Introduction

In Egypt, carcinoma of the prostate is, by far, the most common malignant tumour of the male genital organs. It ranks the 5th most common tumour of all male cancers and the 2nd after bladder cancer in patients over the age of 60 years *(Mokhtar, 1991).*

Prostate cancer is the most commonly diagnosed malignancy among men and the second leading cause of cancer-related deaths in both Western countries and the United States *(Boring et al,1994 ; Parker et al,1996).*

The associated mortality in Japan has also increased in recent years with the westernization of dietary habits *(Tominaga&Kuroishi, 1997).*

However, the underlying molecular genetic events involved in the initiation and progression of prostatic adenocarcinomas remain poorly understood *(Miyake et al,1998).*

Although the current most established prognostic factors in prostate cancer are histologic grade(Gleason system) and tumour stage, the biological behaviour of prostate cancer is still unpredictable in individual patients, ranging from slowly growing, non-life threatening to highly aggressive cancer *(Bubendorf et al,1998).*

Furthermore, among patients with organ confined prostate cancer, one third have micrometastatic disease at the time of surgery and will probably progress to metastatic disease, making essential to detect patients at risk of systemic dissemination among those with clinically localized prostate cancer*(Paradis et al,1998).*

The currently used marker for prostate cancer screening is Prostate-specific antigen (PSA). However, it is neither prostate specific nor made exclusively by prostatic epithelium and also early detection is limited by the fact that increased concentrations of PSA are also found in benign prostatic hyperplasia ***(Cohen et al,1998; Fortier et al,1999).***

So, new prognostic factors that may provide additional prognostic informations shoud be searched for. Increasing attention has turned to molecular markers as a possible mean of obtaining such informations.

CD44 is a widely distributed cell surface adhesion molecule implicated in several biological phenomena such as cell adhesion (aggregation and migration), hyluronate degradation, lymphocytic activation, lymph node homing, myelopoiesis and lymphopoiesis,and release of cytokines ***(Conrad et al,1992; Underhill, 1992; Koopman et al ,1993).*** CD44; located on the short arm of chromosome 11; is encoded by a single gene containing 20 exons, 10 of which (V1-V10) are variant exons, inserted by alternative splicing. The role of CD44 in neoplasia is less well-defined, although metastatic potential can be conferred on non-metastasizing cell lines by transfection with a variant of CD44. High levels of CD44 are associated with several types of malignant tumours e.g. cancers of the breast, colon, pancreas, skin, lung, brain and urinary bladder ***(Rudzki &Jothy,1997; Sneath&Mangham, 1998).***

The p21 gene encodes a 21-Kda nuclear protein, which is a potent inhibitor of cyclin-dependent kinase activity. Induction of p21 gene expression is thought to play an important role in p53-mediated G1/S phase checkpoint control pathways that operate after DNA damage by

ionizing radiation or exposure to anticancer drugs ***(Hartwell & Kastan,1994; Palazzo et al,1997b).***

The p21 gene is transactivated by wild-type p53 protein but not by mutant type, commonly found in human cancers, through p53 DNA binding sequences in its promoter and can itself suppress tumour cell growth in culture. These findings mean that p21-wild type p53 activated fragment, (WAF1)/CIP1 protein is a downstream regulator of the growth-suppressive properties of wild-type p53, therefore, p21 could be expected to reflect the growth suppressive function of p53 and thus show the growth potential of the tumours more directly than can p53 ***(El-Deiry et al,1993; Wakasugiet al, 1997).***

Loss of p21 expression was correlated with poor prognosis in many tumours including breast, colon and uterus. A recent study found an inverse relationship between cellular proliferation and p21 expression in the gastrointestinal tract, but not in the liver, lung, kidney, thyroid or pancreas ***(Fredsdorf et al,1996; Palazzo et al, 1997a;b; Wakasugi et al, 1997).***

In another study it was observed that p21 overexpression seems to be independent of p53 status and is associated with poor differentiation in ductal, but not lobular carcinomas of the breast ***(Rey et al, 1998).***

So, studies specifically addressing p21 expression and patient outcome are needed in order to establish the possible prognostic usefulness of this marker.

Recent studies have evaluated proliferation markers in human cancers in an attempt to predict behaviour. MIB-1 antibody, is a well-recognized, general cell proliferation marker that reacts with a nuclear

antigen; which is coded by a gene on chromosome 10; expressed in proliferating cells during the G1, S, G2 and M phases of the cell cycle ***(Machen&Prayson,1998; van Diest et al, 1998).***

Tumour cell proliferation determined by MIB-1 expression has been suggested as an important predictor for outcome in several human cancers e.g.: breast and ovarian carcinomas and astrocytomas. Although several human prostate cancer studies have shown an association between tumour cellular proliferation and tumour stage, malignancy grade and clinical outcome; conflicting results have been reported ***(Borre et al, 1998; Machen&Prayson,1998; van Diest et al, 1998).***