Cancer is one of the leading causes of death worldwide. There is a definite need for novel approaches to improve the diagnostics and treatment of cancers. The pathological processes leading to carcinoma are associated with the altered expression of a specific gene relevant to malignancy. MicroRNA-125b (miR-125b) is a small non-coding, multipurpose miRNA that plays a key role in several different biological processes. Increasing amounts of evidence indicates that miR-125b may serve as a diagnostic biomarker of certain kinds of cancers. miR-125b may be suitable to be used as a therapeutic target in several human diseases including neoplastic disease. Here, we review the latest progress in the identification and validation of the relationship between cancer-related miR-125b and cancers, and discuss the functions of miR-125b that regulates many processes of diseases, including cell proliferation, differentiation, and apoptosis.

Keywords miR-125b; target gene; gene expression; cancer

Expression of miR-125b in Cancers

Malignancies are mainly caused by internal factors, most importantly the clonal growth of tumorous cells. Emerging evidence indicates that the growth of tumorous cells induces profound changes of miR-125b expression in different tissues and organs. For example, researchers have observed that miR-125b is located at chromosome 11q23-24, one of the regions that is most frequently detected in breast, ovarian, and lung tumors [7,8]. Expression of chromosome 11q23-24 is down-regulated in breast cancer. Iorio et al. [9] also found that aberrant expression of miR-125b gene may take place during the pathogenesis of the breast cancer.

Previous studies have shown that miR-125b is up-regulated or down-regulated in different cancers under pathophysiological conditions [10–13]. In thyroid cancer, miR-125b is significantly over-expressed in thyroid follicular...
miR-125b and Its Biological Functions

miRNAs inhibit gene expression via complementary base pairing and selective binding to the complementary 3′-untranslated region (3′-UTR) of miRNAs [14]. miR-125b is highly conserved among mammals, vertebrates, and nematodes [15]. Mature miRNA-125b originates from two precursors: pre-miR-125b-1 (located at chr11q24.1) and pre-miR-125b-2 (located at chr21q21.1) [16]. The function of miR-125b primarily involves cell proliferation, differentiation, and apoptosis, all of which are taken place in cancers. miR-125b is directly involved in the formation of carcinomas. It has been widely shown that miRNA-125b is under the transcriptional control of nuclear factor-κB, a pro-inflammatory transcription factor widely implicated in cancers and Alzheimer’s disease [17,18]. In this way, miR-125b may be a suitable research focus for the treatment and prevention of cancers.

miR-125b regulates cell proliferation in malignancy

Cancer is a major cause of death due to tumor cell proliferation and metastasis. miR-125b may inhibit the development of malignancy and cell proliferation. The most numerous glial cells in the central nervous system are astrocytes, which perform function in signaling pathway and immunological process [19–21]. miR-125b is up-regulated in the brain tissues of individuals with Alzheimer’s and Down’s syndromes and in those with neurodegenerative disorders associated with astrogliosis. It also regulates many different mRNA targets within healthy brains [1,22–24]. Regarding to molecular triggers of astrogliosis and their role in neurodegenerative disease, recent research has shown that significant up-regulation and high concentrations of miR-125b are strongly associated with glial cell proliferation in the brain [16]. Gliarial fibrillary acidic protein, vimentin, and miR-125b are visibly up-regulated during interleukin (IL)-6-induced proliferation of normal human astrocyte cells. However, anti-miR-125b neutralizes the effects of IL-6 and weakens astrogliosis [16].

miR-125b modulates cell apoptosis in carcinoma

Transcription factor p53 is an important tumor suppressor and a central modulator of the stress reaction, which regulates multiple cellular processes. Activation of p53 during DNA damage or oncogene activation results in cell cycle arrest or apoptosis [25]. It has been recently found that miR-125b is a brain-enriched microRNA [26] and regulates human cells and zebrafish embryos through p53-mediated processes. Over-expression of miR-125b suppresses the endogenous levels of p53 protein and inhibits apoptosis of human neuroblastoma cells and human lung fibroblast cells. However, knockdown of miR-125b increases the protein level of p53 and induces cell apoptosis in human lung fibroblasts and in the brains of zebrafish [2]. In colorectal cancer, Nishida et al. [27] demonstrated that the miR-125b/p53 pathway is of clinical significance and importance as a prognostic indicator. Over-expression of miR-125b has been shown to inhibit the endogenous level of p53 and its downstream molecule, p21. It also has anti-apoptotic effects and can inhibit cell cycle arrest in colorectal cancer cells.

miR-125b suppresses the development of tumor by targeting genes

miR-125b may inhibit the development of malignancy at the post-transcriptional level by binding to specific target gene sequences. Guan et al. [28] found that miR-125b decreases the proliferation of human ovarian cancer (OC) cells, and suppresses the growth of OC cells by targeting BCL3. miR-125b has a tumor repressive function in human bladder cancer, and an important oncogene, E2F3, has been confirmed as a target of miR-125b [29]. Shi et al. [30] detected high miR-125b expression in clinical prostate cancer samples and many cultured CaP cell lines. They also found that miR-125b targets the 3′-UTR of BAK1, which is a member of the Bcl2 protein family and a pro-apoptotic regulator. It was recently confirmed that miR-125b is expressed in a similar manner in osteosarcoma tissues and cell lines. Down-regulation of miR-125b has been frequently observed in these tissues and cells [5]. Nevertheless, exogenous over-expression of miR-125b inhibits cell proliferation and migration by targeting STAT3 in MG-63 and Saos-2 cells that leads to reduced tumorigenesis in nude mice [5]. In our laboratory, we hypothesized that miR-125b might modulate the proliferation and migration of osteosarcoma cells by targeting Cbfβ. An experiment is being performed to test this hypothesis.

Prospects

The discovery that the post-transcriptional regulatory factor, miR-125b, takes part in the transcriptional regulation in humans, is an innovative breakthrough in genetic engineering. These studies described above will broaden our understanding of the function of miR-125b in tumorigenesis and
tumor progression. In the past few years, remarkable advance has been made in the study of miR-125b. miR-125b has been found to be involved in human breast cancer, thyroid cancer, HCC, OSCC, colorectal cancer, bladder cancer, prostate cancer, and osteosarcoma. Confirming the target genes of miR-125b is one of the fundamental problems that remain to be solved. Much more work is needed to confirm that miR-125b is the most significant cause of carcinoma. Studies on miR-125b may promote the development of gene therapy, tissue engineering, and regenerative medicine. A more detailed understanding of the mechanisms underlying the regulation of miR-125b may be a focus in the future. It may provide an effective model for the research of specific diseases in which miR-125b is involved. It may also facilitate the development of theories and practical foundations for the clinical application of gene therapy. If these questions are addressed, it will be a major breakthrough in medical science.

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References