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The Functional Roles of microRNA

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MicroRNAs (miRNAs) are a class of small non-coding RNAs that play important roles in post-transcriptional regulation of gene expression[1]. A large number of miRNAs have been found to be involved in a broad spectrum of biological functions such as regulation of innate and adaptive immunity, cell differentiation and development as well as disease pathogenesis, especially in cancer [2–8]. However, the molecular mechanisms remain largely unknown, which severely blocks the miRNA therapeutic and preventative strategies. Some recent studies have provided valuable information to further unveil the mysteries of miRNA.

High-throughput miRNA microarray and small RNA sequencing have identified a large set of miRNAs involved in development of mammal and plant [6,9]. Dysregulation of the miRNA pathway have great impact on neuronal and glial development in the mammalian brain and could lead to neurodevelopmental and neurodegenerative diseases[4]. Furthermore, wide-ranging functions for miRNAs have been identified using gain- and loss-of-function studies, which provide new perspectives regarding regulation mechanisms of miRNAs in heart development and disease [5]. In plants, miRNAs are predicted to be involved in nearly all biological processes, such as cell development, differentiation, and stress responses[9].

Deregulated expression pattern of large set of miRNAs in cancer and their interactions with oncogenes and tumor suppressor genes demonstrate these miRNAs may be involved in tumorigenesis [10–13]. Recent study from He *et al*. have shown that chromosome gain of miR-151 is a crucial stimulus for tumour invasion and metastasis of hepatocellular carcinoma [11]. Another example, miR-181b is highly expressed in acute myeloid leukemia (AML) and contributed to proliferation of AML cells by targeting MLK2[12]. Furthermore, several differentially expressed miRNAs may be involved in uveal melanoma pathogenesis, and may serves as informative biomarkers for uveal melanoma [13]. Notably, miRNAs have been found to be encoded by animal and plant viral genomes, and many virus-encoded miRNAs have been found to be involved in the cancer development[14–15]. Marek's disease virus (MDV)-encoded miRNAs play key roles in lytic replication, latent infection, T-lymphocyte transformation and tumorigenesis [14]. Lan *et al*. found a miRNA, miR-K12-11, encoded by Kaposi's sarcoma-associated herpesvirus (KSHV), that is critical for the modulation of IFN signaling by targeting IκB kinase ε and can contribute to maintenance of KSHV latency[3]. All the above studies give us great insights into the pathogenesis of miRNA related cancer.

The advantages of high-throughput sequencing (HTS) technology provide us the abilities to illustrate the complexity of genome and transcriptome more comprehensively and generate an unprecedented landscape of miRNA for various species[16–18]. By virtue of the HTS technique, "competitive endogenous RNA" (ceRNA) hypothesis were propose recently [19], which consider messenger RNAs and long non-coding RNAs, a kind of RNA with regulation [20–21], could communicate each other through a new "language" mediated by microRNA-binding sites. Notably, some previous bioinformatic analysis conducted by Zhao *et al*. have provide direct evidence for ceRNA hypothesis [22-23], but which were lack of experimental validation that have been done by several research groups recently. Although the throughput and reproducibility of methods for analyzing miRNAome has improved at a rapid rate, many challenges remain. For example, it is difficult to simultaneously measure miRNA and their targets using HTS technology, and the interpretation of miRNA network involved in various diseases is still be to resolved. In all, the combination of biology, medicine and bioinformatics would greatly facilitate the development of miRNA study in future.

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