MiR-34a: A Key Small Molecule with Great Effects

Nahid Arghiani[1], Maryam M. Matin[1]

1. Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran

Abstract

Cancer remains the third leading cause of death in Iran after cardiovascular diseases and road accidents. MicroRNAs are short, non-coding RNAs which are involved in different pathways like; cell growth, differentiation, development, haematopoiesis, and apoptosis. MiRs function either as oncogenes or as tumour suppressors and, overexpression of oncomiRs and/or downregulation of tumour suppressor miRs can promote cancers. Some miRs like; let7g and miR-34a show a loss of function in different cancer types and represent tumour-suppressive effects. MiR-34a, a tumour suppressor miRNA, is silenced or significantly downregulated in major classes of human cancers like brain, colon, gastric, lung, neuroblastoma, pancreatic, and prostate cancers. Various genetic and epigenetic mechanisms can be involved in miR-34a deregulation. For example, its gene is located in a fragile site that is often deleted in human cancers or, promoter hypermethylation of this miR has been observed in some tumours. MiR-34a exerts its effects by regulateing numerous target genes that function in various cellular pathways. These genes include cyclin D1 (CCND1), cyclin E2 (CCND2), cyclin dependent kinase 4 (CDK4), CDK6, CDC2, CDC25A, CDC25C, E2F transcription factor 1 (E2F1), E2F3, c-MYC, MYCN, silent information regulator 1 (SIRT1), SURVIVIN, Kruppel-like factor 4 (KLF4), metastasis associated 1, family member 2 (MTA2), yinyang1 (YY1), NOTCH1, C-Met, WNT1 and Lymphoid enhancer-binding factor-1 (LEF1). Thus, miR-34a is involved in different biological processes such as cell-cycle arrest, induction of apoptosis and senescence-like phenotypes by regulating the expression of these genes. There are several reports demonstrating that forced expression of miR-34a can induce apoptosis; inhibit cell proliferation, tumour growth and invasion; and modulate sensivity of tumour cells to chemotherapeutic agents. Taken together, different studies demonstrated that miR-34a, may be considerd as a novel and potential diagnostic agents.

Keywords: Cancer, Non-coding RNA, MiR34a, Downregulation, Biomarker

Corresponding Author: Maryam M. Matin

Email: n.arghiani@gmail.com