Revista médica del
Hospital General de México

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EDITORIAL

microRNAs

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Gene expression is controlled by transcription factors and other protein cofactors. However, thanks to studies conducted in the past decade, gene regulation has been proven to be highly complex due to the discovery of non-coding RNAs (ncRNAs), which are key factors in the regulation of gene expression. Roughly 15 years ago, a new path that supports gene expression in animals and plants began to be elucidated. This regulatory pathway is mediated by small non-coding RNAs (ncRNAs), known as microRNAs (miRNAs) (miRNAs; a.k.a. miRs in its shortened form).

miRNAs are a class of short RNA molecules of approximately 19-22 nucleotide residues in length that modulates gene expression. They prevent protein synthesis by means of translation inhibitors through binding to target sites in the 3' untranslated region of the complementary messenger RNA (mRNA) in the cytoplasm. In the nucleus, they modify gene expression through binding to regulatory sequences in genomic DNA.

In 1993, a small ncRNA was described for the first time; it regulates another protein-coding gene, by base pairing to its mRNA. After a decade, the importance of this mechanism was understood as the key to knowing the role of miRNAs in the regulatory networks that govern the biological processes of cell proliferation, differentiation, and death in both normal and aberrant pathways.

Apparently, miRNAs regulate more than a third of all human genes, which makes it one of the largest gene families as it represents approximately 1% of the genome. Recent data state that more than 60% of the human protein-coding genes contain at least one conserved miRNA-binding site. In its latest version of October 2018 (v22), in the miRBase database, miRNA sequences from 271 organisms have been recorded: 38,589 hairpin precursors and 48,860 mature miRNAs. In total, 1917 hairpin precursors and 2654 mature sequences have been recorded in the human genome. Thus, it is expected that the biogenesis and function of miRNAs are well regulated, and their deregulation is associated with human diseases, such as cancer and neurodevelopmental disorders.

MiRNAs and cancer

It has been widely described that miRNAs in cancer are characterized by an abnormal expression (up- or down-regulated), whether related to its precursors or mature miRNAs. This deregulation has been found in a wide range of human carcinogenic tissues, such as lymphomas, breast cancer, colorectal cancer, prostate cancer, and glioma, among others.

The causes of aberrant expression in different types of tumors have not been fully elucidated. Some mechanisms defined as chromosomal alterations, point mutations in coding genes, and modifications of miRNA expression due to transcriptional regulation, epigenetic changes, and alterations in the biogenesis of miRNAs have been described.

In addition, fragile sites and genomic regions related to cancer and miRNAs have been associated. Hence,

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Date of reception: 28-02-2020
Date of acceptance: 03-03-2020
DOI: 10.24875/HGMX.M20000037

Available online: 21-04-2020
Rev Med Hosp Gen Mex. 2020;83(2):45-46
www.hospitalgeneral.mx

alterations in their expression could be a reflection of the chromosomal or genomic changes of cancer-associated genes.

Furthermore, it has been observed that miRNAs discriminate between different types of cancers according to their origin or histopathological subtype. An interesting approach to the study of miRNAs and cancer is whether their expression is up- and/or down-regulated. They are considered oncogenes, when an increase in their expression contributes to a malignant transformation of normal cells, being called oncomiRs. Conversely, if they are down-regulated, they act as tumor suppressors and are called tumor-suppressor miRs.

In the past decade, the way miRNAs intervene in various signaling pathways which are crucial for the development of cancer cells has been described: self-sufficiency in growth signals, insensitivity to anti-growth signals, apoptosis, limitless replicative potential, angiogenesis, invasion, and metastasis.

This has allowed us to focus our attention on these small molecules as possible biochemical markers applied in the diagnosis and prognosis of certain types of cancer. Finally, the use of therapeutic targets against these molecules is still under investigation, given their complexity and difficulty involved in reaching tumor cells accurately without affecting other healthy tissues.