



Tumor marker

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Tumor marker

- a biomarker found in blood, urine, or body tissues that can be elevated by the presence of one or more types of cancer.
- Site. Blood, in body fluids or associated with cell in the cytoplasm or on cell membrane
- Structure

Enzymes , hormones, and protein

- **Oncofetal antigens**

(e.g. alpha-fetoprotein (AFP), Carcinoembryonic antigen (CEA), Pancreatic oncofetal antigen, fetal sulfo-glycoprotein.

- **Tumor associated antigens /Cancer Antigens** e.g. CA125, CA19-9, CA15-3, CA72-4 CA50 etc.
- **Hormones** e.g. Beta human chorionic gonadotropin, calcitonin, placental lactogen etc.
- **Hormone receptors** (e.g. estrogen and progesterone receptors)
- **Enzymes and Isoenzymes** (e.g. prostate specific antigen (PSA), prostatic acid phosphatase (PAP), neuron specific enolase (NSE), glycosyl transferases, placental alkaline phosphatase (PALP), terminal deoxynucleotidyl transferase (TDT), lysozyme, alpha amylase6.
- **Serum and tissue proteins** (beta-2 microglobulin, monoclonal immunoglobulin, protein S-100, ferritin,
- **Other biomolecules** e.g. polyamines

Properties of ideal tumor markers

1. **Have high disease sensitivity** i.e. it should be positive in all patients with particular cancer.

➤ **Sensitivity** of any tumor marker refers to the number of true positives, and it could be calculated as follows:

$$\frac{\text{Number of true positives}}{\text{Number of true positives} + \text{False negatives}} \times 100$$

✓ **True positive** is a malignant case which gives an elevated marker level above the cut-off value.

✓ **False negative** is a malignant case which gives a normal value for the marker whereas it is proved malignant histopathologically.

✓ **Cut-off value** is the highest value obtained by the normal control.

2. **Have high disease specificity** i.e. it should be negative in all normal population.

➤ **Specificity** of any tumor marker refers to the number of true negatives (normal individuals), and it could be calculated as follows:

$$\frac{\text{Number of true negatives}}{\text{Number of true negatives} + \text{False positives}} \times 100$$

✓ **True negative** is a normal case which gives a normal value for the marker.

• **False positive** is a normal case with elevated marker level above the cut-off value

- **Specificity**

- It is a measure of the incidence of negative results in persons known to be free of a disease, that is true negative (TN).

- **Specificity = $TN / \text{All without disease (FP + TN)} \times 100$**

- **Efficiency**

- The efficiency of a test is the number of correct results divided by the total number of tests.

- **Efficiency = $TP + TN / \text{Total number of tests (TP + TN + FP + FN)} \times 100$**

- **Sensitivity**

- It is a measure of the incidence of positive results in patients known to have a condition, that is true positive (TP)

- **Sensitivity = $TP / \text{All with disease (TP + FN)} \times 100$**

- **Predictive values**

- The predictive value of a test is a measure (%) of the times that the value (positive or negative) is the true value, i.e. the percent of all positive tests that are true positives is the Positive Predictive Value (PV_{+ve}).

- **$PV_{+ve} = TP / \text{All positive (TP + FP)} \times 100$**

- **$PV_{-ve} = TN / \text{All negative (TN + FN)} \times 100$**

C- Its level reflects the *stage* of the disease. •

D- Its level must be *stable* i.e. not subjected to marked fluctuation in stable disease state. •

E- *Organ specific* i.e. positive only in certain organ tumor. •

Some benign conditions associated with rise in tumor markers

- Marker Associated non-malignant conditions
- AFP Viral Hepatitis, liver injury, pregnancy
- β -hCG Testicular failure, pregnancy
- CEA Smokers, hepatitis, cirrhosis, pancreatitis, gastritis
- PSA Prostatitis, benign prostatic hyper-plasia

Examples of some clinically important tumor markers

1. AFP (alpha feto protein):

- Alpha fetoprotein is protein that is produced in early fetal life.
 - AFP is the major serum protein of human fetus, and it falls to low levels by one year of age.
 - The cut-off value of AFP is 2-11 ng/ml, but it reaches 500 ng/ml in late pregnancy.
 - However, elevated levels (more than 500 ng/ml) are found in many cases of hepatocellular carcinoma (hepatoma) and testicular carcinoma.
- Furthermore AFP may also be increased in serum of non-neoplastic conditions. In these cases the rise may be transient, and associated with the tissue (usually the liver) response to injury, and usually of lesser magnitude (100-300 ng/ml)

2. CEA (carcino embryonic antigen)

- It is a glycoprotein molecule normally found in the tissue of a developing fetus. Levels of CEA in the blood decrease after birth. CEA is normally found in small amounts in the blood of most healthy people. Cut-off value of CEA is about 5 ng/ml.
- High CEA levels (above 5 ng/ml) have been found in colonic cancer and in some tumors of the lung, pancreas, uterus, and breast.
- Less marked elevations occur in non-neoplastic diseases such as emphysema, ulcerative colitis, pancreatitis and alcoholism, and in serum of heavy smokers.

3. CA 15-3 (Cancer antigen 15-3)

- CA 15.3 is the most reliable and highly specific tumor marker for breast cancer.
- The CA 15.3 level can provide prognostic information in the follow-up management of patients with breast cancer.
- Cut-off value of CA 15-3 is 35 units/ml.

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5. Carbohydrate antigen 19-9 (CA19-9)

- Carbohydrate antigen is a protein that is found in very small amounts on the surface of certain cancer cells. It may be found in the blood when it is shed by tumor cells. It is also found in trace amounts in the pancreas, liver, gall bladder and lungs of healthy adults.
- A CA19-9 test may be done to check:
 - a person's response to treatment for pancreatic cancer, especially advanced pancreatic cancer.
 - if pancreatic cancer is still growing or has come back (recurred) after treatment

6. CA 125 (cancer antigen 125)

- Cancer antigen 125 is a protein produced by a variety of cells, particularly ovarian cancer cells.
- CA125 is most reliable and highly specific tumor marker for ovarian cancer.
- Cut-off value is 0-35 units/ml.

7. PSA (prostatic specific antigen)

- It is widely accepted tumor marker in prostatic cancer.
- PSA is glycoprotein produced only by prostatic epithelial cells and it is organ specific.
- Normal level: 0-4 ng/ml.
- Elevated Level (more than 4 ng/ml) occurs in:
 - ✓ 60% of localized prostatic cancer.
 - ✓ 40% of benign prostatic hypertrophy.

8. Prostatic acid phosphatase (PAP)

- One of the famous enzymes used as tumor marker.
 - The serum level of prostatic acid phosphatase (PAP) is elevated in prostatic carcinoma.
 - Certain precautions must be taken before taking serum samples for prostatic acid phosphatase assay.
 - These include avoidance of rectal examination and passage of catheter at least 7 days before sampling. Also constipation must be avoided.
 - As these factors may result in false positive rise in serum acid phosphatase activity due to squeezing of the prostatic tissues.
- Cut-off value is 0.5-11 units/liter

9. LDH (Lactate dehydrogenase)

- An elevation in all five LDH isoenzymes (LDH₁, LDH₂, LDH₃, LDH₄, LDH₅) can be seen in leukemia and lymphoma.
- Selective increases in LDH isoenzymes LDH₃ and LDH₅ (liver enzyme) may occur in liver carcinoma.
- Cut-off value of total LDH ranges from 48 to 115 units/liter.

10. Calcitonin

- ❖ Patients with medullary thyroid carcinoma can be screened by measuring calcitonin levels.

11. HCG (Human chorionic gonadotropin)

- ❖ Hormone produced by placenta, and used for detection of pregnancy.
 - Reaching maximum level at 8th week of gestation.
 - It increases in testicular carcinoma.