Lack of Association between the MiR146a Polymorphism and Susceptibility to Thai Childhood Acute Lymphoblastic Leukemia

Kochpinchon Chansing¹*, Samart Pakakasama², Suradej Hongeng², Acharawan Thongmee³, Wanida Pongstaporn⁴

Abstract

Background: MiRNAs, small non coding RNAs, play a role in the regulation of hematopoiesis, with effects on cell growth, differentiation, and apoptosis. In addition, MiRNAs are thought to play an important role in tumorigenesis. The miR146a G>C polymorphism can lead to alteration of miR146 expression, which appears to be associated with development and progression of several cancers. This study aimed to investigate the association of the miRNA146a (rs2910164) G>C polymorphism and susceptibility to childhood acute lymphoblastic leukemia (ALL) and clinical outcomes. Materials and Methods: Totals of 100 childhood ALL patients and 200 healthy children were studied for miR146a polymorphisms using polymerase chain reaction-restriction fragment-length polymorphism (PCR-RFLP). Results: The frequency of the miR146a G allele in controls was 0.40 compared with 0.38 in ALL patients. There was no association between miRNA146a (rs2910164) G>C polymorphism and susceptibility to childhood ALL (OR=1.484, 95%CI=0.712-3.093, p=0.290). Moreover, the frequencies of miR146a (rs2910164) G>C polymorphism were not associated with demographic data and clinical outcomes in ALL cases. Conclusions: The miRNA146a polymorphism was not significantly associated with susceptibility to Thai childhood ALL or any clinico-pathological variables.

Keywords: Acute lymphoblastic leukemia - miRNA146a - polymorphism - susceptibility

Introduction

Acute lymphoblastic leukemia (ALL) is the most common type of cancer in children. The peak incidence of ALL occurs between age 2 and 5 years (Inaba, 2013). The improvement of ALL therapy is one of the great successes with long-term survival achieved in over 80% of patients (Pui et al., 2006, Vrooman and Silverman, 2009). However, the remaining cases cannot be cured and has poor prognosis. ALL is a heterogenous leukemia based on the type and stage of lymphoblast. The molecular biology of ALL is not completely understood. Genome-wide association studies show that genetic polymorphisms of some susceptibility genes are associated with the development of childhood ALL (Treviño LR et al., 2009).

Recently, it is discovered that microRNAs (miRNAs) play a role in the regulation of hematopoiesis (Caterine and Ugo, 2012). MiRNAs, small non coding RNAs about 17-22 nucleotide in length, regulate gene expression by translational repression or mRNA degradation (Bartel, 2004). MiR 146a has an important role for negative regulation of acute responses during the activation of the innate immune system and plays a role in the regulation of most biology processes such as differentiation and surveilance of hematopoietic cells. (Caterine and Ugo 2012; Wang et al., 2012). The miR 146a polymorphism (rs2910164) involves a G > C nucleotide substitution which causes change from a G:U pair to a C:U mismatch in the stem structure of miRNA 146a precursor that results in a reduced amount of mature miR146a. (Cong et al., 2011; Palmieri et al., 2014). Up or down regulation of miRNA-146a is observed in human disorders, such as inflammatory diseases and cancers. It has been shown that miRNA-146a (rs2910164) can directly inhibit the expression of IRAK1 and IRAF6, impair nuclear factor (NF)-kB activity, and suppress the expression of NF-kB target genes, such as IL-6, IL-8, IL-1ß, and TNF-α (Caterine and Ugo, 2012; Wang et al., 2012).

The miR146a G>C polymorphism was associated with increased risk of cancer including breast cancer (Hai Lian et al., 2012; Qi P, Wang L et al.,2015), hepatocellular carcinoma (Zhaoming Wang et al., 2014). However, there

¹Department of Biomedical Science, ²Microbiology unit, ³Pathobiology Unit, Department of Biomedical Science, Faculty of Science, Rangsit University, Pathumthani; ⁴Hematology Unit, Pediatric Departments, Faculty of Medicine, Ramathibodi Hospital, Bangkok, Thailand *For correspondence: Kochpinchon@gmail.com