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MicroRNA-210 as a Biomarker in Breast Cancer

Mohamad AlJarallah[1*], Nafise Poorhasan[2]

[1] Jarallah German Specialized Clinic
[2] Department of Cellular and Molecular, Faculty of Life Sciences, North Tehran Branch, Islamic Azad University, Faculty of Biological Sciences, Tehran, Iran
[2] Personalized Medicine Research Center of AmitisGen, Tehran, Iran

**Corresponding author: Mohamad AlJarallah. Jarallah German Specialized Clinic. Email:drmjarallah@gmail.com*

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Abstract

The increasing literature exploring the role of circulating miR-210 has clarified its potential as a promising biomarker for early detection, diagnosis, and prognosis. Measuring circulating miR-210 levels could be a non-invasive method for early cancer detection. Even if, to date, most studies appear to be preliminary, it seems that miR-210 will be a good target for drug development. This study detected the difference in serum miR-210 expression between healthy people and breast cancer patients. A total of 15 breast cancer patients were selected for a breast cancer (BC) group and 15 healthy people as a control group. The results showed that the expression level of miR-210 in the serum of breast cancer patients was significantly higher than controls. Patients with breast cancer showed increased levels of circulating miR-210, so circulating miR-210 may be a potential biomarker of tumor presence and therapeutic response to breast cancer..

INTRODUCTION

MicroRNAs are small, evolutionary conserved, single-stranded, and non-coding RNA molecules that bind target mRNA to prevent protein production by one of two distinct mechanisms: Translation repression or mRNA cleavage [1]. There is a general understanding of miRNA function, but the mechanistic details of miRNA biogenesis and gene silencing are still unclear. Although the biological function of identified miRNAs may be unknown, examining the expression profiles of these molecules provides information on their regulation and function [2]. Such observations have indicated that miRNA expression profiles are altered in specific tumors, implying that miRNA may be involved in the development of cancer and other diseases [3]. Despite the limited knowledge of these molecules, basic expression profiling is clinically relevant to cancer diagnosis, progressions, and outcome. The growing body of experimental evidence suggests a clinical relevance for microRNA miR-210 [4]. There are two versions of miR-210, namely, miR-210-3p and miR210-5p. miR-210-3p is the guide-strand integrated into RISC, whereas miR-210-5p is the passenger-strand inactivated by degradation. miR-210 is up-regulated in most solid tumors, and its levels correlate with negative clinical outcomes [5]. It has been associated with a variety of functionally important targets involved in cancer but also in cell cycle regulation, cell survival, differentiation, angiogenesis, and metabolism. miR-210 is involved in numerous biological processes almost throughout the human body, which is also a regulator of several cellular functions, dependent or independent on hypoxia; among these, neurogenesis is a complex process of many steps [7]. miR-210 has been extensively studied in cancer progression [8]. It is known that miR-210 generally exhibits oncogenic properties, as it is frequently elevated in several cancers, including breast, lung, head and neck, pancreatic cancer, or glioblastoma. miR-210 is overexpressed in numerous cancers, including breast [9], and the induction of miR-210 is a consistent characteristic of the hypoxic response in both normal and transformed cells. This study detected the difference in serum miR-210 expression between health and breast cancer patients.

METHOD AND MATERIALS

A total of 15 breast cancer patients were selected as the breast cancer (BC) group and 15 healthy people (all female; age range, 55-75 years; median age, 65 years) who underwent physical examination in our hospital at the same period were selected as the control group. Venous blood was taken from healthy people and patients with BC, and serum was then isolated immediately using centrifugation in serum-gel tubes at 3,500 x g for 10 min at 4˚C and stored at -80˚C until further experiments were performed. Total RNA was extracted from the serum of healthy and BC groups

by microRNA Purification Kit (NorgenBiotek, Canada) and reverse transcription to cDNA at 42˚C for 60 min and 70˚C for 5 min. The following primer sequences were used: miR-210 forward (F), 5'-CTGTGCGTGTGACAG CGGCTG A-3', reverse (R) primers for universal primer real-time PCR Uni-miR primers (Takara Bio, Inc.); ROD1 F, 5'-AAG GAA ATG AAT GGG CAG CCG TTA G-3', GAPDH F, 5'-GCTCTCTGCTCCTCCTGTTC-3', and R, 5'-GACTCCGACCTTCACCTTCC-3'. GAPDH was used as an internal control. qPCR was performed according to the manufacturer instructions of the RealQ Plus Master Mix Green (Ampliqon, Denmark). Each sample was analyzed in duplicate. The 2^-DDCt method was used to calculate the expression levels of miR-210 and ROD1.

RESULTS

The expression level of mir-210 was measured and compared in the blood serum of breast cancer patients and healthy subjects. The expression level of miR-210 in the serum of breast cancer patients was significantly higher than controls.

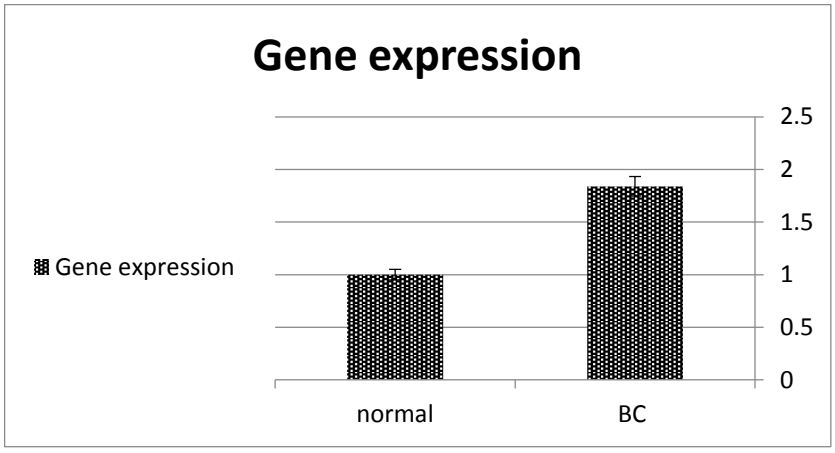

Fig. 1. Significant increase in miR-210 expression in patients compared to healthy subjects

DISCUSSION

After skin cancer, breast cancer is the most common cancer diagnosed in women. In 2020, an estimated 276,480 new cases of invasive breast cancer are expected to be diagnosed in women in the U.S, along with 48,530 new cases of non-invasive (in situ) breast cancer. About 2,620 new cases of invasive breast cancer are also expected to be diagnosed in men in 2020 [10]. A man's lifetime risk of breast cancer is about 1 in 883. MicroRNAs (miRNAs) are a group of small non-coding RNAs (ncRNAs) that regulate post-transcriptional gene expression by targeting their corresponding messenger RNAs (mRNAs). Dysregulated miRNAs have been considered a new type of "oncomiRs" or "tumor suppressors," playing essential roles in cancer initiation and progression [11]. Ubiquitously aberrant expression profiles of miRNAs have been identified in a broad array of human cancers using genome-wide detection methods, showing their great potential as novel diagnostic and prognostic biomarkers of cancer with high specificity and sensitivity [12]. The detectable miRNAs in tissue, blood, and other body fluids with high stability provide an abundant source for miRNA-based biomarkers in human cancers [13]. Even though an increasing number of potential miRNA biomarkers have been reported, the transition of miRNAs-based biomarkers from bench to bedside still requires addressing several challenges. miR-210 is involved in numerous biological processes almost throughout the human body [14]. The increasing literature exploring the role of circulating miR-210 has clarified its potential as a promising biomarker for early detection, diagnosis, and prognosis [15]. Measuring circulating miR-210 levels could be a non-invasive method for early cancer detection. Even if, to date, most studies appear to be preliminary, it seems that miR-210 will be a good target for drug development [16]. This study detected the difference in serum miR-210 expression between health and breast cancer patients as a biomarker. The results showed that the expression level of miR-210 in the serum of breast cancer patients was significantly higher than controls. Patients with breast cancer present increased levels of circulating miR-210, so circulating miR-210 may be a potential biomarker of tumor presence and therapeutic response to breast cancer.

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