MicroRNAs

Clinical trials and potential applications

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MicroRNAs are novel biomolecules with a crucial function in normal cellular physiology and in pathophysiologic conditions, including cancer. Since the first report on the link between microRNAs and cancer was published in 2002, research has revealed the potential clinical implications of microRNAs. Oncology nurses play an important role in educating patients and their families about possible applications of microRNAs in oncology.

AT A GLANCE

- MicroRNAs are critical in regulating various biologic processes engaged in the promotion or inhibition of cancer growth.
- MicroRNAs may be biomarkers for various clinical applications, including diagnosis, prognosis, therapy response, treatment side effects, disease risk, disease progression, and metastasis.
- Numerous clinical trials involving microRNAs and cancer are in progress, with the aim of validating clinical application.

KEYWORDS
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The structure and function of RNA molecules—messenger RNA (mRNA), ribosomal RNA (rRNA), and transfer RNA (tRNA)—have been known for decades. In addition to these known RNA molecules, a class of small noncoding RNA molecules, called microRNA, have been discovered in animals and plants. The first microRNA was discovered in the nematode *Caenorhabditis elegans* (commonly known as roundworm) in 1993 (Lee, Feinbaum, & Ambros, 1993; Wightman, Ha, & Ruvkun, 1993). The existence of microRNAs in humans was first reported in 2000. To date, more than 2,500 microRNAs have been identified in humans and are listed in the miRBase database with their known sequence and annotation (www.mirbase.org; the site is a repository for newly discovered microRNAs and provides stable and consistent names for microRNAs).

MicroRNAs are small, single-stranded molecules of about 19–25 nucleotides in length. Research has determined that microRNAs are important constituents of the gene regulation network, which traditionally was thought to include transcription factors, factors that regulate mRNA stability, factors that regulate translation, and factors that control protein degradation. Research has demonstrated that microRNAs may regulate the expression levels of nearly all genes and modulate the levels of mRNA and proteins in cells (Bhatti, Lee, Lund, & Larvin, 2009). Central dogma, the core principle of molecular biology, illustrates and describes the transfer of genetic information from DNA to RNA to protein (see Figure 1). The term *central dogma* is a misnomer and has been retained only for historical reasons to dictate translation of DNA sequences into proteins through messenger RNAs. The functional understanding of microRNAs led to redefining the central dogma of molecular biology. Because of the immense potential of microRNAs in clinical practice, the discovery of these remarkable molecules has triggered a scientific revolution in a quest to understand their role and importance. Discovery of the profound significance of short RNAs and the process of gene expression regulation by such RNAs, including the small interfering RNAs (or siRNAs), in molecular biology was recognized by the awarding of the Nobel Prize in Physiology or Medicine to Andrew Z. Fire and Craig C. Mello in 2006.

Biogenesis

MicroRNAs are encoded in the genome and synthesized by the RNA polymerase II enzyme as long primary transcripts called primary-microRNAs (pri-miRNAs), which can be several kilobases in length. The pri-miRNAs undergo a series of several biochemical steps to yield mature microRNA molecules containing about 19–25 nucleotides (Siomi & Siomi, 2010) (see Figure 2). Through base pairing, the microRNA may either trigger messenger RNA degradation (because of perfect microRNA–mRNA pairing) or block messenger RNA translation into protein (because of imperfect microRNA–mRNA pairing) (Bartel, 2009). Mature microRNAs can also be transported back into the nucleus to exert their effect on the gene regulation system by targeting hundreds of messenger