RESEARCH ARTICLE

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Contribution of Genetic Polymorphisms of Inflammation Response Genes on Sporadic Colorectal Cancer Predisposition Risk in Malaysian Patients – A Case Control Study

Ravindran Ankathil[1]*, Mohd Aminudin Mustapha[2], Ahmad Aizat Abdul Aziz[1], Siti Nurfatimah Mohd Shahpudin[1], Andee Dzulkarnaen Zakaria[3], Muhammad Radzi Abu Hassan[4], Kamarul Imran Musa[5]

Abstract

AIM: To investigate the frequencies and association of polymorphic genotypes of *IL-8* -251 T>A, *TNF-α* -308 G>A, *ICAM-1* K469E, *ICAM-1* R241G, *IL-6* -174 G>C, and *PPAR-γ* 34 C>G in modulating susceptibility risk in Malaysian colorectal cancer (CRC) patients. **Methods:** In this case-control study, peripheral blood samples of 560 study subjects (280 CRC patients and 280 controls) were collected, DNA extracted and genotyped using PCR-RFLP and Allele Specific PCR. The association between polymorphic genotype and CRC susceptibility risk was determined using Logistic Regression analysis deriving Odds ratio (OR) and 95% CI. **Results:** On comparing the frequencies of genotypes of all single nucleotide polymorphisms (SNPs) in patients and controls, the homozygous variant genotypes *IL-8* -251 AA and *TNF-α* -308 AA and variant A alleles were significantly higher in CRC patients. Investigation on the association of the variant alleles and genotypes singly, with susceptibility risk showed the homozygous variant A alleles and genotypes *IL-8* -251 AA and *TNF-α* -308 AA to be at higher risk for CRC predisposition. Analysis based on age, gender and smoking habits showed that the polymorphisms *IL8* -251 T>A and *TNF – α* 308 G>A contribute to a significantly higher risk among male and female who are more than 50 years and for smokers in this population. **Conclusion:** We observed an association between variant allele and genotypes of *IL-8*-251 T>A and *TNF-α*-308 G>A polymorphisms and CRC susceptibility risk in Malaysian patients. These two SNPs in inflammatory response genes which undoubtedly contribute to individual risks to CRC susceptibility may be considered as potential genetic predisposition factors for CRC in Malaysian population.

Keywords: Colorectal cancer- inflammatory response genes- polymorphisms

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Introduction

With more than one million new cases and half a million deaths every year worldwide, Colorectal cancer (CRC) is a major public health problem, in developed as well as in developing countries (Ferlay et al., 2010). CRC is a multifactorial disease and its onset is attributed to complex interactions between environmental, and host's genetic predisposition factors. In addition to several environmental factors including life style habits and dietary factors, obesity, inflammation and diabetes are also risk factors for CRC (Yehuda-Shnaidman and Schwartz, 2012). Biological, animal, clinical and epidemiological studies had indicated a clear association between CRC and inflammation (Coussens and Werb, 2002; Wang and DuBois, 2013; Nieminen et al., 2013). Patients with inflammatory bowel disease (IBD) including Crohn's disease (CD) and ulcerative colitis (UC) have an increased risk of CRC (Nieminen et al., 2013). Approximately 1:6 individuals with IBD have been reported to develop CRC (Lakatos and Lakatos, 2007). Genetic factors, especially those associated with inflammation have been strongly suggested to be involved in IBD development and an association between inflammatory response genes and IBD development has been established (Garrity-Park et al., 2012). Chronic inflammation is a common underlying cause in the development of many gastrointestinal cancers including CRC and is considered as a predisposing factor for malignant transformation. Despite several evidences strongly implicating chronic inflammation as a culprit in colorectal carcinogenesis, surprisingly, little research has directly addressed the genetic predisposing factors

*[1]Human Genome Centre, [3]Department of Surgery, [5]Department of Community Medicine, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, [2]Center of Pre University Study, Universiti Malaysia Sarawak, Kota Samarahan, Sarawak, [4]Hospital Sultana Bahiya, Alor Setar, Kedah, Malaysia. *For Correspondence: rankathil@hotmail.com*