

# The Genetic Variation A > G at 3' UTR of Nuclear Factor Kappa B 1 A (NFkB1A) Influences Susceptibility of Sporadic Colorectal Cancer in Malaysian Population

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## ABSTRACT

Colorectal Cancer (CRC), represents a significant cause of morbidity and mortality worldwide. Its incidence is increasing in developed and developing countries including Malaysia. Multiple disease pathways including Nuclear Factor Kappa B (NFkB) signaling pathways, have been implicated in Colorectal carcinogenesis. Given the important role of NFkB pathway in Colorectal carcinogenesis, genes and genetic variations influencing NFkB signaling pathway could be candidate CRC predisposition factors. We hypothesized that an A to G variation in the 3' UTR of NFkB1A may be associated with CRC susceptibility risk in Malaysian population.

*Design:* A Case - Control study was designed to investigate the genotype frequencies of A to G polymorphism at 3' UTR of NFkB1A in Malaysian CRC patients and normal Controls and to determine the genetic risk association of the variant genotype on CRC susceptibility.

*Objectives:* To investigate the genotype frequencies of A to G polymorphism at 3' UTR of NFkB1A in Malaysian sporadic CRC patients and healthy controls and to determine the association risk of the variant genotype on CRC susceptibility.

*Materials and Methods:* This study involved 510 subjects with 211 histopathologically confirmed CRC patients as Cases and 299 healthy individuals as Controls. Blood samples from study subjects were collected, DNA extracted and genotyped employing PCR-RFLP technique. Risk associations of specific genotypes with CRC susceptibility were determined by computing Odds Ratios (ORs) and 95% Confidence Intervals (CI).

*Results:* The frequency of homozygous major (AA) genotype was significantly higher ( $p = 0.001$ ) among Controls (44.8%) compared to CRC patients (31.8%) but heterozygous genotype (AG) showed no significant difference between cases and controls. However, the frequency of homozygous variant (GG) genotype was significantly higher in CRC cases (40.7%) compared to controls (24.4%). On investigating the risk, the variant genotype GG showed significant risk association with CRC susceptibility (OR = 2.356, CI: 1.536 - 3.615,  $p = 0.001$ ).

*Conclusion:* From the results, it is reasonable to suggest that the A to G variation in the 3' UTR of NFkB1A could be a predisposition risk factor in colorectal carcinogenesis, mediating through NFkB signaling pathway.

## KEY WORDS

NFkB, NFkB1A, polymorphism, colorectal cancer, predisposition risk

## INTRODUCTION

Colorectal Cancer (CRC) represents a significant cause of morbidity and mortality worldwide. It is a multifactor caused disease with different incidence in different countries. The incidence of CRC

is increasing in developed countries as well as developing countries, including Malaysia. Although the reasons for this difference are still under debate, there are several studies showing that it depends on interaction between polymorphism distributions of various genes involved in various disease pathways with environmental factors. Environmental factors may influence the cancer risk by somatic

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