91	93
Csa	Csa03g033390.1	742	-93	96
Csa	Csa05g087530.1	307	-91	93
Bna	GSBRNA2T00025745001	775	-91	93
Rsa	Rsa1.0_00361.1_g00006.1	793	-91	93
Rsa	Rsa1.0_01246.1_g00003.1	505	-91	93
Esa	Thhalv10008175m	817	-91	93
Tpa	Tp1g26030	832	-93	96

Continue of Table 5

1	2	3	4	5
Bra	XP_009109609.1	757	-91	93
Tha	XP_010551531.1	508	-91	93
Bol	XP_013622999.1	757	-91	93

The interaction schemes of the ath-miR5658-5p with mRNAs of the TCP family TF genes are shown in Figure 1. The given schemes of the interaction of the ath-miR5658-5p with mRNAs of several genes clearly demonstrate the efficiency of our MirTarget program. All nucleotides of the ath-miR5658-5p form hydrogen bonds with mRNA of the AT1G53230.1 and GSBRNA2T00009950001 genes. In the latter case, seven A–C bonds are formed that preserve the double helix structure of the miRNA-mRNA complex, preserving stacking-interactions of all nucleotides. The mRNA of other genes binds the ath-miR5658-5p to form the succession of 19–20 hydrogen bonds that preserve stacking interactions in these regions of the miRNA-mRNA complex [383, p. 614].

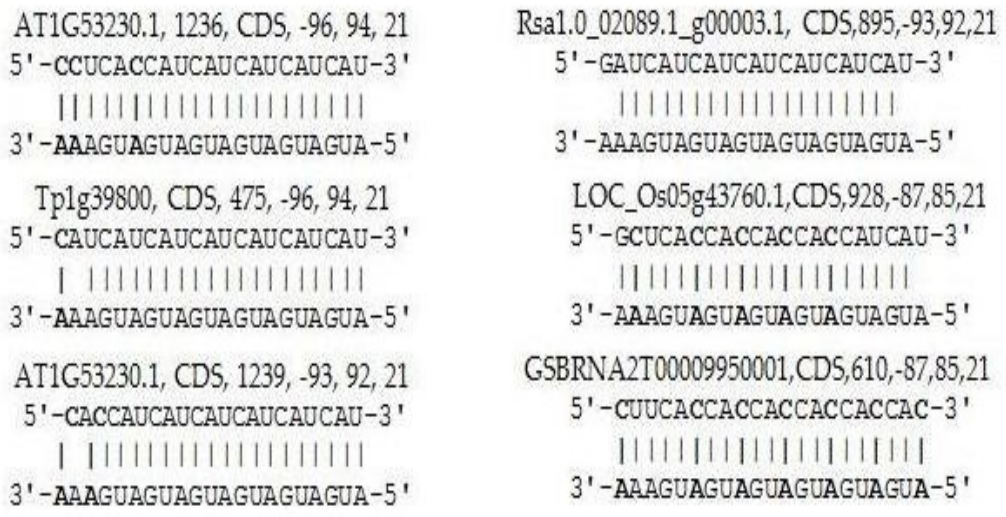


Figure 1 - Schemes of interactions of the ath-miR5658-5p with mRNAs of the TCP family TF-genes [383, P. 614]

Note - Gene; start of the binding site (nt); mRNA region; free energy, Δ*G*, (kJ/mol); Δ*G*/Δ*Gm*, %; miRNA length (nt); upstream and downstream sequences of mRNA and the ath-miR5658-5p, respectively. Bold font indicates nucleotides involved in forming noncanonical pairs, U–G and A–C.

The miRNA binding sites in mRNA of the TCP genes of various plant species encode conservative oligopeptides, evidencing the early occurrence of the functional connection between miRNAs and their target genes preserved for millions of years. The ath-miR5021-5p binding sites were found in mRNA of three genes of *A. thaliana* and in mRNAs of 27 genes of 17 plant species, which encoded

the SSSSSS oligopeptide (*Aar, Aha, Aly, Ath, Bna, Bol, Bra, Bst, Cgr, Cru, Csa, Esa, Rra, Rsa, Sir, Tha,* and *Tpa*). The SSSSSS oligopeptide is highly conservative in these proteins, which is shown in Figure 2c. The AA54G00421 protein of *A. thaliana* contains decaserine, twelve proteins contain octaserine and five proteins contain heptaserine [384]. Binding sites that encode hexaserine consist of synonymous serine codons with the third nucleotide variable (Figure. 2c′). This does not change the oligopeptide composition though it affects the free energy of the ath-miR5021-5p interaction with mRNA of the TCP genes. In this case, the main cause of the amino acid conservatism is the functional importance of hexaserine in comparison with the free energy of interaction of the ath-miR5021-5p with mRNA of the TCP family TF-genes [383, p. 612].

The characteristics of the ath-miR5658-5p binding to mRNA of the TCP genes are shown in Table 6. The target genes for the ath-miR5658-5p were shown to contain the effective binding sites for this miRNA as the ΔG/ΔGm value varied from 90 to 98% [383, p.614].

Table 6 - Characteristics of the potential ath-miR5658-5p binding sites in the CDS region of mRNA of the TCP genes of plants [383, p. 614]

Species	Gene	Start of site, n.	ΔG, kJ/mol	ΔG/ΔGm, %
Gma	Glyma.08G097900.1.p	1078	-100	98
Aly	474447	960	-96	94
Ath	AT1G53230.1	1236	-96	94
Cgr	Cagra.1472s0007.1.p	970	-96	94
Cru	Carubv10009348m	966	-96	94
Csa	Csa14g063740.1	957	-96	94
Rra	RrC11789_p1	817	-96	94
Tpa	Tp1g39800	475	-96	94
Rsa	Rsa1.0_02089.1_g00003.1	895	-93	92
Ath	AT3G02150.2	11183	-91	90
Bst	Bostr.0124s0115.1.p	978	-91	90

The ath-miR5658-5p binding sites encode the HHHHHH hexapeptide in 18 proteins. The data presented show that the HHHHHH hexopeptide is conservative in the TCP-proteins encoded by the ath-miR5658-5p binding sites in mRNAs of 23 genes of 19 plant species: *Aly, Ath, Bdi, Bna, Bol, Bst, Cgr, Cru, Csa, Gar, Ghi, Gma, Gra, Osaj, Rra, Rsa, Tca, Tha,* and *Tpa* (Figure 2d). The ath-miR-5658-5p binding sites in mRNAs of the Bostr.0124s0115.1.p, and Tp1g39800 genes encode octahistidine [383, p. 612].

The nucleotide sequences of the ath-miR5658-5p binding sites that encode hexahistidine consist of synonymous codons, in which the third nucleotide is variable (Figure 2d). A different level of conservatism of the nucleotide composition of the ath-miR5658-5p binding sites and the corresponding amino acids is apparently due to the highly important role of hexahistidine in the TCP proteins as compared with the free energy of binding of this miRNA [383, p. 612].

3.2.2 Characteristics of interaction miRNA with mRNA of the TCP TF genes of *O. sativa*

We performed screening of the possible binding sites for 738 miRNAs in mRNA of 22 TCP family genes of *O. sativa*. Only 14 genes were shown to be the targets for the miR5819-5p, miR5075-3p, miR408-3p, miR319b-3p, miR319a-3p.2-3p, miR2925-5p, miR2919, miR2102-5p, miR2102-3p, miR1861d,h,j-5p, miR1848-5p, miR1846a-c-5p, and miR1437b-5p (Table 7). The LOC_Os07g05720.1 was shown to contain binding sites for the miR2102-5p, miR2925-5p, miR319a-3p.2,b-3p, and miR408-3p. Four miRNAs had binding sites in mRNAS of the LOC_Os03g57190.1 and LOC_Os05g43760.1 genes. Two miRNAs bounded to mRNA of the LOC_Os02g51280.1, LOC_Os01g11550.1, LOC_Os03g49880.1, and LOC_Os06g12230.1, genes. The mRNA of other genes might have bound only one miRNA. The miR2102-5p had eight alternative target genes that indicated an important role of this miRNA in the regulation of several physiological functions in plants. The miRNA binding sites in mRNA of the TCP family genes of *O. sativa* were located in the 5'UTR and CDS regions [385]. The osa-miR2102-5p binding sites in mRNA of two genes of *O. sativa* and the GRMZM2G003944_P01, ONIVA07G01330.1, ORGLA07G0028600.1 and Zpz_sc01752.1.g00080.1.sm.mk genes were shown to encode the AAAAAA hexopeptide [383, p. 610].

Table 7 - Characteristics of interaction miRNA with CDS mRNA of the TCP genes of *O. sativa* [383, p. 614]

Gene	miRNA	Start of site, nt	ΔG, kJ/mol	ΔG/ΔGm, %	Length, nt
1	2	3	4	5	6
LOC_Os03g49880.1	miR1437b-5p	557*	-102	89	21
LOC_Os02g51280.1	miR1846a,b,c-5p	8*	-110	90	21
LOC_Os03g57190.1	miR1848-5p	246*	-113	88	21
LOC_Os02g51280.1	miR1858a,b-5p	1358	-106	88	21
LOC_Os05g43760.1	miR1861d,h,j-5p	706	-106÷-108	88÷91	22
LOC_Os08g43160.1	miR2102-3p	872	-113	88	22
LOC_Os01g11550.1	miR2102-5p	1670	-110	91	20
LOC_Os01g69980.1	miR2102-5p	1007	-110	91	20
LOC_Os05g43760.1	miR2102-5p	428	-108	89	20
LOC_Os06g12230.1	miR2102-5p	644*	-108	89	20
LOC_Os07g05720.1	miR2102-5p	1357	-110	91	20
LOC_Os08g33530.1	miR2102-5p	676	-110	91	20
LOC_Os12g07480.1	miR2102-5p	1180	-108	89	20
LOC107277536	miR2102-5p	997	-110	91	20
LOC_Os03g49880.1	miR2919	827, 836	-96	88	19
LOC_Os07g05720.1	miR2925-5p	912	-100	89	19
LOC_Os03g57190.1	miR319a-3p.2,b-3p	1214	-98	88	20
LOC_Os07g05720.1	miR319a-3p.2,b-3p	1441	-98	88	20
LOC_Os07g05720.1	miR408-3p	904	-106	89	21
LOC_Os01g55750.1	miR5075-3p	965	-108	88	21

Continue of Table 7

1	2	3	4	5	6
LOC_Os06g12230.1	miR5075-3p	642*	-108	88	21
LOC_Os12g42190.1	miR5075-3p	120	-110	90	21
LOC_Os12g42190.1	miR5075-3p	74	-108	88	21
LOC_Os01g11550.1	miR5819-5p	1163	-110	90	21
LOC_Os03g57190.1	miR5819-5p	721	-110	90	21
Note: *-5'UTR					

Binding sites of some miRNAs contain homologous nucleotide sequences, which may be expressed through different open reading frames. For example, the osa-miR2102-5p binding site sequence GCGGCGGCGGCGGCGGCGGCG will encode the AAAAAAA oligopeptide if expressed through the first reading frame, the RRRRRR oligopeptide if expressed through the second reading frame, and the GGGGGG oligopeptide if expressed through the third reading frame. Figure 2e shows the polyglycine-containing protein regions of six plants: *Oba*, *Ogl*, *Ome*, *Oru*, *Osaj*, and *Tae*. The nucleotide sequences of the osa-miR2102-5p binding sites are conservative (Figure 2e′). The osa-miR2102-5p binding sites of 10 TCP family genes of the species *Ogl*, *Oni*, *Osaj*, *Spo*, *Tae*, *Zma*, and *Zpa* were shown to encode hexaalanine. It was shown that protein regions adjacent to the AAAAAA hexapeptide were variable (Figure 2f). This points to the conservatism of the osa-miR2102-5p binding sites in mRNAS of 10 TCP genes. The osa-miR2102-5p binding sites consist of synonymous codons that causes conservatism of the first two nucleotides only (Figure 2f′). Apparently, the functional role of the AAAAAA hexapeptide prevails over the dependence of the gene expression on the osa-miR2102-5p [383, p. 614].

Some TCP proteins of *A.thaliana*, *O. sativa*, *T. aestivum*, and *Z. mays* were shown to contain polyglutamine, polythreonine, polyasparagine, polyproline, and polyaspartate (Table 8).

Table 8 - Oligonucleotides that may be encoded by the miRNA binding sites of *T. aestivum*, *O. sativa*, *Z. mays*, and *A. thaliana* [383, p. 615]

Gene	Species abbreviation	Oligopeptides
1	2	3
AT2G31070.1	*Ath*	QQQQQQ, TTTTTT
AT3G15030.1	*Ath*	QQQQQQQQ
AT3G47620.1	*Ath*	QQQQQQQ
AT5G23280.1	*Ath*	NNNNNNNNNNN, QQQQQQ
LOC_Os01g69980.1	*Osaj*	QQQQQQ
LOC_Os02g51280.1	*Osaj*	QQQQQQQQQQQQQQQQQ
LOC_Os03g57190.1	*Osaj*	QQQQQQ
LOC_Os07g05720.1	*Osaj*	QQQQQQ, QQQQQQQQ
LOC_Os08g43160.1	*Osaj*	QQQQQQQ
LOC_Os09g24480.1	*Osaj*	QQQQQQQ

Continue of Table 8

1	2	3
LOC_Os12g07480.1	*Osaj*	DDDDDD, NNNNNN
TRAES3BF146000020CFD_t1	*Tae*	QQQQQQ, QQQQQQQ
Traes_5BL_2DDBAA0C2.1	*Tae*	QQQQQQ, QQQQQQQ
Traes_5BL_B94C45A8F.1	*Tae*	QQQQQQQ
Traes_6AL_DA27ABCA61.2	*Tae*	QQQQQQQQ
Traes_6DL_136DE13FB.1	*Tae*	QQQQQQQQ
GRMZM2G003944_P01	*Zma*	QQQQQQ
GRMZM2G034638_P01	*Zma*	QQQQQQ, QQQQQQ
GRMZM2G060319_P01	*Zma*	TTTTTT
GRMZM2G077755_P01	*Zma*	QQQQQQQ
GRMZM2G078077_P01	*Zma*	QQQQQQQQ
GRMZM2G089361_P01	*Zma*	PPPPPPP
GRMZM2G089638_P01	*Zma*	QQQQQQ
GRMZM2G107031_P01	*Zma*	DDDDDD
GRMZM2G142751_P01	*Zma*	QQQQQQ
GRMZM2G148022_P02	*Zma*	QQQQQQQ, QQQQQQQ

The nucleotide sequences that encode these oligopeptides form no binding sites for any known miRNA in *A. thaliana*, *O. sativa*, *T. aestivum*, and *Z. mays*. However, these oligopeptides may be encoded by the binding sites for not yet identified miRNAs. In animal and human genes, these oligopeptides are encoded by miRNA binding sites [386-388]. The main features of interactions of miRNAs with mRNAs are similar in plants and animals, indicating the similarity of gene expression regulation by miRNAs in representatives of kingdoms of eukaryotic organisms [383, p. 615].

3.2.3 Characteristics of interaction miRNA with mRNA of the TCP family genes of *Z. mays*

The analysis of binding of 325 miRNAs to mRNAs of 46 TCP family genes of *Z. mays* predicted only seven target genes for the miR319a-d-3p, miR171e,d-5p, miR166a-d,k-5p (Table 9, where * indicates 5'UTR).

Table 9 - Characteristics of interaction miRNA with CDS mRNA of the TCP TF family of *Z. mays* [383, p. 611]

Gene	miRNA	Start of site, nt	ΔG, kJ/mol	ΔG/ΔGm, %	Length, nt
GRMZM2G031905_P01	miR166a,k-5p	123	-104	89	21
GRMZM2G055024_P01	miR166a,k-5p	270	-104	89	21
GRMZM2G062711_P01	miR166a-d,k-5p	112	-98÷-106	88÷91	21
GRMZM2G170232_P01	miR166a-d,k-5p	158*	-98÷-106	88÷91	21
GRMZM2G035944_P01	miR171e,d-5p	328*	-104	91	21
GRMZM2G089361_P01	miR319a-d-3p	1495	-98	88	20
GRMZM2G115516_P01	miR319a-d-3p	1302	-98	88	20

The zma-miR166a-5p and zma-miR166k-5 were shown to bind to mRNA of the GRMZM2G031905_P01, GRMZM2G055024_P01, GRMZM2G062711_P01, and GRMZM2G170232_P01 genes. The mRNA of the GRMZM2G170232_P01and GRMZM2G062711_P01 genes carried binding sites for five miRNAs. The mRNA of the GRMZM2G035944_P01, GRMZM2G115516_P01, GRMZM2G089361_P01, GRMZM2G055024_P01 and GRMZM2G031905_P01 genes had binding sites for several miRNAs. The miRNA binding sites were located in the 5'UTR and CDS regions of mRNAs of the TCP-genes of *Z. mays* (Table 9) [383, p. 610-611].

3.2.4 Characteristics of interaction miRNA with mRNA of the TCP Genes of *T.aestivum*

Screening of 125 miRNAs binding sites for 125 mRNA of the TCP family genes of *T. aestivum* has been carried out in order to reveal miRNAs targeted at the TCP family genes. Four target genes have been revealed for the miR444a,b-3p, miR9780-3p, and miR5086-5p (Table 10). Only one binding site was found for the miR9780-3p. Two or more miRNAs, which bind to mRNA of the same gene, were designated as alternative miRNAs. The Traes_2AL_EA60A06AC.1 and Traes_2BL_36A3AB3A2.1 genes were shown to be alternative target genes with respect to miR444a,b-3p. The Traes_4DS_59A46B69A.1 and Traes_4AL_75D069945.1 genes were alternative targets for the miR5086-5p (Table 10). The miRNA binding sites in mRNAs of the TCP family genes of TCP *T. aestivum* were only located in the CDS regions. The efficacy of a miRNA was determined by the free energy of its interaction with mRNA as well as by the miRNA and mRNA concentration. Either two or more miRNAs or one miRNA, which have several binding sites, may provide upregulation of target genes [383, p. 608].

Table 10 - Characteristics of interaction miRNA with CDS regions of mRNA TCP genes of *T. aestivum* [383, p. 608]

Gene	miRNA	Start of site, nt	ΔG, kJ/mol	ΔG/ΔGm, %	Length, nt
Traes_4AL_75D069945.1	miR5086-5p	132	-98	87	21
Traes_4DS_59A46B69A.1	miR5086-5p	132	-98	87	21
Traes_2BL_36A3AB3A2.1	miR9780-3p	991	-113	88	21
Traes_2AL_EA60A06AC.1	miR444a,b-3p	1062	-102	89	21
Traes_2BL_36A3AB3A2.1	miR444a,b-3p	1089	-102	89	21

The miRNAs target not only the TCP family genes of *T. aestivum* but also the TCP genes of other organisms. The tae-miR319-3p, similar nucleotide sequences of which were found in *A. thaliana*, *O. sativa* and *Z. mays*, bound mRNAs of the TRAES3BF014900010CFD_t1 gene of *T. aestivum*, LOC_Os01g11550.1 gene of *O. sativa*, AC205574.3_FGP006 and GRMZM2G015037_P01 genes of *Z. mays*

and the AT3G15030 and AT1G53230 genes of *A. thaliana* with similar characteristics [383, p. 608].

The accounting of noncanonical pair formation, such as A–C and G–U, increased the free energy of interactions between miRNA and mRNA. The nucleotide sequences of the tae-miR319-3p binding sites in these mRNAs were homologous and encoded the oligopeptide QRGPLQS (Figure 2a). The tae-miR319-3p binding sites encode the conservative oligopeptide QRGPLQS in the TCP transcription factors in 54 plant species (*Aar, Aco, Ain, Aly, Ata, Ath, Atr, Bdi, Bna, Bol, Bra, Bsa, Bst, Ccl, Cgr, Csa, Dol, Egr, Egu, Esa, Gar, Ghi, Gma, Gra, Hvu, Lpe, Mac, Oba, Ogl, Ogu, Ome, Oni, Opu, Oru, Osai, Osaj, Peq, Pha, Ptr, Pvi, Rra, Sbi, Sir, Sit, Sly, Spo, Svi, Tae, Tca, Tha, Tpa, Zja, Zma, Zmr*). The nucleotide sequences of the QRGPLQS oligopeptide encoding binding sites were identical (Figure 2a′) [383, p. 608].

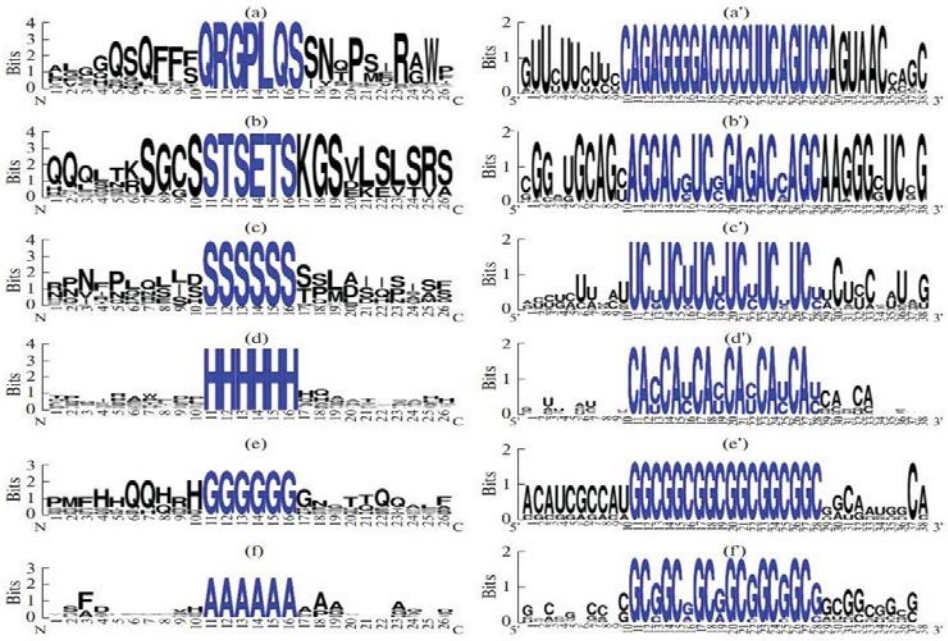


Figure 2 - Amino acid variability in oligopeptides encoded by the miRNA binding sites in mRNAs and nucleotide variability in the binding sites that encode the TCP proteins in different plants [383, p. 609]

Note - (a) The QRGPLQS oligopeptide encoded by the tae-miR319-3p binding sites in mRNAs of 56 genes of 54 plant species; (a′) the CAGAGGGGACCCCUUCAGUCC oligonucleotide of the binding sites that encodes the QRGPLQS oligopeptide. (b) The STSETS oligopeptide encoded by the tae-miR444a-3p binding sites in mRNAs of 29 genes of 28 plant species; (b′) the AGCACGUCGGAGACCAGC oligonucleotide of the binding sites that encodes the STSETS oligopeptide. (c) The SSSSSS oligopeptide encoded by the ath-mir5021-5p binding sites in mRNAs of 30 genes of 17 plant species; (c′) the Weblogo for the nucleotide set that encodes the SSSSSS oligopeptide. (d) The HHHHHH oligopeptide encoded by the ath-miR5658-5p binding sites in mRNAs of 23 genes of 19 plant species; (d′) the Weblogo for the nucleotide set that encodes the HHHHHH oligopeptide. (e) The GGGGGG oligopeptide encoded by the osa-miR2102-5p binding sites in mRNAS of eight genes of six plant species; (e′) the GGCGGCGGCGGCGGCGGC oligonucleotide of the binding sites that encodes the GGGGGG

oligopeptide. (f) the AAAAAA oligopeptide encoded by the osa-miR2102-5p binding sites in mRNAs of ten genes of seven plant species; (f′) the Weblogo for the nucleotide set that encodes the AAAAAA oligopeptide. Variability of amino acid sequences was assessed with the WebLogo program (https://weblogo.berkeley.edu/logo.cgi).

Variability of amino acids adjacent to the QRGPLQS oligopeptide and the variability of nucleotides flanking the binding site shows that it is only the tae-miR319-3p binding to the target genes that were preserved for many million years of divergence of the plant species studied. The nucleotide sequence of the miR444a-3p is known for the *T. aestivum* and *O. sativa* only. This miRNA contains binding sites in the CDS region of mRNAs of two genes of *T. aestivum* and one gene of *Z. mays*. The characteristics of the tae-miR444a-3p binding sites in the mRNAs of the Traes_2AL_EA60A06AC.1, Traes_2BL_36A3AB3A2.1, GRMZM2G020805_P01 genes of the TCP family are similar to one another, and the binding sites were shown to encode the STSETS hexopeptide. The potential binding sites for the tae-miR444a-3p were identified in mRNAs of 29 genes of 28 plant species (*Bdi, Bsa, Dol, Hvu, Lpe, Mac, Oba, Ogl, Ogu, Ome, Oni, Opu, Oru, Osai, Osaj, Oth, Pda, Peq, Pha, Phe, Sbi, Sit, Spo, Svi, Tae, Zja, Zma, Zmt*). The STSETS hexopeptide encoded by the tae-miR444a-3p binding sites is a part of the conservative SSTSETSKGS oligopeptide of the TCP-proteins (Figure 2b). The oligopeptide may be flanked by variable amino acids. The nucleotide sequences of the binding sites, which encode the STSETS hexopeptide, consist of synonymous codons in which only the third nucleotide may vary (Figure 2b′). Hence, the interactions between the tae-miR444a-3p and mRNAs of the TF-genes of the TCP family of the plant species studied have been preserved for millions of years [383, p. 608-610]. The number of genes and miRNAs capable of interacting with one another is different for *T. aestivum*, *O. sativa*, *Z. mays*, and *A. thaliana*. The data obtained show that expression of the TCP genes may be regulated via miRNAs' binding to their mRNAs. A considerable portion of TFs may be targeted for miRNAs, as shown by previous studies [389, 390]. The miRNA binding sites in mRNAs of plant genes are located mainly in the CDS region. Some of the TCP genes have binding sites located in the 5'UTR and 3'UTR regions of the corresponding mRNAs [383, p. 615].

Protein sites, which contain oligopeptides encoded by the miRNA binding sites, are characterized by the following features. In some TCP proteins, flanking amino acids may vary in comparison with oligopeptides encoded by the miRNA binding sites. For some miRNAs, the oligopeptide encoded by the miRNA binding site is conservative together with flanking amino acids (Figure 2). The SPL transcription factors of Arabidopsis were shown to contain the oligopeptide conservative for several proteins, and nucleotide sequences of the miR156j binding sites in mRNAs of the corresponding genes were fully complementary and also conservative [390, p. 2]. In orthologous genes of eight plant species, the ALSLLS oligopeptide, encoded by the miR156a binding sites and nucleotide sequences of these sites, was highly conservative [390, p. 2]. The nucleotide sequences of the miR396 binding sites and oligopeptides that they encode within the GRF

transcription factors were shown to be conservative compared to the flanking nucleotide sequences and amino acids [389, p. 808]. The miRNA binding sites that encode amino acid repeats are of special interest (Figure 1). This property of plant miRNAs resembles that of animal miRNAs, the binding sites of which also encode amino acid repeats [386, p. 2; 387, p. 440]. The main features of interactions between miRNAs and mRNAs are similar in plants and animals, which indicates the similarity of gene expression regulation by miRNAs in different eukaryotic organisms [388, p. 613]. It was shown that the miR319-3p, miR444a-3p, mir5021-5p, and miR5658-5p had binding sites in mRNAs of the TCP family TF genes. These binding sites were shown to encode the QRGPLQS, STSETS, SSSSSS, and HHHHHH oligopeptides, respectively. The miR2102-5p had binding sites that encode the GGGGGG and AAAAAA oligopeptides. The mRNA regions of 18 nt. and more, which function as miRNA binding sites, encode polyserine, polyhistidine, polyglycine, and polyalanine, which may work as phenotypic traits of a protein to point at the dependence of its synthesis on the corresponding miRNAs. The conservatism of oligopeptides encoded by the corresponding miRNA binding sites in genes of a variety of plant species may be considered as the evidence of the evolutionarily early formation of miRNA-dependent regulation of gene expression (Figure 2). The use of the MirTarget program allowed us to predict the quantitative characteristics of interactions between miRNAs and mRNAs of the TCP family of transcription factor genes. Knowledge of these characteristics considerably increases the possibility of considering the interactions of certain miRNAs with mRNAs of the corresponding TF-genes [383, p. 616].

The results of our study lead to the following conclusions: the TCP family target genes of the *T. aestivum*, *O. sativa*, *Z. mays*, and *A. thaliana* for miRNAs have been predicted; for some miRNAs, binding sites in mRNAs of the target genes of different plants are conservative and encode conservative oligopeptides; some miRNAs may have more than one binding sites in one mRNA and for than one target gene; mRNAs of some target genes may have binding sites for two or more different miRNAs; the tae-miR319-3p had conservative binding sites in mRNAs of the TCP gene family of *T. aestivum*, *O. sativa*, *Z. mays*, and *A. thaliana*; miRNA binding sites of plants may be located in the 5'UTR, CDS, and 3'UTR regions; miRNAs, which may bind to mRNAs of genes from different plant transcription factor families, have been identified; the considered properties of plant miRNAs resemble those of animal miRNAs [383, p. 616].

3.3 Characteristics of interaction miRNA with mRNA of the HSF TF genes of *A. thaliana*, *O. sativa, T. aestivum,* and *Z. mays*

The characteristics of the miRNA binding sites in the mRNA of the HSF genes of *A. thaliana, O. sativa, T. aestivum, Z. mays* have been established (Table 11). *A. thaliana* is a model plant organism for modern molecular research and we found binding sites between miRNA and mRNA of their target genes. The binding of 428 ath-miRNAs to mRNA of 24 HSF genes of *A. thaliana* was studied. Only 5 genes were targets for 5 miRNAs. All miRNAs had only one target genes. The

miRNA binding sites were located in 5'UTR and CDS mRNA HSF genes of *A. thaliana*. The quantitative characteristics of 738 osa-miRNAs binding to mRNA of 25 HSF family genes of *O. sativa* were established. Twelve genes were under the control of miRNA. Ten miRNAs were bound to HSF mRNAs, of which the largest number of binding sites had miR5075-3p. It bound to mRNA of seven genes *(LOC_Os06g35960.1, LOC_Os07g44690.1, LOC_Os08g36700.1, LOC_Os08g43334.1, LOC_Os09g28200.1, LOC_Os09g28354.1, LOC_Os09g35790.1)* with free energy from -108 kJ/mole to -113 kJ/mole and ΔG/ΔGm value from 88% to 91%. The miR2102-5p had binding sites in mRNA of four genes with ΔG/ΔGm value equal 88%. Each miRNA of miR2907a,b,d-3p,c-3p had one binding site in the mRNA of *LOC_Os08g43334.1* genes. The miR2925-5p, miR414-5p, miR5077-5p, miR529a-3p, miR5809-3p had only one target gene. The miRNA binding sites were located in 5'UTR and CDS mRNA HSF family genes of *O. sativa*. To identify miRNAs that are targets genes of the HSF transcription factor family, a search was made for the binding sites of 125 tae-miRNAs with the mRNA of 51 genes of the *T. aestivum* HSF family [391]. As a result of the search, it was found that three genes of the HSF family were targets of four miRNAs [391, p. 568-569].

Table 11 - Characteristics of interaction miRNA with the CDS of mRNA of *A. thaliana, O. sativa, T. aestivum, Z. mays* HSF genes [391, p. 568]

Gene	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
1	2	3	4	5	6
A. thaliana					
AT4G11660.1	miR5021-5p	215*	-89	91	20
AT4G18880.1	miR415-5p	752*	-96	90	21
AT4G17750.1	miR5631-3p	728	-93	90	21
AT4G18870.1	miR827-3p	877	-93	90	21
AT1G46264.1	miR834-3p	653	-100	89	21
O. sativa					
LOC_Os01g43590.1	miR2102-5p	616	-106	88	20
LOC_Os03g53340.1	miR2102-5p	961	-106	88	20
LOC_Os06g36930.1	miR2102-5p	395	-106	88	20
LOC_Os09g35790.1	miR2102-5p	937	-106	88	20
LOC_Os08g43334.1	miR2907a-d-3p	987	-117	89	22
LOC_Os09g28200.1	miR2925-5p	1071	-100	89	19
LOC_Os03g53340.1	miR414-5p	1525	-98	88	21
LOC_Os06g35960.1	miR5075-3p	547	-113	91	21
LOC_Os07g44690.1	miR5075-3p	302	-108	88	21
LOC_Os08g36700.1	miR5075-3p	974	-110	90	21
LOC_Os08g43334.1	miR5075-3p	1397	-108	88	21
LOC_Os09g28200.1	miR5075-3p	292	-108	88	21
LOC_Os09g28354.1	miR5075-3p	199*	-108	88	21
LOC_Os09g35790.1	miR5075-3p	1410	-108	88	21
LOC_Os06g36930.1	miR5077-5p	486	-96	90	19
LOC_Os10g28340.1	miR529a-3p	47*	-96	90	20

Continue of Table 11

1	2	3	4	5	6
LOC_Os01g53220.1	miR5809-3p	233	-104	89	20
T. aestivum					
TRAES3BF071100100CFD_t1	miR9778-5p	39	-100	89	21
TRAES3BF021000010CFD_t1	miR9676-5p	41	-104	87	22
Traes_4BL_B64C157DC.1	miR9657b,c-3p	651	-102	87	21
Z. mays					
GRMZM2G118453_P01	miR164a-3p	215*	-100	89	21
RMZM2G301485_P01	miR164a-3p	488	-102	91	21
GRMZM2G179802_P01	miR164d-3p	1214	-96	88	20
GRMZM2G173090_P01	miR164f-3p	687	-102	87	21
GRMZM2G173090_P01	miR167d-3p	1473**	-110	87	23
GRMZM2G002131_P01	miR169c,r-5p	1102	-102	87	21
GRMZM2G089525_P01	miR172c-5p	1181	-93	88	20
Note: *- 5'UTR, **- 3'UTR					

The miR9657a-c-3p, miR9676-5p, miR9778-5p interacted with the mRNA of these genes. Two miRNAs of miR9657b,c-3p family, were bound with mRNA of the Traes_4BL_B64C157DC.1 gene. The miR9778-5p and miR9676-5p interacted with mRNA of TRAES3BF071100100CFD_t1 and TRAES3BF021000010CFD_t1 genes respectively. All discovered miRNA binding sites in mRNA of HSF family genes of *T. aestivum* were located only in the CDS. In the absence of complete complementarity of miRNA interaction with mRNA of genes, unpaired nucleotides appear, leading to the decreased of free energy of interaction of miRNA and mRNA [391, p. 569].

As a result of studying the binding of 325 zma-miRNAs to mRNA 28 HSF family genes of *Z. mays* it was revealed only six genes target for seven miRNA. miR164a,d,f-3p, miR167d-3p, miR169 c,r-5p, miR172c-5p were interacted with mRNA of these genes. The miR164a,d,f-3p family had the largest number of target genes (four). They bound to the mRNA of *GRMZM2G118453_P01*, *GRMZM2G301485_P01*, *GRMZM2G179802_P01*, *GRMZM2G173090_P01* genes with free energy of -96 kJ/mole to -102 kJ/mole and ΔG/ΔGm value from 87% to 91%. In the mRNA of the *GRMZM2G002131_P01* gene, binding sites for miR169c,r-5p were found. The miR167d-3p miR172c-5p had one target gene. The miRNA binding sites were located in 5'UTR, CDS and 3'UTR mRNA HSF genes of *Z. mays* [391, p. 569].

In the present work using the bioinformatics approach, the interactions of miRNA with mRNA of HSF genes *A. thaliana*, *O. sativa*, *T. aestivum*, *Z. mays* were studied. The results of the following research are: the miRNA binding sites for the mRNA genes of the HSF family of *A. thaliana, O. sativa, T. aestivum, Z. mays* were established; the miRNA binding sites are located in 5'UTR, CDS and 3'UTR mRNA target genes; specific miRNAs for different plant species were detected which may affect the expression of heat stress transcription factors [391, p. 569].

3.4 Characteristics of interaction miRNA with mRNA of the MYB TF Genes of *A. thaliana, O. sativa, Z. mays,* and *T. aestivum*

3.4.1 Characteristics of interaction miRNA with mRNAs of the MYB family genes of *A. thaliana*

To identify miRNAs targeting the genes of the MYB TF family, we searched for 428 miRNA binding sites in the mRNA of 144 MYB genes of *A. thaliana*. As a result of this search, it was revealed that with the selection criterion ΔG/ΔGm more than 88%, 32 genes of the MYB family are targets of 15 miRNAs (Table 12). All detected miRNA binding sites are located in the 5'UTR, CDS of mRNA target genes. For miR5021-5p, there are nine target genes with a ΔG/ΔGm value of more than 88%. The miR414-5p has three binding sites in the mRNA of the AT3G18100.1 gene. The ath-miR858 family consists of ath-miR858a and ath-miR858b, differing in two nucleotides at the ends of the sequence. Therefore, their binding sites are differ by one nucleotide. All sites are located in the protein-coding part of the mRNA of the AT5G35550.1 gene. The miR159 had mRNA binding sites for six genes with a ΔG/ΔGm value ranging from 90 to 94% [395, P. 62-65]. The miR5658-5p and miR828-5p had binding sites in mRNA of 12 and four genes, respectively. The rest of the miRNAs had one or two target genes.

Table 12 - Characteristics of miRNA interaction with mRNA of MYB TF genes of *A. thaliana* [395, p. 63, 65]

Gene	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
1	2	3	4	5	6
AT2G32460.1	miR159a,b-3p	1016	-100	92	21
AT2G26950.1	miR159a,c-3p	827	-100	90-92	21
AT3G11440.1	miR159a,c-3p	1212	-98	90	21
AT5G06100.1	miR159a,c-3p	1597	-98	90	21
AT3G60460.1	miR159a-3p	182	-98	90	21
AT5G55020.1	miR159b,c-3p	1338	-100,-102	90,94	21
AT5G55020.1	miR319a,b-3p	1338	-100	92	21
AT4G25560.1	miR413-5p	258	-98	92	21
AT2G32460.1	miR414-5p	1334	-96	90	21
AT3G18100.1	miR414-5p	153-165 (3)*	-96-100	90-94	21
AT3G48920.1	miR5017-5p	482	-91	91	21
AT1G68320.1	miR5021-5p	676	-93	96	20
AT2G32460.1	miR5021-5p	661	-91	93	20
AT3G50060.1	miR5021-5p	222-228 (3)*	-89,-91	91,93	20
AT3G52250.1	miR5021-5p	9*	-89	91	20
AT3G52250.1	miR5021-5p	44-59 (5)*	-89,-91	91,93	20
AT4G18770.1	miR5021-5p	630,633	-91,-93	93,96	20
AT4G32730.1	miR5021-5p	358, 361*	-87,-89	89,91	20
AT5G02320.1	miR5021-5p	81*	-91	93	20
AT5G08520.1	miR5021-5p	348*	-91	93	20
AT5G16600.1	miR5021-5p	799	-89	91	20

Continue of Table 12

1	2	3	4	5	6
AT5G61420.2	miR5640-5p	1184	-93	90	21
AT1G26780.1	miR5658-5p	171	-91	90	21
AT1G49010.1	miR5658-5p	1004,1010	-91	90	21
AT2G36890.1	miR5658-5p	596	-91	90	21
AT3G13890.1	miR5658-5p	418	-93	92	21
AT4G05100.1	miR5658-5p	626-633 (3)	-93÷-100	92÷98	21
AT4G18770.1	miR5658-5p	204	-96	94	21
AT4G18770.1	miR5658-5p	389,636	-91	90	21
AT4G25560.1	miR5658-5p	438	-91	90	21
AT4G37780.1	miR5658-5p	845	-91	90	21
AT5G15310.1	miR5658-5p	846	-91	90	21
AT5G54230.1	miR5658-5p	1129	-96	94	21
AT5G55020.1	miR5658-5p	647,651	-93	92	21
AT5G62470.1	miR5658-5p	813	-91	90	21
AT1G56650.1	miR828-5p	513	-98	90	22
AT1G66370.1	miR828-5p	355	-100	92	22
AT5G52600.1	miR828-5p	460	-102	94	22
AT5G65230.1	miR828-5p	500	-98	90	22
AT5G35550.1	miR858a,b-3p	432	-98,-100	90	21
AT1G68320.1	miR870-3p	815	-93	90	21
Note: *-5'UTR					

3.4.2 Characteristics of the potential miRNA binding sites in mRNA of the MYB family genes of *O. sativa*

The study of the binding of 738 miRNA to mRNA of 124 genes of the MYB *O. sativa* family revealed that only 34 genes were targets for 32 miRNAs (Table 13). Four miRNAs of the miR159c-f-3p family had binding sites in the mRNA of LOC_Os05g41166.1, LOC_Os01g59660.1, LOC_Os06g40330.1, LOC_Os03g38210.1, LOC_Os06g46560.1, LOC_Os04g46384.1 genes of the MYB family with a ΔG/ΔGm value from 89% to 96%. Therefore, miR159 involved in response to stress can affect the expression of studied rice genes [392, 393].

The miR5809-3p had the largest number of binding sites with mRNA of nine genes with the free energy equal -104 kJ/mole and value ΔG/ΔGm of 89%. The miR2102-5p had binding sites in mRNA of eight target genes. The ΔG/ΔGm value, which characterizes the binding energy of miR2102-5p with the mRNA of these genes, ranged from 89% to 93%.

All ten miRNAs of the miR156a-j-5p family bind to the mRNA of the LOC_Os11g03440.1 gene with a ΔG/ΔGm value of 88%. The rest of the miRNAs had only one or two target genes. The miRNA binding sites in the MYB mRNA genes were located in the 5'UTR, CDS, 3'UTR of *O. sativa.*

Table 13 - Characteristics of miRNA interaction with CDS mRNA MYB genes of *O. sativa* [393, p. 105]

Gene	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
LOC_Os06g06740.1	miR1442-5p	867*	-89	91	20
LOC_Os05g41166.1	miR159c,d,e-3p	878	-102,-106	96	21
LOC_Os01g59660.1	miR159c,d,f-3p	1343	-100,-104	89,94	21
LOC_Os06g40330.1	miR159c,d,f-3p	1418	-100,-102	89,92	21
LOC_Os03g38210.1	miR159d-3p	938	-102	91	21
LOC_Os06g46560.1	miR159d-3p	1064	-100	89	21
LOC_Os04g46384.1	miR159f-3p	199	-100	90	21
LOC_Os01g16810.1	miR164d-5p	880	-104	89	21
LOC_Os04g39470.1	miR164e-5p	691	-104	89	21
LOC_Os04g45060.1	miR167d-j-5p	518	-100	89	21
LOC_Os03g27090.1	miR171d,e-5p	369	-102,-106	89,91	21
LOC_Os03g18480.1	miR171i-5p	552	-100	89	21
LOC_Os04g42950.1	miR172d-5p	995	-96	90	20
LOC_Os06g14670.1	miR2098-5p	1150	-102	89	20
LOC_Os01g62410.1	miR2102-5p	441	-110	91	20
LOC_Os01g64360.1	miR2102-5p	453	-110	91	20
LOC_Os02g54520.1	miR2102-5p	1045	-108	89	20
LOC_Os03g25550.1	miR2102-5p	804	-113	93	20
LOC_Os03g26130.1	miR2102-5p	661	-110	91	20
LOC_Os05g48010.1	miR2102-5p	739	-108	89	20
LOC_Os06g46560.1	miR2102-5p	756	-108	89	20
LOC_Os08g33150.1	miR2102-5p	710	-108	89	20
LOC_Os01g65370.1	miR2868-5p	56*	-89	91	20
LOC_Os04g38740.1	miR5075-3p	727	-113	91	21
LOC_Os08g34960.1	miR5075-3p	553	-117	95	21
LOC_Os06g02250.1	miR528-5p	523	-106	91	21
LOC_Os02g02370.1	miR5804-3p	668	-100	89	21
LOC_Os01g36460.1	miR5809-3p	557	-104	89	20
LOC_Os02g46780.1	miR5809-3p	558	-104	89	20
LOC_Os03g25550.1	miR5809-3p	257	-104	89	20
LOC_Os03g27090.1	miR5809-3p	635	-104	89	20
LOC_Os04g39470.1	miR5809-3p	852	-104	89	20
LOC_Os07g31470.1	miR5809-3p	151	-104	89	20
LOC_Os07g44090.3	miR5809-3p	210	-104	89	20
LOC_Os09g26170.1	miR5809-3p	954	-104	89	20
LOC_Os12g33070.1	miR5809-3p	324	-104	89	20
LOC_Os06g46560.1	miR5819-5p	777	-115	93	21
LOC_Os01g18240.1	miR5827-5p	604	-98	92	21
LOC_Os09g23620.1	miR818a-e-3p	1048**	-100	89	22
Note: *-5'UTR; **-3'UTR					

Interaction schemes of miRNA with the MYB *O. sativa* mRNA genes (Figure 3), obtained using the miRTarget program, clearly show the connections between their complementary nucleotides.

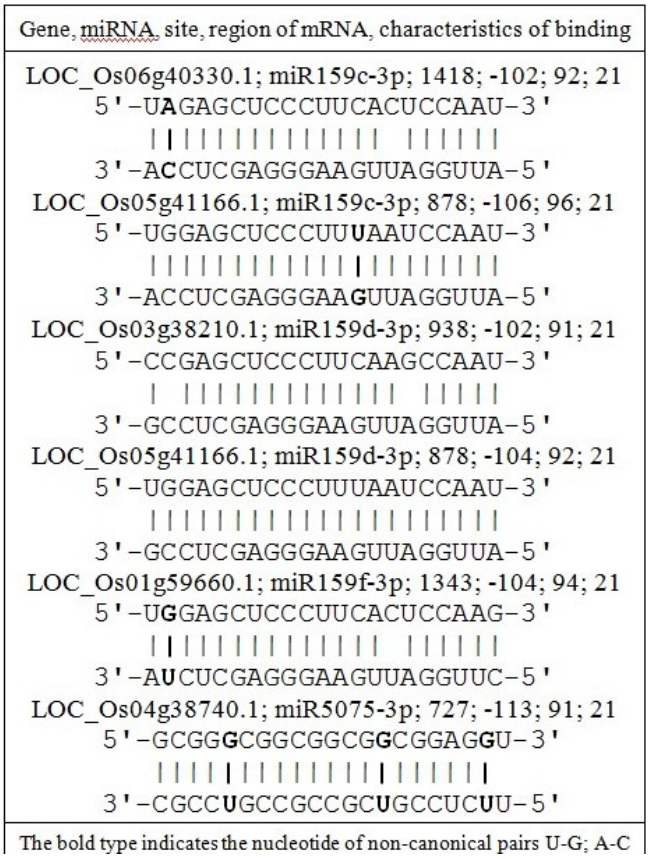


Figure 3 - Schemes of miRNA interaction with mRNA of MYB TF genes in *O. sativa* [393, p. 105]

Above each scheme is the name of the gene, the name of miRNA, the position of the beginning of the binding site (nt.), the binding energy (kJ/mol), the value ΔG/ΔGm (%), and the length of mRNA (nt). The upper and lower nucleotide sequences of mRNA and miRNA, respectively.

3.4.3 Characteristics of miRNA interaction with mRNAs of the MYB family genes of *Z. mays*

To identify miRNAs that target genes of the MYB transcription factor family, a search was done for the binding sites of 325 zma-miRNAs with the mRNAs of 169 genes from the *Zea mays* MYB family (Table 14). As a result, it was found that with the selection criteria ΔG/ΔGm equal 88% and over, 25 genes were the targets for 26 miRNAs. The miRNAs of the zma-miR159 family were bind with mRNA of 13 genes with a ΔG/ΔGm value of 89% -100%. Members of the zma-miR164 family were bound with mRNA of eight genes with a ΔG/ΔGm value 89% and 91% [394]. The rest of the miRNAs had only one or two target genes. The miRNA binding sites in the MYB mRNA genes were located in the 5'UTR, CDS, 3'UTR of *Z. mays.*

Table 14 - Characteristics of miRNA interaction with CDS mRNA MYB genes of *Z. mays* [395, p. 63, 65]

Gene	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
AC217264.3_FGP005	miR159e-3p	1377,1481	-110,-115	100	21
GRMZM2G004090_P01	miR159a,c,d,f,j,k-3p	944	-100	89,90	21
GRMZM2G017268_P01	miR159e-5p	180	-102	89	21
GRMZM2G028054_P01	miR159a,c,d,f,j,k-3p	971	-100	89,90	21
GRMZM2G046443_P01	miR159c,d-3p	292	-100	89	21
GRMZM2G070523_P01	miR159e-3p	1044	-110	100	21
GRMZM2G110135_P01	miR159e-5p	232	-104	91	21
GRMZM2G115859_P01	miR159e-5p	1182	-104	91	21
GRMZM2G139688_P01	miR159c,d,g,h,i-3p	1268	-100,-104	90,92	21
GRMZM2G167088_P01	miR159a,c,d,f,j,k-3p	797	-102	91,92	21
GRMZM2G311059_P01	miR159c,d-3p	1394	-100	89	21
GRMZM2G416652_P01	miR159a,c,d,f,j,k-3p	797	-102	91,92	21
GRMZM2G423833_P01	miR159a,f,j,k-3p	1133	-102	92	21
GRMZM2G121570_P01	miR162-5p	221	-102	89	21
GRMZM2G150680_P01	miR164a-3p	605	-102	91	21
GRMZM2G311059_P01	miR164a-3p	1336	-100	89	21
AC206901.3_FGP005	miR164f-3p	530	-106	91	21
GRMZM2G403620_P01	miR164f-3p	768	-106	91	21
GRMZM2G111731_P01	miR164f-5p	838	-104	89	21
GRMZM2G312419_P01	miR164f-5p	1286	-104	89	21
GRMZM2G038722_P01	miR164g-3p	509	-106	89	21
GRMZM2G056407_P01	miR164h-5p	256*	-104	89	21
GRMZM2G028054_P01	miR319a-d-3p	971	-100	90	20
GRMZM5G833253_P01	miR396c,d-5p	1240**	-102	89	22
GRMZM2G047600_P01	miR396g,h-5p	624	-98	90	21
GRMZM2G097636_P01	miR408a,b-3p	361	-106	89	21
GRMZM2G097638_P01	miR408a,b-3p	361	-106	89	21
GRMZM2G056407_P01	miR529-3p	112*	-100	89	21
Note: *-5'UTR; **-3'UTR					

3.4.4 Characteristics of the potential miRNA binding sites in mRNAs of the MYB family genes of *T. aestivum*

Study of 125 miRNAs binding to mRNAs of 258 MYB family genes of *T. aestivum* revealed that only eight genes were targets for eight miRNAs (Table 15). The miR9780-3p, miR9779-3p, miR5384-3p, miR531-5p, miR397-3p, miR319-3p, miR159a,b-3p bind with mRNAs of these genes [395, p. 61-62].

The miR319-3p binds to mRNAs of two MYB genes. The remaining miRNAs had only one target gene with a ΔG/ΔGm value ranging from 89 to 92%. The miRNA BSs in the mRNA genes of the MYB family of *T. aestivum* are located only in the CDS.

Table 15 - Characteristics of miRNA interaction in CDS mRNA MYB genes of *T. aestivum* [395, p. 61-62]

Gene	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
Traes_6DS_A0EC5D808.1	miR159a,b-3p	688	-100	90	21
Traes_1BL_CF98E922B.1	miR319-3p	838	-102	89	21
TRAES3BF027700010CFD_t1	miR319-3p	955	-102	89	21
Traes_4DS_7BFAC49C2.1	miR397-3p	206	-104	89	21
TRAES3BF026500080CFD_t1	miR531-5p	157	-110	90	21
Traes_2DS_61B920833.1	miR5384-3p	502	-108	89	21
TRAES3BF012200020CFD_t1	miR9779-3p	284	-96	92	20
Traes_2DS_3F5D36630.1	miR9780-3p	958	-115	90	21

3.4.5 Characteristics of miR159-3p interaction with mRNA of MYB TF genes of *T. aestivum, O. sativa, A.thaliana, Z. mays*

Not only MYB family genes of *T. aestivum*, but also genes of other plant species were targets for miRNAs. For instance, tae-miR159a,b-3p has binding sites in the mRNAs of *T. aestivum* Traes_2DL_912473A86.1, Traes_2BL_855A1170C.2, Traes_2AL_0A21FB42C.1 genes as well as in *O. sativa* LOC_Os04g46384.1 gene, *A. thaliana* AT3G60460.1 gene, and *Z. mays* GRMZM2G311059_P01, GRMZM2G046443_P01 genes, which are the members of the MYB family of these plant species (Table 16) [395, p. 62].

Table 16 - Characteristics of miR159-3p interaction in CDS mRNA of MYB TFs genes of *T. aestivum, O. sativa, A.thaliana, Z. mays* [395, p. 63]

Gene	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %
Traes_2DL_912473A86.1	tae-miR159a,b-3p	54	-98	88
Traes_2BL_855A1170C.2	tae-miR159a,b-3p	141	-98	88
Traes_2AL_0A21FB42C.1	tae-miR159a,b-3p	141	-98	88
LOC_Os04g46384.1	osa-miR159f-3p	199	-100	90
LOC_Os04g46384.1	osa-miR159a.1-3p	198	-98	88
AT3G60460.1	ath-miR159a-3p	182	-98	90
AT3G60460.1	ath-miR159c-3p	182	-98	88
AT3G60460.1	ath-miR159b-3p	182	-93	86
GRMZM2G311059_P01	zma-miR159a,f,j,k-3p	1393	-98	88
GRMZM2G311059_P01	zma-miR159c,d-3p	1394	-100	89
GRMZM2G046443_P01	zma-miR159c,d-3p	292	-100	89
GRMZM2G046443_P01	zma-miR159a,f,j,k-3p	292	-96	87

Since the characteristics of miRNA159-3p interaction with mRNA genes of different plant species were close, here we provide data only for the miR159-3p family. The interaction patterns of the nucleotide sequences of miRNA with the mRNAs of these genes presented in Figure 4, clearly show the bonds between their complementary nucleotides. The interaction schemes indicate the participation of

all miRNA nucleotides in binding to mRNA through the formation of canonical and non-canonical nucleotide pairs [395, p. 62].

Gene,miRNA, site,region of mRNA, characteristics of binding	Gene,miRNA, site,region of mRNA, characteristics of binding
Tracs_2DL_912473A86.1, tae-miR159b-3p, 55, -96, 87 5'-U**G**GAGCUCCAUUC**G**AUCCAAA-3' 3'-G**U**CUCGAGGGAAG**U**UAGGUUU-5'	AT3G60460.1, ath-miR159c-3p, 182, -98, 88 5'-UGGAGCUCCAUUC**G**AUCCAAA-3' 3'-UCCUCGAGGGAAG**U**UAGGUUU-5'
Tracs_2BL_855A1170C.2, tae-miR159b-3p, 142, -66, 87 5'-U**G**GAGCUCCAUUCGAUCCAAA-3' 3'-G**U**CUCGAGGGAAGUUAGGUUU-5'	GRMZM2G311059_P01, zma-miR159a-3p, 1394, -96, 87 5'-**UG**GAGCUCCAUUC**G**AUCCAAA-3' 3'-**GU**CUCGAGGGAAG**U**UAGGUUU-5'
LOC_Os04g46384.1, osa-miR159a.1-3p, 198, -98, 88 5'-CUGGAGCUCCAUUC**G**AUCCAAA-3' 3'-GUC-UCGAGGGAAG**U**UAGGUUU-5'	GRMZM2G311059_P01, zma-miR159f-3p, 1394, -96, 87 5'-**UG**GAGCUCCAUUC**G**AUCCAAA-3' 3'-**GU**CUCGAGGGAAG**U**UAGGUUU-5'
LOC_Os04g46384.1, osa-miR159f-3p, 199, -100, 90 5'-U**G**GAGCUCCAUUC**G**AUCCAAAG-3' 3'-A**U**CUCGAGGGAAG**U**UAGGU-UC-5'	GRMZM2G311059_P01, zma-miR159j-3p, 1394, -96, 87 5'-**UG**GAGCUCCAUUC**G**AUCCAAA-3' 3'-**GU**CUCGAGGGAAG**U**UAGGUUU-5'
AT3G60460.1, ath-miR159a-3p, 182, -98, 90 5'-U**G**GAGCUCCAUUC**G**AUCCAAA-3' 3'-A**U**CUCGAGGGAAG**U**UAGGUUU-5'	GRMZM2G046443_P01, zma-miR159a-3p, 292, -96, 87 5'-**UG**GAGCUCCAUUC**G**AUCCAAA-3' 3'-**GU**CUCGAGGGAAG**U**UAGGUUU-5'
AT3G60460.1, ath-miR159b-3p, 182, -93, 86 5'-U**G**GAGCUCCAUUC**G**AUCCAAA-3' 3'-U**U**CUCGAGGGAAG**U**UAGGUUU-5'	GRMZM2G046443_P01, zma-miR159j-3p, 292, -96, 87 5'-**UG**GAGCUCCAUUC**G**AUCCAAA-3' 3'-**GU**CUCGAGGGAAG**U**UAGGUUU-5'
The bold type indicates the nucleotide of non-canonical pairs U-G, A-C.	

Figure 4 - Schemes of miR159-3p interaction with mRNAs of MYB TF genes in *T. aestivum*, *O. sativa*, *A. thaliana* and *Z. mays* [395, p. 63]

It is important to note that the nucleotide sequence of tae-miR159a,b-3p is similar in the *T. aestivum*, *O. sativa*, *A.thaliana* and *Z. mays* genomes in which it was found (miRBase). Six miRNAs of the zma-miR159a,c,d,f,j,k-3p family were bound to mRNAs of GRMZM2G311059_P01 and GRMZM2G046443_P01 genes with a ΔG/ΔGm value of 87 – 89%. Three members of ath-miR159a-c-3p family were bound to mRNA of AT3G60460.1 gene with a ΔG/ΔGm value of 86% and above. Two miRNAs of the osa-miR159a.1,f-3p and tae-miR159a,b-3p had two and three target genes, respectively (Table 17). The tae-miR159a,b-3p binding sites are located in the CDS and encode the WSSIRSK oligopeptide, which is conserved in the 27 proteins of the MYB transcription factors for 22 plant species (Table 17) [395, p. 62].

Table 17 - The variability of amino acid sequences of the MYB family proteins containing oligopeptide WSSIRSK encoded by the binding sites of miR159-3p in the mRNA of genes [395, p. 64]

Gene	Species	Region of transcription factor containing oligopeptide WSSIRSK
1	2	3
GRMZM2G311059_P01	*Zma*	LLRHVLVHGPRD**WSSIRSK**GFLPRTGKSCRL

Continue of Table 17

1	2	3
GRMZM2G046443_P01	*Zma*	LRRHVMENGPRE**WSSIRSK**GLLPRTGKSCRL
LOC_Os04g46384.1	*Osaj*	LLEHVRTHGPMD**WSSIRSK**GLLPRTGKSCRL
Traes_2DL_912473A86.1	*Tae*	LLEHVRTHGPRD**WSSIRSK**GALQRTGKSCRL
Traes_2BL_855A1170C.2	*Tae*	LLEHVRTHGPRD**WSSIRSK**GALQRTGKSCRL
Traes_2DL_912473A86.1	*Tae*	LLEHVRTHGPRD**WSSIRSK**GALQRTGKSCRL
Traes_2BL_855A1170C.2	*Tae*	LLEHVRTHGPRD**WSSIRSK**GALQRTGKSCRL
Traes_2AL_0A21FB42C.1	*Tae*	LLEHVRTHGPRD**WSSIRSK**GALQRTGKSCRL
AT3G60460.1	*Ath*	LINHVKRYGPRD**WSSIRSK**GLLQRTGKSCRL
Bradi5g17600.2.p	*Bdi*	LLEHVRTHGPCD**WSSIRSK**GILPRTGKSCRL
Brast09G163900.1.p	*Bsa*	LLEHVRAHGPCD**WSSIRSK**GILPRTGKSCRL
Do012459.1	*Dol*	LLEHVRAHGPCD**WSSIRSK**GLLPRTGKSCRL
462873087	*Ete*	LREHVRTHGPRD**WSSIRSK**GLLPRTGKSCRL
LPERR04G16870.1	*Lpe*	LREHVRTHGPRE**WSSIRSK**VGLPRTGKSCRL
GSMUA_Achr1P01660_001	*Mac*	LMEYVRKHGPRD**WSSIRSK**GLLARTGKSCRL
OBART04G20790.1	*Oba*	LLEHVRTHGPMD**WSSIRSK**GLLPRTGKSCRL
OB04G27810.1	*Obr*	LLQHVRAHGPMD**WSSIRSK**GLLPRTGKSCRL
ORGLA04G0178400.1	*Ogl*	LLEHVRTHGPMD**WSSIRSK**GLLPRTGKSCRL
OGLUM04G20730.1	*Ogu*	LLEHVRTHGPMD**WSSIRSK**GLLPRTGKSCRL
KN540032.1_FGP006	*Olo*	LLEHVRTHGPMD**WSSIRSK**GLLPRTGKSCRL
OMERI04G17240.1	*Ome*	LLEHVRTHGPMD**WSSIRSK**GLLPRTGKSCRL
OPUNC04G18480.1	*Opu*	LLEHVRTHGPMD**WSSIRSK**GLLPRTGKSCRL
ORUFI04G22380.1	*Oru*	LLEHVRTHGPMD**WSSIRSK**GLLPRTGKSCRL
Pahal.F00780.1	*Pha*	LLRHVREHGPRE**WSSIRSK**GLLPRTGKSCRL
Sobic.006G169700.1.p	*Sbi*	LLEHVRVHGPRD**WSSIRSK**GFLPRTGKSCRL
Seita.6G211500.1.p	*Sit*	LLRHVREHGPRE**WSSIRSK**GLLPRTGKSCRL
Sevir.6G218900.1.p	*Svi*	LLRHVREHGPRE**WSSIRSK**GLLPRTGKSCRL

The zma-miR159c-j,k-3p family consists of zma-miR159c,d-3p, zma-miR159e-3p and zma-miR159f,j,k-3p different in 5'- and 3'-ends of nucleotide sequences [395]. Therefore, their binding sites are identical. Table 18 shows the binding characteristics of mir159-3p with the mRNA of MYB family genes. All sites are located in the CDS of the mRNA target.

Table 18 - Characteristics of miR159-3p family interaction in CDS mRNA of MYB TF genes of *T. aestivum*, *O. sativa*, *A. thaliana* and *Z. mays* [395, p. 65]

Gene	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %
1	2	3	4	5
AT2G32460.1	ath-miR159a-3p	1016	-100	92
AT2G32460.1	ath-miR159b-3p	1016	-96	88
LOC_Os06g46560.1	osa-miR159d-3p	1064	-100	89
Traes_6DS_A0EC5D808.1	tae-miR159a,b-3p	688	-100	90
Traes_6AS_5562B97F7.1	tae-miR159a,b-3p	760	-96	87
AC217264.3_FGP005	zma-miR159a-3p	1377	-96	87
GRMZM2G070523_P01	zma-miR159a-3p	1044	-96	87
AC217264.3_FGP005	zma-miR159c,d-3p	1377	-98	87

Continue of Table 18

1	2	3	4	5
GRMZM2G070523_P01	zma-miR159c,d-3p	1044	-98	87
AC217264.3_FGP005	zma-miR159e-3p	1377	-110	100
GRMZM2G070523_P01	zma-miR159e-3p	1044	-110	100
AC217264.3_FGP005	zma-miR159f,j,k-3p	1377	-96	87
GRMZM2G070523_P01	zma-miR159f,j,k-3p	1044	-96	87

The binding characteristics of miR159-3p in the mRNAs CDS of Traes_6DS_A0EC5D808.1, AT2G32460.1, AC217264.3_FGP005, GRMZM2G070523_P01 genes are shown in Figure 5.

Gene, miRNA, site, region of mRNA, characteristics of binding	Gene, miRNA, site, region of mRNA, characteristics of binding
Traes_6DS_A0EC5D808.1, tae-miR159a-3p, 688, -100, 90 5'-CAGGAGCUCCCUUC**G**AACCAAU-3' 3'-GUC-UCGAGGGAAG**U**UAGGUUU-5'	AC217264.3_FGP005, zma-miR159c-3p, 1377, -110, 100 5'-UGGAGCUCCCUUCAAACCAAU-3' 3'-ACCUCGAGGGAAGUUUGGUUA-5'
AT2G32460.1, ath-miR159a-3p, 1016, 100, 92 5'-UAGAGCU**U**CCUUCAAACCAAA-3' 3'-AUCUCGA**G**GGAAGUUAGGUUU-5'	GRMZM2G070523_P01, zma-miR159c-3p, 1044, -110, 100 5'-UGGAGCUCCCUUCAAACCAAU-3' 3'-ACCUCGAGGGAAGUUUGGUUA-5'
The bold type indicates the nucleotide of non-canonical pairs U-G, A-C.	

Figure 5 - Schemes of miR159-3p BSs interaction in CDS of *T. aestivum*, *A.thaliana, Z. mays* MYB TF mRNAs [395, p. 65]

The nucleotide sequences of miR159-3p interacted along the entire length with the corresponding mRNA. Data from the analysis of miR159-3p binding to the mRNA of 23 genes in 20 plant species are listed in Table 19.

Table 19 - The variability of amino acid sequences of the MYB family proteins containing oligopeptide ELPSNQ encoded by the binding sites of miR159-3p in the mRNA of different plant genes [395, p. 65]

Gene	object names	Region of transcription factor containing oligopeptide ELPSNQ
1	2	3
AC217264.3_FGP005	*Zma*	LPPLSPSPGPRV**ELPSNQ**YGQPAPPTSAAA
GRMZM2G070523_P01	*Zma*	PPLSPSPCPRVV**ELPSNQ**YAQPTPPASAAA
AT2G32460.1	*Ath*	SSFPLGLDNSVL**ELPSNQ**RPTHSFSSSPII
Traes_6DS_A0EC5D808.1	*Tae*	PGMPPLVPPAVQ**ELPSNQ**SPADAGGPLEML
Traes_6AS_5562B97F7.1	*Tae*	LGMPPLVPPSAQ**ELPSNQ**SPADAGGPLEML
LOC_Os06g46560.1	*Osaj*	SSGLPPLPNRPR**ELPSNQ**FETATSGGGGGC
KFK31122.1	*Aal*	GMIKPTSFPLGL**ELPSNQ**TPTHSFTSNTIL
AA32G00526	*Aar*	NITPNSFLLQNL**ELPSNQ**TTSNTNKNGVFL
Araha.1971s0002.1.p	*Aha*	SSFPLGLENSVL**ELPSNQ**TPTHSFSSNPIL
482173	*Aly*	SSFPLGLENSVL**ELPSNQ**TPTHSFSSNPIL

Continue of Table 19

1	2	3
GSBRNA2T00006425001	*Bna*	SYFSLGLDTTVL**ELPSNQ**TPCTSNIMHDNN
XP_013634909.1	*Tha*	SYFSLGLDTTVL**ELPSNQ**TPTQSCTSNIML
Csa05g024410.1	*Csa*	SSFPLGLENTVL**ELPSNQ**TTIDSFTSNPIL
Bostr.23794s0867.1.p	*Bst*	SSFPLGLGNTVL**ELPSNQ**TPTHSFTSNPIL
RrC14648_p1	*Rra*	SYFSLGLDNTVL**ELPSNQ**TPTQLCTSNIML
Rsa1.0_01027.1_g00010.1	*Rsa*	SYFSLGLDNTVL**ELPSNQ**TPTQLCTSNIML
ORUFI06G26670.1	*Oru*	HAXLPPLPNRPR**ELPSNQ**FETATSGGGGGC
ONIVA06G28020.1	*Oni*	SSGLPPLPNRPR**ELPSNQ**FETATSGGGGGG
OMERI06G24960.1	*Ome*	SPSASQANSPPR**ELPSNQ**FETATSGGGGGD
OGLUM06G26120.1	*Ogu*	SSGLPPLPNRPR**ELPSNQ**FETATSGGGGGG
Do015678.1	*Dol*	YSGLPPLPTRPQ**ELPSNQ**FDTSSSGGGGAG
EMT12896	*Ata*	LPGLPPLPTRPR**ELPSNQ**IETASCSGGADG
EMT06644	*Ata*	PGMPPLVPPAVQ**ELPSNQ**SPADAGGPLEML

This data indicates that the relationship between miR159-3p and mRNA of target genes arose millions of years ago, which suggests its important functional significance.

The nucleotides of miR159-3p binding sites are homologous, but encode different oligopeptides (Figure 6 A, B).

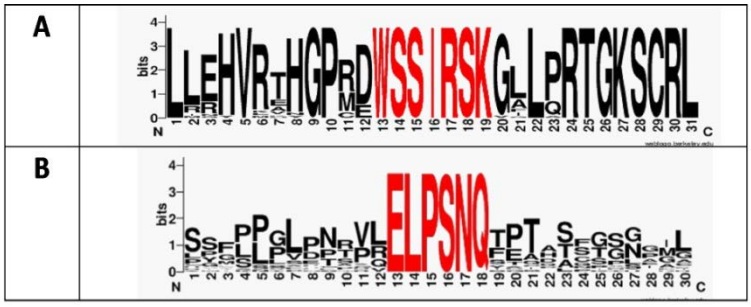
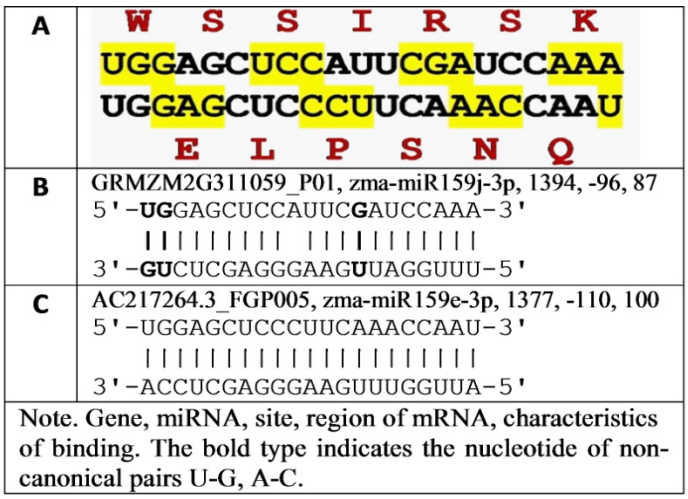


Figure 6 - Variability of the amino acid region of MYB family proteins on the example of tae-miR159a,b-3p binding sites. Note: (A) – oligopeptide WSSIRSK encoded by tae-miR159a,b-3p binding sites in mRNAs of different plant species; (**B)** – oligopeptide ELPSNQ encoded by tae-miR159a,b-3p binding sites located in the third open reading frame in the mRNAs of other plant species [395, p. 66]

The data in Figure 7 explains that mRNA nucleotide sequences can encode different oligopeptides in different reading frames. Therefore, miRNA binding sites in mRNA can also encode different oligopeptides. The binding sites of some miRNAs have homologous nucleotide sequences that can be read in different open reading frames. For example, the nucleotide sequence of miR159j-3p binding sites UGGAGCUCCAUUCGAUCCAAA in the first reading frame will encode the WSSIRSK oligopeptide, and in the third reading frame, miR159e-3p will encode the ELPSNQ oligopeptide (Figure 7) [395, p. 66].



Note. Gene, miRNA, site, region of mRNA, characteristics of binding. The bold type indicates the nucleotide of non-canonical pairs U-G, A-C.

Figure 7 - Scheme of zma-miR159j-3p and zma-miR159e-3p interaction with mRNAs of GRMZM2G311059_P01 and AC217264.3_FGP005 genes [395, p. 66]

Note - **A** – WSSIRSK and ELPSNQ oligopeptide coding scheme by zma-miR159j-3p and zma-miR159e-3p binding sites, respectively (yellow color indicates codons in different open reading frames); **B** – scheme of zma-miR159j-3p interaction with mRNA of GRMZM2G311059_P01gene; **C** – scheme of zma-miR159e-3p interaction with mRNA of AC217264.3_FGP005 gene.

Thus, using the example of the interaction of zma-miR159j-3p and zma-miR159e-3p, which have homologous nucleotide sequences, with mRNAs of the transcription factor genes of many plants, miRNAs binding is observed independently in which reading frame the mRNA nucleotide sequence is translated. Similar data were obtained when analyzing the binding sites of miRNAs in animal mRNAs [386, p. 2; 396].

This work has shown that miRNA families can interact with mRNAs of transcription factor genes of the MYB family and regulate their expression. In mRNAs of MYB genes of *T. aestivum*, *O. sativa*, *A. thaliana*, *Z. mays* all binding sites to mir159-3p were located in the protein-coding part. These binding sites were homologous and encoded oligopeptides WSSIRSK and ELPSNQ. It is important to note that miRNA binding to CDS of the mRNAs encoded by the transcription factor genes is not accidental. Such localization of miRNA binding sites in mRNAs indicates a conserved relationship for many millions of years of divergence in the studied plant species [395, p. 67].

Analysis of interactions of miR159-3p with the different plants of MYB indicates the conserved structure of miRNA binding sites. A high ΔG/ΔGm ratio of miRNAs binding to miRNAs shows that the expression of genes of MYB family can be suppressed strongly by miR159-3p. The established associations of miRNAs and target genes can be used to create plant varieties that are highly productive and resistant to abiotic and biotic stresses [395, p. 67].

3.5 Predicting Characteristics of interaction miRNA with mRNA of the GRAS genes of *A. thaliana, O. sativa, T. aestivum, and Z. mays*

3.5.1 Characteristics of interaction miRNA with mRNAs of the GRAS family genes of *A. thaliana*

As a result of studying the characteristics of the interaction of 428 miRNAs with mRNAs of 37 genes of the *A. thaliana* GRAS family, it was found that only 11 genes were targets for miR171a-3p, miR170-3p, miR842-3p, miR157c-3p, miR414-5p, miR830-3p, miR5021 -5p, miR5658-5p with a ΔG/ΔGm value of 90-100% (Table 20). The miRNA binding sites were located in the CDS and 5'UTR of the mRNA genes. The miR171a-3p and miR170-3p had the same start of binding sites in the mRNA of three genes (AT2G45160.1, AT3G60630.1, AT4G00150.1), since these miRNAs differ by only one nucleotide. The establishment of the complete complementarity of the binding of miR171a-3p nucleotides to the mRNA of these genes indicates a high reliability of the predictions of the MirTarget program. The miR157c-3p had a binding site only in the mRNA of the AT4G00150.1 gene. The miR5021-5p and miR5658-5p each had three target genes. It was revealed that miR842-3p, miR414-5p, miR830-3p each had one binding site in the mRNA of the GRAS genes. The ability of miR171a-3p, miR170-3p, miR157c-3p to bind to AT4G00150.1 mRNA indicates an increased control of this gene expression by these miRNAs [397].

Table 20 - Characteristics of miRNA binding sites in mRNA of target genes of GRAS TF family of *A. thaliana* [397, p. 2]

Gene	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
AT4G00150.1	miR157c-3p	1023	-100	90	21
AT2G45160.1	miR170-3p	1304	-104	96	21
AT3G60630.1	miR170-3p	1100	-104	96	21
AT4G00150.1	miR170-3p	1065	-104	96	21
AT2G45160.1	miR171a-3p	1304	-113	100	21
AT3G60630.1	miR171a-3p	1100	-113	100	21
AT4G00150.1	miR171a-3p	1065	-113	100	21
AT1G14920.1	miR414-5p	479	-96	90	21
AT4G37650.1	miR5021-5p	374	-93	96	20
AT5G41920.1	miR5021-5p	289*	-91	93	20
AT5G52510.1	miR5021-5p	919	-89	91	20
AT5G59450.1	miR5658-5p	119*	-98	96	21
AT1G14920.1	miR5658-5p	442	-93	92	21
AT2G01570.1	miR5658-5p	274	-91	90	21
AT1G55580.1	miR830-3p	1103	-91	90	21
AT1G63100.1	miR842-3p	2635	-102	91	21
Note: *-5'UTR					

Diagrams of the interaction of ath-miRNA with mRNA of the GRAS genes of *A. thaliana* (Figure 8), obtained using the miRTarget program, clearly show the

participation of all miRNA nucleotides in binding to mRNA. Figure 1 shows the schemes of the interaction of osa-miR171a-3p with mRNA of the TF GRAS genes. The interaction of nucleotides occurs along the entire length. The diagrams of the interaction of zma-miRNA with mRNA of genes of the GRAS family shown in Figure 8 show that all nucleotides of miRNA form hydrogen bonds in CDS mRNA. The data obtained indicate the high efficiency of the established associations of miRNAs and TF genes, since in many cases, a completely complimentary interaction of these molecules is observed both due to canonical and non-canonical nucleotide pairs [397, p. 5].

ath-miR171a-3p	ath-miR170-3p
AT2G45160.1; 1304; -113; 100; 21 5'-GAUAUUGGCGCGGCUCAAUCA-3' 3'-CUAUAACCGCGCCGAGUUAGU-5' AT3G60630.1; 1100; -113; 100; 21 5'-GAUAUUGGCGCGGCUCAAUCA-3' 3'-CUAUAACCGCGCCGAGUUAGU-5' AT4G00150.1; 1065; -113; 100; 21 5'-GAUAUUGGCGCGGCUCAAUCA-3' 3'-CUAUAACCGCGCCGAGUUAGU-5'	AT2G45160.1; 1304; -104; 96; 21 5'-GAUAUUGGCGCGGCUCAAUCA-3' 3'-CUAUAACUGUGCCGAGUUAGU-5' AT3G60630.1; 1100; -104;96; 21 5'-GAUAUUGGCGCGGCUCAAUCA-3' 3'-CUAUAACUGUGCCGAGUUAGU-5' AT4G00150.1; 1065; 104; 96;21 5'-GAUAUUGGCGCGGCUCAAUCA-3' 3'-CUAUAACUGUGCCGAGUUAGU-5'
osa-miR171a-3p;	
LOC_Os02g44360.1; 1397; -113;100; 21 5'-GAUAUUGGCGCGGCUCAAUCA-3' 3'-CUAUAACCGCGCCGAGUUAGU-5' LOC_Os02g44370.1; 1522; -113; 100; 21 5'-GAUAUUGGCGCGGCUCAAUCA-3' 3'-CUAUAACCGCGCCGAGUUAGU-5'	LOC_Os06g01620.1; 441; -113; 100; 21 5'-GAUAUUGGCGCGGCUCAAUCA-3' 3'-CUAUAACCGCGCCGAGUUAGU-5' LOC_Os04g46860.1; 1471; -113; 100; 21 5'-GAUAUUGGCGCGGCUCAAUCA-3' 3'-CUAUAACCGCGCCGAGUUAGU-5'
zma-miR171a-3p (20nt)	zma-miR171n-3p (21nt)
GRMZM2G037792_P01; 1280; -106; 100 5'-AUAUUGGCGCGGCUCAAUCA-3' 3'-UAUAACCGCGCCGAGUUAGU-5' GRMZM2G051785_P01; 628; -106; 100 5'-AUAUUGGCGCGGCUCAAUCA-3' 3'-UAUAACCGCGCCGAGUUAGU-5' GRMZM2G098800_P01; 1382; -106; 100 5'-AUAUUGGCGCGGCUCAAUCA-3' 3'-UAUAACCGCGCCGAGUUAGU-5' GRMZM2G110579_P01; 772; -106; 100 5'-AUAUUGGCGCGGCUCAAUCA-3' 3'-UAUAACCGCGCCGAGUUAGU-5' GRMZM2G418899_P01; 46-106; 100 5'-AUAUUGGCGCGGCUCAAUCA-3' 3'-UAUAACCGCGCCGAGUUAGU-5' GRMZM5G825321_P01; 1374; -106; 100 5'-AUAUUGGCGCGGCUCAAUCA-3' 3'-UAUAACCGCGCCGAGUUAGU-5' GRMZM2G011947_P01; 169; -102; 96 5'-AUAUUGGCGCGGCUCAAUUA-3' 3'-UAUAACCGCGCCGAGUUAGU-5' GRMZM2G079470_P01; 1166; -102; 96 5'-AUAUUGGCGCGGCUCAAUUA-3' 3'-UAUAACCGCGCCGAGUUAGU-5' GRMZM2G060265_P01; 1016; -98; 92 5'-AUACUGGCGCGGCUCAACUA-3' 3'-UAUAACCGCGCCGAGUUAGU-5'	GRMZM2G037792_P01; 1279; -113; 100 5'-GAUAUUGGCGCGGCUCAAUCA-3' 3'-CUAUAACCGCGCCGAGUUAGU-5' GRMZM2G051785_P01; 627; -113; 100 5'-GAUAUUGGCGCGGCUCAAUCA-3' 3'-CUAUAACCGCGCCGAGUUAGU-5' GRMZM2G098800_P01; 1381; -113; 100 5'-GAUAUUGGCGCGGCUCAAUCA-3' 3'-CUAUAACCGCGCCGAGUUAGU-5' GRMZM2G110579_P01; 771; -113; 100 5'-GAUAUUGGCGCGGCUCAAUCA-3' 3'-CUAUAACCGCGCCGAGUUAGU-5' GRMZM2G418899_P01; 45; -113; 100 5'-GAUAUUGGCGCGGCUCAAUCA-3' 3'-CUAUAACCGCGCCGAGUUAGU-5' GRMZM5G825321_P01; 1373; -113; 100 5'-GAUAUUGGCGCGGCUCAAUCA-3' 3'-CUAUAACCGCGCCGAGUUAGU-5' GRMZM2G011947_P01; 168; -108; 96 5'-GAUAUUGGCGCGGCUCAAUUA-3' 3'-CUAUAACCGCGCCGAGUUAGU-5' GRMZM2G079470_P01; 1165; -108; 96 5'-GAUAUUGGCGCGGCUCAAUUA-3' 3'-CUAUAACCGCGCCGAGUUAGU-5' GRMZM2G060265_P01; 1015; -104; 92 5'-GAUACUGGCGCGGCUCAACUA-3' 3'-CUAUAACCGCGCCGAGUUAGU-5'
Gene; start of binding site (nt); mRNA region; ΔG (kJ/mole); ΔG/ΔGm, %; length of miRNA (nt). The upper and lower nucleotide sequences of mRNA and miRNA, respectively. The bold type indicates the nucleotide of non-canonical pairs U-G, A-C.	

Figure 8 - Schemes of the interaction of ath-miRNA, osa-miRNA, and zma-miRNA with mRNA of GRAS transcription factor genes of *A. thaliana*, *O. sativa*, and *Z. mays* [397, p. 3]

3.5.2 Characteristics of interaction miRNA with mRNAs of the GRAS family genes of *O. sativa* and *T. aestivum*

It was found that out of 738 miRNAs, only 16 could bind to mRNA of 18 genes from 60 genes of the GRAS *O. sativa* family. The binding sites of these miRNAs were located in the 5'UTR, CDS, and 3'UTR (Table 21). The ΔG/ΔGm value for binding sites of the miR171 family ranged from 92% to 100%, which indicates a high complementarity of the interaction of these miRNAs with the mRNA of the GRAS TF family genes. The miR171a-3p differs from miR171b-f-3p by one nucleotide and by two nucleotides from miR171i-3p. The mRNA of LOC_Os02g44360.1, LOC_Os02g44370.1, LOC_Os04g46860.1, LOC_Os06g01620.1, LOC_Os10g40390.1 genes were targets for all three miR171. The mRNA of the LOC_Os10g40390.1 gene had a binding site for miR415-5p and miR171a-f,i-3p. miR156c,g-3p, miR535-3p, miR5809-3p, miR5819-5p each had two target genes. The mRNA of the LOC_Os04g37440.1 gene contained two miR5819-5p binding sites. The miR5075-3p and miR5819-5p bind to mRNA of the LOC_Os06g03710.1 gene in CDS and 3'UTR, respectively. The mRNA of the LOC_Os04g49110.1 gene contains binding sites for miR11337-5p, miR11342-5p, and miR2926-5p. The rest of the miRNAs each had only one target gene. The obtained data indicate the functioning of many miRNA associations with GRAS TF family genes of the *O. sativa* [397, p. 5-6].

Table 21 - Characteristics of miRNA binding sites in mRNA of target genes of GRAS TF family of *O. sativa* and *T. aestivum* [397, p. 4; 398, p. 7]

Gene	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
1	2	3	4	5	6
LOC_Os04g49110.1	miR11337-5p	285*	-106	94	21
LOC_Os04g49110.1	miR11342-5p	282*	-98	90	21
LOC_Os11g04400.1	miR156c,g-3p	987	-108	91	22
LOC_Os12g04200.1	miR156c,g-3p	891	-108	91	22
LOC_Os02g44360.1	miR171a-f,i-3p	1397	-104,-113	92,100	21
LOC_Os02g44370.1	miR171a-f,i-3p	1522	-104,-113	92,100	21
LOC_Os03g15680.1	miR171h-3p	807	-102	92	21
LOC_Os04g46860.1	miR171a-f,i-3p	1471	-104,-113	92,100	21
LOC_Os06g01620.1	miR171a-f,i-3p	441	-104,-113	92,100	21
LOC_Os10g40390.1	miR171a-f,i-3p	168	-104,-108	92-96	21
LOC_Os04g49110.1	miR2926-5p	838	-100	90	20
LOC_Os04g46860.1	miR319a-3p.2-3p,b-3p	358	-100	90	20
LOC_Os07g40020.1	miR394-5p	1749	-98	90	20
LOC_Os01g67650.1	miR3979-5p	830	-98	90	20
LOC_Os10g40390.1	miR415-5p	1101	-100	90	21
LOC_Os06g03710.1	miR5075-3p	1128	-110	90	21
LOC_Os11g04570.1	miR535-3p	1860	-102	91	21
LOC_Os12g04370.1	miR535-3p	2229	-102	91	21
LOC_Os01g62460.1	miR5793-5p	759	-104	91	21
LOC_Os01g67650.1	miR5809-3p	511	-106	91	20

Continue of Table 21

1	2	3	4	5	6
LOC_Os05g31380.1	miR5809-3p	1440	-106	91	20
LOC_Os04g37440.1	miR5819-5p	327, 402	-110,-115	90,93	21
LOC_Os06g03710.1	miR5819-5p	3555**	-110	90	21
LOC_Os07g39820.1	miR5837.2-5p	774	-106	91	21
T. aestivum					
Traes_4AL_C217A20A1.2	miR399-3p	1469	-91	90	19
Traes_5BL_1E751EF1F.1	miR7757-5p	1799	-100	90	22
Traes_4BL_86941BB78.1	miR530-3p	6	-98	88	21
Traes_5BL_A7C4DAE11.2	miR7757-5p	1811	-98	88	22
Traes_5DL_B89CD8432.1	miR7757-5p	1823	-98	88	22
Note: *-5'UTR;**- 3'UTR					

The study of 125 miRNAs interaction to mRNA of 117 GRAS TF genes of *T. aestivum* revealed only five target genes for three miRNAs with the selection criteria Δ*G*/Δ*G*m equals 88% and over. The miRNA binding sites were located in the protein-coding region (CDS) of mRNA target genes (table 21). It was found that miR399-3p and miR530-3p had only one target gene. The miRNA analysis of target genes showed that miR7757-5p had three binding sites in mRNA of GRAS genes (Traes_5BL_1E751EF1F.1, Traes_5BL_A7C4DAE11.2, Traes_5DL_B89CD8432.1), which indicates a high probability of their significance for the regulation of mRNA translation of the corresponding genes [398].

3.5.3 Characteristics of interaction miRNA with mRNAs of the GRAS family genes of *Z. mays*

The binding of 325 miRNAs to mRNAs of 86 genes of the GRAS family of *Z. mays* was studied. Only 14 genes were targets for eight miRNAs, with a ΔG/ΔGm value of 90-100% (Table 22). The mRNA of these genes interacted with miR159e-5p, miR172a-d-3p, miR172b,d-5p, miR394a,b-5p, and members of the miR171-3p family. The miR171-3p family consists of 14 miRNAs (miR171a-n), differing from each other by several nucleotides. An increase in the probability of miRNA binding in mRNA of GRAS TF family genes is due to the presence of binding sites of the zma-miR171-3p family. The miR171a-n-3p each had six binding sites in the mRNA of the genes GRMZM2G011947_P01, GRMZM2G037792_P01, GRMZM2G051785_P01, GRMZM2G060265_P01, GRMZM2G079470_PG089. The rest of the miRNAs had only one or two target genes. The miRNA binding sites in the mRNA of the genes of the GRAS *Z. mays* family were located only in the CDS [397, p. 6].

The identification of miR171-3p binding sites in the mRNA of GRMZM2G037792_P01, GRMZM2G051785_P01, GRMZM2G098800_P01, GRMZM2G110579_P01, GRMZM2G418899_P01, GRMZM5G825321_P01 maize genes, including a fully complementary interaction, indicates the adequacy of the MirTarget program [397, p. 1-10].

Table 22 - Characteristics of miRNA interaction mRNA of target genes of GRAS TF family of *Z. mays* [397, p. 2]

Gene	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
GRMZM2G146018_P01	miR159e-5p	585	-106	93	21
GRMZM2G011947_P01	miR171a-f,i,j,n-3p	165÷169 (6)	-100÷-108	91÷96	20,21
GRMZM2G037792_P01	miR171a-f,i,j,l,m-3p	1276÷1280 (6)	-100÷-108	92÷100	20,21
GRMZM2G051785_P01	miR171a-f,i,j,l,m-3p	624÷628 (6)	-100÷-108	92÷100	20,21
GRMZM2G055263_P01	miR171b,h,k-3p	757-758	-98÷-102	92	21
GRMZM2G060265_P01	miR171a-f,i,j,l-n 3p	1012÷1016 (6)	-98÷-104	90÷92	20,21
GRMZM2G079470_P01	miR171a-f,i,j,n-3p	1162÷1166 (6)	-100÷-108	91÷96	20,21
GRMZM2G098800_P01	miR171a-f,i,j,l,m-3p	1378÷1382 (6)	-100÷-108	90÷100	20,21
GRMZM2G110579_P01	miR171a-f,i,j,l,m-3p	768÷772 (6)	-102÷-108	92÷100	20,21
GRMZM2G418899_P01	miR171a-f,i,j,l,m-3p	42÷46 (6)	-100÷-108	92÷100	20,21
GRMZM5G825321_P01	miR171a-f,i,j,l,m-3p	1370÷1374 (6)	-100÷-108	90÷100	20,21
GRMZM2G146018_P01	miR172a,b,c,d-3p	1011	-91	90	20
GRMZM2G106356_P01	miR172b,d-5p	2023	-93	90	20
GRMZM2G024973_P01	miR394a,b-5p	2039	-98	90	20
GRMZM5G874545_P01	miR394a,b-5p	602	-98	90	20

The nucleotide sequences of ath-miR171a-3p, osa-miR171a-3p, zma-miR171n-3p were identical and had binding sites in mRNA of *A. thaliana* - 3 genes, *O. sativa* – 4 genes, *Z. mays* – 6 genes of the GRAS family (Figure 9). The presented data indicate high conservation of miR171 nucleotide sequences in three phylogenetically distant plant species but retaining the interaction between miRNA and target genes. It seems important to clarify the function of genes whose expression depends on miR171. The analysis of the functions of the studied target genes carried out in this work showed that miR171 could regulate the expression of genes involved in seed formation (http://www.bar.utoronto.ca/) [397, p. 4].

Figure 9 - Variability of nucleotide sequences of regions containing binding sites ath-miR171a-3p, osa-miR171a-3p, zma-miR171n-3p of GRAS family [397, p. 4]

Note - I - Nucleotide sequences of regions containing binding sites ath-miR171a-3p, osa-miR171a-3p, zma-miR171n-3p; II - Amino acid sequences of regions of the corresponding proteins.

3.6 Characteristics of interaction miRNA with mRNA of the ERF TF genes of *A. thaliana, O. sativa, T. aestivum,* and *Z. mays*

3.6.1 Characteristics of interaction miRNA with mRNAs of the ERF family genes of *A. thaliana*

As a result of studying the interaction of 428 miRNAs of *A. thaliana* in the mRNA of 123 genes of the ERF TF family, it was revealed that with the selection criterion ΔG/ΔGm of 90% or more, 25 genes were targets for eight miRNAs (Table 23). The binding sites were located in the CDS and 5'UTR of mRNA of eight and four target genes, respectively. Eight target genes had miR5658-5p, with a ΔG/ΔGm value of 90-92%. The miR158b-3p, miR774b-3p, miR829-3p.2, miR847-3p, miR859-5p, and miR867-5p each had one target gene. Two miRNAs bound to mRNA of the AT5G18560.1 gene. The miR5021-5p had one to four binding sites in mRNA of 12 genes with a ΔG/ΔGm value from 91% to 96%. The miR5658-5p had mRNA binding sites for eight genes with a ΔG/ΔGm value of 90-92%. The mRNA of the AT1G44830.1 gene contained eight binding sites for miR5658-5p, and the mRNA of the AT4G36900.1 gene contained three binding sites. The data obtained show a strong association of many *A. thaliana* miRNAs with many TF genes of the ERF family [399].

Table 23 - Characteristics of ath-miRNA interaction with mRNA of target genes of ERF TF family of *A. thaliana* [397, p. 5]

Gene	miRNA	Start of site, nt	mRNA region	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
1	2	3	4	5	6	7
AT4G31060.1	miR158b-3p	715	CDS	-93	90	20
AT1G12890.1	miR5021-5p	423	CDS	-89	91	20
AT1G21910.1	miR5021-5p	543	CDS	-91	93	20
AT1G21910.1	miR5021-5p	295÷307 (3)	CDS	-89,-91	91,93	20
AT1G22810.1	miR5021-5p	19÷25 (3)	5'UTR	-91,-96	93,98	20
AT1G25470.1	miR5021-5p	172,175	5'UTR	-89	91	20
AT1G77640.1	miR5021-5p	152,155	CDS	-89,-91	91,93	20
AT1G78080.1	miR5021-5p	821	CDS	-93	96	20
AT2G31230.1	miR5021-5p	718÷727 (4)	CDS	-89,-91	91÷93	20
AT2G44940.1	miR5021-5p	244	CDS	-89	91	20
AT3G25890.1	miR5021-5p	161-170 (3)	5'UTR	-89,-91	91,93	20
AT5G13330.1	miR5021-5p	1176	CDS	-91	93	20
AT5G21960.1	miR5021-5p	186	5'UTR	-89	91	20
AT5G25810.1	miR5021-5p	639	CDS	-93	96	20
AT1G68550.1	miR5658-5p	200	5'UTR	-91	90	21
AT3G16280.1	miR5658-5p	43	CDS	-91	90	21
AT3G61630.1	miR5658-5p	1009	CDS	-93	92	21
AT4G36900.1	miR5658-5p	769÷775 (3)	CDS	-91,-93	90,92	21
AT5G07580.1	miR5658-5p	419	CDS	-91	90	21
AT5G18560.1	miR5658-5p	579	CDS	-93	92	21
AT5G61590.1	miR5658-5p	480	CDS	-91	90	21

Continue of Table 23

1	2	3	4	5	6	7
AT1G44830.1	miR5658-5p	128÷161 (6)	CDS	-91÷-96	90÷94	21
AT3G16770.1	miR774b-3p	939	CDS	-93	90	21
AT5G18560.1	miR829-3p.2	1333	3'UTR	-93	90	21
AT1G49120.1	miR847-3p	568	CDS	-98	90	21
AT1G19210.1	miR859-5p	238	CDS	-96	90	21
AT1G53170.1	miR867-5p	143	5'UTR	-93	92	21

Figure 10 shows examples of the interaction of some miRNAs with mRNAs of ERF genes of *A. thaliana* and *O. sativa*, which illustrate hydrogen bonds between interacting nucleotides. With full complementarity and high interaction of free energy, the probability of miRNAs interaction with mRNA molecules increases. The presented data demonstrate the important role of non-canonical A-C and G-U pairs in increasing the free energy of interaction between miRNAs and mRNAs of target genes. For example, when ath-miR5021-5p, osa-miR11339-5p, osa-miR415-5p interacted with the mRNA of the AT5G21960.1, LOC_Os02g54050.1, and LOC_Os04g46440.1 genes, respectively, two non-canonical A-C pairs and one G-U pair were formed. These schemes demonstrate the advantage of the MirTarget program over other commonly used programs when determining the free energy of interaction between miRNA and their target genes in animals and plants, which is calculated taking into account the formation of non-canonical pairs of nucleotides A and C, G and U [400, p. 49-51].

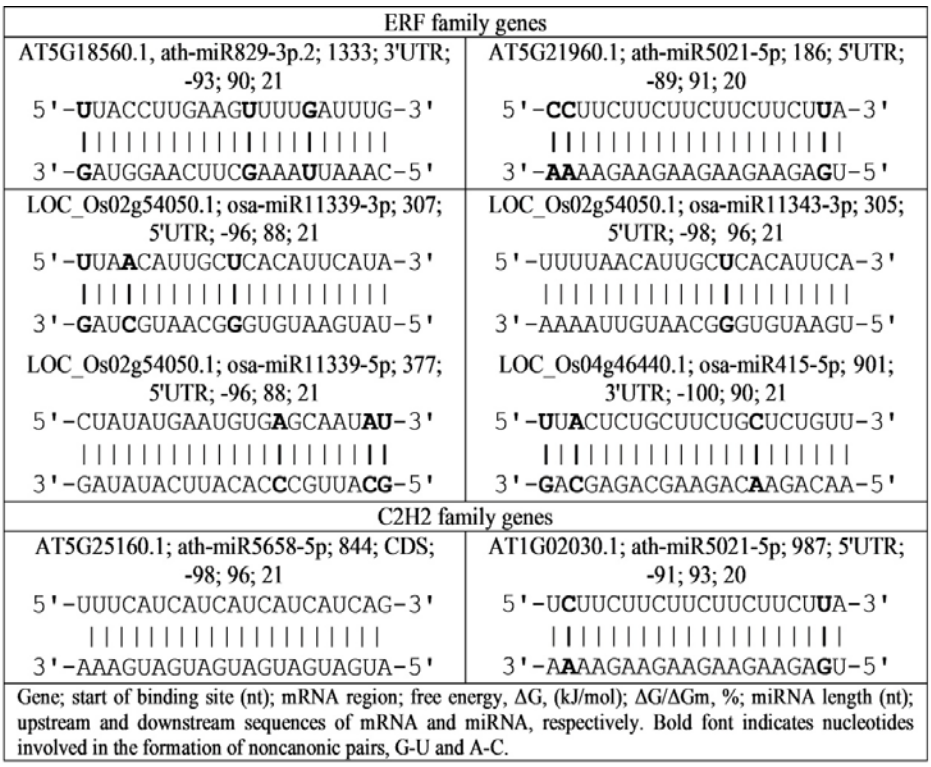


Figure 10 - Schemes of the interaction of ath-miRNA and osa-miRNA with mRNA of the ERF and C2H2 TF genes of *A. thaliana. O. sativa* [400, p. 50]

3.6.2 Characteristics of interaction miRNA with mRNAs of the ERF family genes of *O. sativa, T. aestivum,* and *Z. mays*

Out of 738 *O. sativa* miRNAs, only 13 miRNAs effectively bound to mRNA of 16 ERF genes, which are a family of transcription factors (Table 24). The ΔG/ΔGm value, which characterizes the binding energy of osa-miRNAs with the mRNA of these genes, varied from 90% to 96%. The miR5075-3p and miR5819-5p each have two binding sites in the mRNA of the ERF genes. Table 24 shows that both strands of pre-miR2102 (miR2102-3p and miR2102-5p) can efficiently bind to mRNA of one target gene, which was revealed for the first time in plants [400]. In humans and animals, this phenomenon is more common. The remaining ten osa-miRNAs each have one target gene. The data shown in Table 24 indicate that the miRNA binding sites were located in the 5'UTR, CDS, and 3'UTR.

Table 24 - Characteristics of osa-miRNA interaction in mRNA of ERF TF family target genes of *O. sativa, T. aestivum* [397, p. 5; 398, p. 7]

Gene	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
LOC_Os05g34730.1	miR11339-5p	1590**	-98	90	21
LOC_Os02g54050.1	miR11343-3p	305*	-100	96	21
LOC_Os12g41060.1	miR1427-3p	370	-110	90	21
LOC_Os01g54890.1	miR1846e-5p	284	-104	91	20
LOC_Os07g03250.1	miR2102-3p	465	-117	92	22
LOC_Os04g32790.1	miR2102-5p	965	-110	91	20
LOC_Os02g09650.1	miR2275c-5p	4986**	-104	91	23
LOC_Os06g42990.1	miR3979-5p	214	-100	92	20
LOC_Os04g46440.1	miR415-5p	901**	-100	90	21
LOC_Os03g08490.1	miR5075-3p	355	-110	90	21
LOC_Os02g52670.1	miR5075-3p	739	-110	90	21
LOC_Os05g37640.1	miR531b-5p	620	-110	91	20
LOC_Os04g56150.1	miR5504-3p	188*	-106	91	21
LOC_Os07g47330.1	miR5534a,b-5p	736	-100	90	21
LOC_Os09g11460.1	miR5819-5p	142	-110	90	21
LOC_Os05g28350.1	miR5819-5p	404	-113	91	21
T. aestivum					
Traes_5BL_7F0FD1538.2	miR7757-5p	2096	-102	92	22
Traes_2BL_FC0F8A3DC.1	miR9677b-5p	304	-110	90	21
Traes_1BL_09D8BE2C9.1	miR9778-5p	435	-100	89	21
Traes_1AL_08BAD7CD3.1	miR9778-5p	435	-100	89	21
Traes_5BL_7F0FD1538.2	miR5200-3p	3396	-96	88	21
Note: * 5'UTR; ** 3'UTR					

As a result of studying the interaction of 125 miRNAs with 169 mRNA of *T. aestivum* genes, it was found that only five genes were targets for four miRNAs. Traes_5BL_7F0FD1538.2 gene was the target for miR5200-3p and miR7757-5p. The miR7757-5p bound to mRNA of Traes_5BL_7F0FD1538.2 gene with ΔG/ΔGm value equal 92%, which indicates a strong interaction of these RNAs.

The targets for miR9778-5p were mRNA of two genes in the CDS regions of the ERF family: Traes_1AL_08BAD7CD3.1, Traes_1BL_09D8BE2C9.1 with the value of ΔG/ΔGm equal 89%. The miR9677b-5p had only one target gene. The possibility of binding of several miRNAs to one mRNA or one miRNA at sites of different mRNAs indicates an increased control of the expression of the corresponding genes by miRNAs [398, p. 6; 400].

The binding of 325 miRNAs to the mRNA of 186 genes of the ERF TF family of *Z. mays* was studied. Of the studied genes, only GRMZM2G474326_P01, GRMZM2G060876_P01 were targeted for miR160f-5p and miR529-5p, respectively, with a ΔG/ΔGm value of 90-91%. Consequently, the expression of ERF TFs family of *Z. mays* depends on miRNA to a much less than the expression of ERF TFs families of *O. sativa* and *A. thaliana* [397, p. 7].

3.7 Predicting Characteristics of interaction miRNA with mRNA of the C2H2 TF Genes of *A.thaliana, O. sativa, Z. mays,* and *T. aestivum*

3.7.1 Characteristics of interaction miRNA with mRNAs of the C2H2 family genes of *A. thaliana*

To identify miRNAs targeting genes of the C2H2 transcription factor family, the search for binding sites of 428 miRNAs of *A. thaliana* was carried out in mRNA of 87 C2H2 TF genes (Table 25). As a result of these studies, it was revealed that with the selection criterion ΔG/ΔGm of 90% or more, only 17 genes of the C2H2 family are targets of nine miRNAs. Only three genes of *A. thaliana* were targets of three miRNAs, the binding sites of which were located in the 5'UTR (Table 25). In this case, miR5658-5p had binding sites in the AT2G42410.1 and AT1G34370.1 genes, and the mRNA of the AT1G34370.1 gene could bind to miR854a-e-5p and miR5658-5p. The mRNA of the AT3G57670.1 gene had two binding sites for miR5021-5p, and the mRNA of the AT5G56200.1 gene could interact with miR414-5p and miR5021-5p. The miR414-5p had binding sites for mRNA of three target genes. For ath-miR5021, binding sites were found for the mRNA of AT1G02030.1, AT2G42410.1, AT3G19580.1, AT3G57670.1, AT4G16610.1, and AT5G56200.1 genes [397, p. 1-10].

Table 25 - Characteristics of ath-miRNA binding sites in mRNA of target genes of C2H2 TF family of *A. thaliana* [397, p. 6]

Gene	miRNA	Start of site, nt	mRNA region	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
1	2	3	4	5	6	7
AT5G52010.1	miR2111a,b-5p	1037	CDS	-96	90	21
AT1G26610.1	miR3434-3p	661	CDS	-98	94	20
AT5G56200.1	miR414-5p	887	CDS	-98	92	21
AT5G14010.1	miR414-5p	449	CDS	-98	92	21
AT3G48430.1	miR414-5p	3530	CDS	-96	90	21
AT1G02030.1	miR5021-5p	987	5'UTR	-91	93	20

Continue of Table 25

1	2	3	4	5	6	7
AT2G42410.1	miR5021-5p	551	CDS	-89	91	20
AT3G19580.1	miR5021-5p	318	CDS	-89	91	20
AT3G57670.1	miR5021-5p	612	CDS	-91	93	20
AT3G57670.1	miR5021-5p	297	CDS	-89	91	20
AT4G16610.1	miR5021-5p	277	CDS	-89	91	20
AT5G56200.1	miR5021-5p	776	CDS	-89	91	20
AT4G35610.1	miR5638a-3p	717	CDS	-93	90	21
AT1G34370.1	miR5658-5p	154	5'UTR	-98	96	21
AT1G55110.1	miR5658-5p	903	CDS	-96	94	21
AT2G42410.1	miR5658-5p	201	5'UTR	-91	90	21
AT3G13810.1	miR5658-5p	920	CDS	-93	92	21
AT5G25160.1	miR5658-5p	844	CDS	-98	96	21
AT4G02670.1	miR5662-3p	826	CDS	-96	90	20
AT1G34370.1	miR854a-e-5p	146	5'UTR	-104	91	21
AT5G44160.1	miR860-3p	450	CDS	-96	94	21

The ath-miR5021 binding sites encoded the SSSSSS hexapeptide (Figure 11). The ΔG/ΔGm value for miR5658-5p binding sites in mRNA of five genes ranged from 90% to 96% (Table 25), which indicates a strong interaction of these miRNAs with mRNA of the C2H2 family genes. The remaining six miRNAs (miR2111a,b-5p, miR3434-3p, miR5638a-3p, miR5662-3p, miR854a-e-5p, miR860-3p) each have one target gene. Examples of complementary interaction of miRNA nucleotides with mRNA of two genes are shown in the diagrams (Figure 11) [397, p.7].

3.7.2 Characteristics of interaction miRNA with mRNAs of the C2H2 family genes of *O. sativa, Z. mays*, and *T. aestivum*

Fourteen miRNAs could interact with mRNAs of 17 genes of the C2H2 family *O. sativa* (Table 26). All miRNA binding sites were located in the CDS. The miR5075-3p had binding sites in mRNA of LOC_Os03g13600.1, LOC_Os04g36650.1, LOC_Os04g02510.1, LOC_Os06g10470.1, LOC_Os07g40080.1, and LOC_Os07g44640.1 genes, which indicates the development of its important role in the regulation of rice. On the other hand, LOC_Os07g40080.1 and LOC_Os07g44640.1 genes were targeted by miR2102-5p and miR5075-3p. The miR414-5p and miR5809-3p each have two binding sites in the mRNA of the C2H2 genes. The ath-miR414 binds to mRNA of LOC_Os01g63980.1, LOC_Os04g46670.1 genes with a ΔG/ΔGm value equal 92%. The miR5809-3p interacts with mRNA of LOC_Os01g62190.1, LOC_Os04g39520.1 genes with ΔG/ΔGm value equal to 91% and 96%, respectively. Overall, the results in Table 26 suggest an important role of miRNAs in the regulation of rice growth and development by influencing the C2H2 TF family genes of *O. sativa*. The binding sites of miRNAs with mRNA genes involved in the growth and development of rice were characterized by high

complementarity [397, p. 1-10]. Establishing the properties of miRNA binding sites with mRNA of C2H2 TF genes significantly expands the understanding of the role of miRNA in the regulation of plant gene expression. The data obtained will contribute to creating new varieties of rice to increase their productivity and resistance to stress factors.

Table 26 - Characteristics of miRNA binding sites in CDS mRNA of C2H2 TF target genes of *O. sativa* and *Z. mays* [397, p. 6; 398, p. 7]

Gene	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
O. sativa					
LOC_Os04g39520.1	miR5809-3p	66	-113	96	20
LOC_Os01g62190.1	miR5809-3p	548	-106	91	20
LOC_Os01g66570.1	miR5793-5p	409	-104	91	21
LOC_Os07g39310.1	miR531b-5p	308	-110	91	20
LOC_Os03g13600.1	miR5075-3p	738	-110	90	21
LOC_Os04g02510.1	miR5075-3p	1281	-110	90	21
LOC_Os04g36650.1	miR5075-3p	118	-110	90	21
LOC_Os06g10470.1	miR5075-3p	158	-115	93	21
LOC_Os07g40080.1	miR5075-3p	539	-110	90	21
LOC_Os07g44640.1	miR5075-3p	151	-110	90	21
LOC_Os04g46670.1	miR414-5p	574	-102	92	21
LOC_Os01g63980.1	miR414-5p	621	-102	92	21
LOC_Os03g31240.1	miR2907a-d-3p	548	-119	90	22
LOC_Os09g38610.1	miR2102-5p	229	-117	96	20
LOC_Os07g44640.1	miR2102-5p	161	-110	91	20
LOC_Os07g40080.1	miR2102-5p	440	-115	95	20
LOC_Os06g07020.1	miR2097-5p	452	-110	90	22
LOC_Os01g09850.1	miR1858a,b-5p	667	-113	93	21
LOC_Os07g40780.1	miR1850.3-3p	1578	-98	90	22
Z. mays					
GRMZM2G114660_P01	miR390a,b-5p	484	-108	93	21
GRMZM2G105224_P01	miR169o-3p	1023	-102	92	20
AC211702.2_FGP002	miR166n-5p	9	-104	91	21
AC185655.3_FGP004	miR164d-3p	520	-98	90	20
AC215290.3_FGP002	miR164d-3p	520	-98	90	20
GRMZM2G150011_P01	miR2275d-5p	44*	-96	90	21
T. aestivum					
Traes_5DL_3FBCC4C48.1	miR319-3p	2409	-104	91	21
Traes_5BL_C3F3A871A.1	miR319-3p	3231	-104	91	21
Traes_5AL_903412779.2	miR319-3p	2343	-104	91	21
Traes_1BL_4026DC5011.2	miR10520-5p	373	-91	88	20
Traes_4DL_6EBD74330.2	miR531-5p	360	-108	88	21
Traes_4AS_D20DF472E.1	miR531-5p	270	-108	88	21
Note: *****-5'UTR					

The number of target genes of the C2H2 TF family of *Z. mays* and that bind to miRNA is insignificant (Table 26). This is evidence of the small role of miRNA in the regulation of the expression of members of the C2H2 family of *Z. mays*. It was revealed that miR390a,b-5p, miR169o-3p, miR166n-5p, and miR2275d-5p each have only one target gene, with a ΔG/ΔGm value of 90-93%. The effect of miR164d-3p on the AC185655.3_FGP004 and AC215290.3_FGP002 genes should be noted [397, p. 8].

The analysis of interactions of 125 miRNAs with mRNAs of 211 C2H2 family genes of *T. aestivum* revealed only six target genes for the miR319-3p, miR10520-5p, miR531-5p (Table 26). The miR531-5p interacted with mRNA of Traes_4AS_D20DF472E.1 and Traes_4DL_6EBD74330.2 genes with value of ΔG/ΔGm equal 88%. The miR319-3p had three binding sites in the mRNA of C2H2 TF with the value of ΔG/Δm equal 91%. The miR10520-5p bound to mRNA of Traes_1BL_4026DC5011.2 gene [398, p. 6]. For ath-miR5021-5p, ath-miR5658-5p, osa-miR2102-5p, osa-miR5075-3p, which have several target genes in the C2H2, ERF, GRAS families, it was found that the nucleotide sequences of the binding sites were conserved and encoded conservative oligopeptides (Figure 11) [397, p. 1-10].

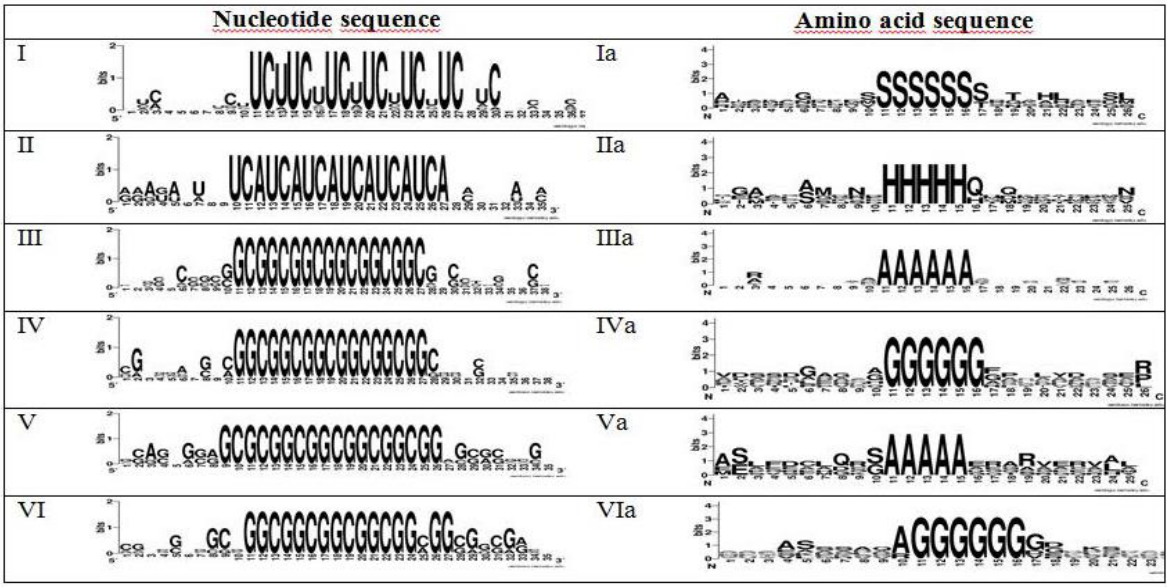


Figure 11 - Nucleotide sequences of ath-miR5021-5p, ath-miR5658-5p, osa-miR2102-5p, osa-miR5075-3p binding sites and their encoded amino acid sequences in GRAS, ERF, C2H2 TF [397, p. 7]

Note - I - nucleotide sequences of ath-miR5021-5p binding sites and Ia - the amino acid sequences encoded by them in proteins; II - nucleotide sequences of ath-miR5658-5p binding sites and IIa - the amino acid sequences encoded by them in proteins; III - nucleotide sequences of osa-miR2102-5p binding sites and IIIa - the amino acid sequences encoded by them in the first open reading frame; IV - nucleotide sequences of osa-miR2102-5p binding sites and IVa - the amino acid sequences encoded by them in the other open reading frame; V - nucleotide sequences of osa-miR5075- binding sites and Va - the amino acid sequences encoded by them in

the first open reading frame; VI - nucleotide sequences of osa-miR5075-3p binding sites and VIa - the amino acid sequences encoded by them in the other open reading frame.

These diagrams are based on table C1-C4 data (Appendix C). Diagram I shows that the nucleotide sequences of the ath-miR5021-5p binding sites are conserved in the first and second positions of the serine codons. In the third position of the codons for serine, different nucleotides are used in different genes, which reduces the free energy of the interaction of miRNA with mRNA, but does not change the encoded SSSSSS oligopeptide [397, p. 8].

Figure 11 shows the nucleotide sequences of the osa-miR2102-5p III and IV binding sites encoding different oligopeptides (IIIa and IVa) in different reading frames. The nucleotide sequences of the osa-miR5075-3p binding sites (V and VI) encoded different oligopeptides (Va and VIa) in different reading frames. It is important for miRNAs to have a binding site without taking into account the oligopeptide that it can encode [397, p. 8].

The results of *in silico* studies of the influence of plant miRNAs on the expression of GRAS, ERF, C2H2 transcription factors family genes of *A. thaliana*, *O. sativa*, and *Z. mays* showed that the studied miRNAs could influence plant growth and development [243, p. 799]. The main problem of determining which miRNAs and how they can influence the key processes will be identifying the target genes of these miRNAs. Due to the MirTarget program, in the present work, it was possible with a high probability to identify target genes for the well-known miRNAs of *A. thaliana*, *O. sativa*, and *Z. mays*. It is important that the established quantitative characteristics of the interaction of miRNA with mRNA make it possible to predict, in a comparative aspect, the effect of different miRNAs on one or several target genes. To carry out successful genetic engineering manipulations on plants, it is necessary to predict side effects [397, p. 9].

Using the MirTarget software to assess the interactions of miRNAs and target genes allows the selection of miRNA and gene associations that can be used to obtain genetically modified organisms. Since many miRNAs are universal regulators of the expression of genes and genomes of many plant species, knowledge of the properties of such miRNAs makes it possible to successfully carry out genetic engineering manipulations with them even in phylogenetically distant plant species [397, p. 9].

Figure 12 shows the participation of some miRNAs in the regulation of the expression of TF genes of various families. Some miRNAs had binding sites in several TF families, while others had binding sites in only one TF family. The miR319-3p, miR159-3p, and miR171-3p had binding sites in mRNA of *A. thaliana, O. sativa, Z. mays,* and *T. aestivum* genes of the TCP, MYB, and GRAS families, respectively. The miR408-3p had binding sites in the mRNA of *O. sativa*, *Z. mays*, and *T. aestivum* genes of three TF families, such as GRAS, ERF, and C2H2. The zma-miR164-3p, zma-miR166-5p, zma-miR169-3p, zma-miR408-3p, osa-miR2102-5p, osa-miR2919, osa-miR5075-3p, ath-5021-5p, ath-5658-5p had binding sites in all studied TF families.

Since the plants studied by us are the most widespread agricultural crops and are used in human nutrition, it is relevant to study the effect of miRNAs of these plants on the regulation of human genes expression, including TF.

Families / miRNAs	TCP				MYB				HSF				GRAS				ERF				C2H2			
	A. thaliana	*O. sativa*	*Z. mays*	*T. aestivum*	*A. thaliana*	*O. sativa*	*Z. mays*	*T. aestivum*	*A. thaliana*	*O. sativa*	*Z. mays*	*T. aestivum*	*A. thaliana*	*O. sativa*	*Z. mays*	*T. aestivum*	*A. thaliana*	*O. sativa*	*Z. mays*	*T. aestivum*	*A. thaliana*	*O. sativa*	*Z. mays*	*T. aestivum*
miR156-3p						+	+		+		+			+	+			+	+					
miR156-5p						+					+			+		+	+	+	+			+	+	
miR159-3p	+	+			+	+	+	+										+					+	
miR159-5p			+												+				+				+	
miR160-3p						+	+							+	+			+	+					
miR160-5p		+												+	+			+	+					
miR164-3p			+				+				+		+		+		+		+				+	
miR164-5p			+			+	+	+		+				+				+	+			+	+	+
miR166-5p		+	+			+	+								+			+	+			+	+	
miR167-3p		+	+				+				+				+				+			+	+	
miR167-5p						+								+		+		+	+		+		+	
miR168-5p			+			+																+	+	
miR169-3p			+				+				+				+		+	+	+				+	
miR169-5p		+				+	+			+	+		+	+	+				+			+		
miR171-3p		+					+	+					+	+	+	+			+			+	+	
miR171-5p			+			+	+											+	+				+	
miR172-3p					+	+			+						+			+	+			+	+	
miR172-5p	+					+					+				+				+			+	+	
miR2102-5p		+				+				+				+				+				+		
miR2919		+				+				+				+				+				+		
miR319-3p	+	+	+	+	+		+	+						+	+									+
miR319-5p			+				+							+					+					
miR395-3p														+					+					
miR395-5p							+								+									
miR396-5p						+	+							+	+		+						+	
miR408-3p			+				+							+	+	+		+	+	+		+	+	+
miR414-5p	+				+	+				+			+	+			+	+			+	+		
miR444-3p				+		+		+			+			+		+		+		+		+		
miR5021-5p	+				+				+				+				+				+			
miR5075-3p		+				+				+				+				+				+		
miR5658-5p	+				+				+				+				+				+			
miR854a-e-5p	+				+								+				+				+			

Figure 12 - Involvement of some miRNAs in the regulation of expression of TF genes of various families [the material obtained in this study by Rakhmetullina A.K]

3.8 Characteristics of the potentially binding sites for maize, wheat, and rice miRNAs in the mRNA of human genes

3.8.1 Characteristics of the interaction of zma-miRNAs with mRNA of human genes

The study of 325 zma-miRNAs interaction to mRNAs of 17508 human genes revealed only 38 target genes for nine zma-miRNAs with the selection criteria ΔG/ΔGm equals 88% and over. The data obtained are shown in Table 27. It was revealed that miR162-5p, miR529-5p, miR827-3p, miR11969-3p have one target gene. The identified target genes for zma-miR529-3p perform various functions in cells, and many of them play a key role in the regulation of many vital processes in the human body (Appendix D, Table D13): distal renal tubular acidosis, epileptic encephalopathy, vulvar squamous cell carcinoma, Hearing loss,

inflammation and platelet-activating factor-induced anaphylaxis, leukemia, schizophrenia, obesity, campomelic dysplasia [401, p. 342-343].

The ΔG/ΔGm value for the zma-miR482-5p binding sites varied from 94% to 96%, which indicates a high complementarity of the interactions of these miRNAs with the human mRNA genes (Table 27). The functions of the identified target genes may be involved in the development of various diseases: Silver-Russell syndrome; Beckwith-Wiedemann syndrome; chronic myeloid leukemia; idiopathic hypogonadotropic hypogonadism; diabetes vellitus, lung cancer, nonsyndromic deafness (Appendix D, Table D13). The zma-miR482-3p target genes are involved in the development of gastric and colon cancer, malignant neoplasm of breast, malignant neoplasm of lung, neurodevelopmental disorder, membranous nephropathy, a congenital disorder of glycosylation, non-small cell lung cancer, spermiogenesis, primary ciliary dyskinesia [401, p. 342-343].

Such a variety of association of zma-miR529-3p, zma-miR482-5p, and zma-miR482-3p with several human target genes may indicate a positive preventive effect of plant miRNAs on the change in the expression level of human genes associated with various diseases (Appendix D, Table D13). In particular, the elucidation of the therapeutic effect of some miRNAs of medicinal plants began to be actively studied. Among the target genes for single zma-miRNAs, 37% participated in oncogenesis, 13% in neurodegenerative diseases, and not a single gene in cardiovascular diseases [401, p. 342-343].

A feature of plant miRNAs is the effect of both strands of pre-miRNAs on human genes. Table 27 shows zma-miR162-5p and zma-miR162-3p, zma-miR482-5p and zma-miR482-3p, zma-miR529-5p and zma-miR529-3p, zma-miR11969-5p and zma-miR11969-3p, can effectively bind to the mRNA of several human target genes [401, p. 342-343].

Table 27 - Characteristics of interaction single zma-miRNAs with mRNA of human genes [401, p. 342-343]

miRNA	Gene	Δ*G*, kJ/mole	Δ*G*/Δ*G*m, %	Length, nt
miR162-5p	*ZNF853*	-104	91	21
miR162-3p	*DNAH3, PLXNA3, RIMS3*	-96÷-98	92÷94	20
miR482-5p	*CDKN1C, FAM168A, FGF17, KCNK16, ROBO4, SLC44A4*	-96÷-98	94÷96	19
miR482-3p	*ATP2A3, CSF1, LARP1, LMBRD2, PTER, SLC35A2, STK32A, TMCO5A, TTC25*	-96÷-98	92÷94	20
miR529-5p	*PPIE*	-102	92	21
miR529-3p	*ATP6V0A4, CHD2, LMO7, LRTOMT, LTB4R, MLL, NUDC, PDE4B, POMC, SOX9*	-102÷-106	91÷94	21
miR827-3p	*AKAP11*	-100	94	21
miR11969-5p	*ADIPOR1, ARAP3, EXOC4, PNPO, POP1, THAP9*	-108	88	24
miR11969-3p	*ZDHHC3*	-108	88	24

Many plant miRNAs differ by one or two nucleotides at the 5-ends or 3-ends, which is the basis for combining them into families. With the most common miRNA length in plants equal to 21-22 nt, the members of the family are 90% similar. Table 28 presents the quantitative characteristics of the interaction of members of the zma-miRNAs families with mRNA of human genes. The data obtained indicate that the families of some zma-miRNAs have from one (zma-miR156j-5p, zma-miR156i-3p, zma-miR160a-e,g-5p, zma-miR164f-5p, zma-miR166b-i-3p, zma-miR168a-3p, zma-miR171g-3p, zma-miR390a,b-3p, zma-miR393a,c-5p, zma-miR396g-3p, zma-miR397a,b-5p, zma-miR397b-3p) up to 16 (zma-miR408a,b-3p) and 18 (zma-miR408b-5p) target genes. Most of the target genes zma-miRNAs are involved in the development of genes for oncological diseases (43%), neurodegenerative diseases (8%), and cardiovascular diseases (2%) (Appendix D, Table D15) [401, p. 342-343].

Table 28 - Characteristics of interaction zma-miRNAs families with mRNA of human genes [401, p. 342-343]

miRNA	Gene	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
1	2	3	4	5
miR156j-5p	*AP2A2*	-104	94	21
miR156i-3p	*SGSM1*	-110	95	22
miR159e-5p	*BZRAP1, FEN1, LZTS1, PDE6B, PRCD*	-104÷-106	91÷93	21
miR159h,i-3p	*ATF6B, DEAF1, DGCR8, DOK6, GPSM3, TMEM229B, TTN, URM1*	-102÷-104	91÷92	21
miR160a-e,g-5p	*DAB2*	-108	93	21
miR164f-5p	*ASXL1*	-110	95	21
miR160f-3p	*ALKBH5, BCL9L*	-110	91	21
miR164b-3p	*DYSF, EXOC7, HPD, ITGA7, PTPRF, ZNF37A*	-100÷-102	92÷94	20
miR166b-i-3p	*CHRM1*	-102	92	20
miR166m-5p	*CCNY, HGS, INSM1, SGIP1, TNFSF13, TSNARE1*	-106÷-110	91÷95	21
miR167e-j-5p	*HSF1, FAM43B, PRICKLE2*	-102÷-106	91÷94	21
miR167j-3p	*FAM57A, FMNL2, GPR107*	-93÷-98	92÷96	20
miR168a-3p	*FLAD1*	-102	92	20
miR169i,j,k-5p	*GRHL3, NCOA6*	-104	92	21
miR169q-3p	*ADRA1D, CA6, CYP1A1, DUOX1, EPHB6, MAP3K12, MARCH10, OXSR1, PIK3C2B, TRMT2A, TUBA3C, WNT16*	-100÷-104	94÷98	19
miR171d,e-5p	*NFATC2, SIRT7*	-104÷-106	91÷93	21
miR171g-3p	*BRD3*	-104	91	21
miR172a-d-3p	*GPR31, LEF1, TECTA, TUFM*	-93÷-96	92÷94	20
miR172c-5p	*GON4L, LASP1, SLC30A8, YY1AP1*	-98÷-100	92÷94	20

Continue of Table 28

1	2	3	4	5
miR2118g-3p	*DYRK1A, XPO6*	-104÷-106	91÷93	22
miR2275a-3p	*GPR22, SACS*	-100÷-102	92÷94	22
miR2275d-5p	*AHCYL2, CER1, FAM205A, SPRR1B*	-98÷-100	92÷94	21
miR319a,c-5p	*PLCD4, RNF157*	-100÷-104	92÷96	20
miR319a-d-3p	*DMAP1, IL4I1*	-102	92	20
miR390a,b-5p	*ASPSCR1, HFE*	-106÷-108	91÷93	21
miR390a,b-3p	*PDAP1*	-102	91	21
miR393a,c-5p	*TMEM136*	-106	93	22
miR393c-3p	*LRP1B, TP53I3*	-106	93	22
miR394a,b-5p	*BIN2, GRIK4, HAVCR2, HNF1B, IGSF3, MICAL3, PGAP1, REXO4, RXFP1*	-100÷-102	92÷94	20
miR394a,b-3p 61	*ALDH4A1, CIB3, PURG*	-100	92	20
miR395a-j,n,p-3p	*CD22, EDN1, TEAD2*	-102÷-108	91÷96	21
miR395k-5p	*CCDC117, MYOM1*	-104÷-106	92÷94	22
miR396a,b-5p	*SCAMP5, SYVN1, VPS13B*	-100÷-102	92÷94	21
miR396g-3p	*EVC2*	-100	92	21
miR397a,b-5p	*PKP3*	-102	91	21
miR397b-3p	*C6orf223*	-106	93	21
miR398a,b-3p	*EPS8, NUAK1, PCDHGA12*	-108	91	21
miR398b-5p	*BAHCC1, NUP62*	-108	91	21
miR399d-3p	*APBB1, CDK18, DDX11, JAGN1, OSTM1*	-106÷-108	91÷93	21
miR399j-5p	*AMMECR1L, CHTF18, EDN3, IKZF3, LARP4B, LDLRAD2, LGI4, SIAH3, SPSB3, SOX18, SPOCK2, TRAK1 157*	-108÷-115	91÷96	21
miR408a,b-3p	*ADARB2, ADCY6, ALPK3, ANO4, EDEM1, ERICH1, FNIP2, KIRREL3, NGB, PAQR6, RBMS2, RLBP1, SMARCC2, TJP3, UBE2K, UNG*	-108÷-113	91÷95	21
miR408b-5p	*ADCY1, ARHGAP30, CPNE6, DYRK1B, GCGR, GPR124, IL6R, MAFK, MAP3K6, NELL2, PLXNA4, PPM1F, PXN, RAB37, TMEM91, TNIP1, WDR46, ZNF132*	-108÷-110	91÷93	21
miR444a,b-3p	*CEP250, CSRNP1, MPDZ*	-100÷-102	92÷94	21
miR528a,b-5p	*CACNB1, CD276, DNAJB6, GSK3B, GTF3C1, PPP1R26, PROB1*	-106÷-108	91÷93	21
miR528a,b-3p	*EXOC7, FREM2, LSM4, MC1R, MGAT3, NFE2L1, RANBP1, RNF14, SPAG5, UIMC1*	-104÷-110	91÷96	21

The most effective characteristic of the interaction of miRNAs with mRNA of target genes is the interaction scheme of the nucleotides of these molecules. Figure 13 shows schematic diagrams of the interaction of several zma-miRNAs with the mRNA of three human target genes.

It can be seen from the diagram that the non-canonical A-C and G-U pairs contribute to an increase in the free energy of interaction between miRNAs and mRNAs. In addition, they maintain stacking interactions between nucleotides in each of the strands of the RNA helix [378, p. 130; 379, p. 210].

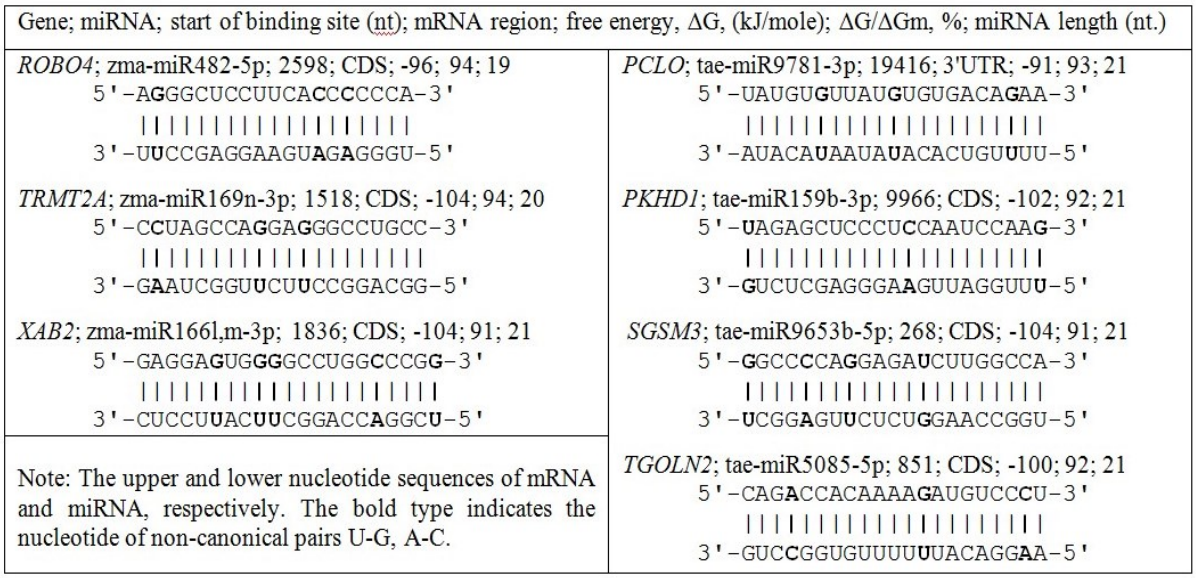


Figure 13 - Schemes of the interaction of nucleotide sequences of zma-miRNA and tae-miRNA with mRNA of human genes [401, p. 342-343]

Table D1 (Appendix D) shows the binding characteristics of zma-miR529-3p to human mRNA genes, which indicate the location of miRNA binding sites in the 5'UTR, CDS, and 3'UTR. It is important for miRNA to have a binding site in any of these regions of the mRNA.

The nucleotide sequences of the zma-miR529-3p binding sites are homologous only in the 5-end and 3-end (Appendix D, Table D2), which play an important role in miRNA binding. The nucleotide sequences of the zma-miR529-3p binding sites are homologous only in the 5-end and 3-end (Appendix D, Table D2), which play an important role in miRNA binding.

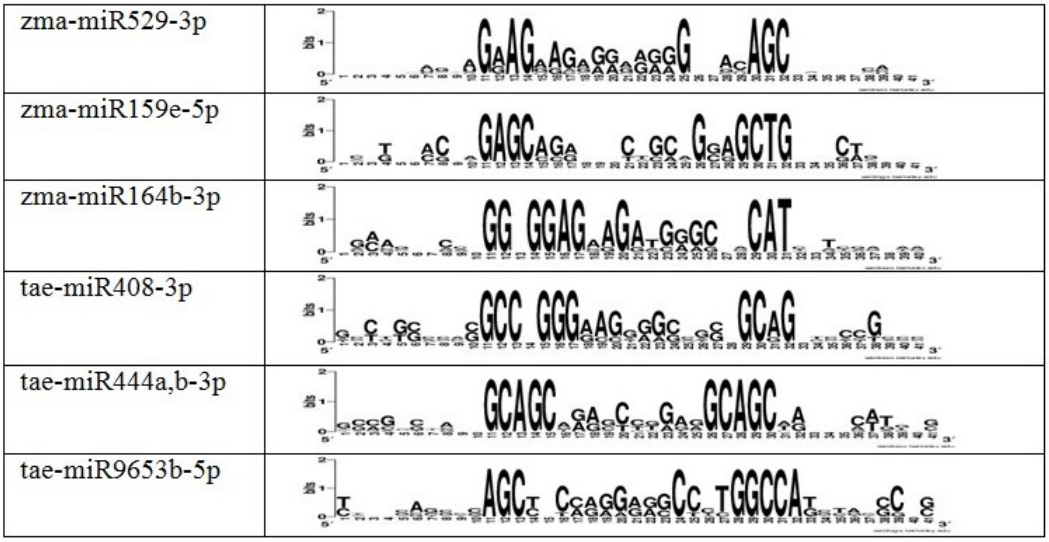


Figure 14 - Schemes of the interaction of nucleotide sequences of zma-miRNA and tae-miRNA with mRNA of human genes [401, p. 342-343]

The WebLogo schemes of the nucleotide sequence variability of mRNA regions of human genes containing the binding sites of zma-miRNA and tae-miRNA showing conserved binding sites at the 5-end and 3-end. This indicates the importance of the 5-end and 3-end in the binding of miRNAs to mRNAs which have an increased GC content, which provides fixation of miRNAs with the highest free interaction energy (Figure 14). Therefore, the determination of the binding site based on only a few nucleotides from the 5-end of the “seed” is inadequate. The entire nucleotide sequence of miRNAs and the binding site is important, which determines the conservation of the entire nucleotide sequence of miRNAs and binding sites for many millions of years in animals and plants. Similar results were obtained when studying the interaction of zma-miR159e-5p (Appendix D, Table D3 and Table D4.) and zma-miR164b-3p (Appendix D, Table D5 and Table D6) with mRNA of human genes [401, p. 342-343].

3.8.2 Characteristics of the interaction of tae-miRNAs with mRNA of human genes

Among the miRNAs presented in Table 29, miR156-5p, miR160-5p, miR164-5p, miR169-3p, miR319-3p, miR396-5p, miR397-3p, miR398-3p, miR399-3p, miR408-3p, miR531-5p are found in many plants and are conservative [168, p. 1706; 229, p. 4; 402-408]. Identified wheat miRNAs (tae-miR5048, tae-miR5384, tae-miR9652-5P, tae-miR9654b, tae-miR9655, tae-miR9656, tae-miR9657b, tae-miR9661, tae-miR9662a, tae-miR9662b, tae-miR9664, tae-miR9666b, tae-miR9667, tae-miR9670, tae-miR9674b, tae-miR9676, tae-miR9677, tae-miR9678, tae-miR9679) also have human target genes. The identified target genes for tae-miRNAs perform various functions in cells, and many of them play a key role in the regulation of many vital processes in the human body and different diseases (Appendix D, Table D14) [401, p. 342-343].

Table 29 - Characteristics of the interaction of single tae-miRNAs with human mRNA genes [401, p. 342-343]

miRNA	Gene	Δ*G*, kJ/mole	Δ*G*/Δ*G*m, %	Length, nt
1	2	3	4	5
miR156-5p	*AP2A2, ZNF652*	-102÷-104	92÷94	21
miR160-5p	*C11orf16, DAB2*	-106÷-108	91÷93	21
miR164-5p	*ASXL1, RASL10B, UGT1A7, UGT1A9*	-106÷-108	91÷93	21
miR169-3p	*AARS2, GTPBP3, LYNX1*	-113÷-119	90÷95	22
miR319-3p	*C15orf55, IL4I1, PTPMT1*	-104	91	21
miR396-5p	*AIM1*	-104	91	21
miR397-3p	*ING1*	-108	93	21
miR398-3p	*EPS8, NUAK1, PCDHGA12*	-108	91	21
miR399-3p	*HSPG2, JAGN1, U2AF2*	-96÷-98	94÷96	19
miR408-3p	*ALPK3, RBMS2, EDEM1, NGB, PAQR6, UNG*	-108÷-113	91÷95	21
miR531-5p	*SLC5A10*	-113	91	21
miR1118-5p	*DCLK1, HECTD3, MDP1, OR51E2*	-106÷-110	89÷93	23
miR1119-3p	*HPDL, KCNA1, SLC27A3*	-119÷-121	89÷90	24
miR1124-3p	*AGRP, ARVCF, CPN1, FNTA, SPRN, URB1*	-110	90	22
miR1129-5p	*CDAN1, ENTPD2, LMO3, SLC47A1, RAX, RERE, WDR45*	-123÷-129	88÷92	24
miR1134-3p	*CCND2, NIPAL4, NOTCH2, TCF7L2, TMEM178B*	-104÷-108	88÷91	24
miR1138-3p	*C21orf2, MFI2, MOG*	-102÷-104	89÷91	23
miR1139-5p	*CDON*	-98	90	22
miR1847-5p	*ATRIP, HSD3B1*	-104	91	21
miR5048-5p	*FLCN*	-100	90	22
miR5050-5p	*MIER1*	-102	91	21
miR5084-3p	*RYR2*	-110	90	24
miR5085-5p	*TGOLN2, ZFHX3*	-100	92	21
miR5086-5p	*DHX30, HBP1, LTBP4, MYO1G, SERPING1, SPTAN1*	-102÷-104	91÷92	21
miR5200-3p	*LYST, TGFBR3*	-100÷-102	92÷94	21
miR5384-3p	*MAF, PAX1*	-110÷-113	91÷93	21
miR9652-5p	*LZTFL1, PTCHD1, STX6*	-98÷-100	90÷92	22
miR9655-3p	*CIB2, GIPR, GPR123, GPR55, TACR1, ZNF488*	-102	91	21
miR9656-3p	*C9orf50*	-106	93	21
miR9661-5p	*DNAH14, GSE1, NUP50, SHANK1*	-102÷-104	91÷92	21
miR9664-3p	*ORAOV1, SIK2*	-102	91	21
miR9667-5p	*REEP3*	-96	94	21
miR9670-3p	*TPM3, USP14*	-98÷-100	92÷94	21
miR9772-5p	*C7*	-100	92	21
miR9773-3p	*CCDC178, CFLAR, INO80D, LRRC34, RHBDD1*	-98÷-100	88÷90	24
miR9774-3p	*NPFF*	-100	90	22
miR9776-5p	*SPRY4, TRAK2*	-102÷-106	91÷94	21

Continue of Table 29

1	2	3	4	5
miR9777-3p	*PDK2*	-93	92	20
miR9778-5p	*SORL1*	-102	91	21
miR9779-3p	*ASRGL1*	-100	96	20
miR9780-3p	*HES4, MEX3C, UBE2K*	-117÷-119	92÷93	21
miR9781-3p	*LRP8, SLC38A2, PCLO, RNASE3*	-89÷-91	91÷93	21
miR9782-3p	*PLEKHG3*	-106	88	24
miR10520-5p	*TCFL5, TSPYL6*	-96÷-98	92÷94	20

The tae-miRNAs families consist of only 2-3 miRNAs that have one to nine target genes (Table 30). The ΔG/ΔGm value varies from 91% to 98%, which indicates a high degree of complementarity between miRNA and mRNA nucleotides. The free energy of interaction between miRNA and mRNA, with a few exceptions, is higher than -100 kJ/mole. Analysis of the function of target genes shows a high proportion (45%) of genes involved in oncogenesis. Candidate genes for neurodegenerative diseases and cardiovascular diseases account for only 18% and 2%, respectively (Appendix D, Table D16). Note that single tae-miRNAs have, as target genes, the proportion of target genes involved in oncogenesis, neurodegenerative and cardiovascular diseases equal to 46%, 13%, and 6%, respectively (Appendix D, Table D14). These proportions are close to those found on the samples of target genes for all zma-miRNAs [401, p. 342-343].

Table 30 - Characteristics of the interaction of tae-miRNAs families with mRNA of human genes [401, p. 342-343]

miRNA	Gene	Δ*G*, kJ/mole	Δ*G*/Δ*G*m, %	Length, nt
1	2	3	4	5
miR159a,b-3p	*KCNJ15, PKHD1*	-102	92	21
miR167a-c-5p	*ARHGEF10, EME1, HSF1, PRICKLE2*	-102÷-108	91÷96	21
miR171b-3p	*LTB4R2*	-102	91	21
miR395a-3p	*CD22, EDN1, TEAD2*	-102÷-108	91÷96	21
miR444a,b-3p	*AP1B1, COL6A3, DOCK1, HIC1, KRT6A, KRT6B, KRT6C, RHBDF1, RUNDC1*	-104÷-108	91÷94	21
miR1120b-3p	*SEMA3A, FAM177A1*	-98	92	21
miR1120c-5p	*EPHA4*	-91	91	21
miR1122c-3p	*KCNAB3*	-100	92	21
miR1127b-3p	*SEMA6A*	-102	92	21
miR1137a-3p	*INO80D*	-96	96	20
miR9653a-3p	*ARHGEF6, CLCN7, ENDOD1, H1FOO, KDM6B, KIF7, PHLDB2*	-102÷-106	91÷94	21
miR9653b-5p	*AOC3, ITIH4, RBM19, TEAD2, TEAD3, TMEM184A*	-104÷-113	91÷98	21
miR9654b-3p	*NEBL*	-104	91	22

Continue of Table 30

1	2	3	4	5
miR9657b-5p	*RNF168*	-104	92	21
miR9662a,b-3p	*DNMT3B, FAM124A, GLI2, HMX3*	-104÷-110	91	21
miR9666b-3p	*HMX3*	-110	91	22
miR9674b-5p	*ROBO3*	-102	92	21
miR9677a-3p	*AKT1, RBFOX3, STAC*	-108	91	22
miR9677b-5p	*ABCA3, CASKIN1, ENC1, GALR1, LRRFIP1, NLGN2, SNX8, SQSTM1*	-113÷-117	91÷95	21

Binding characteristics of tae-miR408-3p interaction with human mRNA six genes are shown in Table D7 (Appendix D), which indicates their effective interaction. Nucleotide sequences of mRNA regions of human genes containing tae-miR408-3p binding sites show (Appendix D, Table D8) conserved nucleotides at the 5-end and 3-end (Figure 14). Similar results were obtained with tae-miR444a,b-3p, which can interact in CDS mRNA of nine genes (Appendix D, Table D9). Based on the nucleotide sequences of the tae-miR444a,b-3p binding sites (Appendix D, Table D10), the constructed Weblogo scheme shows the high conservatism of the GCAGC pentanucleotide, which is identical at the 5-end and 3-end of the binding sites (Figure 14). Four G-C pairs with three hydrogen bonds each provide high free energy of interaction of tae-miR444a, b-3p with mRNA of nine human genes. The characteristics of the interaction of tae-miR9653b-5p with mRNA of seven genes also indicate high efficiency of their interaction (Appendix D, Table D11) and the conservatism of flanking nucleotides (Appendix D, Table D12 and Figure 14) [401, p. 342-343].

Studies have shown that many miRNAs of wheat can bind to mRNA of human genes. These miRNAs are involved in the regulation of gene expression not only in corn and wheat but also in many other plants. Connections between plant miRNAs and genes of animals, including mammals and humans, could have arisen at the early stages of the evolution of higher plants and mammals. Therefore, miRNAs are present in the cells of many plant tissues and organs in relatively large quantities, which makes it possible to determine their functional significance. Since many mammals used plants for food, stable links arose between plant miRNAs and human genes over many millions of years of evolution. Many miRNAs are involved in the regulation of growth, development, and plant resistance to abiotic and biotic factors; therefore, together with food, they enter the human body. For example, mammals consume plants, and their miRNAs enter the digestive system as part of exosomes, which are transported with blood throughout the body and into milk during lactation. Many plant miRNAs enter the human body together with juices, vegetables, and fruits.

The results obtained in this work help to elucidate the possible role of plant miRNAs in the regulation of human gene expression. The influence of plant miRNAs on the expression of the human genome can be both positive and negative. For example, some miRNAs can suppress the expression of oncogenes and inhibit oncogenesis, while other miRNAs, by suppressing oncosuppressors,

will promote tumor development. The regulatory role of miRNAs in the expression of candidate genes for other diseases should also be used to treat these diseases. Consequently, much work remains to be done to elucidate the effect of plant miRNAs on the function of various human genes with a view to using them in medicine [401, p. 342-343].

3.8.3 Characteristics of the interaction of osa-miRNAs with mRNA of human genes

Currently, 738 miRNAs encoded by the rice genome are known. For these osa-miRNAs, target genes from among 17 508 human genes were searched. A total of 82 miRNAs with one to four target genes were identified (Appendix D, Table D17). The miR11339-3p and miR11339-5p; miR1425-3p and miR1425-5p; miR1432-3p and miR1432-5p; miR1870-3p and miR1870-5p; miR2096-3p and miR2096-5p; miR2867-3p and miR2867-5p; and miR390-3p and miR390-5p, originating from the same pre-miRNA, had binding sites in the mRNAs of different genes. The functions of the 162 identified target genes were diverse.

In the group of 49 miRNAs with five or more target genes, there were several miR-3p/miR-5p pairs that originated from the same pre-miRNA (Appendix D, Table D18). The total number of target genes for miRNAs with five or more genes was 479. The number of target genes for miR408-3p, miR5150-3p, miR528-3p, and miR530-3p was comparable to the number of target genes for miR408-5p, miR5150-5p, miR528-5p, and miR530-5p. For miR1847.1-5p, miR1850.1-5p, miR2094-5p, miR2097-5p, miR2102-5p, and miR3979-5p, the set of target genes was significantly larger than that for each corresponding miRNA-3p. Only miR5144-3p had four-fold more target genes compared to the number attributed to miR5144-5p. The miRNAs with the largest number of target genes were miR2102-5p (38 genes), miR5075-3p (36 genes), miR2097-5p (23 genes), and miR2919 (19 genes). Consequently, at high concentrations, these miRNAs could significantly change the metabolism of human recipient cells [367, p. 2].

A total of 641 target genes were identified for 131 single miRNAs, which is approximately 3.7% of the total number of studied human genes.

Table 31 shows the characteristics of the binding of some osa-miRNAs with mRNAs of human genes. Each of the 35 miRNAs could bind to mRNAs of one target gene, six miRNAs had targets with two genes, and four miRNAs had three target genes with a value ΔG/ΔGm equal to 94-98%. The miR2102-5p had 11 target genes with a value ΔG/ΔGm of 94-100%, and the free energy of the interaction of the miRNAs with the mRNAs of these genes varied from -115 kJ/mole to -121 kJ/mole [367, p. 2, 409]. The miR2102-5p binding sites were located mainly in the 5'UTR, which suggests that they have a role in the early inhibition of the translation process. However, this property of miR2102-5p indicates the need to control its plant food-derived concentration in the human body. 19 target genes were associated with miR2919. The miR5075-3p could bind to three mRNAs at binding sites located in the coding domain sequence and the 5'-untranslated region. The high-affinity binding sites were located in the 5'UTR and CDS of the mRNAs with the ΔG/ΔGm value was 94-98%. 17 miRNA binding

sites were located in 5'UTR, 39 in CDS, and 33 in the 3'-untranslated region. Therefore, monitoring the concentrations of miR2102-5p, miR2919, and miR5075-3p in human biological fluids is also necessary [367, p. 3; 410].

Table 31 - Characteristics of interaction single osa-miRNAs with mRNA of human genes [367, p. 3]

Gene	osa-miRNA	Start of site, nt	Region of miRNA	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
1	2	3	4	5	6	7
CPA3	miR1320-3p	671	CDS	-98	96	21
PPAP2B	miR1320-3p	2135	3'UTR	-96	94	21
CNPY1	miR1426-5p	2094	3'UTR	-93	94	21
NSL1	miR1440-5p	4601	3'UTR	-98	94	20
PSEN2	miR1847.1-5p	1785	3'UTR	-108	96	21
MDN1	miR1855-3p	13027	CDS	-106	94	21
KLHDC10	miR1860-3p	3134	3'UTR	-108	96	22
TIE1	miR1860-3p	3139	CDS	-106	94	22
OSTM1	miR2093-3p	848	CDS	-93	96	20
ZNF80	miR2099-3p	2562	3'UTR	-96	94	20
SLC36A3	miR2099-5p	2769	3'UTR	-100	94	22
AFAP1	miR2102-5p	144	5'UTR	-115	95	20
C19orf6	miR2102-5p	193	CDS	-115	95	20
CHSY1	miR2102-5p	348	5'UTR	-117	96	20
DIRC2	miR2102-5p	233	CDS	-117	96	20
KATNAL1	miR2102-5p	80	5'UTR	-117	96	20
NR1D2	miR2102-5p	254	5'UTR	-117	96	20
PDAP1	miR2102-5p	29	5'UTR	-115	95	20
PPP2R5C	miR2102-5p	72	5'UTR	-115	95	20
RHOBTB2	miR2102-5p	158	5'UTR	-115	95	20
UHRF1BP1	miR2102-5p	112	5'UTR	-115	95	20
WT1	miR2102-5p	450	CDS	-121	100	20
ZNF442	miR2866-5p	1020	CDS	-98	96	20
PCDHB15	miR2866-5p	582	CDS	-96	94	20
GPR20	miR2867-3p	455	CDS	-106	94	20
TMEM38A	miR2867-3p	236	CDS	-106	94	20
ATP13A3	miR2867-5p	3035	CDS	-115	95	22
HK2	miR2868-5p	6645	3'UTR	-93	96	20
ZNF395	miR2870-3p	863	CDS	-100	94	21
IQGAP1	miR2876-5p	1234	CDS	-102	94	21
ADAMTS5	miR2919	471	5'UTR	-104	96	19
AKAP11	miR2919	7158	3'UTR	-102	94	19
ATG13	miR2919	259	5'UTR	-102	94	19
BDNF	miR2919	2681	3'UTR	-106	98	19
C1D	miR2919	543	3'UTR	-102	94	19
CDC25B	miR2919	661	5'UTR	-102	94	19
FAM59B	miR2919	257	5'UTR	-102	94	19
FAM83H	miR2919	4348	3'UTR	-102	94	19
GPBP1L1	miR2919	1015	5'UTR	-104	96	19

Continue of Table 31

1	2	3	4	5	6	7
KIAA1161	miR2919	3436	3'UTR	-106	98	19
MINK1	miR2919	4936	3'UTR	-102	94	19
NEUROD2	miR2919	145	5'UTR	-102	94	19
OTUD4	miR2919	4235	3'UTR	-102	94	19
PRDM11	miR2919	8528	3'UTR	-102	94	19
PTGFRN	miR2919	5633	3'UTR	-102	94	19
RGS9BP	miR2919	2857	3'UTR	-102	94	19
SPRY4	miR2919	1576	3'UTR	-102	94	19
ZNF304	miR2919	2752	3'UTR	-102	94	19
ZNF385A	miR2919	1388	3'UTR	-102	94	19
KPNA4	miR2923-5p	7223	3'UTR	-93	94	22
SHISA6	miR2925-5p	71	CDS	-106	94	19
SPON1	miR2925-5p	93	5'UTR	-106	94	19
ZNHIT2	miR2925-5p	559	CDS	-106	94	19
UFSP1	miR2931-5p	960	3'UTR	-91	96	20
IGSF3	miR394-5p	2007	CDS	-102	94	20
PGAP1	miR394-5p	9153	3'UTR	-102	94	20
ZNF425	miR3979-5p	512	CDS	-102	94	20
RBMS2	miR408-3p	7343	3'UTR	-113	95	21
PPM1F	miR408-5p	2987	3'UTR	-110	95	21
GPBP1L1	miR413-5p	400	5'UTR	-102	94	21
C14orf142	miR414-5p	281	CDS	-104	94	21
LMNA	miR414-5p	1902	CDS	-104	94	21
TMEM30B	miR414-5p	1700	CDS	-104	94	21
PVR	miR415-5p	5452	3'UTR	-104	94	21
SNAPC1	miR417-3p	1169	CDS	-98	94	21
FAM120A	miR418-3p	1029	CDS	-98	94	21
ZNF256	miR5071-5p	348	CDS	-102	94	21
NR2F2	miR5075-3p	350	5'UTR	-117	95	21
PARP2	miR5075-3p	32	CDS	-117	95	21
RPS6KA5	miR5075-3p	261	CDS	-121	98	21
NANOG	miR5077-5p	773	CDS	-100	94	19
PPARGC1A	miR5144-5p	1450	CDS	-104	94	21
FREM2	miR528-3p	1921	CDS	-106	94	21
FXYD6	miR530-5p	788	CDS	-100	94	20
LAMC3	miR530-5p	898	CDS	-100	94	20
NDST1	miR530-5p	6055	3'UTR	-100	94	20
SLC35D1	miR5339-5p	795	CDS	-102	96	21
EML1	miR535-3p	2092	CDS	-106	94	21
LRP5	miR5488-5p	4185	CDS	-102	94	21
SLC25A47	miR5510-5p	678	CDS	-108	94	21
PM20D2	miR5514-5p	1280	CDS	-113	95	21
PPARA	miR5515-3p	1497	CDS	-106	94	21
ZSCAN22	miR5526-3p	2638	3'UTR	-102	94	21
SH3BP2	miR5532-3p	8598	3'UTR	-104	94	22
NANOS1	miR5534a-5p	1967	3'UTR	-106	96	21
DUT	miR5543-5p	1619	3'UTR	-93	94	21

Continue of Table 31

1	2	3	4	5	6	7
OTUD4	miR5543-5p	3680	3'UTR	-93	94	21
COX20	miR5833-5p	396	CDS	-117	96	21
AKAP11	miR827-3p	2985	CDS	-100	94	21

Table D17-D19 (Appendix D) shows information about the genes targeted by plant miRNAs that may be involved in the development of various diseases. Most target genes are involved in the development of cancer of various types: *ENAH, MAPT, PRKCE, PRRT2, RBMS2, RHOBTB2, RPS6KA5*, and *ZFHX3* - breast cancer; *ADAMTS5, PRAPRGG1A, PVR, SPRY4* - colorectal cancer; *CHSY1* - colorectal cancer and hepatocellular carcinoma; *PPM1F, FXYD6, DUT, FAM83H* - hepatocellular carcinoma; *HK2* - gallbladder cancer and leukaemia; *C19orf6*– ovarian carcinoma; *AFAP1* - oesophageal adenocarcinoma; *IOGAP1* - pancreatic ductal adenocarcinoma; *PPP2R5C*– lung adenocarcinoma; *PDAP1* - leukemia; *AKAP11, OSTM1, LRP5* - osteoporosis; *WT1* - ovarian cancer and myeloid leukemia; *NR1D2* - various cancers, including glioblastoma; *CDC25B, DIRC2* - renal carcinoma; and *UHRF1BP1* - cell carcinoma of the head and neck. Some genes are associated with other diseases: *NR2F2* - metabolic gene regulation and congenital heart defect; *PRAPA, UFSP1* - with increased cardiovascular disease; and *ATP13A3* - pulmonary tumour arterial hypertension and psychiatric disorder. *BDNF* has an important role in the neurogenesis and neuroplasticity of the brain; *PSEN2* and *LMNA* are associated with Alzheimer's disease; *ZNF442* has a role in psychiatric disorders; and *NANOS1* is associated with retinoblastoma tumors [367, p. 2-3].

The list of oncological diseases caused by the target genes of the osa-miRNAs indicates that miRNAs can participate in the development of cancer not only in the gastrointestinal tract but also in other organs. Therefore, miRNAs that are ingested with food can be transferred to other tissues and organs.

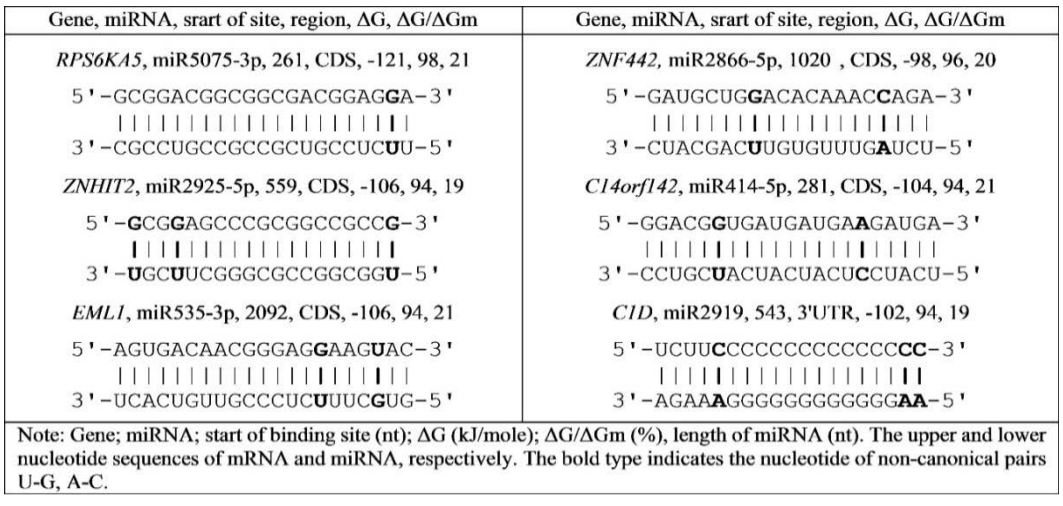


Figure 15 - Schemes of the interaction of the nucleotide sequences of osa-miRNA with mRNA human genes [367, p. 4]

The interaction of miRNAs and mRNA nucleotides of target genes shows how effectively these molecules bind. The schemes presented in Figure 15 show the formation of hydrogen bonds between all the nucleotides of miR5075-3p, miR2866-5p, and miR2919 and the binding sites in mRNA. Because the MirTarget program takes into account the interaction of the noncanonical pairs A–C and G–U, it can be seen that the interaction of miRNAs and mRNAs preserves the spiral structures of both molecules, and therefore, stacking interactions are found between all the nucleotides of the miRNA and mRNA, which stabilize the duplex. The miRNA binding sites are located in the 5'UTR, CDS, and 3'UTR [367, p. 3; 410].

Figure 16 - Logo plots of the nucleotide sequence variability of mRNA regions of human genes containing the binding sites of osa-miRNA [367, p. 5]

One form of evidence for the reliability of miRNA interaction with mRNA is the establishment of a conservative nucleotide sequence of binding sites in the mRNA of target genes. The results of the analysis of the similarity of the nucleotide sequences of the binding sites in mRNA of the target genes miR2102-5p, miR2919, and miR5075-3p are shown in Figure 16. For all miR2102-5p, miR2919, and miR5075-3p binding sites, nucleotide conservation is present compared to the flanking nucleotides of mRNA target genes. With the complete complementarity of the nucleotides miRNA and mRNA (ΔG/ΔGm = 100%) of the target genes, absolute conservatism of the site along the entire binding site should be observed, as previously shown [388-390, 396]. When the ΔG/ΔGm value changes from 94% to 100% (Table 31), the basis for the interaction of the nucleotides miR2102-5p, miR2919, and miR5075-3p and mRNA are G-C pairs. The total number of osa-miRNAs families is 146, and the number of their target genes is equal to 301, which is 1.7% of 17,508 studied human genes. The characteristics of the interaction of 93 osa-miRNAs of all family osa-miRNAs to 86 mRNAs of human genes with values from 94% to 98% were established (Table 32). miRNA of families such as miR156b-3p, miR159a.1,b,f-3p, miR164a-d,f-5p, miR166a,e-5p, miR166b-d,h-5p, miR167a-j-5p, miR172a,d-3p miR172c-3p, miR396d, miR396a,b-3p, miR531b-5p, miR815a,b,c-3p, miR1428b-e-3p and miR1858a,b-5p, has one target gene per family. All members of each miRNA family bind at one site due to the homology of their nucleotide sequences. Therefore, the expression of the target gene for each miRNA family will depend on the total concentration of all miRNA families. The miRNA families miR167e,i-3p, miR168b-5p, miR1846a-c-5p and miR2907a-d-3p had two target genes. The miR2907a-d-3p has target genes *IRAK2* and *SLC25A37* with mRNAs of which these miRNAs interact with large free energy of -123 kJ/mole and -125 kJ/mole, respectively. miR444b.1,c.1-3p had three target genes (*C19orf57*, *KAZN*, *NRG1*) [367, p. 3-4].

Table 32 - Characteristics of interactions of osa-miRNA of families in mRNA of human genes [367, p. 6]

Gene	osa-miRNA	Start of site, nt	Region of miRNA	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
1	2	3	4	5	6	7
ANKRD27	miR1428b-e-3p	244	CDS	-98	96	21
OBFC1	miR156a-j-5p	5427	3'UTR	-100	94	20
ZNF652	miR156a-j-5p	8125	3'UTR	-100	94	20
AP2A2	miR156a-,j,k-5p	3797	3'UTR	-104	94	21
MROH2B	miR156b-3p	4615	CDS	-106	94	21
PKHD1	miR159a.1,b,f-3p	9966	CDS	-108	98	21
ASXL1	miR164a,b,c,d,f-5p	1923	CDS	-110	95	21
CHST11	miR166a,e-5p	986	CDS	-104	94	21
CCNY	miR166b,c,d,h-5p	367	CDS	-110	95	21
PRICKLE2	miR167a-j-5p	1959	CDS	-106	94	21
IL17RB	miR167e,i-3p	137	CDS	-102	94	21

Continue of Table 32

1	2	3	4	5	6	7
KIAA0528	miR167e,i-3p	523	CDS	-102	94	21
APOBR	miR168b-5p	55	CDS	-110	95	21
KLF14	miR168b-5p	623	CDS	-115	98	21
GPR31	miR172a,d-3p	590	CDS	-100	94	21
ATP12A	miR172c-3p	3557	3'UTR	-102	94	21
EIF3B	miR1846a-c-5p	2194	CDS	-119	97	21
FASN	miR1846a-c-5p	11	5'UTR	-117	95	21
C20orf27	miR1858a,b-5p	921	3'UTR	-115	95	21
IRAK2	miR2907a,b,d-3p	1488	CDS	-123	94	22
SLC25A37	miR2907a,b,d-3p	884	CDS	-125	95	22
EDN1	miR395a-q,t,y-3p	1136	3'UTR	-108	96	21
CD22	miR395b,d,e,g,h-t,y-3p	2684	3'UTR	-104	94	21
CMKLR1	miR396a,b-3p	3970	3'UTR	-98	96	20
SCAMP5	miR396a,b-5p	1727	3'UTR	-102	94	21
SYVN1	miR396a,b-5p	854	CDS	-102	94	21
AKAP13	miR396d	1736	CDS	-100	94	20
RHBDF1	miR444a-3p.1, d.1-3p	1071	CDS	-108	94	21
RUNDC1	miR444a-3p.1, d.1-3p	1191	CDS	-108	94	21
CEP250	miR444a-3p.2,b.2-e-3p	1939	CDS	-102	94	21
C19orf57	miR444b.1, c.1-3p	714	CDS	-106	94	21
KAZN	miR444b.1, c.1-3p	4874	3'UTR	-106	94	21
NRG1	miR444b.1,c.1-3p	2444	3'UTR	-106	94	21
ATP6V0A4	miR529a-3p	241	5'UTR	-100	94	20
CCDC94	miR529a-3p	379	CDS	-100	94	20
CHD2	miR529a-3p	6684	3'UTR	-100	94	20
MAP7	miR529a-3p	2137	CDS	-100	94	20
MLL	miR529a-3p	11418	CDS	-100	94	20
PDE4B	miR529a-3p	2270	CDS	-100	94	20
ENAH	miR531b-5p	106	5'UTR	-115	95	20
TIFA	miR815a-c-3p	186	5'UTR	-106	94	21

The miRNAs of the large miR395-3p family had *EDN1* and *CD22* target genes, which are involved in the development of diabetes and in the control of immunity, respectively. If these miRNAs get in food in large quantities, then the probability of their impact on human health is high [367, p. 4].

The miR396a,b-3p can affect the expression of the *CMKLR1* gene, which is involved in cardiovascular disease, and for miR396a,b-5p, the *SCAMP5* and *SYVN1* genes are targeted, the expression of which changes with autism and colon cancer, respectively. The miRNAs of the miR444-3p family have binding sites in the mRNA of six genes (Appendix 4, Table S20, Table S21). Their target genes *RHBDF1, RUNDC1, CEP250, C19orf57, KAZN,* and *NRG1* are involved in oncogenesis and other diseases [367, p. 4].

Therefore, ingestion of these miRNAs with food in humans can significantly affect metabolic processes. The miR529a-3p had binding sites in the mRNA of six genes that are involved in the regulation of several physiological processes

(Appendix D, Table D20, Table D21). If a person in the process of evolution consumed this miRNA as a necessary regulator of the expression of its target genes, then for this miRNA there must be target genes [367, p. 4].

Figure 17 shows the interaction patterns of the nucleotide sequences of some representatives of the miRNA families with the mRNA of their target genes. These data indicate a good predictive power for identifying miRNA associations and target genes. The visibility of the interaction of miRNA and mRNA nucleotides in combination with the quantitative characteristics of binding miRNA and mRNA allows us to consider these associations stable and real [367, p. 4].

Note that the nucleotide sequences miR156, miR166, miR395, miR396, and miR444 did not have homologous miRNAs among 2565 human miRNAs from the miRBase base. Therefore, these miRNAs do not directly have common binding sites for human miRNAs and can independently regulate the expression of their target genes. To confirm the conservatism of the interaction of plant miRNA with human target genes, we plotted the web logo for mRNA sections containing plant miRNA binding sites (Figure 16). The graphs show the high conservatism of these binding sites compared to flanking nucleotide sequences. The miR156a-j-5 family, consisting of 10 miRNAs, was associated with the mRNA of seven genes (Appendix D, Table D20) [367, p. 4].

Gene, miRNA, srart of site, region, ΔG, ΔG/ΔGm	Gene, miRNA, srart of site, region, ΔG, ΔG/ΔGm
NKRD27, miR1428e-3p, 244, CDS, -98, 96 5'-CAAAU**C**CAUGGCAUU**G**UCUUA-3' 3'-GUUUA**A**GUACCGUAA**U**AGAAU-5'	*EIF3B*, miR1846b-5p, 2194, CDS, -119, 97 5'-**G**GCGGCCCCGGCCUCC**C**ACACU-3' 3'-**U**CGCCGGGGCCGGAGG**A**-GUGA-5'
AP2A2, miR156k-5p, 3797, 3'UTR, -104, 94 5'-UGUGCUCGUCUCU**U**U**C**CUGUCA-3' 3'-ACACGAG-AGAGA**G**A**A**GACAGU-5'	*SLC25A37*, miR2907a-3p, 884, CDS, -125, 95 5'-CCG**G**GGCCCUCGC**C**GCGGC**C**GCC-3' 3'-GGC**U**CCGGGAGCG**A**-GCCG**A**CGG-5'
PKHD1, miR159f-3p, 9966, CDS, -108, 98 5'-UAGAGCUCCCU**C**CAAUCCAAG-3' 3'-AUCUCGAGGGA**A**GUUAGGUUC-5'	*CD22*, miR395t-3p, 2684, 3'UTR, -104, 94 5'-GAGUUUCCCCA**G**ACAC**C**G**C**CAC-3' 3'-CUCAAAGGGGU**U**UGUG**A**-**A**GUG-5'
CHST11, miR166a-5p, 986, CDS, -104, 94 5'-CCCUGAACCAGUACA**G**CAUCCC-3' 3'-GGAACUUGGUC-UGU**U**GUAAGG-5'	*SYVN1*, miR396a-5p, 854, CDS, -102, 94 5'-CAGUUCAAGAAAGCUGUG**A**CA**G**-3' 3'-GUCAAGUUCUUUCGACAC**C**-U**U**-5'
CCNY, miR166h-5p, 367, CDS, -110, 96 5'-CCUCG**G**GCCAGCACAA**U**AUUCC-3' 3'-GGAGC**U**CGGUCG-GUU**G**UAAGG-5'	*C19orf57*, miR444b.1-3p, 714, CDS, -106, 94 5'-G**A**CAGCAAGCCUGAGACAGACA-3' 3'-C**C**GUCGUUCGAACUCUGU-UGU-5'
PRICKLE2, miR167d-5p, 1959, CDS, -106, 94 5'-CAG**G**ACAUGCUGGCAGCUUCA-3' 3'-GUC**U**AGUACGACCGUCGAAGU-5'	*PDE4B*, miR529a-3p, 2270, CDS, -100, 94 5'-GAAG**G**AG**G**GAGAGGGA**C**ACAG-3' 3'-CUUC**U**UC**U**CUCUCCC-**A**UGUC-5'
KLF14, miR168b-5p, 623, CDS, -115, 98 5'-UUCCCG**G**GCUGCACCAAAGCCU-3' 3'-AAGGGC**U**CGACGUGGUU-CGGA-5'	*ENAH*, miR531b-5p, 106, 5'UTR, -115, 95 5'-CGGGC**G**CGC**G**GCCCCGGCG**G**G-3' 3'-GCC-G**U**GCG**U**CGGGGCCGC**U**C-5'
GPR31, miR172a-3p, 590, CDS, -100, 94 5'-AUGCAGGCAUCAUCA**G**G**GC**UCU-3' 3'-UACGUC-GUAGUAGU**U**C**UA**AGA-5'	*TIFA*, miR815a-3p, 186, 5'UTR, -106, 94 5'-CCCA**G**UCUCCUC**G**AUUCCCCU**C**-3' 3'-GGGU**U**AGAGGAG**U**UA-GGGGA**A**-5'

Note: Gene; miRNA; start of binding site (nt); ΔG (kJ/mole); ΔG/ΔGm (%), length of miRNA (nt). The upper and lower nucleotide sequences of mRNA and miRNA, respectively. The bold type indicates the nucleotide of non-canonical pairs U-G, A-C.

Figure 17 - Schemes of the interaction of nucleotide sequences of osa-miRNA families with mRNA human genes [367, p. 7]

The miR156a-j-5 binding sites in each of the genes differed in the number of hydrogen bonds (Figure 17) and the value of the free interaction energy. Similar results were obtained for other miRNA families: miR164e-5p, miR168b-5p, miR396c-3p, miR444a-3p.1,d.1-3p, miR529a-3p, miR815a,b,c-3p, miR1846a,b,c-5p, miR1858a,b-5p, miR2118l-3p, miR2275d-3p, miR2907a,b,d-3p, and miR395a-y-3p (Figure 16). The conservatism of such bonds between miRNAs and their target genes was established by us for many associations of miRNAs and their target genes in animals and plants [389, p. 808; 396, p. 7]. These bonds have persisted over tens of millions of years of evolution and indicate the early emergence of the process of regulation by miRNA molecules of target gene expression in animals and plants [367, p. 4].

Based on the results obtained in this work, the fact of the interaction of pl-miRs with mRNA of human genes is beyond question. It is necessary to establish the possibilities for these miRNAs to enter the human and animal organisms. Several studies have shown that miRNAs in various parts of plants are present in exosomes 30-400 nm in size and are distributed in the body as part of these nanoparticles [411-413]. Such compaction of miRNAs in exosomes contributes to their conservation and facilitates miRNAs' entry into animals through the digestive tract [414-416]. Further exosomes together with endogenous exosomes with blood move to many tissues and organs. According to the physicochemical properties, plant miRNAs do not differ from animal miRNAs, which makes them competitive when interacting with mRNA target genes. There are no known limitations for the above-described process of ingestion of plant-miRNAs into humans and animals.

Basically, not all pl-miRs will have human target genes, but the most common and vital pl-miRs present in plants can have target genes in animals and humans for a long time eating them. Such pl-miRs usually participate in maintaining the basic physiological functions of plants (productivity, resistance to biotic and abiotic stresses, growth, and development). For example, developed rice lines overexpressing *MIR529a* have been shown to have increased resistance to oxidative stress [417, 418]. The participation of osa-miR159f, osa-miR1871, osa-miR398b, osa-miR408-3p, osa-miR2878-5p, osa-miR528-5p and osa-miR397a in the regulation of a number of physiological processes of rice has been established [367, p. 4-5; 419].

The expression of miRNA of *Setaria italica* (sit) changed many times: sit-miR1432-3p, sit-miR156a-5p, sit-miR156b-5p, sit-miR164a-5p, sit-miR167b-5p, sit-miR171c-3p, sit -miR2118-3p, sit-miR390-5p, sit-miR394-5p, sit-miR395-3p, sit-miR408-3p, sit-miR529a-3p, sit-miR529b-3p, and sit-miR827, sit-miR159b-3p, sit-miR319c-5p, sit-miR528-5p and sit-miR535-5p under various stresses [420]. In a broader evolutionary context, miRNAs of *Morus notabilis* were compared to those of seven other plants, including five dicotyledons, *A. thaliana*, *G.max*, *Malus domestica*, *Populus trichocarpa*, *Ricinus communis,* and two monocotyledons, *O. sativa* and *Z. mays*. Of the 31 *M. notabilis* miRNA families, 24 were conserved in the seven plant species. These miRNAs were classified into well-conserved miRNA families. Prominent among them were mulberry miR160b, miR164a,

miR167a, miR169a, miR390, and miR396b, which completely matched their counterparties in the seven other plant species, suggesting that those miRNAs were extremely conserved and might play critical physiological roles in both dicotyledons and monocotyledons [367, p. 5-6].

However, seven miRNA families, miR482, miR529, miR858, miR4376, miR4414, miR4995, and miR5523, were found in only one or two plant species. The present data indicated that the conserved miRNA families (miR156, miR166, miR167, miR168, and miR535) miR159, miR160, miR164, miR169, miR171, miR172, miR390, miR396, miR397, miR529 and miR4376, miR162, miR393, miR395, miR398, miR399, miR408 and miR4414 miR319, miR482, miR827, miR828, miR858, miR2111, miR4995 and miR5523 were expressed across a vast range exceeded in all three tissues [421]. In African rice *Oryza glaberrima (ogl*), some miRNAs such as ogl-miR156l, ogl-miR166c, ogl-miR166k, ogl-miR168a, ogl-miR167i, ogl-miR171f, ogl-miR1846d of the control library and ogl-miR408, ogl-miR528, ogl-miR156, ogl-miR390, and ogl-miR396c of the treated library had higher reads than their complementary strand. This is because miRNA-3p and miRNA-5p may function simultaneously to regulate gene expression. It must be understood that the expression of the target gene under the influence of miRNAs can increase with decreasing miRNA concentration below the average physiological level or decrease with increasing miRNA concentration [367, p. 5-6].

The data on changes in miRNA concentration in different plants show that the amount of miRNA consumed with food depends on the stage of plant ontogenesis, growing conditions, plant organs, food processing, etc. [422]. The concentration of pl-miRs after various processing of raw products decreases, but the remaining miR enter the body [315, p. 2; 367, p. 6].

As a result of our study, for the first time, among 17,508 human genes, 942 target genes for 277 osa-miRNAs were established. The identified target genes account for 5.4% of the total number of studied human genes. The miRNA binding sites were found in the CDS, 5'UTR and 3'UTR. The largest number of genes were targeted by osa-miR2102-5p, osa-miR5075-3p, osa-miR2097-5p, and osa-miR2919, which can bind to the mRNA of 38, 36, 23, and 19 genes, respectively. Since osa-miRNAs ingested through plant food have many target genes, they should be controlled in the human body [367, p. 6].

Most osa-miRNA target genes are involved in the development of diseases, which makes it easier to clarify the role of miRNAs in these processes. Many osa-miRNA target genes contribute to the development of breast cancer and other cancer types. The other target genes are involved in cardiovascular and neurodegenerative diseases. Some osa-miRNAs can be effective regulators of human gene expression. The effect of miRNAs can be both positive, contributing to the cure of diseases, and negative, causing a wide range of diseases [367, p. 6].

CONCLUSION

It can be concluded from the study that many miRNAs regulate plant development by controlling the expression of transcription factors, which play an important role in the growth and development process. In the present work, it was established how the studied plant miRNAs interact with the mRNA of target genes: the positions of the binding sites in the 5'UTR, CDS, and 3'UTR were determined; free energy of interaction of miRNA with mRNA was calculated; it is shown how the nucleotides of miRNA and mRNA bind during the interaction of these molecules. Consequently, the obtained information can be used with great confidence when carrying out experiments with miRNAs and their target genes.

1. In the format available for the MirTarget program, the following databases were created: for genes of the TCP, HSF, MYB, GRAS, ERF, C2H2 TF families, consisting of 442 genes of *A. thaliana*, 474 genes of *O. sativa*, 653 genes of *Z. mays* and 834 genes of *T. aestivum*; for 428, 738, 325, and 125 miRNAs of *A. thaliana, O. sativa, Z. mays* and *T. aestivum*, respectively.

2. Based on the quantitative characteristics of the interaction of 428 ath-miRNAs and mRNA of 27 TCP family genes of *A. thaliana* revealed only 11 target genes for five miRNAs. The ath-miR5021-5p binding sites were found in mRNAs of three genes of *A. thaliana* and in mRNAs of 27 genes of 17 plant species. The ath-miR5658-5p binding sites in mRNA of 23 genes of 19 plant species are conservative. Of 738 osa-miRNAs and mRNA of 22 TCP family genes of *O. sativa* only 14 genes were shown to be the targets for 17 miRNAs. The osa-miR2102-5p binding sites encode the AAAAAA and GGGGGG oligopeptides in mRNAs of ten genes of seven plant species and in mRNAs of eight genes of six plant species, respectively. The analysis of binding of 325 zma-miRNAs and mRNA of 46 TCP family genes of *Z. mays* predicted only seven target genes for 11 miRNAs. Of 125 miRNA and 28 mRNA of the TCP family genes of *T. aestivum* revealed only five tae-miRNAs have five mRNA target genes. The tae-miR319-3p binding sites encode the conservative oligopeptide QRGPLQS in the TCP TF in 54 plant species. The tae-miR444a-3p binding sites encode the STSETS oligopeptide in mRNAs of 29 genes of 28 plant species.

3. Of 428 ath-miRNAs and mRNA of 24 HSF genes of *A. thaliana*, only five genes were targets for five miRNAs. Of 738 osa-miRNAs and mRNA of 25 HSF family genes of *O. sativa* 12 genes were under the control of ten miRNAs, of which the largest number of binding sites had miR5075-3p. Of 325 zma-miRNAs and mRNA 28 HSF family genes of *Z. mays* it was revealed only six target genes for seven miRNAs. Of 125 tae-miRNAs and the mRNA of 51 genes of the *T. aestivum* HSF family, it was found that only three genes of the HSF family were targets for four miRNAs.

4. Out of 428 ath-miRNA binding sites in the mRNAs of 144 MYB genes of *A. thaliana* it was revealed that 32 genes are targets of 15 miRNAs. Of 738 osa-miRNA and mRNA of 124 genes of the MYB *O. sativa* family revealed that 34 genes were targets for 32 miRNAs. Of 325 zma-miRNAs and mRNA of 169 genes

of the *Z. mays* MYB family, 25 genes were the targets for 26 miRNAs. Of 125 tae-miRNAs binding and mRNA of 258 MYB family genes of *T. aestivum* revealed that only eight genes were targets for eight miRNAs. The tae-miR159a,b-3p binding sites encode the WSSIRSK oligopeptide, which is conserved in the 27 proteins of the MYB TF for 22 plant species. The proteins of the MYB family of 22 plant species contained the ELPSNQ oligopeptide encoded by miR159e-3p binding sites in mRNAs of 23 genes of 20 plant species.

5. Of 428 ath-miRNAs and mRNA of 37 genes of the *A. thaliana* GRAS family, it was found that only 11 genes were targets for eight miRNAs. Of 738 osa-miRNAs, only 16 miRNAs could bind to mRNA of 18 genes from 60 genes of the GRAS *O. sativa* family. Of 325 zma-miRNAs and mRNA of 86 genes of the GRAS family of *Z. mays*, only 14 genes were targets for eight miRNAs. Of 125 tae-miRNAs interaction with mRNA of 117 GRAS TF genes of *T. aestivum* revealed only five target genes for three miRNAs. The nucleotide sequences ath-miR171a-3p, osa-miR171a-3p, zma-miR171n-3p were identical and had binding sites in mRNA for 13 genes of the TF GRAS family and encode conservative ILARN oligopeptide.

6. Of 428 ath-miRNAs and mRNA of 123 genes of the ERF TF family of *A. thaliana*, it was revealed that 25 genes were targets for eight miRNAs. Of 738 *O. sativa* miRNAs, only 13 miRNAs effectively bound to mRNA of 16 genes from 138 genes. Of 325 miRNAs and mRNA of 186 genes of the ERF TF family of *Z. mays*, only two genes were targets for two miRNAs. Of 125 miRNAs and 169 mRNA of *T. aestivum* genes, it was found that only five genes were targets for four miRNAs.

7. Of 428 ath-miRNAs and mRNA of 87 C2H2 TF genes of *A. thaliana*, only 17 genes were targets of nine miRNAs. Of 738 osa-miRNAs and mRNAs of 105 C2H2 family genes of *O. sativa* revealed only 17 target genes for 14 miRNAs. Of the 325 zma-miRNAs and mRNA of 138 of the C2H2 TF family genes of *Z. mays*, the number of target genes that bind to zma-miRNAs was equal six. Of the 125 miRNAs and mRNA of 211 C2H2 family genes of T. aestivum, only six target genes were identified for three miRNAs.

8. For ath-miR5021-5p, ath-miR5658-5p, osa-miR2102-5p, osa-miR5075-3p, which have several target genes in the C2H2, ERF, GRAS families, it was found that the nucleotide sequences of the binding sites were conserved and encoded conservative oligopeptides: ath-miR5021-5p – SSSSSS, ath-miR5658-5p – HHHHH, osa-miR2102-5p – AAAAAA and GGGGGG, osa-miR5075-3p – AAAAA and GGGGGG.

9. Study of 325 zma-miRNAs interaction to mRNAs of 17508 human genes revealed only 38 target genes for nine single zma-miRNAs and 211 target genes for 94 zma-miRNA families. The study of 125 tae-miRNAs interaction with mRNA of 17508 human genes revealed only 116 target genes for 44 single tae-miRNAs and 57 target genes for 23 tae-miRNA families. Among 17,508 human genes with 738 osa-miRNAs, 942 target genes for 277 osa-miRNAs were established. A total of 641 target genes were identified for 131 single miRNAs.

Most of the studied target genes of zma-miRNA, tae-miRNA, osa-miRNA may influence on human genes which participate in the development of oncological, neurodegenerative, and cardiovascular diseases.

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Appendix A.

ҚАЗАҚСТАН РЕСПУБЛИКАСЫ

РЕСПУБЛИКА КАЗАХСТАН

СВИДЕТЕЛЬСТВО

О ВНЕСЕНИИ СВЕДЕНИЙ В ГОСУДАРСТВЕННЫЙ РЕЕСТР ПРАВ НА ОБЪЕКТЫ, ОХРАНЯЕМЫЕ АВТОРСКИМ ПРАВОМ

№ 15600 от «2» марта 2021 года

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Appendix B.

Table B1. Database of TCP family genes of *A. thaliana*, *O. sativa*, *Z. mays*, and *T. aestivum* [the list of genes was obtained in this study by Rakhmetullina A.K. based on PlantTFDB data]

TCP family	
Species	TF ID
A. thaliana	AT1G30210.1, AT1G30210.2, AT1G35560.1, AT1G53230.1, AT1G58100.1, AT1G58100.2, AT1G67260.1, AT1G67260.2, AT1G68800.1, AT1G69690.1, AT1G72010.1, AT2G31070.1, AT2G37000.1, AT2G45680.1, AT3G02150.1, AT3G15030.1, AT3G18550.1, AT3G27010.1, AT3G45150.1, AT3G47620.1, AT4G18390.1, AT5G08070.1, AT5G08330.1, AT5G23280.1, AT5G41030.1, AT5G51910.1, AT5G60970.1
O. sativa	LOC_Os01g11550.1, LOC_Os01g55750.1, LOC_Os01g69980.1, LOC_Os02g42380.1, LOC_Os02g51280.1, LOC_Os02g51310.1, LOC_Os03g49880.1, LOC_Os03g57190.1, LOC_Os04g11830.1, LOC_Os04g44440.1, LOC_Os05g43760.1, LOC_Os06g12230.1, LOC_Os07g05720.1, LOC_Os08g33530.1, LOC_Os08g43160.1, LOC_Os09g24480.1, LOC_Os09g34950.1, LOC_Os11g07460.1, LOC_Os12g02090.1, LOC_Os12g07480.1, LOC_Os12g42190.1, LOC107277536
Z. mays	AC190734.2_FGP003, AC199782.5_FGP003, AC205574.3_FGP006, AC213524.3_FGP003, AC233950.1_FGP002, AC234521.1_FGP006, GRMZM2G003944_P01, GRMZM2G015037_P01, GRMZM2G015037_P02, GRMZM2G020805_P01, GRMZM2G020805_P02, GRMZM2G031905_P01, GRMZM2G034638_P01, GRMZM2G035944_P01, GRMZM2G055024_P01, GRMZM2G060319_P01, GRMZM2G062711_P01, GRMZM2G064628_P01, GRMZM2G077755_P01,GRMZM2G078077_P01, GRMZM2G088440_P01, GRMZM2G089361_P01, GRMZM2G089638_P01, GRMZM2G092214_P01, GRMZM2G093895_P01,GRMZM2G096610_P01, GRMZM2G107031_P01, GRMZM2G110242_P01,GRMZM2G113888_P01, GRMZM2G115516_P01, GRMZM2G120151_P01,GRMZM2G135461_P01, GRMZM2G142751_P01, GRMZM2G148022_P02,GRMZM2G166687_P01, GRMZM2G166946_P01, GRMZM2G170232_P01,GRMZM2G178603_P01, GRMZM2G180568_P01, GRMZM2G359599_P01,GRMZM2G414114_P01, GRMZM2G416524_P01, GRMZM2G424261_P01, GRMZM2G445944_P01, GRMZM2G458087_P01, GRMZM2G465091_P01
T. aestivum	TRAES3BF002700090CFD_t1, TRAES3BF014900010CFD_t1, TRAES3BF146000020CFD_t1, Traes_1AL_79B8C6F15.1, Traes_2AL_B05A4E316.1, Traes_2AL_EA60A06AC.1, Traes_2AS_1A307CE26.1, Traes_2BL_36A3AB3A2.1, Traes_2BL_4B6057E06.1, Traes_2BS_03909B330.1, Traes_2DL_01D9C842D.1, Traes_2DS_4C8E5F416.1, Traes_4AL_75D069945.1, Traes_4AL_E57587E16.1, Traes_4BS_6A0B5C129.1, Traes_4BS_DC076554D.1, Traes_4DS_59A46B69A.1, Traes_4DS_9C2FD9F381.2, Traes_5BL_19F383CC71.1, Traes_5BL_2DDBAA0C2.1, Traes_5BL_B94C45A8F.1, Traes_5BS_77558D2A3.2, Traes_5DL_46A3B0DAB1.1, Traes_5DS_643EDFE5B.2

Table B2. Database of HSF family genes of *A. thaliana*, *O. sativa*, *Z. mays*, and *T. aestivum* [the list of genes was obtained in this study by Rakhmetullina A.K. based on PlantTFDB data]

HSF family	
Species	TF ID
1	2
A. thaliana	AT1G32330.1, AT1G46264.1, AT1G67970.1, AT1G77570.1, AT2G26150.1, AT2G41690.1, AT3G02990.1, AT3G22830.1, AT3G24520.1, AT3G51910.1, AT3G63350.1, AT4G11660.1, AT4G13980.1, AT4G17750.1, AT4G18870.1, AT4G18880.1, AT4G19630.1, AT4G36990.1, AT5G03720.1, AT5G16820.1, AT5G43840.1, AT5G45710.1, AT5G54070.1, AT5G62020.1
O. sativa	LOC_Os01g39020.1, LOC_Os01g43590.1, LOC_Os01g53220.1, LOC_Os01g54550.1, LOC_Os02g13800.1, LOC_Os02g29340.1, LOC_Os02g32590.1, LOC_Os03g06630.1, LOC_Os03g12370.1, LOC_Os03g25120.1, LOC_Os03g53340.1, LOC_Os03g58160.1, LOC_Os03g63750.1, LOC_Os04g48030.1, LOC_Os05g45410.1, LOC_Os06g35960.1, LOC_Os06g36930.1, LOC_Os07g08140.1, LOC_Os07g44690.1, LOC_Os08g36700.1, LOC_Os08g43334.1, LOC_Os09g28200.1, LOC_Os09g28354.1, LOC_Os09g35790.1, LOC_Os10g28340.1
Z. mays	AC205471.4_FGP003, AC206165.3_FGP007, AC216247.3_FGP001, GRMZM2G002131_P01, GRMZM2G003489_P03, GRMZM2G005815_P01, GRMZM2G010871_P02, GRMZM2G025685_P01, GRMZM2G026742_P01, GRMZM2G059851_P01, GRMZM2G086880_P01, GRMZM2G088242_P01, GRMZM2G089525_P01, GRMZM2G098696_P01, GRMZM2G105348_P01, GRMZM2G115456_P01, GRMZM2G118047_P01, GRMZM2G118453_P01, GRMZM2G118485_P01, GRMZM2G125969_P01, GRMZM2G132971_P01, GRMZM2G139535_P01, GRMZM2G164909_P01, GRMZM2G165272_P01, GRMZM2G173090_P01, GRMZM2G179802_P01, GRMZM2G301485_P01, GRMZM2G384339_P02
T. aestivum	TRAES3BF002300100CFD_t1, TRAES3BF021000010CFD_t1, TRAES3BF025700020CFD_t1, TRAES3BF025700030CFD_t1, TRAES3BF025700040CFD_t1, TRAES3BF025700050CFD_t1, TRAES3BF029100010CFD_t1, TRAES3BF071100100CFD_t1, Traes_1AL_A4B5C1474.2, Traes_2AL_D3B2C21A7.1, Traes_2AS_53BFA14C7.2, Traes_2AS_5C7B75BC5.1, Traes_2AS_66F050AC7.1, Traes_2BL_33410A32A.1, Traes_2BS_1484A7516.1, Traes_2BS_3B77DC6C3.1, Traes_2BS_ECF9B4EB4.1, Traes_2DL_481253665.1, Traes_2DS_070CE3D50.1, Traes_2DS_B6872CB84.1, Traes_3AL_463ABD4BF.1, Traes_3DL_C5832B670.1, Traes_4AL_ABD465CB6.1, Traes_4AS_02B607421.1, Traes_4AS_52EB860E7.2, Traes_4BL_2E125A702.1, Traes_4BL_5091DE58E.1, Traes_4BL_86572BB6D.1, Traes_4BL_B64C157DC.1, Traes_4BL_F3AB558D4.1, Traes_4BL_F6C3B5069.1, Traes_4DL_66D0047A7.1, Traes_4DL_9A51D1EB2.2, Traes_4DL_EE941086E.1, Traes_4DL_FA07D8414.1, Traes_4DS_A980F512E.4, Traes_5AL_16AD8DEEC.1, Traes_5AL_D369204D3.1, Traes_5BL_8D23DFA4A.1, Traes_5BL_A847CD732.1

Continue of Table B2

1	2
T. aestivum	Traes_5BL_FCB1625F3.1, Traes_5DL_431CCA490.1, Traes_5DL_6EB179C88.1, Traes_6AS_1537629B3.1, Traes_6BS_25E162197.1, Traes_6DS_C59B6322F.1, Traes_7AL_6931AA68B.1, Traes_7AS_937121AF8.1, Traes_7BS_03F39ED94.1, Traes_7DL_82722EDAD.2, Traes_7DS_10A9C68FA.1

Table B3. Database of HSF family genes of *A. thaliana*, *O. sativa*, *Z. mays*, and *T. aestivum* [the list of genes was obtained in this study by Rakhmetullina A.K. based on PlantTFDB data]

MYB family	
Species	TF ID
1	2
A. thaliana	AT1G06180.1, AT1G08810.1, AT1G09540.1, AT1G09770.1, AT1G14350.1, AT1G16490.1, AT1G17950.1, AT1G18570.1, AT1G18710.1, AT1G22640.1, AT1G25340.1, AT1G26780.1, AT1G34670.1, AT1G35515.1, AT1G48000.1, AT1G49010.1, AT1G56160.1, AT1G56650.1, AT1G57560.1, AT1G63910.1, AT1G66230.1, AT1G66370.1, AT1G66380.1, AT1G66390.1, AT1G68320.1, AT1G69560.1, AT1G73410.1, AT1G74080.1, AT1G74430.1, AT1G74650.1, AT1G79180.1, AT2G02820.1, AT2G16720.1, AT2G23290.1, AT2G25230.1, AT2G26950.1, AT2G26960.1, AT2G31180.1, AT2G32460.1, AT2G36890.1, AT2G37630.1, AT2G38090.1, AT2G39880.1, AT2G47190.1, AT2G47460.1, AT3G01140.1, AT3G01530.1, AT3G02940.1, AT3G06490.1, AT3G08500.1, AT3G09230.1, AT3G09370.1, AT3G11280.1, AT3G11440.1, AT3G11450.1, AT3G12720.1, AT3G12820.1, AT3G13540.1, AT3G13890.1, AT3G18100.1, AT3G23250.1, AT3G24310.1, AT3G27785.1, AT3G27810.1, AT3G27920.1, AT3G28470.1, AT3G28910.1, AT3G29020.1, AT3G30210.1, AT3G46130.1, AT3G47600.1, AT3G48920.1, AT3G49690.1, AT3G50060.1, AT3G52250.1, AT3G53200.1, AT3G55730.1, AT3G60460.1, AT3G61250.1, AT3G62610.1, AT4G00540.1, AT4G01680.1, AT4G05100.1, AT4G09460.1, AT4G12350.1, AT4G13480.1, AT4G17785.1, AT4G18770.1, AT4G21440.1, AT4G22680.1, AT4G25560.1, AT4G26930.1, AT4G28110.1, AT4G32730.1, AT4G33450.1, AT4G34990.1, AT4G37260.1, AT4G37780.1, AT4G38620.1, AT5G01200.1, AT5G02320.1, AT5G04760.1, AT5G05790.1, AT5G06100.1, AT5G06110.1, AT5G07690.1, AT5G07700.1, AT5G08520.1, AT5G10280.1, AT5G11050.1, AT5G11510.1, AT5G12870.1, AT5G14340.1, AT5G14750.1, AT5G15310.1, AT5G16600.1, AT5G16770.1, AT5G17800.1, AT5G23000.1, AT5G23650.1, AT5G26660.1, AT5G35550.1, AT5G39700.1, AT5G40330.1, AT5G40350.1, AT5G40360.1, AT5G40430.1, AT5G49330.1, AT5G49620.1, AT5G52260.1, AT5G52600.1, AT5G54230.1, AT5G55020.1, AT5G56110.1, AT5G57620.1, AT5G58850.1, AT5G59780.3, AT5G60890.1, AT5G61420.2, AT5G62320.1, AT5G62470.1, AT5G65230.1, AT5G65790.1, AT5G67300.1
O. sativa	LOC_Os01g03720.1, LOC_Os01g04930.1, LOC_Os01g07450.1, LOC_Os01g09590.1, LOC_Os01g12860.1, LOC_Os01g16810.1, LOC_Os01g18240.1, LOC_Os01g19330.1, LOC_Os01g19970.1, LOC_Os01g36460.1, LOC_Os01g45090.1, LOC_Os01g49160.1

Continue of Table B3

1	2
O. sativa	LOC_Os01g52410.1, LOC_Os01g59660.1, LOC_Os01g62410.1, LOC_Os01g63160.1, LOC_Os01g63460.1, LOC_Os01g63680.1, LOC_Os01g64360.1, LOC_Os01g65370.1, LOC_Os01g74410.1, LOC_Os01g74590.1, LOC_Os02g02370.1, LOC_Os02g09480.1, LOC_Os02g17190.1, LOC_Os02g36890.1, LOC_Os02g40530.1, LOC_Os02g41510.1, LOC_Os02g42850.2, LOC_Os02g42870.1, LOC_Os02g46780.1,LOC_Os02g49250.1, LOC_Os02g49986.1, LOC_Os02g51799.1,LOC_Os02g54520.1, LOC_Os03g04900.1, LOC_Os03g13310.1,LOC_Os03g18480.1, LOC_Os03g19120.1, LOC_Os03g20090.1,LOC_Os03g25550.1, LOC_Os03g26130.1, LOC_Os03g27090.1,LOC_Os03g29614.1, LOC_Os03g38210.1, LOC_Os03g51110.1,LOC_Os03g56090.1, LOC_Os04g28090.1, LOC_Os04g30890.1,LOC_Os04g38740.1, LOC_Os04g39470.1, LOC_Os04g42950.1,LOC_Os04g43680.1, LOC_Os04g45020.1, LOC_Os04g45060.1,LOC_Os04g46384.1, LOC_Os04g50680.1, LOC_Os04g50770.1,LOC_Os05g04210.1, LOC_Os05g04820.1, LOC_Os05g28320.1,LOC_Os05g35500.1, LOC_Os05g37060.1, LOC_Os05g37730.1,LOC_Os05g38460.1, LOC_Os05g41166.1, LOC_Os05g46610.1,LOC_Os05g48010.1, LOC_Os05g49310.1, LOC_Os06g02250.1,LOC_Os06g06740.1, LOC_Os06g10350.1, LOC_Os06g11780.1,LOC_Os06g14670.1, LOC_Os06g14700.1, LOC_Os06g40330.1,LOC_Os06g43090.1, LOC_Os06g46560.1, LOC_Os07g04700.1,LOC_Os07g04700.2, LOC_Os07g04700.6, LOC_Os07g12130.1,LOC_Os07g14110.1, LOC_Os07g25370.1, LOC_Os07g31470.1,LOC_Os07g37210.1, LOC_Os07g43420.1, LOC_Os07g43580.1,LOC_Os07g44090.3, LOC_Os07g48870.1, LOC_Os08g05520.1,LOC_Os08g15020.1, LOC_Os08g33150.1, LOC_Os08g33660.1,LOC_Os08g33800.1, LOC_Os08g33940.1, LOC_Os08g34960.1,LOC_Os08g37970.1, LOC_Os08g43550.1, LOC_Os09g01960.1,LOC_Os09g23620.1, LOC_Os09g24800.1, LOC_Os09g26170.1,LOC_Os09g36250.1, LOC_Os09g36730.1, LOC_Os10g20990.1,LOC_Os10g33810.1, LOC_Os10g35660.1, LOC_Os11g03440.1,LOC_Os11g10130.1, LOC_Os11g35390.1, LOC_Os11g45740.1,LOC_Os11g47460.1, LOC_Os12g03150.1, LOC_Os12g07610.1,LOC_Os12g07640.1, LOC_Os12g13570.1, LOC_Os12g33070.1,LOC_Os12g37690.1, LOC_Os12g37970.1, LOC_Os12g38400.2
Z. mays	AC165178.2_FGP004, AC197146.3_FGP002, AC203535.4_FGP001, AC206901.3_FGP005, AC213884.3_FGP002, AC217264.3_FGP005, GRMZM2G000818_P01, GRMZM2G001223_P03, GRMZM2G001824_P01, GRMZM2G001875_P01,GRMZM2G002128_P01, GRMZM2G003406_P01, GRMZM2G004090_P01, GRMZM2G005066_P01, GRMZM2G006352_P01, GRMZM2G011422_P01, GRMZM2G013581_P01, GRMZM2G015021_P01, GRMZM2G017268_P01, GRMZM2G017520_P01, GRMZM2G020772_P01, GRMZM2G022686_P01, GRMZM2G024468_P01, GRMZM2G027697_P01, GRMZM2G028054_P01, GRMZM2G031323_P01, GRMZM2G032655_P01, GRMZM2G037650_P01, GRMZM2G038722_P01, GRMZM2G040924_P01, GRMZM2G041415_P01, GRMZM2G043792_P01, GRMZM2G044824_P01, GRMZM2G045748_P01, GRMZM2G046443_P01, GRMZM2G047600_P01,

Continue of Table B3

1	2
Z. mays	GRMZM2G047626_P01, GRMZM2G048136_P02, GRMZM2G048295_P01, GRMZM2G048910_P01, GRMZM2G050305_P01, GRMZM2G050550_P01, GRMZM2G051256_P01, GRMZM2G051528_P01, GRMZM2G051793_P01, GRMZM2G052377_P01, GRMZM2G052606_P01, GRMZM2G054111_P01, GRMZM2G055158_P01, GRMZM2G056407_P01, GRMZM2G056986_P01, GRMZM2G057027_P02, GRMZM2G064630_P01, GRMZM2G064744_P01, GRMZM2G069325_P02, GRMZM2G070523_P01, GRMZM2G070849_P01, GRMZM2G073836_P01, GRMZM2G077147_P01, GRMZM2G077789_P01, GRMZM2G078820_P01, GRMZM2G079123_P01, GRMZM2G079458_P01, GRMZM2G081557_P01, GRMZM2G081919_P01, GRMZM2G083239_P01, GRMZM2G084583_P01, GRMZM2G084799_P01, GRMZM2G087955_P01, GRMZM2G088189_P01, GRMZM2G088783_P01, GRMZM2G089244_P01, GRMZM2G089686_P01, GRMZM2G090837_P01, GRMZM2G093647_P01, GRMZM2G093660_P01, GRMZM2G093789_P01, GRMZM2G095904_P01, GRMZM2G096358_P01, GRMZM2G097636_P01, GRMZM2G097638_P01, GRMZM2G098179_P01, GRMZM2G102790_P01, GRMZM2G104551_P01, GRMZM2G104789_P01, GRMZM2G105137_P01, GRMZM2G106558_P02, GRMZM2G108959_P01, GRMZM2G110135_P01, GRMZM2G111045_P01, GRMZM2G111117_P01, GRMZM2G111731_P01, GRMZM2G115859_P01, GRMZM2G117244_P01, GRMZM2G119693_P01, GRMZM2G121570_P01, GRMZM2G123202_P01, GRMZM2G124715_P01, GRMZM2G125522_P01, GRMZM2G126566_P01, GRMZM2G127490_P01, GRMZM2G127857_P01, GRMZM2G130149_P01, GRMZM2G131442_P01, GRMZM2G131937_P01, GRMZM2G134279_P01, GRMZM2G138427_P01, GRMZM2G139284_P01, GRMZM2G139688_P01, GRMZM2G143046_P01, GRMZM2G143274_P01, GRMZM2G143328_P01, GRMZM2G145444_P01, GRMZM2G147346_P01, GRMZM2G147698_P01, GRMZM2G149958_P01, GRMZM2G150680_P01, GRMZM2G150841_P01, GRMZM2G151205_P01, GRMZM2G158700_P01, GRMZM2G159547_P01, GRMZM2G160838_P01, GRMZM2G160840_P01, GRMZM2G161512_P01, GRMZM2G162434_P01, GRMZM2G162709_P01, GRMZM2G166337_P01, GRMZM2G167088_P01, GRMZM2G167829_P01, GRMZM2G169316_P01, GRMZM2G169356_P01, GRMZM2G170049_P01, GRMZM2G171781_P01, GRMZM2G172327_P01, GRMZM2G172487_P01, GRMZM2G172575_P01, GRMZM2G173633_P01, GRMZM2G175232_P01, GRMZM2G176327_P01, GRMZM2G302549_P01, GRMZM2G305856_P01, GRMZM2G308034_P01, GRMZM2G311059_P01, GRMZM2G312419_P01, GRMZM2G322490_P01, GRMZM2G325907_P01, GRMZM2G330475_P01, GRMZM2G343068_P01, GRMZM2G356718_P02, GRMZM2G369799_P01, GRMZM2G392823_P01, GRMZM2G395672_P01, GRMZM2G403620_P01, GRMZM2G405094_P01, GRMZM2G416652_P01, GRMZM2G419239_P01, GRMZM2G423833_P01, GRMZM2G425427_P01, GRMZM2G428555_P01, GRMZM2G431156_P01, GRMZM2G455869_P01, GRMZM2G460869_P01, GRMZM2G470307_P01, GRMZM2G496770_P01, GRMZM2G701063_P01, GRMZM5G803308_P01, GRMZM5G803355_P01, GRMZM5G833253_P01, GRMZM5G870592_P01
T. aestivum	TRAES3BF012200010CFD_t1, TRAES3BF012200020CFD_t1, TRAES3BF012200030CFD_t1, TRAES3BF016200140CFD_t1, TRAES3BF018800030CFD_t1, TRAES3BF019300020CFD_t1, TRAES3BF024100110CFD_t1, TRAES3BF026200120CFD_t1,

Continue of Table B3

1	2
T. aestivum	TRAES3BF026500080CFD_t1, TRAES3BF027700010CFD_t1, TRAES3BF034000040CFD_t1, TRAES3BF039800050CFD_t1, TRAES3BF044400110CFD_t1, TRAES3BF049800070CFD_t1, TRAES3BF058700130CFD_t1, TRAES3BF059600070CFD_t1, TRAES3BF063000030CFD_t1, TRAES3BF065400010CFD_t1, TRAES3BF071400020CFD_t1, TRAES3BF076000070CFD_t1, TRAES3BF080800010CFD_t1, TRAES3BF082500050CFD_t1, TRAES3BF100100070CFD_t1, TRAES3BF104600030CFD_t1, TRAES3BF142600060CFD_t1, Traes_1AL_1A93B0C96.1, Traes_1AL_206AE5B76.1, Traes_1AL_25726E5E7.1, Traes_1AL_28010F812.1, Traes_1AL_343F2D219.1, Traes_1AL_50CECDF43.1, Traes_1AL_51EBF8930.1, Traes_1AL_91299CB97.1, Traes_1AL_B68E59AAB.2, Traes_1AL_C7FD90C13.2, Traes_1AL_F0688BFDE.2, Traes_1AS_1EE692FDC.1, Traes_1AS_36AF74187.2, Traes_1AS_61D017632.2, Traes_1BL_02507996C.1, Traes_1BL_4D9406708.1, Traes_1BL_C25B5DDB4.2, Traes_1BL_C664E8E1E.1, Traes_1BL_CF98E922B.1, Traes_1BS_403DBC53C.1, Traes_1BS_92EA1F290.1, Traes_1BS_B44ECE28C.1, Traes_1DL_2714E3604.1, Traes_1DL_57F246ADF.1, Traes_1DL_918A8F357.1, Traes_1DL_B26A733D4.1, Traes_1DL_B7E76AFE6.1, Traes_1DL_FCDEFA244.1, Traes_1DS_47E2D90AC.1, Traes_1DS_5BAD8947E.1, Traes_1DS_5EEED86AD.2, Traes_1DS_711044AD5.1, Traes_2AL_097BADCFE.1, Traes_2AL_0A21FB42C.1, Traes_2AL_1D7D3D0DE.1, Traes_2AL_2D4100475.1, Traes_2AL_41B71F83C.1, Traes_2AL_5EE86C5BC.1, Traes_2AL_605C25CDF.2, Traes_2AL_962A9D448.1, Traes_2AL_AF9357B4C.1, Traes_2AL_B01AE830F.1, Traes_2AL_CC403D182.1, Traes_2AL_E5B3B79F7.1, Traes_2AL_FBC0ED0EE.2, Traes_2AS_1161E1D2E.2, Traes_2AS_25C93FD29.1, Traes_2AS_40FA27AE7.1, Traes_2AS_4C9807337.1, Traes_2AS_731C703DE.2, Traes_2AS_CD74215DB.1, Traes_2AS_FA7059723.1, Traes_2BL_03F3475CD.1, Traes_2BL_0501BC320.2, Traes_2BL_230A3A2D0.2, Traes_2BL_34A0848F2.1, Traes_2BL_35241DE8D.1, Traes_2BL_361925B62.1, Traes_2BL_560CCE975.1, Traes_2BL_604FE7639.1, Traes_2BL_79F1B50DF.1, Traes_2BL_7CEC6A8D7.1, Traes_2BL_855A1170C.2, Traes_2BL_88BBF0441.1, Traes_2BL_C843D1851.1, Traes_2BL_FD8C2F815.1, Traes_2BS_1DB727AD1.1, Traes_2BS_2A12B5E70.2, Traes_2BS_CA02DC5B2.1, Traes_2BS_E1E541767.1, Traes_2BS_E8D2BD66E.1, Traes_2BS_F1B450FA4.2, Traes_2DL_25FD0FFB4.1, Traes_2DL_54D11D5E7.1, Traes_2DL_54E6F0446.1, Traes_2DL_5A0300CE0.1, Traes_2DL_5F686B67C.1, Traes_2DL_6BD0572DF.1, Traes_2DL_7183519F8.1, Traes_2DL_912473A86.1, Traes_2DL_A03AB7608.1,

Continue of Table B3

1	2
T. aestivum	Traes_2DL_BDECC07BD.2, Traes_2DL_C964675DE.1, Traes_2DL_D39684C41.1, Traes_2DS_3569AEDFB.1, Traes_2DS_3F5D36630.1, Traes_2DS_49959692B.1, Traes_2DS_61B920833.1, Traes_2DS_9430AAD52.1, Traes_3AL_152A7186A.1, Traes_3AL_386795528.1, Traes_3AL_7C031019E.1, Traes_3AL_825A1B8BD.1, Traes_3AL_A8AF980F3.1, Traes_3AL_E3BF20F0D.2, Traes_3AS_09025DA2E.1, Traes_3AS_5E49D47AF.1, Traes_3B_934488D20.1, Traes_3DL_429583AEC.1, Traes_3DL_46F83C41D.1, Traes_3DL_68BC65ED4.1, Traes_3DL_6BBC889A1.1, Traes_3DS_901181FDD.1, Traes_3DS_A0676BAEA.1, Traes_4AL_40E835A94.2, Traes_4AL_7800B74E3.2, Traes_4AL_7A841CAD2.1, Traes_4AL_8B52D54FD.2, Traes_4AL_9BF07972C.2, Traes_4AL_CC5803BED.1, Traes_4AL_D05736670.1, Traes_4AL_DACD935B2.1, Traes_4AS_3883DC244.1, Traes_4AS_4EFBA88E4.1, Traes_4AS_759D8DDBB.1, Traes_4AS_A79A68739.1, Traes_4AS_E4294BADC.1, Traes_4BL_532725AD5.1, Traes_4BL_545A5716E.1, Traes_4BL_B181F1FD2.2, Traes_4BL_F49830790.1, Traes_4BL_FE8B8ABC4.1, Traes_4BS_189002AB8.1, Traes_4BS_5690C215A.1, Traes_4BS_61B30E3E4.1, Traes_4BS_6253482BD.1, Traes_4BS_AAFB56987.1, Traes_4BS_F83CB32DD.1, Traes_4DL_14C563681.1, Traes_4DL_26A958CDD.1, Traes_4DL_4EE7DFCCD.1, Traes_4DL_8A9D9ACCB.1, Traes_4DL_9023F3504.1, Traes_4DL_967152326.1, Traes_4DL_ADB23D42F.1, Traes_4DL_D41CB81EA.1, Traes_4DL_DFCF4A15A.1, Traes_4DL_FD6DBA41D.2, Traes_4DS_0ECE7A421.2, Traes_4DS_2A5B4C4C4.1, Traes_4DS_7BFAC49C2.1, Traes_4DS_90B64301A.1, Traes_4DS_926486EE0.1, Traes_4DS_F6E1A4F88.1, Traes_5AL_56F30392D.1, Traes_5AL_78AD0AF8E.1, Traes_5AL_8008803A5.1, Traes_5AS_62CC650D3.1, Traes_5BL_30D8E6BE2.1, Traes_5BL_3C4ECAB6D.1, Traes_5BL_486D0D865.1, Traes_5BL_557E7700B.1, Traes_5BL_632EBAD09.1, Traes_5BL_87924B626.1, Traes_5BL_9B80DEC84.1, Traes_5BL_A848F629F.1, Traes_5BL_AED68C680.1, Traes_5BL_C1D4586B1.2, Traes_5BL_D85C0EF26.1, Traes_5BS_2CB91C54A.1, Traes_5BS_95A52A87F.2, Traes_5BS_B41FDD6AA.1, Traes_5BS_E635B0A281.2, Traes_5DL_0B2C5ADF6.1, Traes_5DL_1521D205A.1, Traes_5DL_1868E2A6C.1, Traes_5DL_1CD39D4D0.1, Traes_5DL_1D036F8B5.1, Traes_5DL_36CD3229A.1, Traes_5DL_46D39C394.1, Traes_5DL_4F38323F3.3, Traes_5DL_8ABCB84A7.1, Traes_5DL_92CBBE968.1, Traes_5DS_8F3BD4450.2, Traes_5DS_AACA2EBA3.2, Traes_5DS_DE2C70E4C.2, Traes_6AL_2BA02CAA9.1, Traes_6AL_30B272DDD.2, Traes_6AL_52227091B.1,

Continue of Table B3

1	2
T. aestivum	Traes_6AL_54D562BC2.1, Traes_6AL_89BA7115C.1, Traes_6AL_BB730675A.1, Traes_6AL_C13753B31.1, Traes_6AL_D10CBA40D.1, Traes_6AL_E1D3D8DAA1.1, Traes_6AL_FF1508B19.1, Traes_6AS_5562B97F7.1, Traes_6AS_7C1FD879C.1, Traes_6BL_0D6CD031E.1, Traes_6BL_5A2DB8F78.1, Traes_6BL_7755E4A8A.1, Traes_6BL_7E2D1D34C.3, Traes_6BL_8E4A831B6.1, Traes_6BL_CE61B9510.1, Traes_6BL_E5A9546C9.1, Traes_6BS_B2C9F123A.1, Traes_6DL_29EF04226.1, Traes_6DL_2CD01D459.1, Traes_6DL_41CBE9959.1, Traes_6DL_499F64524.1, Traes_6DL_67FD04DA0.1, Traes_6DL_8BAAC240D.1, Traes_6DL_8BF29D46C.1, Traes_6DL_991931CF9.2, Traes_6DL_A014E9069.1, Traes_6DL_BBAC725C3.2, Traes_6DL_FCDEB9A8B.1, Traes_6DL_FDFCBA57D.1, Traes_6DS_59260A671.2, Traes_6DS_8F05AE571.2, Traes_6DS_A0EC5D808.1, Traes_7AL_04D939077.1, Traes_7AL_0AD4A7A87.1, Traes_7AL_0BCF482E8.1, Traes_7AL_5B57EF9FC.2, Traes_7AS_2EE7C2628.11, Traes_7AS_A337F362A.1, Traes_7AS_B6ADF4159.1, Traes_7AS_B8E8A2F55.1, Traes_7BS_5F17B1022.2, Traes_7BS_7E91DE546.1, Traes_7BS_D28CCE3B8.1, Traes_7DL_1FA87027B.1, Traes_7DL_20EC9096A.2, Traes_7DL_5BD0D4BD1.1, Traes_7DL_AD4395F8F.1, Traes_7DL_FAF2AE9FB.1, Traes_7DS_469ED3135.1, Traes_7DS_5100A9609.1, Traes_7DS_8DF2537B8.1, Traes_7DS_91CCCF6DB.1, Traes_7DS_E27ECBC6E.1

Table B4. Database of GRAS family genes of *A. thaliana*, *O. sativa*, *Z. mays*, and *T. aestivum* [the list of genes was obtained in this study by Rakhmetullina A.K. based on PlantTFDB data]

GRAS family	
Species	TF ID
1	2
A. thaliana	AT1G07520.1, AT1G07530.1, AT1G14920.1, AT1G21450.1, AT1G50420.1, AT1G50600.1, AT1G55580.1, AT1G63100.1, AT1G66350.1, AT2G01570.1, AT2G04890.1, AT2G29060.1, AT2G29065.1, AT2G37650.1, AT2G45160.1, AT3G03450.1, AT3G13840.1, AT3G46600.1, AT3G49950.1, AT3G50650.1, AT3G54220.1, AT3G60630.1, AT4G00150.1, AT4G08250.1, AT4G17230.1, AT4G36710.1, AT4G37650.1, AT5G17490.1, AT5G41920.1, AT5G48150.1, AT5G52510.1, AT5G59450.1, AT5G66770.1, AT5G67411.1
O. sativa	LOC_Os01g45860.1, LOC_Os01g62460.1, LOC_Os01g65900.1, LOC_Os01g67650.1, LOC_Os01g67670.1, LOC_Os01g71970.1, LOC_Os02g10360.1, LOC_Os02g21685.1, LOC_Os02g44360.1, LOC_Os02g44370.1, LOC_Os02g45760.1, LOC_Os03g09280.1, LOC_Os03g15680.1, LOC_Os03g29480.1, LOC_Os03g31880.1,

Continue of Table B4

1	2
O. sativa	LOC_Os03g49990.1, LOC_Os03g51330.1, LOC_Os04g35250.1, LOC_Os04g37440.1, LOC_Os04g46860.1, LOC_Os04g49110.1, LOC_Os04g50060.1, LOC_Os05g31380.1, LOC_Os05g31420.1, LOC_Os05g40710.1, LOC_Os05g42130.1, LOC_Os05g49930.1, LOC_Os06g01620.1, LOC_Os06g03710.1, LOC_Os06g10900.1, LOC_Os06g40780.1, LOC_Os07g16330.1, LOC_Os07g36170.1, LOC_Os07g38030.1, LOC_Os07g39470.1, LOC_Os07g39820.1, LOC_Os07g40020.1, LOC_Os10g22430.1, LOC_Os10g40390.1, LOC_Os11g03110.1, LOC_Os11g04400.1, LOC_Os11g04570.1, LOC_Os11g04590.1, LOC_Os11g06180.1, LOC_Os11g11600.1, LOC_Os11g31100.1, LOC_Os11g47870.1, LOC_Os11g47890.1, LOC_Os11g47900.1, LOC_Os11g47910.1, LOC_Os11g47920.1, LOC_Os12g02870.1, LOC_Os12g04200.1, LOC_Os12g04370.1, LOC_Os12g04380.1, LOC_Os12g06540.1, LOC_Os12g38490.1
Z. mays	AC198366.3_FGP004, AC200124.3_FGP005, AC204621.4_FGP006, AC234164.1_FGP004, GRMZM2G001426_P01, GRMZM2G011947_P01, GRMZM2G013016_P01, GRMZM2G015080_P01, GRMZM2G018254_P01, GRMZM2G019060_P01, GRMZM2G023872_P01, GRMZM2G024973_P01, GRMZM2G028039_P02, GRMZM2G028438_P01, GRMZM2G028608_P01, GRMZM2G037286_P01, GRMZM2G037792_P01, GRMZM2G049159_P01, GRMZM2G051785_P01, GRMZM2G055263_P01, GRMZM2G060265_P01, GRMZM2G070371_P01, GRMZM2G073779_P01, GRMZM2G073805_P01, GRMZM2G073823_P01, GRMZM2G079470_P01, GRMZM2G082387_P01, GRMZM2G089636_P01, GRMZM2G089662_P01, GRMZM2G089782_P01, GRMZM2G091656_P01, GRMZM2G097456_P01, GRMZM2G098517_P01, GRMZM2G098784_P01, GRMZM2G098800_P01, GRMZM2G104342_P01, GRMZM2G106336_P01, GRMZM2G106356_P01, GRMZM2G106548_P01, GRMZM2G109869_P01, GRMZM2G110067_P01, GRMZM2G110579_P01, GRMZM2G114680_P01, GRMZM2G116638_P01, GRMZM2G117949_P01, GRMZM2G125501_P01, GRMZM2G129154_P01, GRMZM2G131516_P01, GRMZM2G132794_P01, GRMZM2G133169_P01, GRMZM2G140085_P01, GRMZM2G140094_P01, GRMZM2G143433_P01, GRMZM2G144744_P01, GRMZM2G146018_P01, GRMZM2G153333_P01, GRMZM2G157679_P01, GRMZM2G159475_P01, GRMZM2G163427_P01, GRMZM2G169636_P01, GRMZM2G172657_P01, GRMZM2G173429_P01, GRMZM2G176537_P01, GRMZM2G179325_P01, GRMZM2G313078_P01, GRMZM2G317287_P01, GRMZM2G335814_P01, GRMZM2G342217_P01, GRMZM2G346706_P01, GRMZM2G348780_P01, GRMZM2G359304_P01, GRMZM2G368909_P01, GRMZM2G386362_P01, GRMZM2G408012_P01, GRMZM2G418899_P01, GRMZM2G420280_P01, GRMZM2G425366_P01, GRMZM2G431309_P01, GRMZM5G821439_P01, GRMZM5G825321_P01, GRMZM5G826526_P01, GRMZM5G868355_P01, GRMZM5G874545_P01, GRMZM5G885274_P01, GRMZM5G889326_P01, GRMZM5G895672_P01
T. aestivum	TRAES3BF021600230CFD_t1, TRAES3BF043700070CFD_t1, TRAES3BF071100020CFD_t1, TRAES3BF071100030CFD_t1, TRAES3BF071100040CFD_t1, TRAES3BF090100150CFD_t1, TRAES3BF091600190CFD_t1, TRAES3BF108400020CFD_t1, TRAES3BF178300020CFD_t1, TRAES3BF267500030CFD_t1, TRAES3BF267500040CFD_t1, TRAES3BF267500050CFD_t1,

Continue of Table B4

1	2
T. aestivum	Traes_1AL_FB0C83DD9.1, Traes_1AS_1104A122D.1, Traes_1AS_D3AEB9F29.1, Traes_1AS_D967CFB69.2, Traes_1AS_F3E49A47C.1, Traes_1BL_DF66FC4FE.1, Traes_1DS_5998ADCA3.1, Traes_2AL_1B22EA0AD.2, Traes_2AS_455BD2CA1.1, Traes_2AS_620B821281.1, Traes_2AS_960C7E44E.1, Traes_2AS_D0B21BF981.2, Traes_2AS_E17243D52.1, Traes_2BL_46E59998A1.1, Traes_2BL_88A78A71E.1, Traes_2BL_B2811EA531.2, Traes_2BS_015167E00.1, Traes_2BS_4600D4B54.2, Traes_2BS_736EF207B1.2, Traes_2BS_D007D6598.1, Traes_2BS_D32231DB0.1, Traes_2BS_FDABA21A7.1, Traes_2DS_2D035BAFD.1, Traes_2DS_3B4535629.1, Traes_2DS_6DAFEC37F.1, Traes_2DS_7B6E75DD2.1, Traes_2DS_9A08AAEE4.1, Traes_2DS_CCA2FCCAD.1, Traes_2DS_FB1D2D1A7.1, Traes_3AL_60B6CD0A5.2, Traes_3AL_6E16C8167.1, Traes_3B_A25F058E5.1, Traes_3DL_13B382BD2.1, Traes_3DL_A3AC10E58.1, Traes_3DL_BF7D83705.1, Traes_4AL_04B7D5758.1, Traes_4AL_0A3D7BB7F.1, Traes_4AL_77F4CC833.1, Traes_4AL_7B4A599EC.1, Traes_4AL_884BA5746.1, Traes_4AL_977AF4963.1, Traes_4AL_C217A20A1.2, Traes_4AL_E769BB5A6.1, Traes_4AL_F023A8691.1, Traes_4AL_FB3CE240C.1, Traes_4AL_FF199F127.1, Traes_4AS_19FA06316.1, Traes_4AS_C30034054.1, Traes_4BL_340D5E00A.1, Traes_4BL_86941BB78.1, Traes_4BL_CDCFB216C.1, Traes_4BL_E20E75836.1, Traes_4BL_EDA8441F6.1, Traes_4BS_071700C53.1, Traes_4BS_2EA81743E1.2, Traes_4BS_2EE4988CD.1, Traes_4BS_344A932261.3, Traes_4BS_A05D3DC53.1, Traes_4BS_A79538646.4, Traes_4BS_DCA6E2BE0.2, Traes_4BS_EC11C40EC.1, Traes_4DL_25E90F954.1, Traes_4DL_5B3B57371.1, Traes_4DL_E50C77AEC.3, Traes_4DS_050789E2A.1, Traes_4DS_258687ACC.1, Traes_4DS_2B4E99BE4.2, Traes_4DS_2CE9E3235.1, Traes_4DS_5644BB36D.3, Traes_4DS_82065CB2C.1, Traes_4DS_A5CD70F30.3, Traes_4DS_ADBA6E30A.1, Traes_4DS_AE4107C25.1, Traes_4DS_C7C37A73D.1, Traes_4DS_F8FC0C699.6, Traes_5AL_1A7387EDC.1, Traes_5AL_4C72C5BCB.1, Traes_5AL_83E515188.2, Traes_5AL_886E8DACD.1, Traes_5AL_9AE0ED26A.1, Traes_5AL_BF8D0B7C0.1, Traes_5AS_710247B67.1, Traes_5BL_04BDEB5D8.2, Traes_5BL_1E751EF1F.1, Traes_5BL_700283665.2, Traes_5BL_A7C4DAE11.2, Traes_5BL_C02570726.1, Traes_5BL_C8BEC527F.1, Traes_5BL_DF8EC4A24.2, Traes_5BL_ED508277A.2, Traes_5BS_ED54C58C5.1, Traes_5DL_3EC609F62.1, Traes_5DL_88247E2B8.1, Traes_5DL_8FD0CF6B9.2, Traes_5DL_A39210547.2, Traes_5DL_B89CD8432.1, Traes_5DL_E275797CE.1, Traes_5DS_C06FE6037.2,

Continue of Table B4

1	2
T. aestivum	Traes_6AL_4084532FC1.1, Traes_6AS_74635BB63.1, Traes_6BL_972224088.1, Traes_6DL_26DDCA106.1, Traes_6DS_A08A13944.1, Traes_7BS_54E859139.1, Traes_7DL_44FCA17C4.1

Table B5. Database of ERF family genes of *A. thaliana*, *O. sativa*, *Z. mays*, and *T. aestivum* [the list of genes was obtained in this study by Rakhmetullina A.K. based on PlantTFDB data]

ERF family	
Species	TF ID
1	2
A. thaliana	AT1G01250.1, AT1G03800.1, AT1G04370.1, AT1G06160.1, AT1G12610.1, AT1G12630.1, AT1G12890.1, AT1G12980.1, AT1G15360.1, AT1G19210.1, AT1G21910.1, AT1G22190.1, AT1G22810.1, AT1G22985.1, AT1G24590.1, AT1G25470.1, AT1G28160.1, AT1G28360.1, AT1G28370.1, AT1G33760.1, AT1G36060.1, AT1G43160.1, AT1G44830.1, AT1G46768.1, AT1G49120.1, AT1G50640.1, AT1G53170.1, AT1G53910.1, AT1G63030.1, AT1G64380.1, AT1G68550.1, AT1G71130.1, AT1G71450.1, AT1G71520.1, AT1G72360.1, AT1G74930.1, AT1G75490.1, AT1G77200.1, AT1G77640.1, AT1G78080.1, AT1G80580.1, AT2G20350.1, AT2G20880.1, AT2G22200.1, AT2G23340.1, AT2G25820.1, AT2G31230.1, AT2G33710.1, AT2G35700.1, AT2G36450.1, AT2G38340.1, AT2G40220.1, AT2G40340.1, AT2G40350.1, AT2G44840.1, AT2G44940.1, AT2G46310.1, AT2G47520.1, AT3G11020.1, AT3G14230.1, AT3G15210.1, AT3G16280.1, AT3G16770.1, AT3G20310.1, AT3G23220.1, AT3G23230.1, AT3G23240.1, AT3G25890.1, AT3G50260.1, AT3G57600.1, AT3G60490.1, AT3G61630.1, AT4G06746.1, AT4G11140.1, AT4G13040.1, AT4G13620.1, AT4G16750.1, AT4G17490.1, AT4G17500.1, AT4G18450.1, AT4G23750.1, AT4G25470.1, AT4G25480.1, AT4G25490.1, AT4G27950.1, AT4G28140.1, AT4G31060.1, AT4G32800.1, AT4G34410.1, AT4G36900.1, AT4G39780.1, AT5G05410.1, AT5G07310.1, AT5G07580.1, AT5G11190.1, AT5G11590.1, AT5G11590.1, AT5G13330.1, AT5G13910.1, AT5G18450.1, AT5G18560.1, AT5G19790.1, AT5G21960.1, AT5G25190.1, AT5G25390.1, AT5G25810.1, AT5G43410.1, AT5G44210.1, AT5G47220.1, AT5G47230.1, AT5G50080.1, AT5G51190.1, AT5G51990.1, AT5G52020.1, AT5G53290.1, AT5G61590.1, AT5G61600.1, AT5G61890.1, AT5G64750.1, AT5G65130.1, AT5G67000.1, AT5G67010.1, AT5G67190.1
O. sativa	LOC_Os01g04020.1, LOC_Os01g07120.1, LOC_Os01g10370.1, LOC_Os01g12440.1, LOC_Os01g21120.1, LOC_Os01g46870.1, LOC_Os01g54890.1, LOC_Os01g58420.1, LOC_Os01g59780.1, LOC_Os01g64790.1, LOC_Os01g66270.1, LOC_Os01g73770.1, LOC_Os02g06330.1, LOC_Os02g09650.1, LOC_Os02g10760.1, LOC_Os02g13710.1, LOC_Os02g29550.1, LOC_Os02g32040.1, LOC_Os02g32140.1, LOC_Os02g34260.1, LOC_Os02g34270.1, LOC_Os02g35240.1, LOC_Os02g38090.1, LOC_Os02g42585.1, LOC_Os02g43790.1, LOC_Os02g43820.1, LOC_Os02g43940.1, LOC_Os02g43970.1, LOC_Os02g45420.1, LOC_Os02g45450.1, LOC_Os02g51670.1, LOC_Os02g52670.1, LOC_Os02g54050.1,

Continue of Table B5

1	2
O. sativa	LOC_Os03g07830.1, LOC_Os03g07940.1, LOC_Os03g08460.1, LOC_Os03g08470.1, LOC_Os03g08490.1, LOC_Os03g08500.1, LOC_Os03g09170.1, LOC_Os03g15660.1, LOC_Os03g22170.1, LOC_Os03g60120.1, LOC_Os03g64260.1, LOC_Os04g18650.1, LOC_Os04g32620.1, LOC_Os04g32790.1, LOC_Os04g34970.1, LOC_Os04g44670.1, LOC_Os04g46220.1, LOC_Os04g46240.1, LOC_Os04g46250.1, LOC_Os04g46400.1, LOC_Os04g46410.1, LOC_Os04g46440.1, LOC_Os04g48350.1, LOC_Os04g52090.1, LOC_Os04g55520.1, LOC_Os04g56150.1, LOC_Os04g57340.1, LOC_Os05g25260.1, LOC_Os05g27930.1, LOC_Os05g28350.1, LOC_Os05g29810.1, LOC_Os05g34730.1, LOC_Os05g36100.1, LOC_Os05g36100.1, LOC_Os05g37640.1, LOC_Os05g39590.1, LOC_Os05g41760.1, LOC_Os05g41780.1, LOC_Os05g49010.1, LOC_Os05g49700.1, LOC_Os06g03670.1, LOC_Os06g06540.1, LOC_Os06g06970.1, LOC_Os06g07030.1, LOC_Os06g08340.1, LOC_Os06g09390.1, LOC_Os06g09717.1, LOC_Os06g09760.1, LOC_Os06g09790.1, LOC_Os06g09810.1, LOC_Os06g10780.1, LOC_Os06g11860.1, LOC_Os06g11940.1, LOC_Os06g36000.1, LOC_Os06g40150.1, LOC_Os06g42990.1, LOC_Os06g44750.1, LOC_Os06g47590.1, LOC_Os07g03250.1, LOC_Os07g10410.1, LOC_Os07g12510.1, LOC_Os07g22730.1, LOC_Os07g22770.1, LOC_Os07g38750.1, LOC_Os07g42510.1, LOC_Os07g47330.1, LOC_Os07g47790.1, LOC_Os08g07700.1, LOC_Os08g27220.1, LOC_Os08g31580.1, LOC_Os08g34360.1, LOC_Os08g35240.1, LOC_Os08g36920.1, LOC_Os08g41030.1, LOC_Os08g42550.1, LOC_Os08g43200.1, LOC_Os08g43210.1, LOC_Os08g44960.1, LOC_Os08g45110.1, LOC_Os09g11460.1, LOC_Os09g11480.1, LOC_Os09g13940.1, LOC_Os09g20350.1, LOC_Os09g26420.1, LOC_Os09g28440.1, LOC_Os09g35010.1, LOC_Os09g35020.1, LOC_Os09g35030.1, LOC_Os09g39810.1, LOC_Os09g39850.1, LOC_Os10g22600.1, LOC_Os10g25170.1, LOC_Os10g26590.1, LOC_Os10g30840.1, LOC_Os10g38000.1, LOC_Os10g41130.1, LOC_Os10g41330.1, LOC_Os11g06770.1, LOC_Os11g13840.1, LOC_Os12g39330.1, LOC_Os12g40960.1, LOC_Os12g41030.1, LOC_Os12g41060.1
Z. mays	AC187157.4_FGP001, AC198403.3_FGP001, AC198979.4_FGP009, AC200038.4_FGP011, AC206951.3_FGP016, AC206951.3_FGP017, AC209257.4_FGP006, AC213666.3_FGP003, AC233933.1_FGP001, GRMZM2G000520_P01, GRMZM2G002119_P01, GRMZM2G003466_P01, GRMZM2G005301_P01, GRMZM2G006745_P01, GRMZM2G007406_P01, GRMZM2G008234_P01, GRMZM2G009598_P01, GRMZM2G010100_P01, GRMZM2G011110_P01, GRMZM2G011236_P01, GRMZM2G015281_P01, GRMZM2G016079_P01, GRMZM2G016434_P01, GRMZM2G018138_P01, GRMZM2G018398_P01, GRMZM2G018984_P02, GRMZM2G019443_P01, GRMZM2G020016_P01, GRMZM2G020054_P01, GRMZM2G020150_P01, GRMZM2G021369_P01, GRMZM2G021573_P02, GRMZM2G021790_P01, GRMZM2G023708_P01, GRMZM2G024871_P01, GRMZM2G025062_P01, GRMZM2G026926_P01, GRMZM2G028151_P02, GRMZM2G028386_P01, GRMZM2G028969_P01, GRMZM2G029323_P01, GRMZM2G033656_P01,

Continue of Table B5

1	2
Z. mays	GRMZM2G039112_P01, GRMZM2G039870_P01, GRMZM2G040664_P01, GRMZM2G041839_P01, GRMZM2G042756_P01, GRMZM2G044077_P01, GRMZM2G047918_P01, GRMZM2G047999_P01, GRMZM2G048621_P01, GRMZM2G050851_P01, GRMZM2G052667_P01, GRMZM2G052720_P01, GRMZM2G055070_P01, GRMZM2G055180_P01, GRMZM2G055204_P01, GRMZM2G057386_P01, GRMZM2G059939_P01, GRMZM2G060206_P01, GRMZM2G060249_P01, GRMZM2G060465_P01, GRMZM2G060517_P01, GRMZM2G060876_P01, GRMZM2G061487_P01, GRMZM2G066158_P01, GRMZM2G067463_P01, GRMZM2G068967_P01, GRMZM2G069082_P01, GRMZM2G069126_P01, GRMZM2G069146_P01, GRMZM2G072926_P01, GRMZM2G073047_P01, GRMZM2G073258_P01, GRMZM2G076896_P01, GRMZM2G079653_P01, GRMZM2G079825_P01, GRMZM2G080516_P01, GRMZM2G081892_P01, GRMZM2G084264_P01, GRMZM2G085678_P01, GRMZM2G085964_P01, GRMZM2G087040_P01, GRMZM2G087059_P01, GRMZM2G089995_P01, GRMZM2G093595_P01, GRMZM2G097081_P01, GRMZM2G097182_P01, GRMZM2G100727_P01, GRMZM2G100982_P01, GRMZM2G103085_P01, GRMZM2G104260_P01, GRMZM2G104866_P01, GRMZM2G105266_P01, GRMZM2G106591_P01, GRMZM2G110333_P01, GRMZM2G111415_P01, GRMZM2G113060_P01, GRMZM2G114820_P01, GRMZM2G119865_P01, GRMZM2G120401_P01, GRMZM2G123119_P01, GRMZM2G124011_P01, GRMZM2G124037_P01, GRMZM2G125460_P01, GRMZM2G129674_P01, GRMZM2G129777_P01, GRMZM2G131266_P03, GRMZM2G131281_P01, GRMZM2G132185_P01, GRMZM2G132223_P01, GRMZM2G133168_P01, GRMZM2G135452_P01, GRMZM2G137341_P01, GRMZM2G138396_P01, GRMZM2G139740_P01, GRMZM2G139765_P01, GRMZM2G141219_P03, GRMZM2G141679_P01, GRMZM2G142179_P01, GRMZM2G146028_P01, GRMZM2G148333_P01, GRMZM2G149756_P01, GRMZM2G151542_P01, GRMZM2G156006_P01, GRMZM2G156737_P01, GRMZM2G160971_P01, GRMZM2G163745_P01, GRMZM2G165257_P01, GRMZM2G169382_P01, GRMZM2G171179_P01, GRMZM2G171569_P01, GRMZM2G172936_P01, GRMZM2G173771_P01, GRMZM2G174347_P01, GRMZM2G174917_P01, GRMZM2G175525_P01, GRMZM2G175543_P01, GRMZM2G175856_P01, GRMZM2G300924_P01, GRMZM2G301860_P01, GRMZM2G307119_P01, GRMZM2G307152_P01, GRMZM2G309731_P01, GRMZM2G310368_P01, GRMZM2G317596_P01, GRMZM2G322672_P01, GRMZM2G323172_P01, GRMZM2G328197_P01, GRMZM2G348307_P01, GRMZM2G363052_P01, GRMZM2G368838_P01, GRMZM2G369472_P01, GRMZM2G376255_P01, GRMZM2G379652_P01, GRMZM2G380377_P01, GRMZM2G381441_P01, GRMZM2G384386_P01, GRMZM2G399098_P01, GRMZM2G399598_P01, GRMZM2G419901_P01, GRMZM2G421033_P01, GRMZM2G425798_P02, GRMZM2G429378_P01, GRMZM2G434203_P01, GRMZM2G438202_P01, GRMZM2G457562_P01, GRMZM2G458437_P01, GRMZM2G461907_P01, GRMZM2G466044_P01, GRMZM2G474326_P01, GRMZM2G475678_P01, GRMZM2G477287_P01, GRMZM2G478965_P01, GRMZM2G480434_P01, GRMZM2G481668_P01, GRMZM2G544539_P01, GRMZM5G805505_P01, GRMZM5G806839_P01, GRMZM5G816314_P01, GRMZM5G837876_P01, GRMZM5G842961_P01, GRMZM5G846057_P01, GRMZM5G852704_P01, GRMZM5G889719_P01

Continue of Table B5

1	2
T. aestivum	TRAES3BF017100030CFD_t1, TRAES3BF024700170CFD_t1, TRAES3BF046300130CFD_t1, TRAES3BF051200070CFD_t1, TRAES3BF064700080CFD_t1, TRAES3BF073700060CFD_t1, TRAES3BF075600040CFD_t1, TRAES3BF075600050CFD_t1, TRAES3BF084200010CFD_t1, TRAES3BF091400270CFD_t1, TRAES3BF108400040CFD_t1, TRAES3BF171600010CFD_t1, TRAES3BF176500010CFD_t1, Traes_1AL_08BAD7CD3.1, Traes_1AL_258E7F2A3.1, Traes_1AL_7BE5906B2.1, Traes_1AL_88D49649D.1, Traes_1AL_A9FB6BF52.1, Traes_1BL_09D8BE2C9.1, Traes_1BL_8E4911A3C.1, Traes_1BL_BDF0801D01.2, Traes_1BL_E0397871B.1, Traes_1BL_E39CD252E.1, Traes_1DL_CD3D9CDE7.1, Traes_2AL_0B28B6DBE.1, Traes_2AL_0F08552FB.1, Traes_2AL_158F8EE88.2, Traes_2AL_3FB37A3E7.1, Traes_2AL_43491B9E0.1, Traes_2AL_45E6314EF.1, Traes_2AL_61DB73424.1, Traes_2AL_6B6086A7C.2, Traes_2AL_9E90C2488.1, Traes_2AL_E5A9615E2.3, Traes_2AL_F24D031AA.1, Traes_2AL_FC6DD1383.1, Traes_2AS_72E9B68D2.2, Traes_2BL_0B09B840B.1, Traes_2BL_1E57B73B21.5, Traes_2BL_304012B04.1, Traes_2BL_3A3353970.1, Traes_2BL_593E1CCC2.1, Traes_2BL_5BA37F95E.1, Traes_2BL_5DC21F3CD.1, Traes_2BL_970693C1F.1, Traes_2BL_984787AC0.1, Traes_2BL_9CD6E043A.2, Traes_2BL_B397F2CE3.1, Traes_2BL_CF47A74CC.2, Traes_2BL_E5F50498D.1, Traes_2BL_E7871AFBA.1, Traes_2BL_FC0F8A3DC.1, Traes_2BS_0EE99D4A6.1, Traes_2BS_5E7287209.1, Traes_2BS_B1A73C7A8.1, Traes_2DL_2536A1C8C.2, Traes_2DL_A336122501.1, Traes_2DL_B32203C91.1, Traes_2DL_CB03F0D2A.1, Traes_2DL_D2EA554EA.1, Traes_2DS_9698ADBC2.1, Traes_2DS_A6A088AFC.1, Traes_3AL_7ECC5258D.1, Traes_3AS_62742A0471.1, Traes_3DL_83B339561.1, Traes_3DS_70F9BD124.1, Traes_4AL_1A0E673DC.1, Traes_4AL_5E86DF14B.1, Traes_4AL_D2D7703821.2, Traes_4AL_F18648C49.1, Traes_4AS_094442636.2, Traes_4AS_0D75149B5.1, Traes_4AS_18663793B.1, Traes_4AS_8A64DBE8E.1, Traes_4AS_9450AD3F4.1, Traes_4AS_A1A963CC4.1, Traes_4AS_FA4BBDBF9.2, Traes_4BL_21E038CCB.1, Traes_4BL_39AE2989D.1, Traes_4BL_5B2AF2556.1, Traes_4BL_71E35BBC1.1, Traes_4BL_762F09E09.1, Traes_4BL_7EC2BFC7B.1, Traes_4BS_180379032.1, Traes_4BS_591F7718A.1, Traes_4BS_DD5E68382.1, Traes_4DL_A739DE8B2.1, Traes_4DL_CB92B5ABB.1, Traes_4DL_D96E9236F.1, Traes_4DL_FB8B5AAEB.2, Traes_4DL_FE7B7E018.1, Traes_4DS_97AC77E13.1, Traes_4DS_9C01B536B.1, Traes_4DS_AB2BEFAB3.1, Traes_5AL_14D9A9844.2, Traes_5AL_27FB6BB0C.2, Traes_5AL_E9FE08F07.1, Traes_5BL_027509D0D.1,

Continue of Table B5

1	2
T. aestivum	Traes_5BL_0C3609EF0.2, Traes_5BL_199A847E4.1, Traes_5BL_310D4BA71.1, Traes_5BL_4D65B66E2.1, Traes_5BL_4E044468C.1, Traes_5BL_5299B6B33.1, Traes_5BL_60510E4A7.1, Traes_5BL_60FC12DA6.2, Traes_5BL_63E444E80.2, Traes_5BL_6647931E2.1, Traes_5BL_7F0FD1538.2, Traes_5BL_7F84602F3.1, Traes_5BL_8D6C8E27F.1, Traes_5BL_98D063967.2, Traes_5BL_B6A784025.1, Traes_5BL_B795CE108.2, Traes_5BL_C94A0F1D4.1, Traes_5BL_F5D379AFC.1, Traes_5BL_FBC7AF288.1, Traes_5BS_80C46D9C4.2, Traes_5DL_41E3B1B23.1, Traes_5DL_45B242D3E1.2, Traes_5DL_6003530B1.1, Traes_5DL_62A4CE1CC.2, Traes_5DL_96CF2E239.2, Traes_5DL_B49D156B7.1, Traes_5DL_BFA40F938.1, Traes_5DS_1BDB9837E.1, Traes_6AL_13895C140.1, Traes_6AL_2CA7515B31.2, Traes_6AL_3C182DED5.1, Traes_6AL_9BE9CB5E8.1, Traes_6AL_AFC0B56BD.1, Traes_6AL_DAA2D7F8A.1, Traes_6AL_DFEC1189D.1, Traes_6AL_DFEC1189D1.1, Traes_6AL_E6DAE246D.1, Traes_6AS_84E7FEDB3.1, Traes_6AS_8E7166D79.1, Traes_6AS_A9D28899F.1, Traes_6BL_6AEADC565.2, Traes_6BL_A8D141E69.1, Traes_6BS_2291F7F98.1, Traes_6BS_4C945B9F1.1, Traes_6DL_3019F176A.1, Traes_6DL_31D678054.1, Traes_6DL_5CA0A526A.1, Traes_6DL_7892214C8.1, Traes_6DL_7B2EC9B84.1, Traes_6DL_901793D6D.2, Traes_6DL_DD82BD107.2, Traes_6DL_FA861D610.2, Traes_6DL_FD6D63D1A.1, Traes_6DL_FECA3FE13.1, Traes_6DS_43372C0A6.2, Traes_6DS_E6A0BE6CD.1, Traes_7AL_0D52C1D87.1, Traes_7AL_C5F8733D0.3, Traes_7AS_89D49F177.1, Traes_7AS_D9A440FE2.1, Traes_7BL_0712EF0CA.2, Traes_7BL_9FED7F55E.1, Traes_7BL_E5CC8C8E7.1, Traes_7BL_EB1DCAB4B.1, Traes_7BS_51188D64E.1, Traes_7DL_538583735.1, Traes_7DL_E1D7A51C8.1, Traes_7DL_FBE71A7AE.2, Traes_7DS_3570A0055.2, Traes_7DS_433704E8E.1, Traes_7DS_433704E8E1.1

Table B6. Database of C2H2 family genes of *A. thaliana*, *O. sativa*, *Z. mays*, and *T. aestivum* [the list of genes was obtained in this study by Rakhmetullina A.K. based on PlantTFDB data]

C2H2 family	
Species	TF ID
1	2
A. thaliana	AT1G02030.1, AT1G03840.1, AT1G04445.1, AT1G08290.1, AT1G10480.1, AT1G13290.1, AT1G14580.1, AT1G24625.1, AT1G25250.1, AT1G26590.1, AT1G26610.1, AT1G27730.1, AT1G30970.1, AT1G34370.1, AT1G34790.1, AT1G51220.1, AT1G55110.1, AT1G66140.1, AT1G68130.1, AT1G72050.1,

Continue of Table B6

1	2
A. thaliana	AT2G45120.1, AT3G10470.1, AT3G13810.1, AT3G19580.1, AT3G20880.1, AT3G23130.1, AT3G29340.1, AT3G44750.1, AT3G45260.1, AT3G46070.1, AT3G46080.1, AT3G46090.1, AT3G48430.1, AT3G49930.1, AT3G50700.1, AT3G53600.1, AT3G53820.1, AT3G57480.1, AT3G57670.1, AT3G58070.1, AT3G60580.1, AT4G02670.1, AT4G06634.1, AT4G12240.1, AT4G16610.1, AT4G17810.1, AT4G25610.1, AT4G27240.1, AT4G35280.1, AT4G35610.1, AT4G35700.1, AT5G01860.1, AT5G03150.1, AT5G03510.1, AT5G03740.1, AT5G04240.1, AT5G04340.1, AT5G04390.1, AT5G05120.1, AT5G06070.1, AT5G06650.1, AT5G10970.1, AT5G14010.1, AT5G14140.1, AT5G15480.1, AT5G22890.1, AT5G22990.1, AT5G25160.1, AT5G27880.1, AT5G42640.1, AT5G43170.1, AT5G43540.1, AT5G44160.1, AT5G52010.1, AT5G56200.1, AT5G57520.1, AT5G59820.1, AT5G60470.1, AT5G61470.1, AT5G63280.1, AT5G66730.1, AT5G67450.1
O. sativa	LOC_Os01g09850.1, LOC_Os01g14010.1, LOC_Os01g39110.1, LOC_Os01g57020.1, LOC_Os01g57650.1, LOC_Os01g62130.1, LOC_Os01g62190.1, LOC_Os01g63980.1, LOC_Os01g65080.1, LOC_Os01g66570.1, LOC_Os01g67970.1, LOC_Os01g68160.1, LOC_Os01g70870.1, LOC_Os02g01090.1, LOC_Os02g02424.1, LOC_Os02g08510.1, LOC_Os02g31890.1, LOC_Os02g34680.1, LOC_Os02g35460.1, LOC_Os02g36360.1, LOC_Os02g44120.1, LOC_Os02g44130.1, LOC_Os02g45054.1, LOC_Os02g57550.1, LOC_Os02g57790.1, LOC_Os03g05480.1, LOC_Os03g05690.1, LOC_Os03g10140.1, LOC_Os03g13400.1, LOC_Os03g13600.1, LOC_Os03g15790.1, LOC_Os03g17150.1, LOC_Os03g31240.1, LOC_Os03g32220.1, LOC_Os03g49132.1, LOC_Os03g55540.1, LOC_Os03g60560.1, LOC_Os03g60570.1, LOC_Os03g62230.1, LOC_Os04g02510.1, LOC_Os04g08060.1, LOC_Os04g08290.1, LOC_Os04g08600.1, LOC_Os04g36650.1, LOC_Os04g39050.1, LOC_Os04g39520.1, LOC_Os04g46670.1, LOC_Os04g46680.1, LOC_Os04g47860.2, LOC_Os04g50070.1, LOC_Os04g59380.1, LOC_Os05g01550.1, LOC_Os05g02390.1, LOC_Os05g03020.1, LOC_Os05g14130.1, LOC_Os05g20930.1, LOC_Os05g37190.1, LOC_Os05g38600.1, LOC_Os05g38620.1, LOC_Os05g51830.1, LOC_Os06g07020.1, LOC_Os06g10470.1, LOC_Os06g20020.1, LOC_Os06g40960.1, LOC_Os06g51140.1, LOC_Os07g01180.1, LOC_Os07g23450.1, LOC_Os07g38240.1, LOC_Os07g39310.1, LOC_Os07g39970.1, LOC_Os07g40080.1, LOC_Os07g40780.1, LOC_Os07g40950.1, LOC_Os07g44640.1, LOC_Os08g17640.1, LOC_Os08g20580.1, LOC_Os08g36390.1, LOC_Os08g37904.1, LOC_Os08g37920.1, LOC_Os08g39390.1, LOC_Os08g44050.1, LOC_Os08g44190.1, LOC_Os08g44830.1, LOC_Os09g03500.1, LOC_Os09g10980.1, LOC_Os09g13680.1, LOC_Os09g26210.1, LOC_Os09g27650.2, LOC_Os09g31140.1, LOC_Os09g38340.1, LOC_Os09g38610.1, LOC_Os09g39660.1, LOC_Os10g07080.1, LOC_Os10g28330.1, LOC_Os11g06840.1, LOC_Os11g25610.1, LOC_Os11g30484.1, LOC_Os11g47620.1, LOC_Os11g47630.1, LOC_Os11g48000.1, LOC_Os12g07280.1, LOC_Os12g18150.1, LOC_Os12g38940.1, LOC_Os12g38960.1, LOC_Os12g39400.1

Continue of Table B6

1	2
Z. mays	AC149475.2_FGP005, AC149818.2_FGP008, AC183950.2_FGP002, AC185108.3_FGP011, AC185655.3_FGP004, AC185655.3_FGP005, AC198081.2_FGP005, AC198506.3_FGP001, AC201740.3_FGP003, AC206217.2_FGP006, AC211702.2_FGP002, AC211756.4_FGP001, AC211891.4_FGP001, AC215290.3_FGP002, AC233952.1_FGP008, AC234522.1_FGP009, AF546187.1_FGP012, GRMZM2G000103_P01, GRMZM2G000126_P01, GRMZM2G000836_P01, GRMZM2G001205_P01, GRMZM2G002805_P01, GRMZM2G003234_P01, GRMZM2G003927_P01, GRMZM2G006282_P01, GRMZM2G011357_P01, GRMZM2G021587_P01, GRMZM2G022213_P01, GRMZM2G023988_P01, GRMZM2G027333_P01, GRMZM2G027960_P01, GRMZM2G028046_P01, GRMZM2G028766_P01, GRMZM2G035103_P01, GRMZM2G035625_P01, GRMZM2G037574_P01, GRMZM2G038291_P01, GRMZM2G042666_P01, GRMZM2G048154_P01, GRMZM2G050939_P01, GRMZM2G058197_P01, GRMZM2G058868_P01, GRMZM2G061545_P01, GRMZM2G061897_P01, GRMZM2G068710_P07, GRMZM2G069176_P01, GRMZM2G071101_P01, GRMZM2G074032_P01, GRMZM2G074793_P01, GRMZM2G075956_P01, GRMZM2G081782_P01, GRMZM2G081812_P01, GRMZM2G084014_P01, GRMZM2G086277_P01, GRMZM2G086530_P01, GRMZM2G089557_P01, GRMZM2G090332_P01, GRMZM2G090595_P01, GRMZM2G093305_P01, GRMZM2G100146_P01, GRMZM2G104516_P01, GRMZM2G105092_P01, GRMZM2G105224_P01, GRMZM2G106026_P01, GRMZM2G108818_P01, GRMZM2G110107_P02, GRMZM2G112799_P01, GRMZM2G113860_P01, GRMZM2G114660_P01, GRMZM2G115388_P01, GRMZM2G120794_P01, GRMZM2G123094_P02, GRMZM2G129261_P01, GRMZM2G129428_P01, GRMZM2G132057_P01, GRMZM2G132756_P01, GRMZM2G134998_P01, GRMZM2G136494_P01, GRMZM2G137736_P01, GRMZM2G139160_P01, GRMZM2G140016_P01, GRMZM2G140033_P01, GRMZM2G141031_P01, GRMZM2G142502_P02, GRMZM2G143723_P01, GRMZM2G150011_P01, GRMZM2G150776_P01, GRMZM2G151309_P01, GRMZM2G157197_P01, GRMZM2G158141_P01, GRMZM2G159032_P01, GRMZM2G161255_P01, GRMZM2G165355_P01, GRMZM2G166782_P01, GRMZM2G170520_P01, GRMZM2G171073_P02, GRMZM2G172605_P01, GRMZM2G175000_P01, GRMZM2G177693_P01, GRMZM2G179677_P01, GRMZM2G302891_P01, GRMZM2G307402_P01, GRMZM2G320287_P01, GRMZM2G327741_P01, GRMZM2G329159_P01, GRMZM2G338056_P01, GRMZM2G344974_P01, GRMZM2G345155_P01, GRMZM2G350621_P01, GRMZM2G357688_P01, GRMZM2G359589_P01, GRMZM2G376061_P01, GRMZM2G380515_P01, GRMZM2G400714_P01, GRMZM2G402027_P01, GRMZM2G403590_P01, GRMZM2G408436_P01, GRMZM2G409452_P01, GRMZM2G417574_P01, GRMZM2G431157_P01, GRMZM2G435357_P01, GRMZM2G436344_P01, GRMZM2G443109_P01, GRMZM2G445684_P01, GRMZM2G455889_P01, GRMZM2G459540_P01, GRMZM2G459614_P01, GRMZM2G464580_P01, GRMZM2G465595_P01, GRMZM2G470422_P01, GRMZM2G703281_P01, GRMZM5G828179_P01, GRMZM5G883760_P01, GRMZM5G884137_P01, GRMZM5G885700_P01, GRMZM5G887286_P01, GRMZM5G898314_P02

Continue of Table B6

1	2
T. aestivum	TRAES3BF035900060CFD_t1, TRAES3BF042100060CFD_t1, TRAES3BF044200110CFD_t1, TRAES3BF048700110CFD_t1, TRAES3BF060000010CFD_t1, TRAES3BF064300010CFD_t1, TRAES3BF070600040CFD_t1, TRAES3BF094600010CFD_t1, TRAES3BF095600020CFD_t1, TRAES3BF099700020CFD_t1, TRAES3BF104200040CFD_t1, TRAES3BF105800110CFD_t1, TRAES3BF114300150CFD_t1, TRAES3BF127400030CFD_t1, TRAES3BF153400010CFD_t1, TRAES3BF153400050CFD_t1, TRAES3BF182900010CFD_t1, TRAES3BF231500020CFD_t1, Traes_1AL_319447519.1, Traes_1AL_7A2072713.1, Traes_1AL_80D0BD0DC.1, Traes_1AS_21ACC7F67.1, Traes_1AS_8B624F2DA.1, Traes_1AS_8F01029FE.1, Traes_1AS_B282BFB83.1, Traes_1AS_CD57D000A.1, Traes_1AS_DC6B18EE0.1, Traes_1BL_3EEA722DF.1, Traes_1BL_4026DC5011.2, Traes_1BS_0DEFAACB9.1, Traes_1BS_22E395F75.1, Traes_1BS_527ED00B9.1, Traes_1BS_7B7D5282B.1, Traes_1BS_CF75D4172.2, Traes_1DL_63D5C4C8E.2, Traes_1DS_0BBC3B5D3.1, Traes_1DS_75AF80583.1, Traes_1DS_CE96E8BF0.1, Traes_1DS_D1F453705.1, Traes_1DS_F40AC713C.2, Traes_2AL_3035352F3.1, Traes_2AL_7ABA7B7C8.1, Traes_2AL_C81692E4F.1, Traes_2AS_099955797.1, Traes_2AS_1913BF8B3.1, Traes_2AS_5A6E08D4E.1, Traes_2AS_D917848B7.1, Traes_2AS_DBA88CF6F.2, Traes_2AS_E9A1F35CB.1, Traes_2AS_FA70DB417.1, Traes_2BL_0A51FACEC1.1, Traes_2BL_41168D652.2, Traes_2BL_41EDFCA77.1, Traes_2BL_58A855C7B.2, Traes_2BL_78C496B63.1, Traes_2BL_9E38243B0.1, Traes_2BS_0544D9D4B.1, Traes_2BS_11131541B.1, Traes_2BS_13A816248.1, Traes_2BS_2C75C54A9.1, Traes_2BS_31F130A79.1, Traes_2BS_494F02775.1, Traes_2BS_67D862F4A.2, Traes_2BS_705DDDDC8.2, Traes_2BS_9C5982D89.1, Traes_2BS_ACA52BC08.1, Traes_2BS_C270C0C9F.2, Traes_2BS_DA786DC5B.1, Traes_2BS_DD07C2EE6.2, Traes_2DL_540050272.2, Traes_2DL_BF4319E7D.1, Traes_2DL_FE8D235D5.1, Traes_2DS_035AA95E3.1, Traes_2DS_11ADF414D.1, Traes_2DS_2CE71025C.1, Traes_2DS_B06BAC02B1.1, Traes_2DS_E1537CBD1.1, Traes_3AL_00FAACD5D.1, Traes_3AL_35CA14632.1, Traes_3AL_A8E345835.2, Traes_3AS_413E4DDF6.1, Traes_3AS_88AAED4BB.1, Traes_3B_4F4479FAF.1, Traes_3DL_0284E68CC1.1, Traes_3DL_8407DBC44.1, Traes_3DL_C1684BF20.2, Traes_3DL_D03A43799.3, Traes_3DS_4F293F5BA.1, Traes_3DS_9A5A4FE3E.1, Traes_4AL_24A54C8BA.2, Traes_4AL_37D98E743.1, Traes_4AL_76355F5F2.1, Traes_4AL_784CF40E5.1, Traes_4AL_A6AA602BC.1, Traes_4AL_FC7AEBB05.1, Traes_4AS_2718699A7.1, Traes_4AS_501676A91.1, Traes_4AS_D20DF472E.1, Traes_4AS_D4763E468.1, Traes_4AS_F7A905B43.1, Traes_4BL_38E55D7B4.1, Traes_4BL_3B919C814.1, Traes_4BL_581E788ED.1, Traes_4BL_C7F1E5ECA.1,

Continue of Table B6

1	2
T. aestivum	Traes_4BL_D10DEA6E9.1, Traes_4BL_DB9678C4C.2, Traes_4BS_23455E24F.1, Traes_4BS_6BEE72C38.1, Traes_4BS_86704D746.1, Traes_4BS_86704D7461.1, Traes_4BS_FE945D2FC.2, Traes_4DL_184FFC74B.2, Traes_4DL_3BEA40EE1.1, Traes_4DL_6EBD74330.2, Traes_4DL_7AC6C149F.1, Traes_4DL_AA51A43E7.1, Traes_4DL_D73F1E523.1, Traes_4DL_DF1F43E16.1, Traes_4DS_276818E4F.1, Traes_4DS_A0186B942.1, Traes_4DS_B63507774.1, Traes_5AL_78701B16C.1, Traes_5AL_81EFE5211.1, Traes_5AL_903412779.2, Traes_5AS_7E3208FD4.1, Traes_5BL_096B0BDA8.2, Traes_5BL_13B5BB344.2, Traes_5BL_388501B7C.1, Traes_5BL_3A9D3CEEF.2, Traes_5BL_3B50B6963.1, Traes_5BL_3E6B0CD61.1, Traes_5BL_46BDE583B.1, Traes_5BL_5391EC4A0.1, Traes_5BL_56E52A2FC.1, Traes_5BL_630A8A142.4, Traes_5BL_63AE36D3A.1, Traes_5BL_6888AE9CB.1, Traes_5BL_6F2D345E2.4, Traes_5BL_7F56360BF.1, Traes_5BL_8DB8274DB1.1, Traes_5BL_9301719551.1, Traes_5BL_9C687EE11.5, Traes_5BL_B038BE0A3.1, Traes_5BL_BA26BA910.1, Traes_5BL_BB99746DD.6, Traes_5BL_C2576EA84.1, Traes_5BL_C3F3A871A.1, Traes_5BL_D53A846BE.1, Traes_5BL_F2AF1D802.1, Traes_5BL_F74D668D9.1, Traes_5BS_23717182B.1, Traes_5BS_AF63E8E5C.2, Traes_5BS_CD57D000A.1, Traes_5DL_0C5F4342D.1, Traes_5DL_13706ACAF.2, Traes_5DL_3FBCC4C48.1, Traes_5DL_4831C18DC.1, Traes_5DL_4B4927090.1, Traes_5DL_4E890ABF3.1, Traes_5DL_50E35B4F3.1, Traes_5DL_6CBF61AA4.1, Traes_5DL_81A859497.1, Traes_5DL_90F570468.7, Traes_5DL_98FA0887C.1, Traes_5DL_9D713AD9C.1, Traes_5DL_AB989ABB3.1, Traes_5DL_B97546DA11.1, Traes_5DL_CE45A9676.1, Traes_5DL_DD8A0F6BE.1, Traes_5DL_F269EF70D.1, Traes_5DL_F8AEA5040.1, Traes_5DS_4C00D348F.1, Traes_5DS_818C09355.1, Traes_5DS_976CBF9EB.2, Traes_5DS_CB3830B22.2, Traes_6AL_1A07854E2.2, Traes_6AL_3DEF1B023.1, Traes_6AL_BA6465E82.1, Traes_6AL_BA6465E821.1, Traes_6AL_BA6465E822.1, Traes_6AS_448C7608C.2, Traes_6AS_AE7376F74.1, Traes_6AS_C15119294.1, Traes_6BL_CC009B78A.2, Traes_6BL_D87B09F77.1, Traes_6BS_D373D1A96.2, Traes_6DL_244C908B5.2, Traes_6DL_3B9E63F04.2, Traes_6DL_434BF5425.1, Traes_6DL_88DFCF552.1, Traes_6DL_9FC9C02351.1, Traes_6DL_F47CFC6D9.1, Traes_6DS_1E1A89D33.1, Traes_6DS_2B2F9C290.2, Traes_6DS_DE865EA6D.1, Traes_7AL_0BC1C3E70.1, Traes_7AL_1070DBD71.1, Traes_7AS_09344A629.1, Traes_7AS_8054DC45D.1, Traes_7AS_B60BC1735.1, Traes_7BL_83946C3EC.1, Traes_7BL_A86A9614E.1,

Continue of Table B6

1	2
T. aestivum	Traes_7DL_36AA043D1.2, Traes_7DL_38929DD1E.1, Traes_7DL_B0F38D6EB.3, Traes_7DL_BF9C602A5.2, Traes_7DL_EC744E159.2, Traes_7DL_F970BC94B.1, Traes_7DS_5084227F2.1

Appendix C

Table C1. Nucleotide sequences of ath-miR5021-5p binding sites in mRNA of C2H2, ERF, GRAS TF genes and their encoded amino acid sequences of *A. thaliana* [397, p. 8]

Gene	Nucleotide sequences of mRNA regions
AT5G52510.1	UUCACCGAGCUCUUCUUCUUCGUCUUCUUCGCCUUCUA
AT1G06160.1	CUCCUAUUCAUCUUCUUCGUCUUCUUCUUCUUUGUCGU
AT1G21910.1	AUCACCAUCUUCUUCUUCUUCUUCAUCUUCUUCCUCGU
AT1G77640.1	CUCUCAUUCUUCAUCUUCUUCUUCUUCUUCAACGUCGG
AT2G31230.1	AAAGCGAUCCUCUUCUUCUUCUUCUUCUUCUUCUAAUU
AT2G44940.1	ACCUACUACAUCUUCCUCUUCUUCGUCAUCAACAAAUU
AT3G23230.1	UCCUUAUGCUUCUUCUUCUUCGUCGUCGUCAUCGGGUU
AT5G13330.1	UUCAACGCCUUCUUCAUCUUCUUCUUCCUCCCAACAGA
AT3G57670.1	GCUCAUGAUGUCUUCUUCUUCCUCUUCCUCGAGGACCA
AT2G42410.1	UAAUUUUAGCUCUUCUUCUUCCUCUUCAACAACAACAG
AT3G19580.1	UCACAGCCCUUCUUCGUCUUCUUCCUCACCGCCUCGAU
AT4G16610.1	CUCGGUCUAUUCUUCUUCUUCCUCUUCCUCCGAUGGUA
AT3G13810.1	AAACGUCUCUUCUUCUUCAUCUUCCUCCCACAACCACA
AT5G57520.1	UUCCAUGUCUUCUUCUUCAUCUUCUUCCACGAACUCAU
Gene	Encoded amino acid sequences
AT5G52510.1	NPNPVLSFSPSSSSSSSSPSTASTTT
AT1G06160.1	SSPSSSSSYSSSSSSSLSSRSRKQS
AT1G21910.1	KEMPLSSSPSSSSSSSSSSSSSCKN
AT1G77640.1	TTSSSSLSHSSSSSSSTSALRHQSC
AT2G31230.1	RNRPRGKKRSSSSSSSSNSSSCSSS
AT2G44940.1	SASLSSSPTTSSSSSSTNSNFIEED
AT3G23230.1	DDYSLRPPYASSSSSSSSGSTSTNVS
AT5G13330.1	LFSQPFSTPSSSSSSQQTQQQQLQQ
AT3G57670.1	AQEMASLLMMSSSSSSSRTTHHHEDM
AT2G42410.1	PIANPNPNFSSSSSSSTTTAHLEPSL
AT3G19580.1	RSKRQRSHSPSSSSSSPPRSRPKSQN
AT4G16610.1	ARKKLGDSVYSSSSSSSDGKALAYGL
AT3G13810.1	HQTQPTINVSSSSSSSHNHNIINSLH
AT5G57520.1	ELVLEPSSMSSSSSSSTNSSSCLEQP

Table C2. Nucleotide sequences of ath-miR5658-5p binding sites in mRNA of C2H2, ERF, GRAS TF genes and their encoded amino acid sequences of *A. thaliana* [397, p. 8]

Gene	Nucleotide sequences of mRNA regions
AT1G14920.1	GAAGAGAGAUCAUCAUCAUCAUCAUCAUCAAGAUA
AT4G36900.1	AGGGAAUCGUCAUCAUCAUCAUCAUCAACAUCAAC
AT5G25160.1	GGAUAAUUUUCAUCAUCAUCAUCAUCAGAUGAUGA
AT1G55110.1	AAAUUCUCCUCAUCAUCAUCAUCAUCAAACACAAC
Gene	Encoded amino acid sequences
AT1G14920.1	GGAELSMKRDHHHHHHQDKKTMMMN
AT4G36900.1	LEAAGAGGNRHHHHHQHQRGNHDYV
AT5G25160.1	IGKFPSMDNFHHHHHQMMMMAPSVN
AT1G55110.1	PIMIQASNSPHHHHHQTQQNIGFSS

Table C3. Nucleotide sequences of osa-miR2102-5p binding sites in mRNA of C2H2, ERF, GRAS TF genes and their encoded amino acid sequences in different open reading frames of *O. sativa* [397, p. 8]

Gene	Nucleotide sequences of mRNA regions
1	2
LOC_Os03g07940.1	UACAACGCCGGCGGCGGCGGCGGCGGCGUCGUCGACGG
LOC_Os04g32790.1	CUCCUCGCCGGCGGCGGCGGCGGCGGCAGGCUCGCACG
LOC_Os06g11860.1	GCAGGCCGGGGCGGCGGCGGCGGCGGCGGCCGGCGGCA
LOC_Os06g42990.1	ACGCCGUCGCGCGGCGGCGGCGGCGGCGCCAUCAGCCC
LOC_Os07g22730.1	CGGGGCGGGGGCGGCGGCGGCGGCGGCGGGCUUCAUCG
LOC_Os01g09850.1	CGCCCACAUGGCGGCGGCGGCGGCGGCGAGCACGCACA
LOC_Os01g14010.1	CGGGGCCGCCGCGGCGGCGGCGGCGGCCACGGCCACGU
LOC_Os01g62190.1	CGACCCCGCCGCGGCGGCGGCGGCGGCGGCCGAGAGGG
LOC_Os11g47630.1	GUGGACGGCGGCGGCGGCGGCGGCGGCGACAAUGUCCG
Gene	Encoded amino acid sequences
LOC_Os03g07940.1	QWRRRRCTTPAAAAAASSTDPCRSPA
LOC_Os04g32790.1	DFASYSSSSPAAAAAAGSHGMYFEEG
LOC_Os06g11860.1	PRAQPMKQAGAAAAAAAGGKMYRGVR
LOC_Os06g42990.1	RGRGRSRRRRAAAAAAPSAPASEAPP
LOC_Os07g22730.1	AARKEEGGAGAAAAAAGFIGVRKRPW
LOC_Os01g09850.1	TTRPSSHAHMAAAAAASTHNSSSSAA
LOC_Os01g14010.1	ARLNAASGAAAAAAAATATSLCGQSY
LOC_Os01g62190.1	LQAKLLSDPAAAAAAAAERDRARVHE
LOC_Os11g47630.1	DDTMSTTWTAAAAAAATMSGSSSEER
Gene	Nucleotide sequences of mRNA regions
LOC_Os05g40710.1	CGCGCACGCCGGCGGCGGCGGCGGCGGGCGCGCGCAGC
LOC_Os06g40780.1	GAGGGAAGCAGGCGGCGGCGGCGGCGGCGGCGACCACA
LOC_Os02g09650.1	UGGUGGAGGCGGCGGCGGCGGCGGCGGCUUUGGCUGUG
LOC_Os07g44640.1	CGACGCGGGCGGCGGCGGCGGCGGCGGCGGGCUCCUCU
LOC_Os09g38340.1	CGGCAACCACGGCGGCGGCGGCGGCGGCUUCCCUUCUC
LOC_Os07g38750.1	CGUGAAGCAAGGCGGCGGCGGCGGCGGCGCACCAACGG
Gene	Encoded amino acid sequences
LOC_Os05g40710.1	VLARHGFAHAGGGGGGRAQLVAAACP
LOC_Os06g40780.1	AVVTIAEREAGGGGGGGDHIDDLPRR
LOC_Os02g09650.1	FDLNLPPGGGGGGGGFGCAYDDEEL

Continue of Table C3

1	2
LOC_Os07g44640.1	DWESDGDDAGGGGGGGLLCLFCSAR
LOC_Os09g38340.1	VTSSGLAGNHGGGGGGFPSLYNSSEP
LOC_Os07g38750.1	TDSCDGAVKQGGGGGGAPTDASEVYR

Table C4 Nucleotide sequences of osa-miR5075-3p binding sites in mRNA of C2H2, ERF, GRAS TF genes and their encoded amino acid sequences in different open reading frames of *O. sativa* [397, p. 8]

Gene	Nucleotide sequences of mRNA regions
LOC_Os11g04570.1	GCAGCGGAGCGCGGCGGCGGCGGCGGAGCGCGCGC
LOC_Os12g04370.1	GCAGCGGAGCGCGGCGGCGGCGGCGGAGCGCGCGC
LOC_Os06g09810.1	GCAGAAGAGCGCGGCGGCGGCGGCGGACGGCGGCA
LOC_Os04g02510.1	CGACUGCGGCGCGGCGGCGGCGGCGGCGCAGCAGG
LOC_Os06g10470.1	AGGCGGCGGCGCGGCGGCGGCGGCGGGGGAGACGA
Gene	Encoded amino acid sequences
LOC_Os11g04570.1	ASLFDCLQRSAAAAAERARVERVLL
LOC_Os12g04370.1	ASLFDCLQRSAAAAAERARVERVLL
LOC_Os06g09810.1	MEPVSFMQKSAAAAADGGSAAQAAA
LOC_Os04g02510.1	ASSGRAHDCGAAAAAAQQAGGCRAM
LOC_Os06g10470.1	EEAEEEAGGGAAAAAGETRRFECHY
Gene	Nucleotide sequences of mRNA regions
LOC_Os01g64790.1	CGUCGUGGCGGGCGGCGGCGGCGGCGGCGGCGACG
LOC_Os04g32790.1	AGCAGCAGCAGGCGGCGGCGGCGGAGGGAGGGAAU
LOC_Os04g46400.1	GGCGCAGGCGGGCGGCGGCGGCGGCGGCGUCGACA
LOC_Os05g28350.1	CAGCGGCGCCGGCGGCGGCGGCGGAGGGGGGAGAA
LOC_Os02g45054.1	CCUGCAGCGCGGCGGCGGCGGCGGCGGCGACGGCG
LOC_Os07g44640.1	CGACGACGCGGGCGGCGGCGGCGGCGGCGGCGGGC
Gene	Encoded amino acid sequences
LOC_Os01g64790.1	MVSALARVVAGGGGGGGDGDGDQWA
LOC_Os04g32790.1	YFYSSSAAAAGGGGGGGEKKSSSSS
LOC_Os04g46400.1	NAAASGKAQAGGGGGGVDSSSTCTA
LOC_Os05g28350.1	AETAASSSGAGGGGGGGRTKKKAAG
LOC_Os02g45054.1	QHEVKFSLQRGGGGGGDGDVTRDFL
LOC_Os07g44640.1	DDWESDGDDAGGGGGGGGLLCLFCS

Appendix D.

Table D1. Binding characteristics of zma-miR529-3p to human mRNA genes [401, p. 342-343]

Gene	Start of BS, nt	Region of RNA	ΔG, kJ/mole	ΔG/ΔGm, %
ATP6V0A4	241	5'UTR	-106	94
CHD2	6684	3'UTR	-106	94
MLL	11418	CDS	-106	94
PDE4B	2270	CDS	-106	94
LMO7	4210	CDS	-102	91
LRTOMT	1111	CDS	-102	91

Continue of Table D1

1	2	3	4	5
LTB4R	3117	3'UTR	-102	91
NUDC	455	CDS	-102	91
POMC	1055	CDS	-102	91
SOX9	92	5'UTR	-102	91

Table D2. Nucleotide sequences of mRNA regions of human genes containing zma-miR529-3p binding sites [401, p. 342-343]

Gene	Nucleotide sequences of mRNA regions
ATP6V0A4	UCUCUGAAGA**GAAGAAGAGAGAGAGACACAGC**CAAGACCGA
CHD2	UUGGGGUGGA**GAAGUAGAGAGAGGGCAACAGC**UUCCACAAC
MLL	CCCCAAUGAU**GAAGAAGAGGAGGAGGUACAGC**UGAAGUCAG
PDE4B	AAGGACCUGA**GAAGGAGGGAGAGGGACACAGC**UAUUUCAGC
LMO7	AACCCGAGCA**GGAGAAGAGGAGAGGAGACAGC**CACAAGAGG
LRTOMT	GGAACCCCAU**GGAGGAAGAGAAAGGGUAUAGC**AGGCCCUGG
LTB4R	GAGUGGAGUG**GAAGAAGAGGGAGAGGUGGAGC**AAAGUGAGG
NUDC	GCUAACUGAU**GAAGAGGCAGAGAGGCUGCAGC**UAGAGAUUG
POMC	ACGCCUACAA**GAAGGGCGAGUGAGGGCACAGC**GGGGCCCCA
SOX9	CUUUGCAGGA**GGAGAAGAGAAGGGGUGCAAGC**GCCCCCACU

Table D3. Binding characteristics of zma-miR159e-5p to human mRNA genes [401, p. 342-343]

Gene	Start of BS, nt	Region of mRNA	ΔG, kJ/mole	ΔG/ΔGm, %
BZRAP1	72	5'UTR	-104	91
FEN1	1040	CDS	-104	91
LZTS1	1524	CDS	-106	93
PDE6B	218	CDS	-104	91
PRCD	755	3'UTR	-104	91

Table D4. Nucleotide sequences of mRNA regions of human genes containing zma-miR159e-5p binding sites [401, p. 342-343]

Gene	Nucleotide sequences of mRNA regions
BZRAP1	GCAGUCCCCA**GAGCAGAGGCCAGCAGGGGCUG**AGACUAUGA
FEN1	AAUUCCACCU**GAGCCGGAUUCUGCAGGAGCUG**GGCCUGAAC
LZTS1	UCCUCGACGA**GAGCAGAUGGCUGCAGCAGCUG**CCAGACCUA
PDE6B	AGGUGGAGGA**GAGCACGGCGCUGCUGGAGCUG**GUGCAGGAU
PRCD	CCAGAUCCAG**GAGCAGACCCUGCAGGCAGCUG**CUCCUGAUG

Table D5. Binding characteristics of zma-miR164b-3p to human mRNA genes [401, p. 342-343]

Gene	Start of BS, nt	Region of mRNA	ΔG, kJ/mole	ΔG/ΔGm, %
1	2	3	4	5
DYSF	5983	CDS	-100	92
EXOC7	2252	CDS	-102	94

Continue of Table D5

1	2	3	4	5
HPD	954	CDS	-100	92
ITGA7	3496	CDS	-102	94
PTPRF	3163	CDS	-100	92
ZNF37A	5222	3'UTR	-102	94

Table D6. Nucleotide sequences of mRNA regions of human genes containing zma-miR164b-3p binding sites [401, p. 342-343]

Gene	Nucleotide sequences of mRNA regions
DYSF	UGAGCCUCAC**GGGGGAGAAGAUGAGCGACAU**UUAUGUGAA
EXOC7	UCAAGUACGG**GGUGGAGCAGGUGGGCGACAU**GAUCGAUCG
HPD	CACACACCCU**GGUGGAGAAGAUGAACUACAU**CGGCCAAUU
ITGA7	AGCAGUUCAA**GGAGGAGAAGACGGGCACCAU**CCUGAGGAA
PTPRF	CGCCAGUGCU**GGCGGAGAGGAACGGGCGCAU**CAUCAGCUA
ZNF37A	GGAAGGGACA**GGGGGAGGAGAUGGGCAGCAU**UGUUGAGAG

Table D7. Binding characteristics of tae-miR408-3p to human mRNA genes [401, p. 342-343]

Gene	Start of BS, nt	Region of mRNA	ΔG, kJ/mole	ΔG/ΔGm, %
RBMS2	7343	3'UTR	-113	95
NGB	218	5'UTR	-108	91
ALPK3	602	CDS	-108	91
EDEM1	354	CDS	-108	91
PAQR6	1079	CDS	-110	93
UNG	260	CDS	-108	91

Table D8. Nucleotide sequences of mRNA regions of human genes containing tae-miR408-3p binding sites [401, p. 342-343]

Gene	Nucleotide sequences of mRNA regions
RBMS2	GCUGUGAUAG**GCCAGGGGAGUAGGCUGUGCAG**UGACGGCUU
NGB	UCUCUCCCGC**GCCAGGGAAGGAGCGGCUGCGG**CCCCCGCCG
ALPK3	GUCGGGCCAG**GCCAGGGGAGGGACAGCAGCAG**GUGACGACG
EDEM1	GGCUGCAGCC**GCCGGGGACCGGGGCAGCGCAG**AGCCCGCGC
PAQR6	GCCUGGCCCG**GCCCGGGAAGAGGCAGGGGCAG**AUGCCUUCC
UNG	AGCUGCGGAC**GCCUGGGAAGGGGCCGCUGCAG**CUCUUGAGC

Table D9. Binding characteristics of tae-miR444a,b-3p to human mRNA genes [401, p. 342-343]

Gene	Start of BS, nt	Region of mRNA	ΔG, kJ/mole	ΔG/ΔGm, %
1	2	3	4	5
AP1B1	2787	CDS	-104	91
COL6A3	9106	CDS	-104	91

Continue of Table D9

1	2	3	4	5
DOCK1	1960	CDS	-104	91
HIC1	2077	CDS	-104	91
KRT6A	460	CDS	-104	91
KRT6B	299	CDS	-104	91
KRT6C	299	CDS	-104	91
RHBDF1	1071	CDS	-108	94
RUNDC1	1191	CDS	-108	94

Table D10. Nucleotide sequences of mRNA regions of human genes containing tae-miR444a,b-3p binding sites [401, p. 342-343]

Gene	Nucleotide sequences of mRNA regions
AP1B1	GAGGCUGCGA**GCAGCAAGCUGCAGAGCAGCAA**CAUCUUCAC
COL6A3	GCCAGCAACG**GCAGCGAAGCCUGUAGCAGCAA**AGCCAGCAG
DOCK1	CCAGCCUGCU**GCAGCAGAACUUGAGGCAGCUG**AUGAAAGUC
HIC1	UCACGGCCGA**GCAGCUGAGCCUGAAGCAGCAG**GACAAGGCG
KRT6A	GGCGGCUAUG**GCAGCAGAGCCGGAGGCAGCUA**UGGCUUUGG
KRT6B	GGCGGCUAUG**GCAGCAGAGCCGGAGGCAGCUA**UGGCUUUGG
KRT6C	GGCGGCUAUG**GCAGCAGAGCCGGAGGCAGCUA**UGGCUUUGG
RHBDF1	GCCCUGGACC**GCAGCGAGCUUGAGCGCAGCCA**CCUGAUGCU
RUNDC1	ACAGAGUGAA**GCAGCUAGCCUUGAGGCAGCAG**CCACAUGAC

Table D11. Binding characteristics of tae-miR9653b-5p to human mRNA genes [401, p. 342-343]

Gene	Start of BS, nt	Region of mRNA	ΔG, kJ/mole	ΔG/ΔGm, %
ITIH4	3084	3'UTR	-106	93
TMEM184A	2137	3'UTR	-104	91
AOC3	1250	CDS	-113	98
LOC101927064	489	CDS	-104	91
RBM19	1949	CDS	-104	91
TEAD2	245	CDS	-104	91
TEAD3	360	CDS	-104	91

Table D12. Nucleotide sequences of mRNA regions of human genes containing tae-miR9653b-5p binding sites [401, p. 342-343]

Gene	Nucleotide sequences of mRNA regions
ITIH4	UUCCACUGUC**AGCUCUCAAGAGCCCAUGGCCA**GGAAGGCCC
TMEM184A	UCCACACGCC**AGCCACAGGGGAGCCCUGGCCA**GGCGCCCAG
AOC3	UUAUGAGAUA**AGCCUCCAAGAGGCCUUGGCCA**UCUAUGGUG
LOC101927064	UCCACACGCC**AGCCACAGGGGAGCCCUGGCCA**GGCGCCCAG
RBM19	CUGGCGGCCC**AGCUGCAGGAGACCUUCGGCCA**UUUUGGCAG
TEAD2	CAUUGAGCAG**AGCUUCCAGGAGGCCCUGGCCA**UCUAUCCAC
TEAD3	CAUCGAGCAG**AGCUUCCAGGAGGCCCUGGCCA**UCUACCCGC

Table D13. Single zma-miRNA target human genes involved in biological processes [401, p. 342-343]

Gene	Gene involvement in disease
1	2
ADIPOR1	Kidney failure DOI: 10.3109/0886022X.2013.830975
AKAP11	Osteoporosis DOI:10.7150/ijms.25369
ARAP3	Papillary thyroid carcinoma Doi: 10.2147/OTT.S115668
ATP2A3	Gastric and colon cancer DOI: 10.1002/mc.22978
ATP6V0A4	Distal renal tubular acidosis DOI:10.5414/CN107505
CDKN1C	Silver-Russell syndrome Doi: 10.1186/s13148-020-00945-y. Beckwith-Wiedemann syndrome (BWS) DOI: 10.1136/jmedgenet-2020-107401
CHD2	Epileptic encephalopathy DOI: 10.1212/WNL.0000000000001305
CSF1	Malignant neoplasm of breast DOI: 10.1016/j.bbagrm.2018.10.008
DNAH3	Breast cancer DOI: 10.1186/s12967-018-1504-9
EXOC4	Alzheimer disease Doi: 10.1001/jamaneurol.2013.3545
FAM168A	Chronic myeloid leukemia DOI: 10.1186/s12885-019-5898-4
FGF17	Idiopathic hypogonadotropic hypogonadism Doi: 10.1016/j.fertnstert.2019.08.069
KCNK16	Diabetes Mellitus, Non-Insulin-Dependent Doi: 10.18388/abp.2018_2632.
LARP1	Malignant neoplasm of lung Doi: 10.1016/j.bbrc.2018.06.172.
LMBRD2	Neurodevelopmental disorder DOI: 10.1136/jmedgenet-2020-107137
LMO7	Vulvar squamous cell carcinoma Doi: 10.3892/or.2019.7138
LRTOMT	Hearing loss (HL) DOI: 10.1186/s12881-020-01061-7
LTB4R	Inflammation and platelet-activating factor-induced anaphylaxis DOI: 10.1084/jem.192.3.433
LUZP2	Low-grade glioma DOI: 10.1155/2020/9716720
MLL	Leukemia DOI:10.1073/pnas.88.23.10735
NUDC	Acute lymphocytic leukemia Doi: 10.3109/10428190009113375
PDE4B	Schizophrenia Doi: 10.1016/j.pnpbp.2019.109729
PLXNA3	Endometrial Carcinoma DOI: 10.1158/1541-7786.MCR-11-0213
PNPO	Neonatal epileptic encephalopathy DOI: 10.3389/fphar.2019.01086
POMC	Obesity DOI: 10.1093/jmcb/mjz053
POP1	Anauxetic dysplasia DOI: 10.1002/ajmg.a.37839
PPIE	Bipolar Disorder DOI: 10.1038/sj.mp.4002001
PTER	Membranous nephropathy (MN) DOI: 10.1186/1423-0127-21-32
RIMS3	Autistic Disorder DOI: 10.1136/jmg.2008.065821
ROBO4	lung cancer DOI: 10.1038/s41598-020-78882-2
SLC35A2	Solute carrier family 35 member A2 congenital disorder of glycosylation DOI: 10.1002/humu.23731
SLC44A4	Nonsyndromic Deafness DOI: 10.1093/hmg/ddw394
SOX9	Campomelic dysplasia DOI: 10.1016/j.braindev.2017.09.002
STK32A	Non-small cell lung cancer DOI: 10.1186/s12885-020-07056-0
THAP9	Pediatric Septic Shock DOI: 10.1155/2020/7170464
TMCO5A	Spermiogenesis DOI: 10.1002/mrd.23108
TTC25	Primary ciliary dyskinesia DOI: 10.1016/j.ajhg.2016.06.014
ZDHHC3	Malignant neoplasm of breast Doi: 10.1158/0008-5472.CAN-17-1536
ZNF853	Neurophysiological processes doi: 10.1183/23120541.00123-2018
Note - genes involved in the development of diseases are indicated as: oncological - purple, neurodegenerative - blue, others - yellow and green color	

Table D14. Single tae-miRNA target human genes involved in biological processes [401, p. 342-343]

Gene	Gene involvement in disease
1	2
AARS2	Late-Onset Dilated Cardiomyopathy Doi: 10.1161/CIRCGEN.120.003086
AGRP	Obesity Doi: 10.1186/1471-2350-10-63
AIM1	Prostate cancer DOI: 10.1038/s41467-017-00084-8
ALPK3	Autosomal Dominant Adult-onset Hypertrophic Cardiomyopathy Doi: 10.1161/CIRCGEN.120.003127
AP2A2	Coronary artery disease DOI:10.1186/s12872-018-0905-2
ARVCF	Schizophrenia DOI: 10.4088/JCP.10m06491
ASRGL1	Endometrial carcinoma DOI: 10.1016/j.ygyno.2015.03.055
ASXL1	Myeloid leukemia DOI: 10.1080/10428194.2018.1433298
ATRIP	Essential role in preventing DNA damage accumulation during unchallenged replication Doi: 10.1038/s41419-020-03227-w.
RBMS2	Tumor suppressor in breast cancer DOI: 10.1186/s13046-018-0968-z
HES4	Osteosarcoma Doi: 10.1002/pbc.26318
UBE2K	Embryonic stem cells Doi: 10.1038/s42003-020-0984-3
C15orf55	Hepatocellular carcinoma (HCC) DOI: 10.1111/cas.13884
C21orf2	Amyotrophic lateral sclerosis DOI: 10.1016/S1474-4422(17)30401-5
C7	Meningococcal disease DOI: 10.1016/j.molimm.2009.10.017
C9orf50	Colorectal cancer DOI: 10.1371/journal.pone.0050266
CCDC178	Hepatocellular carcinoma Doi: 10.1038/onc.2017.10
CFLAR	Cerebral ischaemia-reperfusion injury Doi: 10.1016/j.biopha.2019.109155
INO80D	Aortic hypoplasia DOI: 10.1161/CIRCGENETICS.113.000233
LRRC34	Spermatogonial stem cells Doi: 10.24920/003680
RHBDD1	Colorectal cancer Doi: 10.1186/s13046-018-0709-3
CCND2	Hepatocellular carcinoma DOI: 10.12659/MSM.927444
CDAN1	Congenital dyserythropoietic anemia type I DOI: 10.1016/j.exphem.2020.09.201
CDH9	Autism spectrum disorders DOI: 10.1186/s13041-019-0461-4
CDON	Holoprosencephaly 11 DOI: 10.1016/j.ajhg.2011.07.001
CIB2	Deafness, autosomal recessive 48 DOI: 10.1007/s00405-016-4330-9
CLDN10	Clear cell renal cell carcinoma (ccRCC) DOI: 10.2217/epi-2020-0256
CNST	Tumorigenesis of Osteosarcoma Cells DOI: 10.1177/0963689720926147
CPN1	Breast cancer Doi: 10.2174/1871520620666200703191135.
DAB2	Coronary artery disease risk Doi: 10.3389/fcell.2020.624159
DCLK1	Colorectal Carcinoma DOI: 10.1093/carcin/bgz157
DHX30	Neurodevelopmental Disorder doi: 10.1016/j.ajhg.2017.12.016
DNAH14	Lung Diseases in Cystic Fibrosis DOI: 10.1513/AnnalsATS.201706-451OC
GSE1	Breast cancer DOI: 10.1016/j.bbrc.2016.01.168
DOCK10	Senescence DOI: 10.1016/j.heliyon.2019.e01391
EDEM1	Colorectal cancer DOI: 10.18632/aging.202354
ENTPD2	Biliary cirrhosis DOI: 10.1136/jim-52-07-42
EPS8	Malignant tumours DOI: 10.3892/or.2021.7927
FLCN	Birt-Hogg-Dubé (BHD) syndrome DOI: 10.1097/CM9.0000000000000442
FNTA	Malignant Neoplasms DOI: 10.1111/j.1365-2141.2011.08817.x
GIPR	Diabetes Mellitus, Non-Insulin-Dependent DOI: 10.3389/fendo.2019.00075
GPR123	Neuronal signal transduction. DOI: 10.1111/j.1471-4159.2006.04281.x
GPR55	Malignant Neoplasms DOI: 10.1172/jci.insight.122947

Continue of Table D14

1	2
TACR1	Hepatocellular Carcinoma DOI: 10.2147/CMAR.S259243
NIPAL4	Autosomal recessive congenital ichthyosis DOI: 10.1111/ced.12740
GTPBP3	Primary angle closure glaucoma DOI: 10.1089/dna.2019.5079
HBP1	Osteoarthritis DOI: 10.3892/etm.2020.9541
HECTD3	Malignant Neoplasms DOI: 10.1007/s00018-019-03339-3
HPDL	Neurodegenerative disease DOI: 10.1038/s41436-020-01010-y
HSD3B1	Malignant neoplasm of prostate DOI: 10.1210/en.2019-00366
HSPG2	Schwartz-Jampel Syndrome, Type 1 DOI: 10.1016/j.nmd.2016.07.004
IL4I1	Melanoma DOI: 10.1002/eji.201041119
ING1	Colon cancer DOI: 10.1038/s41392-020-0206-y
JAGN1	Severe congenital neutropenia DOI: 10.1111/bjh.17135
KCNA1	Episodic ataxia type 1 DOI: 10.1016/j.neuroscience.2008.09.022
PDK2	Neoplasms DOI: 10.18632/oncotarget.16991
LMO3	Central neuroblastoma DOI: 10.1016/j.bbrc.2009.12.010
LRP8	Schizophrenia DOI: 10.1016/j.schres.2017.05.002
SLC38A2	Breast cancer DOI: 10.1038/s41416-020-01113-y
PCLO	Major Depressive Disorder DOI: 10.1016/j.jad.2012.01.028
RNASE3	Cerebral malaria (CM) DOI: 10.1371/journal.pone.0029465
LTBP4	Muscular Dystrophy, Duchenne DOI: 10.1002/ana.23819
LYNX1	Ovarian cancer Doi: 10.1155/2020/1392674
LYST	Chediak-Higashi Syndrome DOI: 10.1038/s41598-019-42159-0
LZTFL1	Breast cancer DOI: 10.1186/s12885-019-5951-3
MAF	Esophageal cancer DOI: 10.3960/jslrt.19002
MDP1	Malignant neoplasm of stomach PMID: 28678323
MEX3C	Carcinoma of bladder DOI: 10.2147/OTT.S199667
MFI2	Colorectal Cancer DOI: 10.1007/s10620-020-06064-1
MIER1	Breast carcinoma DOI: 10.4267/2042/46943
MIER3	Malignant Neoplasms DOI: 10.1038/s41598-017-11374-y
MLPH	Prostate Cancer DOI: 10.2147/OTT.S225023
MOG	Narcolepsy-Cataplexy Syndrome DOI: 10.1016/j.ajhg.2011.08.007
MYO1G	Neoplasm Metastasis DOI: 10.1002/prca.201900030
NGB	Alzheimer's Disease DOI: 10.1016/j.neuroscience.2019.05.039
NOM1	Diabetes DOI: 10.3892/etm.2016.3576
NOTCH2	Hajdu-Cheney Syndrome DOI: 10.1007/s00198-013-2298-5
NPFF	Central nervous system Doi: 10.1096/fj.201902978R
NUAK1	Nasopharyngeal carcinoma DOI: 10.1007/s00405-018-5095-0
NUP50	Nuclear protein export DOI: 10.1128/mcb.20.15.5619-5630.2000
OR51E2	Prostate cancer DOI: 10.18632/oncotarget.13836
ORAOV1	Hepatocellular carcinoma. PMID: 33161447
SIK2	Pancreatic cancer DOI: 10.1002/cbin.11396
PAQR6	Nongenomic actions of rapid steroid response. DOI: 10.1089/dna.2011.1262
UNG	Somatic hypermutation and class switch recombination DOI: 10.1093/intimm/dxu071
PAX1	Otofaciocervical Syndrome DOI: 10.1111/cge.13085
PCDHGA12	Lung cancer DOI: 10.3892/ol.2018.8699
PLEKHG3	Autistic Disorder DOI: 10.1002/aur.186
PRR11	Tongue squamous cell carcinoma (TSCC). DOI: 10.7150/jca.29265; Esophageal carcinoma DOI: 10.3892/ol.2020.11615

Continue of Table D14

1	2
PTCHD1	Intellectual Disability DOI: 10.1038/s41598-019-49781-y
PTPMT1	Malignant Neoplasms DOI: 10.1016/j.ebiom.2018.11.007
RASL10B	Tumor suppressor potential DOI: 10.1007/s10529-006-9176-6
RAX	Anophthalmos DOI: 10.1210/jc.2018-02316
REEP3	Autistic Disorder DOI: 10.1038/sj.ejhg.5201785
RYR2	Ventricular tachycardia, catecholaminergic polymorphic, 1 DOI: 10.1016/j.jelectrocard.2017.10.002
SERPING1	Hereditary Angioedema Type I DOI: 10.1186/s13023-014-0103-y
SHANK1	Autism spectrum disorders (ASD) DOI: 10.1007/s11427-015-4892-6
SLC27A3	Autism spectrum disorders Doi: 10.1038/srep16239
SLC47A1	Type 2 diabetes PMID: 28775995
SLC5A10	Arteriosclerosis DOI: 10.1038/s41598-019-42202-0
SORL1	Alzheimer's disease DOI: 10.1186/s13041-020-00681-7
SPRN	Creutzfeldt-Jakob disease DOI: 10.1038/s41598-019-51625-8
SPRY4	Colorectal cancer doi: 10.1080/19768354.2020.1784274
TRAK2	Osteosarcoma Doi: 10.1002/jbt.22511
SPTAN1	Autosomal recessive hereditary spastic paraplegia DOI: 10.1038/s10038-019-0669-2
STX6	Progressive supranuclear palsy DOI: 10.1016/j.parkreldis.2013.01.019
TCF7L2	Diabetes Mellitus, Non-Insulin-Dependent transcription factor 7-like 2 DOI: 10.1111/nmo.13724
TCFL5	Transcription factor-like 5, Spermiogenesis DOI: 10.1111/j.2047-2927.2013.00069.x
TGFBR3	Oesophageal squamous cell carcinoma DOI: 10.1111/iep.12380
TGOLN2	Bipolar disorder Doi: 10.1002/ajmg.b.31068
TMEM178B	Melanoma DOI: 10.1038/onc.2016.486
TPM3	Breast cancer DOI: 10.1002/2211-5463.12759
USP14	Adenocarcinoma Doi: 10.1007/s10735-020-09934-0
TSPYL6	Breast Carcinoma DOI: 10.18632/oncotarget.10754
U2AF2	Malignant Neoplasms DOI: 10.1021/acs.biochem.7b00551
UGT1A7	Pancreatic cancer DOI: 10.7314/apjcp.2015.16.4.1651
UGT1A9	Propofol metabolism in children. DOI: 10.2147/PGPM.S231329
URB1	Colorectal cancer DOI: 10.1111/cas.14643
VCAN	Hyaloideoretinal degeneration of Wagner DOI: 10.1038/ejhg.2012.137
WDR45	Neurodegeneration with brain iron accumulation 5 DOI: 10.1080/15548627.2019.1630224
ZFHX3	Atrial Fibrillation DOI: 10.1111/apha.13322
ZNF488	Nasopharyngeal carcinoma DOI: 10.2147/CMAR.S200001
ZNF652	Prostate cancer DOI:10.3892/or_00000731 Breast cancer DOI:10.1002/jcb.23214
Note - genes involved in the development of diseases are indicated as: oncological - purple, neurodegenerative - blue, cardiovascular - green, others – yellow and mustard color	

Table D15. Family zma-miRNA target human genes involved in biological processes [401, p. 342-343]

Gene	Gene involvement in disease
1	2
ADARB2	Brain function DOI: 10.1093/nar/gkz815
ADCY1	Deafness, autosomal recessive 44 Doi: 10.1093/hmg/ddu042
ADCY6	Luminal-like breast cancer. DOI: 10.1002/jcb.29633

Continue of Table D15

1	2
ADRA1D	Hypertensive disease DOI: 10.1371/journal.pone.0037145
AHCYL2	Insulin metabolism and lipid metabolism pathways DOI: 10.1093/jas/skz031
ALDH4A1	Hyperprolinemia type 2 DOI: 10.1159/000028400
ALKBH5	Malignant neoplasm of breast DOI: 10.1186/s13046-019-1159-2
ALPK3	Autosomal Dominant Adult-onset Hypertrophic Cardiomyopathy Doi: 10.1161/CIRCGEN.120.003127
AMMECR1L	Linked to a new syndrome with growth, bone, heart, and kidney alterations DOI: 10.1002/humu.23373
ANO4	Stimulated Aldosterone Secretion. Doi: 10.1161/HYPERTENSIONAHA.119.13287
AP2A2	Coronary artery disease DOI:10.1186/s12872-018-0905-2
APBB1	Cancer stem cell(CSC) DOI: 10.1016/j.bbrc.2016.11.030
ARHGAP30	Tumor suppressor in lung cancer DOI: 10.2147/OTT.S175255
ASPSCR1	Alveolar Soft Part Sarcoma DOI: 10.1016/j.urology.2019.04.002
ASXL1	Myeloid leukemia DOI: 10.1080/10428194.2018.1433298
ATF6B	Asthmatics DOI: 10.4168/aair.2014.6.2.142
BAHCC1	Human acute leukemia DOI: 10.1038/s41588-020-00729-3
BCL9L	Osteosarcoma Cells Doi: 10.3389/fcell.2020.594135
BIN2	Alzheimer's Disease DOI: 10.1038/s41598-017-17999-3
BRD3	Acetylation in H2A.Z. DOI: 10.1002/pro.4006
BZRAP1	Hepatocellular carcinoma doi: 10.1186/s12967-019-02145-6.
C6orf223	Age related macular degeneration DOI: 10.1038/ncomms7063
CA6	Dental caries DOI: 10.3390/ijms20112673
CACNB1	Malignant tumor of colon DOI: 10.1016/j.gene.2018.02.007
CCDC117	Coiled-coil-domain-containing 117 Doi: 10.1038/s41598-019-39078-5
CCNY	Hypertension and hypertension of renal origin DOI:10.5603/EP.a2018.0079
CD22	B-cell inhibition to keep humoral immunity in check DOI:10.1038/s41467-017-00836-6
CD276	Hepatocellular Carcinoma DOI: 10.2147/OTT.S271891
CDK18	Glioblastoma Doi: 10.1038/s41467-019-10993-5.
CEP250	Usher syndrome which is characterized by early-onset sensorineural hearing loss (SNHL) and a relatively mild retinitis pigmentosa DOI:10.1080/13816810.2018.1466338
CER1	Early embryogenesis in primates and rodents PMID: 16596263
CHRM1	Asthma Doi 10.1007/s11033-014-3060-6
CHTF18	Ensures the quantity and quality of the ovarian reserve DOI: 10.1093/biolre/ioaa036
CIB3	Male fertility DOI: 10.1590/1414-431X20176177
CPNE6	Glioblastoma Multiforme DOI: 10.1155/2018/4246703
CSRNP1	Hypoxic-Ischemic Encephalopathy DOI: 10.4103/1673-5374.264469
CYP1A1	Wider roles in cancer progression and prevention DOI: 10.1186/1471-2407-9-187
DAB2	Cystic Fibrosis Doi: 10.2174/138161282266616100616103 3
DDX11	Warsaw breakage syndrome DOI: 10.3390/genes9110564
DEAF1	The Transcription Factor Deaf1, Regulate Skin Appendage Fate Doi: 10.1016/j.jid.2019.05.007
DGCR8	DiGeorge syndrome Doi: 10.1038/s41467-019-10831-8

Continue of Table D15

1	2
DMAP1	Pancreatic cancer DOI: 10.1186/s12943-018-0919-5
DNAJB6	Esophageal Squamous Cell Carcinoma Doi: 10.1007/s10620-019-05929-4
DOK6	Scute myeloid leukemia (AML) DOI: 10.1002/cam4.2540
DUOX1	Chronic obstructive pulmonary disease (COPD) DOI: 10.1172/jci.insight.142189
DYRK1A	Ocular pathology DOI: 10.3390/genes12020234
DYRK1B	Mediator of transcription repression on damaged chromatin DOI: 10.1073/pnas.2002193117
DYSF	Calcium-activated plasma membrane repair Doi: 10.1042/BCJ20200773
EDEM1	Colorectal cancer DOI: 10.18632/aging.202354
EDN1	Diabetic foot DOI: 10.4149/BLL_2019_009
EDN3	Hirschsprung Disease DOI: 10.1097/GIM.0b013e3181c371b0
EPHB6	Colorectal Carcinoma DOI: 10.1038/srep43702
EPS8	Malignant tumours DOI: 10.3892/or.2021.7927
ERICH1	Tumour suppressor genes in PDAC DOI: 10.1159/000178871
EVC2	Ellis-Van Creveld Syndrome DOI: 10.1007/s00438-015-1151-2
EXOC7	Cervical Cancer Doi: 10.7754/Clin.Lab.2019.191203
FAM205A	Intracerebral hemorrhage (ICH) DOI: 10.3892/br.2018.1104
FAM43B	Hepatocellular carcinoma DOI: 10.1007/s11010-011-0800-y
FAM57A	Postoperative pathological remission DOI: 10.19723/j.issn.1671-167X.2019.03.025
FEN1	Malignant neoplasm of lung DOI: 10.1002/1878-0261.12058
FLAD1	Gastric Cancer Doi: 10.7150/ijms.48162
FMNL2	Melanoma progression Doi: 10.26355/eurrev_201906_18200
FNIP2	Neoplasms DOI: 10.18632/oncotarget.14221
FREM2	Fraser syndrome DOI:10.1002/ajmg.a.32091
GCGR	Diabetes Mellitus, Non-Insulin-Dependent DOI: 10.1002/prot.25807
GON4L	Regulates notochord boundary formation and cell polarity Doi: 10.1038/s41467-018-03715-w
GPR107	Prostate Cancer Doi: 10.3390/jcm9061703
GPR124	Ischemic stroke Doi: 10.1111/cns.13457
GPR22	Osteoarthritis DOI: 10.1002/art.27184
GPR31	Malignant neoplasm of colon and/or rectum DOI: 10.3748/wjg.v24.i41.4679
GPSM3	Rheumatoid arthritis DOI: 10.1038/gene.2016.3
GRHL3	Neural tube defects DOI:10.2217/epi-2018-0016 Colorectal cancer cells DOI:10.1007/s11596-017-1821-x
GRIK4	Major depressive disorder (MDD) doi: 10.1016/j.neurol.2019.11.009
GSK3B	Alzheimer's Disease DOI: 10.1007/s12035-018-1103-z
GTF3C1	Triple-negative breast cancer (TNBC) DOI: 10.1007/s10549-020-05874-1
HAVCR2	Acute myeloid leukemia DOI: 10.1182/blood.2020006921
HFE	Hemochromatosis, type 1 DOI: 10.1016/j.tracli.2019.05.003
HGS	Hepatoblastoma HuH6 and colorectal HCT116 DOI: 10.1186/s12885-015-2037-8
HNF1B	Maturity-onset diabetes of the young (MODY) DOI: 10.1530/EDM-20-0092
HPD	Tyrosinemia, Type III DOI: 10.1006/cbir.2002.0896
HSF1	Malignant Neoplasms DOI: 10.2174/1568009618666181018162117
IGSF3	Identification of an IGSF3 mutation in a family with congenital nasolacrimal duct obstruction DOI:10.1111/cge.12321
IKZF3	Lung adenocarcinoma DOI: 10.3389/fmolb.2020.571641

Continue of Table D15

1	2
IL4I1	Human Cutaneous Melanoma DOI: 10.1016/j.jid.2018.06.178
IL6R	Mental Depression DOI: 10.1016/j.bbi.2017.11.020
INSM1	Small cell carcinoma of lung DOI: 10.1002/cncy.22177
ITGA7	Duchenne muscular dystrophy (DMD) DOI: 10.1089/hum.2015.062
JAGN1	Syndromic severe congenital neutropenia Doi: 10.24953/turkjped.2020.02.022
KIRREL3	Intellectual disability DOI: 10.1016/j.ajhg.2008.10.020
LARP4B	Liver cancer DOI: 10.1155/2019/1569049
LASP1	Esophageal squamous cell carcinoma Doi: 10.1002/mc.23269
LDLRAD2	Gastric cancer Doi: 10.18632/aging.102359
LEF1	Chronic Lymphocytic Leukemia DOI: 10.1093/ajcp/aqw208
LGI4	Arthrogryposis multiplex congenita (AMC) DOI: 10.1016/j.ajhg.2017.02.006
LRP1B	Malignant neoplasm of prostate DOI: 10.1002/cam4.2375
LSM4	Ovarian cancer doi: 10.1016/j.prp.2020.153275
LZTS1	Neuronal delamination DOI: 10.1242/dev.195404
MAFK	Antituberculous drug-induced liver injury (ATDILI) DOI: 10.1002/phar.2349
MAP3K12	Neurodegenerative Disorders DOI: 10.1021/acs.jmedchem.7b00843
MAP3K6	Familial gastric cancer DOI: 10.1371/journal.pgen.1004669
MARCH10	Spermiogenesis DOI: 10.1074/jbc.M111.256875
MC1R	Major determinant of skin pigmentation and phototype DOI: 10.1111/pcmr.12400
MGAT3	Alzheimer's Disease DOI: 10.3233/JAD-2011-101950
MICAL3	Breast Cancer stem-like cells DOI: 10.1073/pnas.1806851116
MPDZ	Severe congenital hydrocephalus DOI: 10.1136/jmedgenet-2012-101294
MYOM1	Important role in sarcomere assembly DOI: 10.1111/jcmm.16268
NCOA6	Melanoma DOI: 10.1002/ijc.27648
NELL2	Regulator for the morphological development for neuronal polarization and axon growth DOI: 10.14348/molcells.2020.0032
NFATC2	Potential regulator of cellular sensitivity to ionizing radiation DOI: 10.3389/fonc.2020.589168
NFE2L1	Lung adenocarcinoma DOI: 10.1002/cam4.3270
NGB	Alzheimer's Disease DOI: 10.1016/j.ijbiomac.2018.10.021
NUAK1	Non-Small Cell Lung Cancer Doi: 10.2147/CMAR.S277524
NUP62	Bilateral striatal necrosis DOI: 10.1002/ana.20902
OSTM1	Malignant osteopetrosis DOI:10.1038/ejhg.2017.96
OXSR1	Hepatocellular carcinoma progression DOI: 10.1080/21655979.2020.1814659
PAQR6	Nongenomic actions of rapid steroid response DOI: 10.1089/dna.2011.1262
PCDHGA12	Lung cancer DOI: 10.3892/ol.2018.8699
PDAP1	Childhood acute lymphoblastic leukemia DOI:10.1016/j.exphem.2018.04.002 Glioma DOI:10.1016/j.biocel.2016.07.016
PDE6B	Human retinitis pigmentosa DOI: 10.18240/ijo.2016.08.02
PGAP1	Cerebral visual impairment and intellectual disability caused by PGAP1 variants DOI:10.1038/ejhg.2015.42
PIK3C2B	Neoplasm Metastasis DOI: 10.18632/oncotarget.7761
PKP3	Ovarian cancer Doi: 10.1016/j.bbrc.2018.11.163.
PLCD4	Malignant neoplasm of breast DOI: 10.1186/1476-4598-3-15
PLXNA4	Alzheimer disease Doi: 10.1002/ana.24219.
PPM1F	Hepatocellular carcinoma DOI:10.1186/s12943-018-0909-7 Tumour recurrence DOI:10.1111/cpr.12444

Continue of Table D15

1	2
PPP1R26	Breast cancer DOI: 10.1186/s12943-017-0696-6
PRCD	Essential for high-fidelity photoreceptor disc formation Doi: 10.1073/pnas.1906421116.
PRICKLE2	Tissue polarity or planar polarity PMID:12525887
PROB1	Keratoconus (KTCN) DOI: 10.1038/ejhg.2016.130
PTPRF	Gastric adenocarcinoma DOI: 10.2147/OTT.S178152
PURG	Inhibition of oncogenic transformation PMID: 12894583
PXN	Cervical cancer Doi: 10.2217/fon-2017-0474
RAB37	Nasopharyngeal carcinoma (NPC) DOI: 10.1158/1078-0432.CCR-18-0532
RANBP1	Cortical neuron polarity DOI: 10.1016/j.celrep.2018.07.107
RBMS2	Tumor suppressor in breast cancer DOI: 10.1186/s13046-018-0968-z
REXO4	Infertility DOI: 10.1007/s00439-020-02143-5
RLBP1	Fundus Albipunctatus DOI: 10.1136/bjo.2010.189076
RNF14	Malignant tumor of colon DOI: 10.1038/embor.2013.19
RNF157	Serves as a novel node integrating oncogenic signaling pathways with the cell cycle machinery and promoting optimal cell cycle progression in transformed cells DOI: 10.1074/jbc.M117.792754
RXFP1	Cancer therapy DOI: 10.1016/j.mce.2019.02.001
SACS	Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) DOI: 10.1038/s41598-019-48047-x
SCAMP5	Autism DOI:10.1093/hmg/ddq013
SGIP1	Hepatocellular carcinoma DOI: 10.4149/neo_2020_200623N657
SGSM1	Nasopharyngeal carcinoma DOI: 10.1158/0008-5472.CAN-18-1754
SIAH3	Neurodegenerative diseases DOI: 10.18632/aging.102435
SIRT7	Breast cancer metastasis DOI: 10.1038/s41467-017-00396-9
SLC30A8	Type 1 diabetes; type 2 diabetes. DOI: 10.2174/1573399812666151123104540
SMARCC2	Gastric cancer DOI: 10.1016/j.canlet.2018.01.032
SOX18	Augmented angiogenic transcription factor; asthma exacerbation Doi: 10.1080/02770903.2020.1771727
SPAG5	Hepatocellular carcinoma DOI: 10.1186/s12943-018-0872-3
SPOCK2	Ovarian cancer DOI: 10.18632/aging.102538
SPRR1B	Squamous metaplasia DOI: 10.1167/iovs.07-0685
SPSB3	Malignant Neoplasms DOI: 10.1038/onc.2017.370
SYVN1	Colon cancer DOI:10.1007/s11010-018-3447-0
TEAD2	Hepatocellular carcinoma Doi: 10.3892/or.2020.7578
TECTA	Hearing loss DOI: 10.3390/genes10100744
TJP3	Antioxidant activity DOI: 10.3390/md17010023
TMEM136	Exfoliation syndrome DOI: 10.1097/IJG.0000000000000903
TMEM229B	Transmembrane protein 229B DOI: 10.1111/sji.12832
TMEM91	Regulation of cell migration and invasion, constructs ion channels, and participates in the immune response Doi: 10.1155/2018/1705478
TNFSF13	Triple-negative breast cancer DOI: 10.1007/s00109-020-01952-5
TNIP1	Systemic lupus erythematosus DOI: 10.1016/j.gene.2018.05.062
TP53I3	BRCA-like tumor suppressor DOI: 10.1016/j.cancergen.2019.04.061
TRAK1	Mitochondrial dysfunction DOI: 10.1007/s12035-020-02175-y
TRMT2A	Cell cycle regulator that suppresses cell proliferation DOI: 10.1016/j.bbrc.2018.11.104

Continue of Table D15

1	2
TSNARE1	Schizophrenia doi: 10.1007/s00702-014-1348-2
TTN	Regulatory roles in cardiac and skeletal muscles Doi: 10.1002/humu.22611
TUBA3C	Teratozoospermia DOI: 10.1007/s13353-011-0078-5
TUFM	Combined Oxidative Phosphorylation Deficiency 4 DOI: 10.1038/s10038-019-0592-6
UBE2K	Schizophrenia DOI: 10.1016/j.jpsychires.2019.03.005
UNG	Somatic hypermutation and class switch recombination DOI: 10.1093/intimm/dxu071
URM1	Hepatocellular Carcinoma DOI: 10.2147/OTT.S258843
VPS13B	Cohen syndrome doi: 10.1186/s12881-020-01075-1.
WDR46	Aspirin-Exacerbated Respiratory Disease doi: 10.4168/aair.2012.4.4.199
WNT16	Osteoporosis DOI: 10.1155/2019/8503148
XPO6	Prostate cancer DOI: 10.2741/s445
YY1AP1	Colon adenocarcinoma DOI: 10.1016/j.bbrc.2017.10.060
ZNF132	Esophageal squamous cell carcinoma DOI: 10.1038/s41419-018-1236-z
ZNF853	Zinc finger protein 853 DOI: 10.1038/nature21683
Note - genes involved in the development of diseases are indicated as: oncological - purple, neurodegenerative - blue, others – yellow and green color	

Table D16. Family tae-miRNA target human genes involved in biological processes [401, p. 342-343]

Gene	Gene involvement in disease
1	2
ABCA3	Surfactant Metabolism Dysfunction, Pulmonary, 3 DOI: 10.1002/humu.23416
AKT1	Schizophrenia DOI: 10.1038/mp.2011.91
AOC3	Lung fibrosis DOI: 10.1096/fj.201600935R
AP1B1	Ichthyosis, Deafness, and Photophobia DOI: 10.1016/j.ajhg.2019.09.021
ARHGEF6	Hearing loss (ARHGEF6 belongs to the family of guanine nucleotide exchange factors (GEFs) DOI: 10.3389/fnmol.2018.00362
ARHGEF10	Putative tumor suppressor in pancreatic ductal adenocarcinoma DOI: 10.1038/s41388-019-0985-1
CLCN7	Osteopetrosis Autosomal Dominant Type 2 DOI: 10.1016/j.bone.2018.02.031
ENDOD1	Carcinogenesis DOI: 10.1186/s12885-017-3330-5
GLI2	Castration-resistant prostate cancer DOI: 10.3892/ijo.2020.5044
H1FOO	Oocytic growth Doi: 10.1095/biolreprod.104.032474
KDM6B	Modulates MAPK pathway mediating multiple myeloma cell growth and survival DOI: 10.1038/leu.2017.141
CASKIN	Tyrosine phosphorylation DOI: 10.1186/1478-811X-10-36
CD22	B-cell inhibition to keep humoral immunity in check DOI:10.1038/s41467-017-00836-6
COL6A3	Osteosarcoma Doi: 10.1590/1806-9282.66.6.740
DOCK1	Claudin-Low Breast Cancer Cells DOI: 10.3390/cancers11111762
DNMT3B	Glioblastoma DOI: 10.1007/s11060-010-0520-2
EDN1	Diabetic foot DOI: 10.4149/BLL_2019_009
EME1	Malignant Neoplasms DOI: 10.1002/prot.25644
ENC1	Malignant Neoplasms DOI: 10.1093/hmg/ddh315

Continue of Table D16

1	2
EPHA4	Amyotrophic Lateral Sclerosis DOI: 10.1186/s40478-019-0759-6
FAM124A	Mycoplasma pneumoniae pneumonia doi: 10.1186/s40246-017-0101-y
FAM177A1	Juvenile arthritis DOI: 10.1089/dna.2009.0970
GALR1	Squamous cell carcinoma of the head and neck Doi: 10.1371/journal.pone.0193275
LRRFIP1	Tumor Cell Invasion DOI: 10.1016/j.canlet.2015.05.023
NLGN2	Schizophrenia doi: 10.1038/s41398-019-0660-x.
HIC1	Miller Dieker syndrome DOI: 10.1093/hmg/9.3.413
HMX3	Hearing and Vestibular Function Doi: 10.1002/ajmg.a.32705
HSF1	Malignant Neoplasms DOI: 10.2174/1568009618666181018162117
INO80D	Aortic hypoplasia, premature atherosclerosis, and arterial stiffness DOI: 10.1161/CIRCGENETICS.113.000233
ITIH4	Hepatocellular Carcinoma DOI: 10.1007/s12253-017-0285-4
KCNAB3	Genetic epilepsy with febrile seizures plus (GEFS+) DOI: 10.1002/brb3.1859
KCNJ15	Esophageal Squamous Cell Carcinoma DOI: 10.1245/s10434-019-08189-8
KIF7	Acrocallosal Syndrome DOI: 10.1038/s41431-017-0019-9
KRT6A	Lung Adenocarcinoma Doi: 10.1177/1533033820921248
KRT6B	Hepatocellular carcinoma PMCID: PMC4659127
KRT6C	Lung adenocarcinoma Doi: 10.1007/s13258-019-00889-5
LTB4R2	Asthma DOI: 10.1165/rcmb.2008-0445OC
NEBL	Colorectal Cancer DOI: 10.15171/mejdd.2018.107
PHLDB2	Colorectal Cancer Doi: 10.1186/s12935-019-0903-1
PKHD1	Autosomal recessive polycystic kidney ARPKD DOI:10.1038/s10038-018-0550-8 Congenital hepatic fibrosis (CHF) DOI:10.1097/MEG.0000000000001295
PRICKLE2	Tissue polarity or planar polarity PMID:12525887
RBFOX3	Epilepsy DOI: 10.1371/journal.pone.0164164
RBM19	Nucleolar protein expressed in crypt/progenitor cells of the intestinal epithelium DOI: 10.1016/j.modgep.2005.05.001
RHBDF1	Head and neck squamous cancer cells DOI:10.1096/fj.08-112771
RUNDC1	p53 activity, p53 protein is a sequence-specific transcription factor that plays a crucial role in tumor suppression DOI:10.4161/cc.5.16.3140
RNF168	Riddle Syndrome DOI: 10.1002/ajmg.a.38208
ROBO3	Myeloid leukemia DOI: 10.1177/1535370220988246
SEMA3A	Prostate cancer DOI: 10.1002/cbin.11554
SEMA6A	Receptor Specificity in Clostridial Toxins, Lethal toxic shock syndrome associated with gynecological infections DOI: 10.1016/j.cell.2020.06.005
SNX8	Critical component in innate immune response to cytosolic DNA and DNA virus DOI: 10.1371/journal.ppat.1007336
SQSTM1	Amyotrophic Lateral Sclerosis DOI: 10.1080/13816810.2019
STAC	Sleep Disorders DOI: 10.1017/S0033291717003191
TEAD2	Hepatocellular carcinoma Doi: 10.3892/or.2020.7578
TEAD3	Pancreatic ductal adenocarcinoma Doi: 10.1016/j.pan.2020.12.003. Transcriptional enhanced associated domain (TEAD) transcription factors
TMEM184A	Confirmation of Heparin Receptor Identity Doi: 10.3791/55053
Note - genes involved in the development of diseases are indicated as: oncological - purple, neurodegenerative - blue, cardiovascular - green color	

Table D17. osa-miRNA list of 1-4 human target genes [367, p. 1-9]

osa-miRNA	Gene	osa-miRNA	Gene
miR11336-3p	*CIB3*	miR2103-5p	*GIPC1, KLHL26, SKA3*
miR11339-3p	*LAMB2*	miR2105-3p	*FAM13A*
miR11339-5p	*RASSF1*	miR5151-5p	*CHI3L1*
miR11343-3p	*CYTH2, RAB3B*	miR5152-5p	*MBTPS1*
miR11344-3p	*ALOX12B, UBE2I*	miR5154-3p	*MLL4, PCDHA12, PCDHA3*
miR1320-3p	*CPA3, PPAP2B*	miR5155-5p	*FAT1*
miR1423-3p	*CHST5, CHST6, TTC40*	miR5156-5p	*ENAH, LETM1, TMEM194B*
miR1424-3p	*FBXO8*	miR5158-3p	*LMF1*
miR1425-3p	*C20orf195, ZBTB24*	miR5161-3p	*PTGDR2, SYNGAP1*
miR1425-5p	*C6orf225, FREM2*	miR5162-5p	*ARHGAP19, PAFAH2, SAMD9L*
miR1426-5p	*CNPY1, MOB3B, TBCD*	miR5338-5p	*CDS2*
miR1430-3p	*CPSF1, CRTC1, LRRC45*	miR5339-5p	*SLC35D1*
miR1432-3p	*MIIP, RPA1*	miR535-3p	*EML1, L1CAM*
miR1432-5p	*GARNL3*	miR5487-5p	*ATP2A3*
miR1435-5p	*CHD4, LRRIQ3, MKS1, WIPF1*	miR5488-5p	*LRP5*
miR1436-3p	*CD2BP2, KRT222, RNF19B,*	miR5492-5p	*C6orf48*
miR1439-3p	*EVI5L, SMAD2*	miR5493-3p	*CST6, SIX3*
miR1848-5p	*LTB4R, ZNF516*	miR5494-5p	*ITPRIPL1*
miR1853-5p	*SUB1, ZC3H4*	miR5496-5p	*PCNX*
miR1854-3p	*PIK3C2A, PLCD4, SLC7A11*	miR5497-5p	*ADAMTSL3, GRHL3*
miR1859-3p	*DCAF4L1, ERCC2*	miR5498-5p	*ETNK1*
miR1864-3p	*MUC5B, PDE6B, SLC2A3*	miR5501-3p	*GPR85, LARP6, TUBGCP6*
miR1868-5p	*ATRIP, LIG4*	miR5503-3p	*ATP1B4*
miR1869-5p	*HAND1, SPON1*	miR5509-5p	*RASGRF2UNC5D, ZNF846*
miR1870-3p	*AVPR1B, MAST4*	miR5511-3p	*CD27, WBSCR27*
miR1870-5p	*ALPPL2, TMEM178B*	miR5515-3p	*ETV6, PPARA, ZNF282*
miR1871-3p	*ASRGL1, RUFY3, UHRF1BP1L*	miR5518-3p	*AHNAK2, CLECL1*
miR1872-3p	*SPSB4*	miR5519-5p	*XYLT1*
miR1874-3p	*FN1, FRK*	miR5523-3p	*ZSCAN5A*
miR1876-3p	*ENTPD1, USH2A*	miR5524-3p	*SETD1B*
miR1877-3p	*GNAZ, MFAP5*	miR5526-3p	*C12orf5, IKZF4, ZSCAN22*
miR2090-5p	*CEP170, MLLT3, RAD54L, RGS21*	miR5529-3p	*GJB7, WTIP*
miR2092-3p	*APEH, DFFB, OSTM1, XKR8*	miR5530-5p	*RGS8*
miR2095-3p	*ACTR1B, SYT11*	miR5532-3p	*KIAA0586, SH3BP2, TET1*
miR2096-3p	*GSTO2*	miR5534a-5p	*NANOS1*
miR2096-5p	*JUN*	miR5537-3p	*C15orf23*
miR2098-5p	*ATP13A1*	-	-

Table D18. osa-miRNA list of 5 or more human target genes [367, p. 1-9]

osa-miRNA	Gene
1	2
miR1438-5p	*AZIN1, C18orf63, CAMTA1, CMYA5, MAGEB2, POGZ, REXO1L1, RGPD1, RGPD2, STX6, TMEM194A, TMPRSS15*
miR1440a-5p	*AIMP1, CUX2, FOLH1, FOLH1B, LPP, MAMDC4, NSL1, SSX2IP*
miR1847.1-5p	*ACIN1, EIF3A, GJB4, GJB5, PRSS58, PSEN2, VGLL1*
miR1847.2-3p	*C1QL4, CHRNG*
miR1850.1-5p	*C10orf105, EBF1, ELFN2, GPANK1, NACC2, PPP1R18, TP73, ZMYM6*
miR1850.2-5p	*CDC42BPA*
miR1850.3-3p	*LRRC10, TP53TG5, UBXN2B*
miR1855-3p	*ANTXR1, CACHD1, MDN1, PADI1, PDK2, SMO*
miR1860-3p	*C15orf39, COL4A5, KLHDC10, RABEP2, TIE1*
miR1860-5p	*AMMECR1L*
miR1866-3p	*AKAP9, ALS2CR12, CA11, CEP135, ERCC6, FAM198A, FAT4, GEN1, WDR43*
miR1873-5p	*ASTN1, DHX37, KCNN1, ROM2, USH2A*
miR1879-3p	*ADAMTS7, RBM3, REXO1, SPOCK2, TBC1D3B, TBC1D3F, TBC1D3H, XYLB*
miR2091-3p	*CHST5, KIF1A, LDLRAD2, ZXDA, ZXDB*
miR2094-3p	*CAD, KCNC1, LYPD3, PIDD*
miR2094-5p	*ADAMTS15, B3GALT4, BMP8B, C16orf55, ERN2, GGA3, KLHDC4, METRN, MYH6, MYH7*
miR2097-3p	*CNNM2, FANCM*
miR2097-5p	*ATP1A2, BHLHE40, CAMKK1, CELF6, CLEC11A, CNGB1, DAZAP2, DUSP8, HIPK2, LHX3, LRRC32, MARK4, MUC5B, OLFML2A, PSCA, RAB3A, RAP1GAP2, RASA4B, SH3PXD2B, SYT, SYT3, TAP2, ZNF592*
miR2099-3p	*ATP10D, CUX1, GCNT3, MED12L, SAMD11, SLC36A3, ZNF80*
miR2101-5p	*ADAM12, ASPM, DYNC1H1, PDCD10, PDGFRA, RNF148, TEAD1, ZNF770*
miR2102-3p	*MRPL19, PDK2, SMG5*
miR2102-5p	*ABHD17B, ADAMTS5, ADRBK1, AFAP1, BRWD1, C11orf75, C19orf6, C1orf173, C1QL2, C2orf72, CHSY1, CUX1, DIRC2, EVX2, FAM108B1, GLTSCR2, HCN2, KATNAL1, KCNA3, KCNMB4, LMO2, NANS, NR1D2, PDAP1, PPP2R5C, RALGAPA1, RHOBTB2, RIN3, TAB3, TGFBR1, UHRF1BP1, UNCX, VAT1L, WT1, XKR7, ZBTB10, ZFHX3, ZNF286B*
miR2104-3p	*ADCYAP1R1, C9orf172, EMX1, FAM120A, FAM184B, PAK1, PSIP1, PTPN5, UTF1*
miR2122-5p	*AADACL3, ARHGEF26, KLHL32, PTPRK, SLC25A12, SLC25A31, UBE2H, ZNF347*
miR2866-5p	*BICD1, LAMB3, PCDHB15, ZNF442, ZNF648*
miR2878-3p	*IFNAR1, LRPPRC, CUX1, KRTAP9-2, KRTAP9-3, KRTAP9-8*
miR2919	*ADAMTS5, AKAP11, ATG13, BDNF, C1D, CDC25B, FAM59B, FAM83H, GPBP1L1, KIAA1161, MINK1, NEUROD2, OTUD4, PRDM11, PTGFRN, RGS9BP, SPRY4, ZNF304, ZNF385A*
miR2923-5p	*ANO6, CSE1L, HSPA1B, KPNA4, MLF1, RD3, RP2, STC2, SYNJ2, TIPRL*
miR2924-3p	*CTBP1, KIFC1, NDUFA2, NR2F2, POMZP3, STAU2*
miR394-5p	*BIN2, GRIK4, HAVCR2, HNF1B, IGSF3, MICAL3, PGAP1, REXO4, RXFP1*
miR3979-3p	*C19orf24, LRRC16B, LY6H*
miR3979-5p	*C1orf65, CACNA1H, CUX2, DSC3, FAM49A, GPR124, MYBL1, ZNF425*

Continue of Table D18

1	2
miR408-3p	*ADARB2, ADCY6, ALPK3, ANO4, EDEM1, ERICH1, FNIP2, KIRREL3, NGB, PAQR6, RBMS2, RLBP1, SMARCC2, TJP3, UBE2K, UNG*
miR408-5p	*CCL22, COG4, CPNE6, GATA5, IGF1R, IL2RB, INPP1, MAFK, MAP2K2, PFKL, PPM1F, PRKX, RAB37*
miR414-5p	*APLP2, BAZ2B, C14orf142, C9orf43, CASQ1, CASZ1, CENPB, CHD8, LMNA, MAP4K4, MTERFD2, RNF34, SPOCK1, SUGP2, TAF7L, TMEM30B*
miR5075-3p	*AGAP1, B4GALT5, BOD1, C4orf32, CNRIP1, COL23A1, DLX2, ECI1, GALNT2, GOLPH3, HDAC3, HNRNPL, HOXD13, IVNS1ABP, KCNA7, LLGL1, MAPK8IP1, MNX1, NKD2, NR2F2, PARP2, RABGAP1, RHOQ, RPRD2, RPS6KA5, RPS6KC1, SFRP5, SLC9A6, SMAD2, SMG7, SOX11, ST3GAL2, TCF24, TRIP10, TWIST1, URI1*
miR5144-3p	*AKAP9, BAZ1B, C10orf54, CLCN6, EPB41L2, FFAR3, FLYWCH2, HMCN1, LOXL1, MAU2, MYH6, PEAK1, PROM2, SKI, SLC13A5, SLC34A1, TMEM207*
miR5144-5p	*CSTF2, PACS2, PPARGC1A, WDR19*
miR5147-3p	*JAG2, LRFN5, OSGIN1, PDE4B, SBNO2*
miR5150-3p	*BIRC7, CER1, CLEC4M, FITM1, GNAO1, HIVEP3, JMJD7-PLA2G4B, PLA2G4B, RAVER1,*
miR5150-5p	*B4GALNT4, IL17RC, KIAA1407, KIF1A, MAPT, MCM3AP, MCM3AP, MFN2, MUM1L1, PDE4DIP, SETD1B, TK1, ZNF469*
miR528-3p	*EXOC7, FREM2, LSM4, MC1R, MGAT3, RPS4Y1, RPS4Y2, SPAG5*
miR528-5p	*CACNB1, CD276, DNAJB6, GSK3B, GTF3C1, PPP1R26, PROB1, RGS9BP*
miR530-3p	*ACRBP, C21orf2, CARD14, CECR6, DISP2, EGR4, FPGS, IL9R, IRF2, MTUS2, TMEM11*
miR530-5p	*AATK, FXYD6, LAMC3, MEGF6, NDST1, NOTCH2, SEPT2*
miR5489-3p	*CUL7, CUX2, FAM124A, MYOF, TCEA2, UBAC1, ZBTB7A*
miR5504-3p	*AP1M1, HEXDC, IRX1, MED15, TLR6, TMEM229B*
miR5508-5p	*AGAP2, APBB1IP, GPR56, HCCS, KIAA0556,OTUD7A*
miR5510-5p	*BRD2, COL4A2, SLC25A47, TBX3, TRIM44*
miR5514-5p	*BNIPL, FTCD, MTA1, OPN3, PM20D2, TMEM88*
miR5527-5p	*ALS2CL2, BFAR, FZR1, LRRC71, RBM15, SMIM5, TBC1D2, TREM2, VPS13C, WIZ, ZNF469*
miR5531-5p	*AFF1, NF1, PHF15, PKN1, PRKCE, SEPT3, SMAD4*
miR5536-3p	*COL5A1, E2F1, FAM65A, NKD1, PCDHAC1*
miR5543-5p	*DUT, GLS, HOXD3, OTUD4, SPDL1*
miR5791-3p	*ATP13A2, COL6A3, CPNE9, HNRNPUL1, NSD1*
miR5819-5p	*CLASRP, FBXO7, HMGXB3, RHOA, UBE2I, ZNF839*
miR5826-3p	*C4BPA, C8orf31, CAV3, CERS4, RBM14*
miR5833-5p	*ADRM1, CHD5, COX20, EXOC7, MIER2, TOB2, XYLT1*

Table D19. osa-miRNA of target human genes involved in biological processes [367, p. 1-9]

Gene	Function
1	2
CPA3	Fibromyalgia https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4888802/ Chronic prostatitis https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4089501/
PSEN2	Alzheimer's disease https://www.ncbi.nlm.nih.gov/pubmed/31235344; https://www.ncbi.nlm.nih.gov/pubmed/31182772
KLHDC10	Cell death Apoptosis https://www.ncbi.nlm.nih.gov/pubmed/23102700
OSTM1	Malignant osteopetrosis https://www.ncbi.nlm.nih.gov/pubmed/28612835
WT1	Ovarian cancer https://www.ncbi.nlm.nih.gov/pubmed/28367736 Myeloid leukemia https://www.ncbi.nlm.nih.gov/pubmed/31102358 Myelodysplastic syndrome and aplastic anemia in children https://www.ncbi.nlm.nih.gov/pubmed/31210595 Myelodysplastic syndromes https://www.ncbi.nlm.nih.gov/pubmed/31207708
KATNAL1	Intellectual disability https://www.ncbi.nlm.nih.gov/pubmed/24664804 Azoospermia https://www.ncbi.nlm.nih.gov/pubmed/24913027
NR1D2	Cryptorchidism https://www.ncbi.nlm.nih.gov/pubmed/27562222 Various cancers glioblastoma https://www.ncbi.nlm.nih.gov/pubmed/29773903
CHSY1	Hepatocellular carcinoma https://www.ncbi.nlm.nih.gov/pubmed/28652022 Sarcomas https://www.ncbi.nlm.nih.gov/pubmed/26997434 Colorectal cancer https://www.ncbi.nlm.nih.gov/pubmed/21468578
DIRC2	Renal carcinoma https://www.ncbi.nlm.nih.gov/pubmed/21692750 Cell carcinoma https://www.ncbi.nlm.nih.gov/pubmed/11912179
RHOBTB2	Epileptic Encephalopathy https://www.ncbi.nlm.nih.gov/pubmed/29276004 Breast cancer https://www.ncbi.nlm.nih.gov/pubmed/24485767; https://www.ncbi.nlm.nih.gov/pubmed/24356943; https://www.ncbi.nlm.nih.gov/pubmed/27941885
UHRF1BP1	Cell carcinoma of the head and neck https://www.ncbi.nlm.nih.gov/pubmed/28886272 Lupus erythematosus https://www.ncbi.nlm.nih.gov/pubmed/21326321
PDAP1	Childhood acute lymphoblastic leukemia https://www.ncbi.nlm.nih.gov/pubmed/29656114 Glioma https://www.ncbi.nlm.nih.gov/pubmed/27448842
PPP2R5C	Lung adenocarcinoma https://www.ncbi.nlm.nih.gov/pubmed/26986830 Human overgrowth https://www.ncbi.nlm.nih.gov/pubmed/25972378 Hepatic Glucose and Lipid Homeostasis https://www.ncbi.nlm.nih.gov/pubmed/26440364
AFAP1	Oncogenic role in retinoblastoma https://www.ncbi.nlm.nih.gov/pubmed/29654169 Various cancers https://www.ncbi.nlm.nih.gov/pubmed/29544748 Esophageal adenocarcinoma https://www.ncbi.nlm.nih.gov/pubmed/23333711
C19orf6	Ovarian carcinoma https://www.ncbi.nlm.nih.gov/pubmed/16084606
ZNF442	Psychiatric disorder https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3098561/
ATP13A3	Pulmonary arterial hypertension https://www.ncbi.nlm.nih.gov/pubmed/29650961 Cellular aging and tumor suppression https://www.ncbi.nlm.nih.gov/pubmed/11867234/
HK2	Cancer stem cell expansion https://www.ncbi.nlm.nih.gov/pubmed/31201299 Gallbladder cancer https://www.ncbi.nlm.nih.gov/pubmed/30825877 Tumor including acute myeloid leukemia https://www.ncbi.nlm.nih.gov/pubmed/29663500 Cancer cells https://www.ncbi.nlm.nih.gov/pubmed/30650008

Continue of Table D19

1	2
KIAA1161	Myoblast differentiation https://www.ncbi.nlm.nih.gov/pubmed/19706595/
BDNF	Neurogenesis and Neuroplasticity of the brain https://www.ncbi.nlm.nih.gov/pubmed/29858545
GPBP1L1	Protein Interaction Network Analysis https://www.ncbi.nlm.nih.gov/pubmed/29513927/
ADAMTS5	Osteoarthritis https://www.ncbi.nlm.nih.gov/pubmed/30652828/ Colorectal cancer https://www.ncbi.nlm.nih.gov/pubmed/29143120/
UFSP1	Cardiovascular disease https://www.ncbi.nlm.nih.gov/pubmed/20639392
RBMS2	Breast cancer https://www.ncbi.nlm.nih.gov/pubmed/30514345/
PPM1F	Hepatocellular carcinoma https://www.ncbi.nlm.nih.gov/pubmed/30470261 Tumour recurrence https://www.ncbi.nlm.nih.gov/pubmed/29473240
RPS6KA5	Breast cancer https://www.ncbi.nlm.nih.gov/pubmed/29358704 Colorectal cancer https://www.ncbi.nlm.nih.gov/pubmed/28314603
NR2F2	Metabolic gene regulation https://www.ncbi.nlm.nih.gov/pubmed/30481528 Congenital heart defect and dysmorphic features https://www.ncbi.nlm.nih.gov/pubmed/29663647
PARP2	DNA repair https://www.ncbi.nlm.nih.gov/pubmed/27708353; https://www.ncbi.nlm.nih.gov/pubmed/30104678
SLC35D1	Cartilage and skeletal development https://www.ncbi.nlm.nih.gov/pubmed/17952091
PM20D2	Synthesis of carnosine and homocarnosine https://www.ncbi.nlm.nih.gov/pubmed/24891507
NANOS1	Retinoblastoma tumor https://www.ncbi.nlm.nih.gov/pubmed/25100735
COX20	Mitochondrial encephalocardiomyopathies https://www.ncbi.nlm.nih.gov/pubmed/24403053

Table D20. list of osa-miRNA families of human target genes [367, p. 1-9]

osa-miRNA	Gene
1	2
miR1428b,c,d-3p	*ANKRD27*
miR1437a,b-3p	*CYP11B2, DLK1, DUSP1, GNG2, IL17C, LPCAT2, NUDT21, PKD2, UNCX, VWA9*
miR1437b-5p	*AP4S1, EPB41L1, SRRM2, STK25*
miR156a-j-5p	*ADCY2, AP2A2, C6orf7, MYBBP1A, OBFC1, ZFP62, ZNF652*
miR156c,g-3p	*KBTBD4, KIF20B, LOC100132703*
miR159a.2-3p	*ESPL1, PTK7, TESK1, TLN1, TXNDC12*
miR160a-d-5p	*C11orf16, DAB2*
miR160d-3p	*ALKBH5, IFFO1, PDE7B, PRADC1*
miR160f-3p	*KDM4E, KRT38, PADI4, TACR2, UNC5A*
miR160f-5p	*C4A, C4B, C11orf16, ESPNL, GLYCTK, TNKS1BP1*
miR162b-3p	*C14orf80, CSPG4, GPR123, KCNJ5, RIMS3*
miR164a,b,f-5p	*ASXL1, KCNJ14, RASL10B, UGT1A9, UGT1A7*
miR164c,d-5p	*ASXL1, B3GNT7, BMP2K, KCNJ14, LRRTM2, MXD4, TRAK1*
miR164e-5p	*B3GNT7, H6PD, KCNJ14, MAFA, RCAN3, SP5, SLC30A10, TMC6*
miR166a,b,c,d,f,j-3p	*MOGS*
miR166a,e-5p	*ARRDC1, CHST11, NAV1, TJP1*

Continue of Table D20

1	2
miR166b-5p	*CCNY, IGDCC4*
miR166h-5p	*CCNY, FKBP15, HGS, INSM1, SGIP1, TSNARE1, TNFSF13*
miR166i-5p	*RSAD2, STIL, VARS2*
miR167a-j-5p	*ARHGEF10, FAM43B, HSF1, PRICKLE2*
miR167c-3p	*CORO1A, LRTM2, SEZ6, SDK1*
miR168a-3p	*GALNT6*
miR168b-5p	*ADAMTS4, AP1M1, APOBR, DYNC1H1, KLF14, KLF16, PSEN2, RPL29*
miR169h-m-5p	*GRHL3, NCOA6, RNF44*
miR169q-5p	*ADCY8, PCED1A, RAP1GAP2, WDFY3*
miR169r-3p	*LLGL1, LLGL2, NUMBL*
miR171a-3p	*RPGRIP1L*
miR171d-5p	*MTX1, YARS*
miR172a,d-3p	*GPR31*
miR172d-5p	*C11orf88, MEIS3*
miR1846a,b,c-5p	*CDH24, DNAJB6, EIF3B, HOXD9, LACC1, LYSMD2, OLIG1*
miR1846a,b-3p	*FBRSL1, FRMPD2, TRIM24*
miR1858a,b-5p	*ACADM, ACSL4, ATXN2L, AQP2, BRD7, C1QL4, COL7A1, C20orf27, FAM178B, HOXB3, KCNC3, KIF13B, SP6, SSTR1, TYRO3, TMEM91, TPM2, UBIAD1*
miR1861a,d,o-5p	*CRLF1, IL17RB, METTL17, SHBG, ZNF284*
miR1882a-h-5p	*GNPAT, KCNK10*
miR2118l-3p	*ABCA9, DYRK1A, DOCK2, HEMK1, MKL2, TTC5*
miR2275c-5p	*A2M, CACNA1E, SCAF4, RPGR, ZNF641*
miR2275d-3p	*CKAP5, DNAH5, MYH7B, MACF1, NCAPG, PRRT2, RPL39L, RAP1GAP2, RPL39, SCN8A, SLC12A1, SYF2*
miR2907a-d-3p	*CAMKK2, E2F1, FBRSL1, IRAK2, KDSR, PRKAR2B, SLC25A37, SLC24A3, TNK2, ZNF275*
miR319a-3p.2,b-3p	*DMAP1, IL4I1, TPSG1*
miR395a-3p	*DEPDC1B, EDN1, MKL1, SCAMP4, TEAD2*
miR395b-e,g-s,y-3p	*CD22, EDN1, TEAD2*
miR396a,b-3p	*CMKLR1, LRRC32, SCAMP5, SYVN1, VPS13B*
miR396c-3p	*C1orf65, CNNM4, DNAH7, KIF9, NFIX, PNKD, RASD2, TRIL*
miR396c-5p	*KIAA1755, RARG*
miR398a-3p	*C1orf198, FAM216B, IL4I1, PRRC2B*
miR399i-3p	*APBB1, CTIF, CDK18, DDX11, JAGN1, OSTM1*
miR439a-i-3p	*ASIC3*
miR444a-3p.1,d.1-3p	*AP1B1, C9orf170, COL6A3, DVL1, DOCK1, EBF2, EIF5A, HIC1, KRT6A, KRT6B, KRT6C, RUNDC1, RHBDF1, SEPT9, SPECC1L, ZFHX3*
miR5079a,b-5p	*SCML4, SPIN4*
miR5148a,b,c-3p	*LRRC47, RBM8A, TMEM19, ZCCHC24*
miR529a-3p	*ADORA2A, ATP6V0A4, BZRAP1, CCDC94, CHD2, CLIC5, HCLS1, ITGA2B, KIAA0195, LRIG1, MAP3K15, MAP7, MLL, OPHN1, PDE4B, RANBP2, RGPD1, RGPD2, RGPD3, RGPD4, RGPD5, RGPD6, RGPD8, TMEM181, USF2, VEGFA*
miR529b-5p	*PHF2, SPEN*

Continue of Table D20

1	2
miR531a,c-5p	*DHX34, HPRT1, SLC3A2, SLC30A7*
miR531b-5p	*ENAH, MAP3K3, RAP2B, SHISA8, SLC30A7, VSX1*
miR6249a,b-5p	*ARTN, CHRD, FAM110B, NTRK3, POLR3D*
miR815a,b,c-3p	*ABAT, FCHSD1, FKBP4, OLFML2A, PPRC1, RHOBTB3, STAT5B, TIFA, ZBTB7A*

Table D21. osa-miRNA families of target human genes involved in biological processes [367, p. 1-9]

Gene	Function
1	2
ABCA9	Papillary thyroid cancer DOI:10.1002/jcp.29048
AKAP13	Blood pressure DOI:10.1038/jhg.2010.167 Colorectal cancer DOI:10.1007/s10238-009-0065-x Hepatocellular carcinoma PMC4637775 Prostate cancer DOI:10.1016/j.urolonc.2005.04.002 Breast cancer DOI:10.1093/carcin/bgl164
ANKRD27	Trafficking of melanogenic enzymes to epidermal melanocytes DOI:10.1038/ncomms6593; Endosomal trafficking DOI:10.1111/tra.12406
AP2A2	Coronary artery disease DOI:10.1186/s12872-018-0905-2
APOBR	Hypothyroidism DOI: 10.3892/mmr.2018.9499
ASXL1	Myeloid leukemia DOI: 10.1080/10428194.2018.1433298
ATP12A	Mucus dysfunction DOI:10.1038/s41598-018-20444-8 Non-gastric proton pump in human colorectum DOI:10.2170/jjphysiol.52.317
ATP6V0A4	Distal renal tubular acidosis DOI:10.5414/CN107505
C19orf57	Cervical cancer DOI:10.1007/s10142-019-00706-y
C20orf27	Diabete DOI: 10.2337/dc10-0452
CCDC94	Protects cells from ionizing radiation DOI:10.1371/journal.pgen.1002922
CCNY	Hypertension and hypertension of renal origin DOI:10.5603/EP.a2018.0079
CD22	B-cell inhibition to keep humoral immunity in check DOI:10.1038/s41467-017-00836-6
CEP250	Usher syndrome which is characterized by early-onset sensorineural hearing loss (SNHL) and a relatively mild retinitis pigmentosa DOI:10.1080/13816810.2018.1466338
CHD2	Neurodevelopmental Disorders PMID:26677509
CHST11	Chondroitin and dermatan sulfate synthesis in different tissues. DOI:10.1074/jbc.M002443200
CMKLR1	Male fertility and reproductive hormones DOI: 10.1093/humrep/dey310 Cardiovascular disease DOI: 10.1161/JAHA.116.004421
DNAH7	Testicular cancer DOI:10.1002/ijc.31604
EDN1	Diabetic foot DOI: 10.4149/BLL_2019_009
EIF3B	Ovarian cancer DOI: 10.1016/j.biopha.2018.10.027
ENAH	Ovarian cancer DOI: 10.1073/pnas.1715998115
FASN	Gastric adenocarcinoma DOI: 10.1016/j.lfs.2019.03.056
GPR31	Prostate cancer DOI:10.1096/fj.201500076
GRHL3	Neural tube defects DOI:10.2217/epi-2018-0016 Colorectal cancer cells DOI:10.1007/s11596-017-1821-x

Continue of Table D21

1	2
H6PD	Controls cancer cell proliferation DOI: 10.1096/fj.201700870RR
IL17RB	Colorectal cancer stem cells DOI:10.1073/pnas.1900251116
IRAK2	Non-small cell lung cancer DOI:10.1002/ijc.31660
KAZN	Desmosome assembly, cell adhesion, cytoskeletal organization, and epidermal differentiation DOI:10.1242/jcs.029538, DOI:10.1083/jcb.200312123
KIAA0528	Cell growth and migration DOI:10.1074/mcp.M113.036699
KLF14	Colorectal cancer DOI: 10.3892/ijo.2018.4546
MAP7	Essential role in microtubule function required for spermatogenesis PMID: 12755995 Proliferation and differentiation of human intestinal epithelial cells DOI:10.1002/cm.10124
MLL	Leukemia DOI:10.1073/pnas.88.23.10735
MROH2B	maestro heat like repeat family member 2B doi: 10.1186/s12864-016-2423-x
NCAPG	Hepatocellular carcinoma DOI:10.7717/peerj.7436
NRG1	Lung cancer DOI:10.2174/092986732466617091117055 4,DOI:10.1158/1078-0432.CCR-14-0854 Schizophrenia, and bipolar disorder (BPD) DOI:10.1002/ajmg.b.32428 Hirschsprung disease DOI:10.1186/s12887-018-1265-x
OBFC1	Regulates telomere maintenance in ALT cancer cells DOI:10.1016/j.yexcr.2017.03.058 Affect telomere function DOI:10.1371/journal.pgen.1007523
PDE4B	Schizophrenia DOI:10.1371/journal.pone.0147092
PKHD1	Autosomal recessive polycystic kidney ARPKD DOI:10.1038/s10038-018-0550-8, PMID:30595564 Congenital hepatic fibrosis (CHF) DOI:10.1097/MEG.0000000000001295
PRICKLE2	Tissue polarity or planar polarity PMID:12525887
RHBDF1	Head and neck squamous cancer cells DOI:10.1096/fj.08-112771
RUNDC1	p53 activity p53 protein is a sequence-specific transcription factor that plays a crucial role in tumor suppression DOI:10.4161/cc.5.16.3140
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