

Forum Minireview

**MicroRNAs and Their Therapeutic Potential for Human Diseases:
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1-1-20 Shinmachi, Nishitokyo-shi, Tokyo 202-8585, Japan**Received May 27, 2010; Accepted June 1, 2010***Keywords:** RNA interference (RNAi), microRNA (miRNA), primary miRNA (pri-miRNA), precursor miRNA (pre-miRNA)

RNA interference (RNAi) is a cellular mechanism to regulate eukaryotic gene expression in a sequence-specific manner by either inducing degradation of a messenger RNA (mRNA) or inhibiting its translation (1). The RNAi is triggered by two classes of RNA molecules, small interfering RNAs (siRNAs) and microRNAs (miRNAs). The siRNAs are either endogenously encoded (1) or derived from longer double-stranded RNA, which are transcribed from various vectors or are directly introduced into cells by transfection. The miRNAs are processed from stem-loop precursors (pre-miRNAs) that are encoded within the host genome (2 – 4).

The miRNAs are initially transcribed as long RNA precursors, termed primary miRNAs (pri-miRNAs), that require the RNase III enzyme, Drosha, in the nucleus to trim them into pre-miRNAs. The pre-miRNAs are characterized by a stem-loop or hairpin structure of 70 – 100 nucleotides and are exported to the cytoplasm by the nuclear export factor, exportin-5. The pre-miRNA are subsequently cropped to become mature miRNA by another RNase III enzyme, Dicer, in the cytoplasm (5).

It is increasingly evident that miRNAs play an important role in regulation of gene expression. Although our understanding of the specific roles of miRNAs in cellular function is only beginning, recent studies revealed that miRNAs play a pivotal role in the most critical biological events such as development, proliferation, differentiation, apoptosis, signal transduction, and carcinogenesis (4). The mature miRNAs are conserved about 2-nucleo-

tide non-coding RNAs that anneal to inexact complementary sequences in the 3'-untranslated regions (3'-UTR) of target mRNA of a protein-coding gene, resulting in silencing of the target gene. While the mechanism of action of miRNAs is yet to be fully understood, the widely-known mode of gene regulation by miRNAs occurs at the post-transcriptional level by either specific inhibition of translation or induction of mRNA cleavage (6, 7). More recently, it has also been suggested that miRNAs are capable of modifying chromatin (7).

Over 1,000 miRNAs have been estimated to exist in human cells, and they are involved in the regulation of up to 30% of all genes and almost every genetic pathway (5). Increasing evidence also suggests that a wide range of miRNAs are linked to a variety of human diseases (5). In this series of forum minireviews (8 – 10), we will discuss possible involvement of miRNAs in some diseases, including allergic bronchial asthma, muscular dystrophy, amyotrophic lateral sclerosis, Alzheimer's disease, cancer, and so on, based on our recent findings (11 – 14). The information would also provide us new insight that miRNAs are significant pharmacological targets for the treatment of certain diseases.

This forum minireview series is based on the symposium at the 83rd Annual Meeting of The Japanese Pharmacological Society held on March 16, 2010.

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