

# Glutathione S Transferase PI, MI and TI Genotypes and Risk for Colorectal Cancer Development in Malaysian Population

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## ABSTRACT

**Background:** Colorectal cancer (CRC) is a multifactorial disease with factors including dietary and lifestyle habits and genetic predisposition contributing to its etiopathogenesis. Even though the genetic predisposing factors are still unclear, genetic polymorphisms of genes encoding enzymes involved in xenobiotic metabolic pathways that activate or inactivate dietary carcinogens have been proposed as candidate genes. Three members of the Glutathione S-Transferase (GSTs) family GSTP1, GSTT1 and GSTM1 have been analyzed in Malaysian population for polymorphic variants, and to elucidate their role in colorectal carcinogenesis.

**Objective:** To determine the frequencies of GSTP1, GSTT1 and GSTM1 genotypes in 111 histopathologically confirmed CRC patients and 128 healthy controls and to evaluate the association risk of GSTP1, GSTT1 and GSTM1 genotypes on CRC predisposition.

**Material and Methods:** Peripheral blood from the study subjects were collected in EDTA tubes and genomic DNA extracted using QIAGEN kit. The GSTP1 Ile105Val polymorphism was analyzed by PCR-RFLP technique using BsmAI restriction enzyme. The presence or absence of GSTM1 and GSTT1, genes were determined using a multiplex PCR protocol with albumin as the housekeeping gene. The resulting PCR fragments were separated on 2.0% agarose gel for GSTP1 and 3.0% agarose gel electrophoresis for the GSTT1 and GSTM1.

**Results and Conclusion:** On evaluating the CRC risk association with variant genotypes singly, GSTT1 null genotype was associated significantly with an elevated risk (OR 1.804, 95% CI: 1.065-3.361,  $p=0.027$ ). When the polymorphic genotypes were analyzed in combination, the combination genotypes of GSTP1 Val/Val/GSTM+/GSTT1+ (OR 4.000), Val/Val/GSTM-/GSTT1- (OR 3.000), and GSTP1 Ile/Ile/GSTM+/GSTT1- (OR 2.833) showed higher associated risk for CRC susceptibility, however the risk values were not statistically significant. Further studies involving larger sample size may help to identify the more specific risk groups and to determine factors of importance in CRC development.

## KEY WORDS

colorectal cancer (CRC), susceptibility risk, *Glutathione S Transferase*, genetic polymorphism

## INTRODUCTION

Colorectal cancer (CRC) is the second most common cancer in developed and developing countries and third cause of cancer deaths in Malaysia. CRC is a multifactorial disease and the risks of developing CRC include dietary and lifestyle habits on one hand and also genetic

predisposition on the other hand. Exposure to environmental carcinogens such as aromatic amines found in overcooked, charred and preserved meat as well as tobacco smoke are associated with an increased risk of CRC (Norat, 2002). However not all individuals who are exposed to these carcinogens develop CRC. It is known that each individual differ in their susceptibility to cancer and this clearly indicates

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