RESEARCH ARTICLE

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MLH1 rs1800734 Pathogenic Variant among Patients with Colorectal Cancer in the Lower Northeastern Region of Thailand

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Abstract

Background: The -93G > A (rs1800734) polymorphism within the core promoter region of *MLH1* gene is associated with *MLH1* CpG island hypermethylation. This polymorphism has recently been proposed as a low penetrance variant for colorectal cancer. Many published studies have evaluated the association between the *MLH1* -93G > A polymorphism and colorectal cancer risk. However, the results remain conflicting rather than conclusive. The aim of this study was to assess the association between the *MLH1* -93G > A polymorphism and the risk of colorectal cancer in patients with colorectal cancer in the lower northeastern region of Thailand. **Methods:** One hundred fifty one samples from colorectal cancer patients and 100 samples from healthy control group were analyzed. Genomic DNA was extracted from white blood cell of all samples. The real-time polymerase chain reaction (qPCR) was used to demonstrate genetic polymorphism of *MLH1* rs1800734. **Results:** This study demonstrated that the frequency of *MLH1* rs1800734 in patients with colorectal cancer was higher than healthy control group. The *MLH1* rs1800734 polymorphism variant AA was associated with an increased risk of colorectal cancer ($p < 0.05$). The *MLH1* polymorphism variant AA carriers presented 1.36-folds high risk of colorectal cancer and the alcohol consumption was linked to their likelihood of developing colorectal cancer and their tumor's grade. **Conclusion:** This study showed that *MLH1* rs1800734 genotype AA was associated with colorectal cancer risk in the lower northeastern region of Thailand.

Keywords: *MLH1* rs1800734 - colorectal cancer risk - Thailand

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Introduction

Colorectal cancer (CRC) is one of the most prevalent and incident cancers worldwide, as well as a significant cause of mortality. It is a heterogenous disease associated with the number of genetic or somatic mutations. Diagnostic markers are used for risk stratification and early detection, which might prolong overall survival. Both genetic and environmental factors play an important part in the etiology of colorectal cancer. Several genome-wide association studies have identified polymorphisms associated with colorectal cancer risk (Ilyas et al., 1999). The majority of colorectal cancers are sporadic; approximately three-quarters of patients have a negative family history. Impaired mismatch repair during replication gives rise to accumulation of DNA mutations (Jasperson et al., 2010). Lifestyle factors influence the risk of developing colorectal cancer. The risk is increased by smoking, alcohol intake and increased body weight. The loss of genomic and epigenomic stability accelerates the accumulation of mutations and epigenetic alterations in tumor suppressor genes and oncogenes, which drive the malignant transformation of colon cells through rounds of clonal expansion that select for those cells with the most aggressive and malignant behavior (Grady and Carethers, 2008).

Single nucleotide variations in genomic sequences are called SNPs. SNP is the third generation of molecular marker and one of the most common genetic variations in human. The SNP is a single base change in a DNA sequence, with a usual alternative of two possible nucleotides at a given position. SNPs may fall within coding regions, non-coding regions or in intergenic regions. Their diverse roles in disease pathogenesis are reported through both experimental and computational methods. SNPs in gene coding regions can lead to change in the biological properties of the encoded protein, SNPs in non-coding gene regulatory regions may affect gene expression levels in an allele-specific manner and these functional SNPs represent an important but relatively

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