Sarcoma Research - International

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Mini Review

The Role of MicroRNA in Ewing's Sarcoma

Sohn EJ*
College of Korean Medicine, University of Kyung Hee, South Korea

***Corresponding author:** Sohn EJ, College of Korean Medicine, University of Kyung Hee, Dongdaemun-gu, South Korea

Received: October 19, 2016; **Accepted:** December 01, 2016; **Published:** December 03, 2016

Abstract

The Ewing's sarcoma is very aggressive and bone tumor arising in children and adolescent. Ewing Sarcoma (EWS) tumors resulted from chromosomal translocation between the EWSR1 gene and ETS members. MicroRNAs (miRNAs), as non-coding RNAs play an important role in cancer acting as both suppressors and oncogenes. Also, microRNAs involve in malignant phenotype or metastasis of Ewing sarcoma tumor. Understanding biological aspects of miRNA may give important information for pathogenesis of Ewing's sarcoma.

Keywords: Ewing's sarcoma; MicroRNA; ETS

Introduction

The Ewing's Sarcoma (EWS) is very aggressive and second malignant bone tumor after osteosarcoma arising in young [1]. EWS tumors resulted from chromosomal translocation between the EWSR1 gene located on chromosome 22 and Ewing's Family Tumors (ETS) members such as leukemia virus integration 1 (FLI), Fifth Ewing Sarcoma Variant (FEV), ETS-Related Gene(ERG), or ETS Variant Gene1(ETV1) [2-4]. Chromosomal translocations of fusion are as follows; EWS/FLI-1 t(11;22)(q24;q12), EWS/FEV1 t(2;22)(q35;q12), EWS/ERG t(21;22)(q22;q12) ,EWS/ETV1 t(7;22)(p22;q12) [5]. In 85% of Ewing's sarcoma, the ETS domain is resulted from 11q24 (FLI-1), producing an EWS/FLI-1 chimera by a t(11;22)(q24;q12) translocation [6]. Though radiotherapy, surgical resection, and multiagent chemotherapy have improved the survival outcome in Ewing sarcoma patients [7-9], the survival after relapse or with metastasis in the Ewing sarcoma patient is still low [10].

MicroRNAs

MicroRNAs (miRNAs) are non-coding RNAs involving in post transcriptional regulation [11]. Also, microRNA binds to the complementary sequences in the 3′UTR (the three prime Untranslated Region) to degrade or inhibit of target mRNAs. MiRNAs was involved in various cellular processes such as aging [12], apoptosis [13], and metastasis [14]. MicroRNA acts both as suppressors or oncogenes in cancer [15]. Also, MicroRNA acts as a prognostic indicator because of its stability and robust expression within clinical samples [16].

The Biological Roles of MicroRNA in Ewing's Sarcoma

Several studies showed that MicroRNA expression was altered in EWS tumor. Thirty five different microRNAs in Ewing sarcoma were identified from the Ewing sarcoma tumor and cell lines [17]. Among these, miRNA-106b, miRNA-93, miRNA-181b, miRNA-101, and miRNA-30b were highly expressed, while the expression of miRNA-145, miRNA-193a-3p, miRNA-100, miRNA-22, miRNA-21, and miRNA-574-3p was low from the Xenograft Ewing sarcoma model [18]. Eun et al reported that the expression of mature let 7g was low in Ewing sarcoma compared to osteosarcoma [19] miRNA 34a was expressed at the low level in Ewing sarcoma tumor [20]. The profile of MicroRNA expression could be important in diagnosis and understanding clinical source of EWS.

Michal et al reported that that let-7 negatively regulates HIF, which is an aggressive metastatic factor in Ewing's Sarcoma [21]. Li et al. also reported that miRNA-31 showed the proliferative and invasive abilities in Ewing sarcoma cell line suggesting as a tumor suppressor in Ewing's sarcoma [22]. Zhang et al showed that let-7a repressed malignant phenotype of Ewing's sarcoma via targeting STAT 3, and NF-kappa B [23]. Thus, these studies imply that MicroRNA may be essential in the tumorigenesis of Ewing's sarcoma.

Conclusion

Recently, MicroRNA has been suggested as a promising therapeutic target for cancer treatment. Finding a novel intracellular signaling pathway targeting of microRNAs in Ewing sarcoma pathogenesis may provide important source in diagnosis. Therefore, understanding the role of MicroRNA in Ewing's sarcoma is providing important information for therapeutic targets in Ewing's sarcoma.

Acknowlegement

This work was supported by the National Research Foundation of Korea (NRF) grant funded by Basic Research Program (2015R1C1A1A02036842).

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Citation: Sohn EJ. The Role of MicroRNA in Ewing's Sarcoma. Sarcoma Res Int. 2016; 3(3): 1035.

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Sarcoma Res Int - Volume 3 Issue 3 - 2016
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