

## Tumour Markers

### Introduction

Cancer is the uncontrolled growth and spread of cells that may affect almost any tissue of the body. Lung, prostate, breast, colorectal and stomach are the five most common cancers in the world. More than 10 million people are diagnosed with cancer every year.

### Tumour Markers

Tumour markers are biological substances which can be measured in blood and other body fluids. Increased concentration indicates the presence of a tumour. Many different substances can be used as tumour markers, but the term generally refers to substances produced by the tumour cells and generally found in very low concentration in the body fluids of normal individuals. An ideal tumour marker should be used for screening, diagnosis and monitoring of disease progression. Unfortunately there is no ideal tumour marker.

### Screening

There is no tumour marker currently recommended for screening of the general population. The most likely candidate is PSA for prostate cancer, however there is no agreement whether screening reduces premature mortality. Most tumour markers have too low sensitivity to make screening feasible.

## DiaSorin Tumour Markers Assays

Cancer form	Tumour Marker	Cancer form	Tumour Marker
Brain	S100B, NSE	Pancreas	CA 19-9™, CEA
Thyroid	Tg, CEA, Calcitonin	Colorectal	CEA, CA 19-9™, TPA®
Lung	CEA, TPA®, NSE	Bladder	TPA®
Breast	CA 15-3®, CEA, TPA®	Ovary	CA 125 II™, CA 72-4™ *, AFP, hCG
Blood	TK*, β <sub>2</sub> -microglobulin, Ferritin	Prostate	PSA, fPSA
Liver	AFP, CEA	Cervix, Uterus	CA 125 II™, CEA, TPA®
Stomach	CA 72-4™*, CEA, CA 19-9™	Testes	AFP, hCG
		Skin	S100B
			* under development

TK - Thymidine Kinase  
TPA - Tissue Polypeptide Antigen

### Diagnosis

Tumour markers are occasionally useful as pointers towards a specific diagnosis. Very high concentration of a specific marker will make some cancer forms exceedingly likely. However tumour markers should never be used alone to establish a diagnosis.

### Prognosis

Prognosis may be of help to assess optimal therapeutic regime. Several tumour markers have additional value to the traditional staging system and often a correlation between tumour marker concentration and survival time exists.

### Monitoring of Treatment and Follow-up

Monitoring of disease progression is the main clinical use of tumour markers. Regular measurements of tumour markers assist in demonstrating the effectiveness of a treatment intervention. Reduced levels of the marker indicate successful treatment, increased levels indicate progressive disease. In the follow-up the markers may detect progression prior to the appearance of clinical symptoms.

## Tumour Markers Characteristics

Tumour Marker	Substance	Reference range	Clinical indication	False positives
AFP	Glycoprotein MW 68 000	< 5.5 IU/mL	Liver cell carcinoma Germ-cell tumours	Liver disease, Crohn's disease, polyposis
β <sub>2</sub> -microglobulin	The light chain of the MHC class I antigens MW 10 800	0.9-2.0 mg/L	Lymphoproliferative disease, myeloma	Renal insufficiency
Calcitonin	Polypeptide MW 3600	<10 pg/mL	Medullary thyroid cancer	Renal insufficiency
CA 15-3	Glycoprotein defined by two monoclonal antibodies (115 D8 and DF3)	<30 U/mL	Mammary carcinoma	Liver disease Diseases of the ovaries, lung and breast
CA 19-9	Glycolipid, hapten of the Lewis-a-blood group determinant. Defined by the monoclonal antibody 1116NS-19-9	<19 U/mL with greyzone up to 37 U/mL	Carcinomas of the gastro-intestinal tract especially pancreatic carcinoma	Hepatitis, biliary disease, pancreatitis, cystic fibrosis
CA 125	High molecular weight glycoprotein defined by the monoclonal antibodies OC 125 and M11	< 35 U/mL	Carcinomas of the ovaries	Benign gynaecological disease, endometrioses, liver disease, pancreatitis
CA 72-4*	Glycoprotein defined by the monoclonal antibodies CC49 and B72-3	< 4 U/nL	Carcinoma of the gastro-intestinal tract, especially stomach, oesophagus and ovarian	Liver disease
CEA	Glycoprotein MW 180 000	< 4 µg/L	Colorectal carcinoma, secondary marker in pancreas, lung, breast, prostate	Liver disease, Colitis ulcerosa Lung emphysema
Ferritin	Iron containing protein MW 460 000	Male: 18.2-341.2 µg/mL Female: 4.0-104.2 µg/mL (< 45 years) 4.9-232.3 ng/mL (> 45 years)	Leukaemia, Hodgkin, non-Hodgkin, breast, bronchial carcinoma, neuroblastoma	Idiopathic haemo-chromatosis, Intrathecal haemorrhage
hCG	Dimeric glycoprotein consisting of an α-and β-subunit MW 37 000	Female: < 2.4 mIU/mL Male: < 1.1 mIU/mL	Germinal tumours of testis and ovary	Pregnancy
NSE	The γ-form of enolase, an enzyme in the glycolytic pathway MW 87 000	< 18.3 µg/L	Small-cell bronchial carcinoma, neuroblastoma	Head trauma
PSA	Glycoprotein, a serine protease MW 34 000	< 3 ng/mL with grey zone up to 10 ng/mL f/t PSA < 0.1 in prostate cancer patients	Carcinoma of the prostate	Acute prostatitis and benign prostate hyperplasia. Determination of free PSA/total PSA improves discrimination
S100B	Protein, member of the S100 family consisting of 20 proteins MW subunits 11 000	< 0.15 µg/L	Malignant melanoma	Brain damage
Thyroglobulin	Glycosylated iodoprotein MW 660 000	0.2-70 µg/L	Thyroid carcinoma (papillary, follicular)	Goitre, Basedow's disease
TK	Cellular enzyme involved in DNA synthesis MW subunits 58 000	< 8 U/L	Haematological malignancies	Infections
TPA	Circulating complex from cytokeratin 8, 18 and 19	up to < 75 U/L	Carcinomas of the lung, breast, gastro-intestinal tract	Liver disease, Infections

\* under development