UNIVERSITI TEKNOLOGI MARA

DEVELOPMENT OF A PCR BASED METHOD FOR DETECTION OF GENETIC POLYMORPHISM OF MLH1 IN COLORECTAL CANCER

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ABSTRACT

Colorectal cancer (CRC) is the second most common disease that relate to cancer in most developed countries. The loss of normal mismatch repair functions causes a mutator phenotype which is indicated by changes in the length of microsatellite sequences that results in abnormality of genome. Germline mutations in the DNA mismatch repair (MMR) genes *hMLH1* are responsible for contribution of hereditary nonpolyposis colorectal cancer (HNPCC). MutL homolog 1(MLH1), a colon cancer-related human gene which is found on Chromosome 3, is a gene that is commonly related with HNPCC. This gene has been identified as a locus that is commonly mutated in HNPCC. In this study, development of polymerase chain reaction based method was conducted and successfully developed and validated. A two-steps PCR method was successfully developed.

CHAPTER 1

INTRODUCTION

1.1 Introduction

1.1.1 Physiology and Anatomy of the Colorectum

Colorectal cancer (CRC) is the second most common cause of cancer-related deaths in developed countries (Westra, Plukker, Buys, & Hofstra, 2004). The colorectum is a component of human digestive system responsible for absorption of water, sodium, and chloride, while excreting potassium and bicarbonate (Gervaz, Bucher, & Morel, 2004). The large intestine is capable of passively absorbing short-chain fatty acids, main fuel for the colonic epithelium (Gervaz et al., 2004). The large intestine is also capable for waste products storage as it will be eliminated from the body. The colon is divided into sections that include the cecum, ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon, sigmoid, and rectum (Welch, Ottinger, & Welch, 1980). The lowermost is the extraperitoneal rectum that lies entirely below the peritoneal floor and averages about 8 cm in length (Welch et al., 1980). The upper portion of the rectum is the intraperitoneal rectum; it is also about 8 cm in length and extends upward to the sigmoid, which is marked by the transition to a definite mesentery (Welch et al., 1980).