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Mini Review

Identification of Mirnas, Their Targets, and Their Activities, as well as the Prediction of Functional Microrna Targets using Integrative Modelling of Data on Mirna Binding and Target Expression

Ching Chang*

Harbin Medical University, Harbin, China

*Corresponding Author's E-mail: changching7878@yahoo.com

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Abstract

Small endogenous non-coding RNAs called microRNAs (miRNAs) serve as the universal specificity elements in post-transcriptional gene silencing. Understanding the normal biological activities of miRNAs and their involvement in the emergence of illness have depended critically on the discovery of miRNAs, the identification of their targets, and subsequent inference of miRNA functions. In this study, we concentrate on computational approaches for integrating heterogeneous data sources to infer miRNA functions, including as miRNA functional annotation and inferring miRNA regulatory modules. We also give a brief overview of the work in the fields of miRNA discovery and miRNA-target identification, focusing on the difficulties in computational biology (Price JH et al., 2002).In order to empirically discover the genes that are downregulated by 25 miRNAs, we conduct a large-scale RNA sequencing investigation. To systematically identify miRNA targeting characteristics that are indicative of both miRNA binding and target downregulation, this RNA-seq dataset is coupled with publicly available miRNA target binding data. We create and verify a better computational model for the prediction of miRNA targets across the genome by incorporating these common traits into a machine learning framework (Kutay H et al., 2006).

Keywords: miRNA; functional annotation; Functional miRNA-mRNA regulatory modules

INTRODUCTION

The goal of this study is to provide information on genetic and regulatory pathways, as well as miRNA-mediated control of the expression of key genes or transcription factors (TFs). Additionally, data on target prediction and validation, computational tools, and databases for plant miRNAs are specifically focused on their exploration for engineering abiotic stress tolerance in plants (Wei L et al.,2017). These factors are all related to adaptive mechanisms involved in plant responses to abiotic stress. An organism's genetic makeup, or genome, is crucial in encoding both the cellular structure and the regulatory apparatus that regulates cell homeostasis and internal processes including DNA replication and reaction to external cues (Singh I 1997). The complex biological processes produced from the genome entail a multitude of interacting and co-functioning RNA molecules as well as various protein structures, even though the genome is encoded by DNA. Non-coding RNAs of 19–26 nucleotides, known as microRNAs (miRNAs), attach to mRNAs and use their interactions with them to control how those mRNAs are translated. MiRNAs have a role in a number of physiological processes and are linked to the emergence of illnesses like cancer (Tian T et al., 2010). As a result, comprehension of miRNA regulation on targets is essential for comprehending illness causes and acquiring a more effective treatment. Prediction of these targets is hampered in animals by the poor base complementarity between miRNAs and mRNA.

Sequence information supplied by the user or typed by them is used to identify miRNAs. Numerous sequencing programmes might produce sequencing data. For instance, miRNA expression in tissue samples might be compared with and without a transcription factor that has been suppressed by siRNA in a comparative sequencing effort. In the majority of physiological activities, miRNAs are essential (Hamilton JA et al., 2002). It is not shocking that poor control of miRNAs has been associated with a variety of illnesses, including cancer, metabolic syndrome, and neurological disorders. A single miRNA may really be able to bind up to 200 different gene targets, according to bioinformatic assessments. One-third of all human genes might possibly be regulated by miRNAs collectively. (See our recent webinar on the identification of circulating biomarkers.) MiRNA expression analysis in certain cell types may have significant diagnostic utility, and restoring aberrant miRNA levels in disease states offers exciting therapeutic potential (Craveiro Sarmento AS et al., 2018).

Gene regulatory modules are cooperative collections of molecules that are crucial parts of biological systems. In-depth analysis of gene structures, functions, and activities inside individual cells and in different tissues during development is required in order to comprehend the makeup of these modules and their functions in an organism. The patterns of gene expression and their regulation or dysregulation, however, are what have the biggest impact on normal biology and disorders since gene structure and function remain largely stable from one cell to another or from one species to another (Connor RF et al., 2007).

The review discusses the regulatory role of miRNAs in plant growth, development, and abiotic stresses. HTS technologies are used to create large libraries of small RNAs (sRNAs) for conventional screening of known and novel abiotic stress-responsive miRNAs, which complicates the regulatory networks in plants. In this review, we highlight and discuss the recent findings of miRNA-mediated tolerance to a variety of abiotic stressors, including salt, drought, cold, heat stress, nutritional deficiencies, UV radiation, and oxidative stress, hypoxia, and heavy metal toxicity (Ibba M 2002).

Although a variety of factors can affect how a gene expresses itself, post-transcriptional gene regulation involving microRNAs (miRNAs) is particularly fascinating because of the range of interactions that are made possible by the synergistic/combinatorial relationships that these molecules have with their target genes. A developing family of non-protein-coding RNAs with a length of 22 nt defines miRNAs. They are expressed from longer transcripts that are encoded in single-celled eukaryotes, viruses, plants, animals, and plants. Due to their functions as guide strands for mRNA degradation and translational inhibition, which are mostly accomplished through the logic of complementary base pairing, miRNAs are also a fascinating issue for system modelling and computer science (Andreini C et al., 2012).

Growing evidence points to miRNAs as important regulators of cellular homeostasis and development due to their influence over a variety of biological functions. Target mRNAs are controlled by miRNAs, which also fine-tune protein production. Therefore, abnormal miRNA function can result in human illnesses. Various cancer forms, including breast cancer, lung cancer, prostate cancer, colon cancer, ovarian cancer, and head and neck cancer, have been linked to differently regulated miRNAs in recent research. Numerous neurological conditions, such as schizophrenia, multiple sclerosis, and Alzheimer's disease, are also thought to be impacted by miRNAs. Determining miRNAs, targets, and their functional regulatory networks is therefore essential to understanding miRNAs' normal biological functions and their contributions to the emergence of illness (Feig AL et al., 2002).

In recent years, significant efforts have been undertaken to find miRNAs, identify miRNA targets, and infer miRNA functions using both biological and computational techniques. The quantity of miRNA and mRNA data at both the expression and sequencing levels has significantly expanded as a result of these endeavours. However, because to the time-consuming procedures required, it is not viable to scientifically investigate the complexity and variety of miRNAs and their targets using biological approaches in a combinatorial matrix. Fortunately, computational techniques provide insight into biological research by generating statistically significant hypotheses from the vast amount of biological observations, facilitating experimental validation (Vuong P et al., 2008).

As these strategies have already been thoroughly discussed elsewhere, in this review we just briefly touch on bioinformatics approaches to miRNA discovery and target identification with a focus on the difficulties in computational biology. Computational techniques for miRNA functional annotation and inferring miRNA regulatory modules will receive further focus (MRMs). This innovative and difficult new discovery in integrated genomics has the potential to give miRNA and miRNA-associated gene networks a more robust and concrete functional annotation (Alic AS et al., 2016).

Small non-coding RNAs called microRNAs (miRNAs) play a significant role in a wide range of biological activities. MiRNA expression can be dysregulated, which can result in a number of disorders. Over 2000 human miRNAs have been identified in miRBase as of this writing. Both computational and experimental investigations show that one or more miRNAs influence the majority of human protein-coding genes. Finding the genes that the miRNA target is a crucial initial step in the investigation of functional miRNAs. In order to do this, the majority of research use computational algorithms to initially select interesting target candidates that are then subjected to experimental validation. Given the crucial role that target prediction plays in characterising how miRNAs work, a variety of computational techniques

have been created over the past ten years, each of which has steadily improved target identification performance. In example, new models have been created recently based on advances in experimental techniques and fresh perceptions of the processes governing miRNA target regulation. Many common characteristics have been identified for miRNA target regulation, including precise matching of the miRNA 5'-end (seed region) to the target site and very low target site GC content, which increases site accessibility for miRNA binding (Kelley DR et al., 2010).

MicroRNAs (miRNAs) are a particular subclass of endogenous short non-protein coding RNAs with a length of 20 to 24 nucleotides that regulate post-transcriptional and translational gene expression in both plants and animals. Mature miRNA recognise and complementarily bind to the open reading frame or untranslated regions (UTRs) of target genes to negatively control gene expression. Mature miRNA is produced from longer pri-RNA by nuclease cleavage mechanisms. A single miRNA may influence the expression of several genes, and multiple miRNAs can affect the expression of a single gene. The strong complementarity between miRNA and its targets in plants leads to RNA-induced silencing complexes that either destroy the target mRNA or prevent it from being translated. Because of this, miRNA-mediated gene silencing is crucial for a number of fundamental plant biological processes, such as developmental control, hormone secretion, cell differentiation, and proliferation, as well as environmental adaptation and response to factors like salinity, drought, and low temperature. Similar to this, certain miRNAs influence the relationships between plants and microbes, which points to their involvement in activities like symbiosis events and plant-pest interactions. Understanding miRNAs' regulatory functions in plants, however, is challenging since they are known to be spatiotemporally specialised (Salmela L et al., 2011).

CONCLUSION

To anticipate miRNA genes or miRNA: target relationships, the majority of computational methods created to date heavily rely on evolutionary conservation. This demonstrates how little we all understand about the complex laws governing miRNA biogenesis and target specificity. We appear to be leaving out an important piece of the puzzle since the cell cannot select among all potential stem-loops or all potential targets using the filter of evolutionary conservation. Future research should concentrate on the requirement to construct more precise models for these fundamental issues. Animal miRNA precursors are still being studied in an effort to identify their distinctive properties. Even after accounting for size and GC content, it has already been proven that the known miRNAs have extremely low-energy structures when compared to other RNAs. Additionally, as would be predicted for effective Drosha detection, these stem-loops appear to be resilient in relation to their genomic settings. They are also stable in the sense that the thermodynamic ensemble, which contains the stem-loop most frequently, consists of a collection of suboptimal structures, all of which exhibit a consistent base-pairing pattern. Another characteristic of miRNA precursors that has been proposed is mutational resilience, which is more likely to be seen in older, well-conserved pre-miRNAs than in more recent, non-conserved precursor stem-loops.

The recent suggestion of a thermodynamic model with target accessibility has given the field of target prediction a new boost. But a crucial filter for limiting false positives is seed matches. The seed hypothesis, which is almost universally accepted by current target prediction methods, has recently been supported by a study that determined the structure of a key silencing complex component bound to a DNA guide strand and establishes the biochemical rationale for the function of seed sites. However, at least some targets that have undergone experimental confirmation appear to go against the seed rule by including mismatches or G: U pairings. The biggest barrier to the creation of better prediction methods as well as the systematic evaluation of the efficacy of existing tools is the current lack of miRNA targets that have been confidently validated, establishing not only miRNA-target associations but also precisely identifying the hybridization sites.

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