MINI-REVIEW

MicroRNAs: Biogenesis, Roles for Carcinogenesis and as Potential Biomarkers for Cancer Diagnosis and Prognosis

Nowroji Kavitha¹, Soundararajan Vijayarathna¹, Subramanion Lachumy Jothy¹, Chern Ein Oon¹, Yeng Chen², Jagat Rakesh Kanwar³, Sreenivasan Sasidharan¹*

Abstract

MicroRNAs (miRNAs) are short non-coding RNAs of 20-24 nucleotides that play important roles in carcinogenesis. Accordingly, miRNAs control numerous cancer-relevant biological events such as cell proliferation, cell cycle control, metabolism and apoptosis. In this review, we summarize the current knowledge and concepts concerning the biogenesis of miRNAs, miRNA roles in cancer and their potential as biomarkers for cancer diagnosis and prognosis including the regulation of key cancer-related pathways, such as cell cycle control and miRNA dysregulation. Moreover, microRNA molecules are already receiving the attention of world researchers as therapeutic targets and agents. Therefore, in-depth knowledge of microRNAs has the potential not only to identify their roles in cancer, but also to exploit them as potential biomarkers for cancer diagnosis and identify therapeutic targets for new drug discovery.

Keywords: Cell cycle control - cancer - miRNA dysregulation - oncogene

Introduction

MicroRNAs (miRNAs) are small, single stranded and genomically encoded RNA molecules of approximately 19 to 25 nucleotides in length that are found in all higher eukaryotes including mammals, fungi and plants. miRNA lin-4 was the first miRNA discovered in 1993, which regulates the developmental timing of larva by translation repression of the gene lin-14 in the nematode Caenorhabditis elegans (Lee et al., 1993). The discovery of miRNA was proven to be continued when a second miRNA, let-7, which was discovered in 2000 (Reinhart et al., 2000), repressed lin-41, lin-14, lin-28, lin-42, and daf-12 expression during alteration of the developing stage in C. elegans. Subsequently, let-7 was found to be homologous in other species, including humans, and revealed that the existence of miRNAs is quite common in eukaryotes, which is the one of the most exciting scientific breakthroughs in the last decade. Since then, thousands of non-coding RNAs have been studied and 940 distinct miRNA molecules that exist in human genomes were identified and catalogued (Berezikov et al., 2005; Griffiths-Jones et al., 2008; Baumhoer et al., 2012; Chaudhry and Lhakhang, 2012). Each miRNA is predicted to have hundreds of mRNA targets caused by the imperfect base pairing (Lim et al., 2005) to the 3’ untranslated region (UTR) of the target mRNAs and signalling the target for mRNA degradation. Thus, miRNAs have been identified as performing significant regulatory functions in various cellular, biological and pathological processes, including the differentiation, progression, apoptosis, and proliferation of cancer cells (Heneghan et al., 2010; Farooqi et al., 2014). These molecules characteristically moderate the translation and stability of mRNAs, including those genes that mediate processes in carcinogenesis, including the immune response, metabolism, inflammation, cell cycle control, viral replication, stem cell differentiation and human development (Farazi et al., 2013).

miRNAs, known as gene regulators, expressed more than 30% of protein-coding genes in the human genome at the post transcriptional stage and simultaneously targeted multiple genes in the initiation and progression of human malignancies (Croce, 2009). Recent studies also indicated the differences of miRNA expression profiling between tumour and normal cells that revealed that miRNAs are involved in the pathogenesis of all types of human cancer (Heneghan et al., 2010; Kobayashi et al., 2012; Su et al., 2013). Furthermore, miRNAs play numerous roles as tumour suppressors due to the aberrant expression, which can lead to carcinogenesis by inhibiting the malignant potential, or react as an oncogene by triggering malignant