Quantitative analysis of the expression of p53 gene in colorectal carcinoma by using real-time PCR

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Abstract. Colorectal carcinoma ranks third among ten leading causes of cancer in Malaysia. The colorectal carcinoma tumourigenesis involves the inactivation of tumour suppressor genes, and activation of proto-oncogenes. The p53 is one of the tumour suppressor genes that is involved in the colorectal carcinogenesis. The p53 gene is located on human chromosome 17p13.1 and comprises of 11 exons. Deficiencies in the p53 gene can cause the cancerous cells to spread to distant organs such as liver, lungs, lymph nodes, spine and bone. The most common p53 abnormalities that can lead to the metastasis of colorectal tumours are mutation and deregulation of the gene. In this study, nine colorectal carcinoma samples were used to establish a simple and sensitive strategy in the study on in vivo p53 expression by using real-time LightCycler SYBR Green I technology.

INTRODUCTION

In Malaysia, colorectal carcinoma is the third leading cause of cancer in the population (Lim & Halimah, 2003). Colorectal carcinoma develops through a cascade of histopathological and genetic defects, which is known as adenoma to carcinoma sequence (Kinzler & Vogelstein, 1996). The p53 genetic aberration is involved in the late stage of colorectal tumourigenesis (Vogelstein & Kinzler, 1996). This tumour suppressor gene has been mapped to human chromosome 17p13.1 and it plays an important role in cellular growth control (McBride et al., 1986). Under stress condition, the wild type p53 binds to DNA, stimulates transcription of several genes and mediates cell cycle arrest in the G1 phase for DNA repair or initiates apoptosis when the damaged DNA cannot be successfully repaired (Kumudini et al., 2002). If the p53 gene is mutated, the damaged DNA remains unrepaired and mutations become fixed in the dividing cells. Subsequently, malignant transformation of the cancerous cells occurs and starts to accumulate the mutated p53 gene (Kumudini et al., 2002).

Consequently, mutations and deregulation of the p53 gene are commonly found in cancers (Wunderlich et al., 2000). More than 75% of colorectal carcinomas are due to mutation in the p53 gene (Erhan et al., 2002), while over-expression of the gene is associated with advanced malignancies (Auvinen et al., 1994). Recent preliminary reports revealed that over-expression of p53 are an indicator of poor prognosis and survival in the patient (Remvikos et al., 1992; Sun et al., 1992; Zhao et al., 2005). However, other reports correlated low expression of the p53 gene and adverse outcome (Kumudini et al., 2002). Whether p53 expression level is associated with patient survival and stages of the diseases in colorectal tumour is still uncertain and remains to be scrutinized.