

MicroRNAs in model and complex organisms

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Abstract Non-coding RNAs such as microRNAs (miRNAs) are very tiny ribonucleotides having an essential role in gene regulation at both post-transcriptional and translational levels. They are very conserved and expressed in worms, flies, plants, and mammals in a sequence-specific manner. Furthermore, it is now possible to clone miRNAs using the new genome editing tool CRISPR/cas9, which shows benefit in control of untargeted effect. In this special issue, we tried to cover researches associated with functional roles of miRNAs across model and complex organisms.

Keywords miRNAs · Noncoding RNAs · CRISPR/Cas · Plant and human genome

In 2000, when scientist presented the first draft of human genome, they were stunned by the fact that more than 97% of that has no revealed protein coding function. This part, referred as “junk DNA” was thought as evolutionary remnants and natural parasitic part of human genome which can reproduce and spread themselves across the genome (Lander et al., 2001). However, this term of “junk DNA” have revealed a giant stumble in following years and in fact, the “junk DNA”

have come out as an big source of hidden treasures which scientist are still trying to understand. Apparently, the “junk DNA” has many important regulatory functions for maintenance of cellular life at the expressional, transcriptional and translational levels and the pieces of treasures are still in the process of discovery.

In recent years, a critical hidden molecule from the pool of junk DNA is discovered; microRNAs (miRNAs). miRNAs are an extensive class of small regulatory RNAs, which are the keystones controlling gene expression at the post transcriptional levels (Alptekin et al. 2016; Budak et al. 2015a; Budak and Akpınar 2015). These tiny ribo-regulators are widely existed in all eukaryotic organisms and they are involved in the regulation of many important pathways both in animals and plants (Alptekin et al. 2017; Budak et al. 2014; Eulalio et al. 2008; Zhang 2015; Zhang et al. 2007). miRNA-based gene expression regulation is critical in several diseases such as cancer, Alzheimer, Parkinson and they possess a potential of use as “biomarkers” for detection of such diseases and disease stages (Bekris and Leverenz 2015; Kosaka et al. 2010). In plants, they are contributed to stress tolerance together with environmental adaptation process and they have revealed a huge potential for crop improvement with the shed of several researches (Akpınar et al. 2015; Akpınar and Budak 2016; Budak et al. 2015b; Budak and Akpınar 2011). Considering the essential roles of them in many aspect of molecular life, miRNAs have attracted a considerable attention from scientific research community as well as industries in past 15 years (Lucas and Budak 2012; Kantar et al. 2012; Budak and Kantar 2015); however, many crucial points about these molecules still remain elusive.

Considering the importance of miRNAs, this special issue focuses on some exciting research questions associated with functional roles of miRNAs both in animals and plants with the contribution of 18 valuable papers (Alptekin et al. 2016;

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Alptekin and Budak 2016; Azevedo-Pouly et al. 2016; Baddela et al. 2016; Deniz and Erman, 2016; Esmaeili et al. 2016; Ferdous et al. 2016; Giusti et al. 2016; Gu et al. 2016; Gupta et al. 2017; Liu et al. 2016; Qiu et al. 2016; Reis et al. 2016; Soltani et al. 2016; Wang et al. 2017; You et al. 2017; Zhang et al. 2016; Zhao et al. 2016): How are the miRNAs involved in drought tolerance in plants? What is the role of miRNAs under biotic stress conditions? Are miRNAs crucial for cellular maintenance and survival in cancer tissues? What is the role of miRNAs in the developmental processes? In addition to research papers, three review paper are included in the special issue where the several controversial issues associated with miRNAs are discussed in a comprehensive and comparative way (Alptekin et al. 2016; Deniz and Erman 2016; Reis 2016). Overall, this issue gathers the papers from world-wide leading scientists of miRNA researches with the aim of providing up-to-date answers to miRNA-associated questions. Here, we highlight some of the particular subjects from this issue:

In spite the presence of several hypothesis about history of miRNAs and gene silencing at the post transcriptional levels, there are many points remain unexplained and not well-understood, particularly in plants (Voinnet 2009; Alptekin et al. 2017). In this special issue, Alptekin and Budak investigates the origin of miRNAs in bread wheat by performing an *in silico* identification and comparative analysis of miRNA repertoires of bread wheat and its diploid progenitors/relatives; their results provided important insight into the diversification and distribution of miRNA genes, which should contribute to the elucidation of miRNA evolution of Poaceae family (Alptekin and Budak 2016). Also, Reis reviews entangled history of animal and plant miRNAs in the consideration of current refinements and new hypothesis regarding to evolution of miRNAs (Reis 2016). This paper also provided detail information about miRNA and siRNA biogenesis and particular proteins involved in the biogenesis pathway. Also, You and colleagues focused on transcription start site of the *Arabidopsis* miRNAs which provide insight about miRNA biogenesis (You et al. 2017). Furthermore, Deniz and Erman described the long non-coding RNA molecules, their function and specific association between miRNAs (Deniz and Erman, 2016). These papers also provided a collection of studies which might be useful for gaining comprehensive information about miRNA biogenesis, miRNA evolution, and association of miRNAs with other sRNA molecules.

miRNAs are essential elements of stress adaptation and cell survival for plants under both biotic and abiotic stress condition (Budak et al. 2015b). In this special issue, Alptekin and colleagues reviewed the current progress about abiotic stress associated miRNAs and their targets as well the potential application of miRNA-based biotechnology on improvement of crop tolerance to abiotic stresses (Alptekin et al. 2016; Zhang 2015), particularly in wheat and barley (Alptekin et al. 2016). In addition, six research papers explore the miRNA response

to abiotic stress as well as hormone treatment in several plant species (Esmaeili et al. 2016; Ferdous et al. 2016; Giusti et al. 2016; Liu et al. 2016; Gupta et al. 2017; Zhao et al. 2016) and detected miRNAs have shown that they play important roles in plant response to environmental adaptation. Liu and colleagues surveyed the miRNAs responsive to water-deficiency stress in four type of durum wheat (Liu et al. 2016). Ferdous and colleagues showed that overexpression of miR827 confers the drought tolerance in barley and it represented a potential for maintenance of drought tolerance in cereals (Ferdous et al. 2016). In addition to the cereals, drought and osmotic stress associated miRNAs are also characterized in peach and almond (Esmaeili et al. 2016; Giusti et al. 2016). Also, Gupta and colleagues were analyzed and identified miRNAs and tasiRNAs under phosphate deficient conditions (Gupta et al. 2017). Furthermore, the miRNAs from grapevine berries in response to ethylene hormone treatment were surveyed by Zhao and colleagues (Zhao et al. 2016). Overall, these studies highlighted many miRNA candidates which might contribute crop improvement.

miRNAs have also been detected as showing a differential expression pattern under several diseases in humans and possess a potential to be used as a biomarker. Gu and colleagues showed that miR-106b/25 presents a oncogene potential by utilization of myeloma cells and they were able to decrease the malignant progression of cancer by inhibiting this miRNA family (Gu et al. 2016). In another study, Azevedo-Pouly and colleagues demonstrated that miR-216 and miR-217 expression was reduced in transgenic mouse models of pancreatic adenocarcinoma. Knockout of miR-216/miR-217 host gene was lethal at embryonic level (Azevedo-Pouly et al. 2016). Additionally, Soltani and colleagues discussed the role of miRNAs in imatinib-resistant chronic myeloid leukemia and their results shed a light to new therapeutical approaches for this type of cancer which might also be helpful for inhibition of potential anticancer drug resistance (Soltani et al. 2016).

miRNAs might also contribute the regulation of developmental pathways both in animals and plants. Baddela and colleagues researched on the miRNAs which are effective on the development of ovarian follicular granulosa cells (GC) and their maturation which are particularly located on the chromosome 21 in cows and chromosome 20 in buffalos (Baddela et al. 2016). In another study, Qiu and colleagues provided evidence on infection of a novel rhizobium, *Azorhizobium caulinodans* ORS571 on wheat and the potential role of miRNAs during maturation of symbiosis process (Qiu et al. 2016). Zhang and colleagues also identified miRNAs from parasitic plant toot-knot nematode *Meloidogyne incognita* which contribute the understanding of host-plant interaction process and development (Zhang et al. 2016). In addition to these valuable researches, Wang and colleagues investigated the miRNAs which are involved

in oil and oleic acid production during embryogenesis in *Carya cathayensis* (Wang et al. 2017). Thus, these miRNAs showed the importance of miRNAs in developmental process both at organismal and inter-organismal level.

In summary, this issue highlights the importance and essentialness of miRNAs for regulation of many important processes such disease resistance, stress tolerance and development. Described miRNAs in the shed of several valuable research papers presents a huge potential for the solution of today's critical problems like drug resistance or crop improvement. It is highly likely that future decades will show us the utilization of miRNAs in every aspects of science from medicine to agriculture. Given the need for a revised naming prescription, mis-identification and annotation of current miRNAs, CRISPR/Cas9 system in gene editing should be an innovative strategy in modulation of miRNA expression in model and complex organisms. Recently, Chen et al. (2016) employed CRISPR/Cas9 to knockout miR-126a gene, their results show the expression of miR-126 is significantly low and the knockout of miR-126a severely affected the formation of parachordal lymphangioblasts and thoracic duct in zebrafish embryos (Chen et al. 2016). Disruption of miR-137 via CRISPR/Cas9 inhibited the apoptosis in A2780 ovarian cells (Li et al. 2016). We believe CRISPR/Cas9 is becoming a powerful tool for studying the function of miRNAs as well improving traits for disease and pests in plants.

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