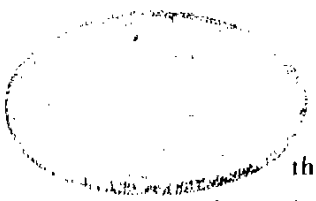
Tumour Markers in Genitourinary Oncology



Thesis submitted for partial fulfilment of master degree in urology.

Presented by :

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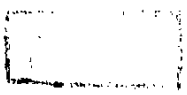

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A C K N O W L E D G M E N T

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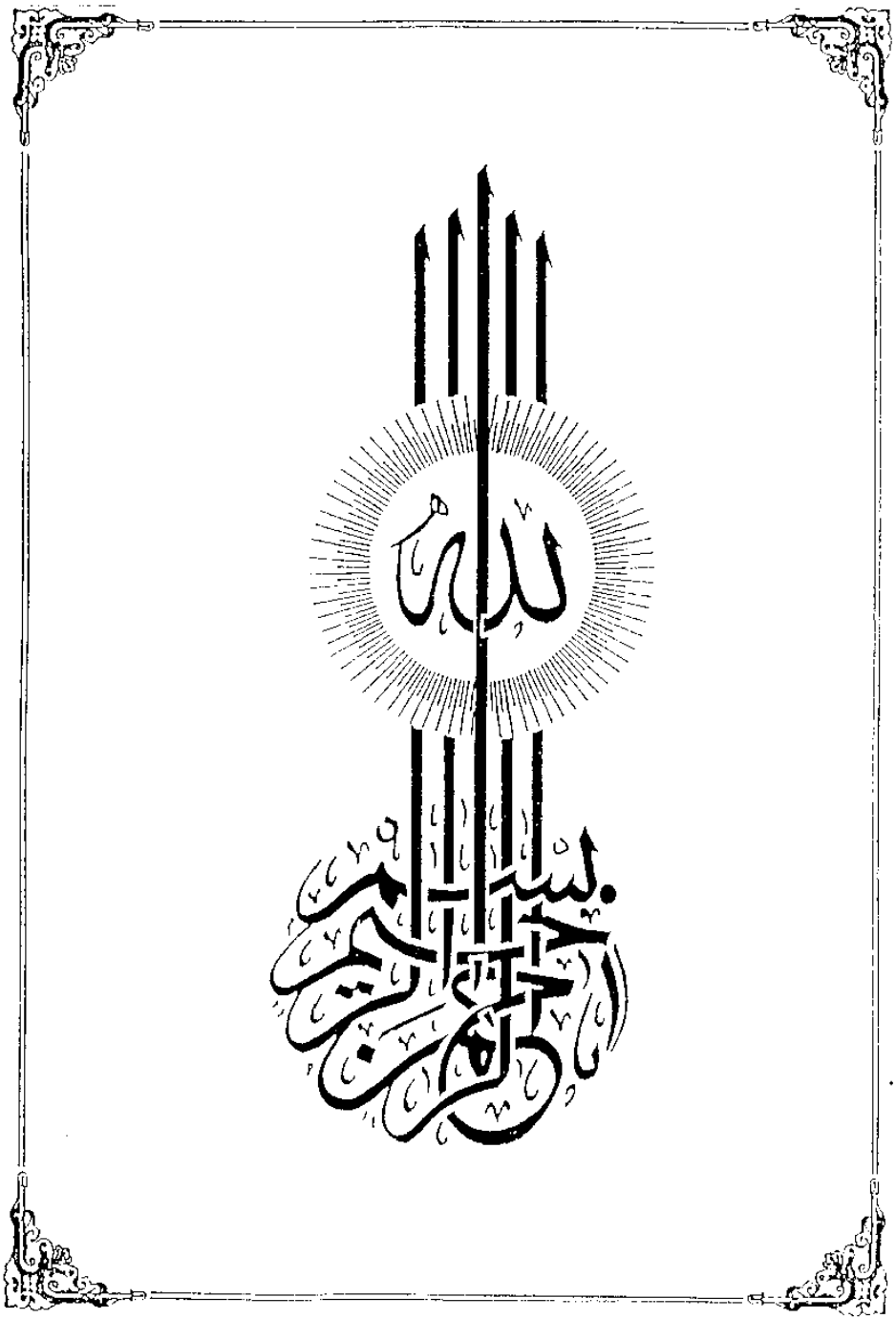
Thanks to all the staff of urology department of Ain Shams University for their valuable and pronounced help.



C O N T E N T S

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LIST OF ABBREVIATIONS

-	Prostatic acid phosphatase.	PAP
-	Serum prostatic acid phosphatase.	SPAP
-	Serum acid phosphatase.	SAP
-	Prostatic specific antigen.	PSA
-	Bone marrow acid phosphatase.	BMAP
-	Radioimmunoassay.	RIA
-	Counterimmunoelectrophoresis.	CIEP
-	Enzyme linked immunosorbent assay.	ELISA
-	Benign prostatic hypertrophy.	BPH
-	Immunoperoxidase.	IP
-	Peroxidase - anti - peroxidase.	P-anti-P
-	Radioimmunodetection.	RID
-	Radioimmunotherapy.	RIT
-	Immunofluorescence.	IF
-	Indirect Immunofluorescence.	IIF
-	Alkaline Phosphatase.	ALP
-	Total alkaline phosphatase.	TAP
-	Placental alkaline phosphatase.	PLAP
-	Bone alkaline phosphatase.	BAP
-	Non seminomatous germ cell tumor.	NSGCT
-	Adenosine diphosphate.	ADP
-	Adenosine triphosphate.	ATP
-	Aspertate aminotransferase.	AST
-	Leucine aminopeptidase.	LAP
-	Gamma glutamyl transpeptidase.	GGT
-	Glucose - 6 - phosphate dehydroginase.	G6PD

- Galactosyl transferase.	GT
- Aryl sulfatase A.	ASA
- Aryl sulfatase B.	ASB
- Alpha feto protein.	AFP
- Carcinofetal antigen.	CFA
- Svedberg unit.	S
- Human chorionic gonadotrophin.	HCG
- Carcinoembryonic antigen.	CEA
- Human leucocytic locus A antigen.	HLA
- Transitional cell carcinoma.	TCC
- Serum prostatic specific antigen.	SPSA
- Placental specific protein.	SPI
- Syncytiotrophoblastic giant cells.	STGC
- Luteinizing hormone.	LH
- Follicle stimulating hormone.	FSH
- Thyroid stimulating hormone.	TSH
- Dihydrotestosterone.	DHT
- Carcinoma in situ.	CIS
- Lactate Dehydroginase.	LD

I N T R O D U C T I O N

The management of cancer has changed dramatically during the past 2 decades. Treatment modalities have been refined to the point that all produce significant positive results by themselves. The most important added knowledge were the early detection of cancer for better treatment and the prognosis of recurrences to decrease it. So any system of analysis that can detect chemical or immunological differences between normal and malignant cells may add potentially valuable information to complement histologic data to achieve our goals.

The term tumor marker denotes any chemical or biological factor that identifies a tumor.

The advance in this field is hasty. It begins by the early cytologic detection in the beginning of this century then the discovery and improvements in detection of acid phosphatase in the 1930s. This is followed by rapid advance in methodology and technology of detection qualitatively and estimation quantitatively. Because most of the recently available markers lack the characters of ideal ones. We hope to reach early the ideal markers which is so sensitive to detect minor changes in level and so used for survey and early detection, as well as so specific not to confuse with other malignencies or benign conditions.

Some enzymes studied in cancer

- Acid phosphatase
- Alkaline phosphatase
- Creatine kinase
- Lactate dehydrogenase
- Glycosyltransferases
- Ribonuclease
- 5'-nucleotide phosphodiesterase
- Arylsulfatases
- Glycolytic enzymes
- Catechol-o-methyltransferase
- Terminal transferase

Table 1

Van Lente, and Shamberger, 1983

Diverse theories have been proposed to explain the changes in enzymatic activity in tumor cells (Winhouse, 1982). According to the deletion theory, certain enzymes are absent from cancer cells. The glycolysis theory attributes the elevation of glycolytic enzymes in certain tumors to increase glycolytic activity. The disdifferentiation theory blames abnormal gene expression in tumor cells. The dedifferentiation or embryonic theory states that enzymes normally produced by the fetus are abnormally produced by cancer cells.

It is generally accepted that different genes produce individual isoenzymes, therefore, alteration in gene expression in tumors may alter isoenzymes. This type of change has been observed in tissue culture following the neoplastic transformation of normal cells. However, it is not clear whether changes in the composition of isoenzymes can be traced to homogeneous cells in the tumor or to the presence of more than one kind of cell. It is conceivable that the alteration of some isoenzymes is a side effect of tumor-cell proliferation rather than a stable characteristic of the tumor itself. Normal tissue undergoing regeneration can alter isoenzymes.

Enzymes can provide clues to the location of tumors. For example, serum alkaline phosphatase is elevated in patients with metastatic bone cancer. Abnormalities in several liver enzymes including gamma glutamyl transferase and 5' - nucleotidase, have been associated with liver metastasis.

Unfortunately, a given abnormality in enzyme production is not always associated with a particular tumor, either qualitatively or quantitatively. This ambiguity-probably stemming from the heterogeneity

of the neoplastic process - hampers the use of enzymes in diagnosing cancer (Van lente and Shamberger, 1983). Nevertheless recognizing enzymatic changes induced by cancer has clinical value as will be discussed.

The enzymes of interest in our subject are :

- Phosphatases (Acid and Alkaline).
- Creatine Kinase.
- Lactate Dehydroginase.
- Leucine Aminopeptidase.
- Urinary - B - Glucuronidase.
- Urinary Lysozymes.
- Others.

PHOSPHATASES

Phosphatases are enzymes capable of hydrolyzing phosphoric esters, both aliphatic and aromatic with the liberation of inorganic phosphate, including a portion of the phorsphoric esters of the circulating red blood cells and those present, in small amounts, in blood plasma. In the fetus and growing animals the greatest relative quantity of phosphatase in found in the bones and teeth. In the adult animal, the intestinal mucosa contains the greatest amount per unit of weight.

Two types of phosphomonoesterases of clinical significance may be differentiated on the basis of their activity at different PH ranges :

1) Acid Phosphatase :

A type with aptimum activity at acidic PH, which can be further differentiated into 2 types +

a) One has optimum activity at PH 6, and present in mammalian erythrocytes.