UNIVERSITI TEKNOLOGI MARA

IN SILICO IDENTIFICATION OF HUMAN ENDOPEPTIDASE INHIBITOR PROTEIN, ALPHA 1-ANTITRYPSIN; APPROACH TOWARD COLON CANCER BIOMARKER IDENTIFICATION.

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ABSTRACT

Alpha 1-Antitrypsin (AAT) is a major plasma protease inhibitor synthesized in hepatocytes and macrophages. AAT is a globular glycoprotein of molecular weight 52 kilodalton (kD) with the unique chain of 394 amino acids and 3 lateral chains of carbohydrate linked by 3 residues of asparagines. Hepatocyte is the primary source of AAT but other cells including monocytes, macrophages, and lung and intestinal epithelial cell may also synthesis low quantities of the protein. AAT has one active site known as SERPIN profile which is responsible for the anti-protease activity. The absent of AAT leads to destruction of colon and rectum membrane by protease, leaving the colon and rectum vulnerable to cancer development. Absent of AAT can occur through few ways (1) a reduction in the levels of AAT as occurs in AAT heterozygotes; (2) a reduction in the functional levels of AAT as might occur in cigarette smokers; or (3) an increase in the local concentration of proteases such as neutrophil elastase, as might occur in acute inflammatory states. AAT-degrading activity of Matrix Metalloproteinases (MMP) could contribute to tumor progression not only via the inactivation of the proteinase inhibitory activity of AAT, but also via the generation of a biologically active peptide, AAT-C. In *silico* identification and characterization of AAT provide preliminary information on the structure and function of the protein in human. In addition, comparative modeling is becoming a useful technique in the field of bioinformatics because the knowledge of the of protein structure would be an invaluable aid to understand the details of a particular protein. The predicted secondary-dimensional model may be further used in characterizing the interest protein in wet laboratory. The methods in this study can be used to get more information about biosystem by identifying and characterization of other genes and biomolecules.

CHAPTER 1

INTRODUCTION

1.1 Colon cancer

Colon cancer is one of the most common diseases in western country accounting for about 15% of all cancers and are occurs equally in men and women, mainly between the ages 55 to 70 (King, 2000). About half of the patients survive after the first five years of detection, but this depends on the degree of spread (stage) when the cancer is first detected. They usually divide the degree of spread in to three categories depending on whether the cancer is localize (A), has invaded through the colon wall (B), or has spread outside the colon (C). The cancer can be metastasizes through several routes, the first one is by direct invasion through the colonic mucosa which is result in peritoneal outgrowth whereas liver is the major site for blood-borne spread.

Among the presenting symptoms include irregular and problematic bowel movement and the appearance of blood in the feces. There are several types of colon cancer according to the degree and familial involvements. About 80% is sporadic meanwhile the remaining 20% exist in two heredity form; the first one is Familial Adenomatous Polyposis coli (FAP) and the second form is heredity Non-Polyposis Colon Cancer (HNPCC) or Lynch's Syndrome. Usually, both of the familial type occurs before age of 50, earlier than the sporadic cancer.