



Novel Biomarkers in cancer

Cancer biomarker:

Cancer biomarker :is a “biological molecule produced either by the tumor cell or by human tissues in response to cancer that is objectively measured and evaluated as an indicator of cancerous processes within the body.

Ideal tumor biomarker should be :

1. Produced only by the tumor cells.
2. Present in measurable quantities in the blood of cancer patients at early or preclinical stages.
3. Undetectable in the blood of healthy individuals.
4. Easy to measure even in small amounts and with little preparation, by means of a reliable test, cost-effective and associated with high analytical sensitivity.

Types of Cancer Biomarkers

cancer biomarkers are currently distinguished:

1. Prognostic

Prognostic markers are important at the time of initial diagnosis of malignancy and in cancers that vary widely in patients’ outcome.

2. Predictive

Predictive biomarkers assess that the tumor will respond to the drug, and allow a level of personalization to be introduced into the treatment regimen.

3. Pharmacodynamic markers

Pharmacodynamic markers provide information on the effects of the drug on the body.

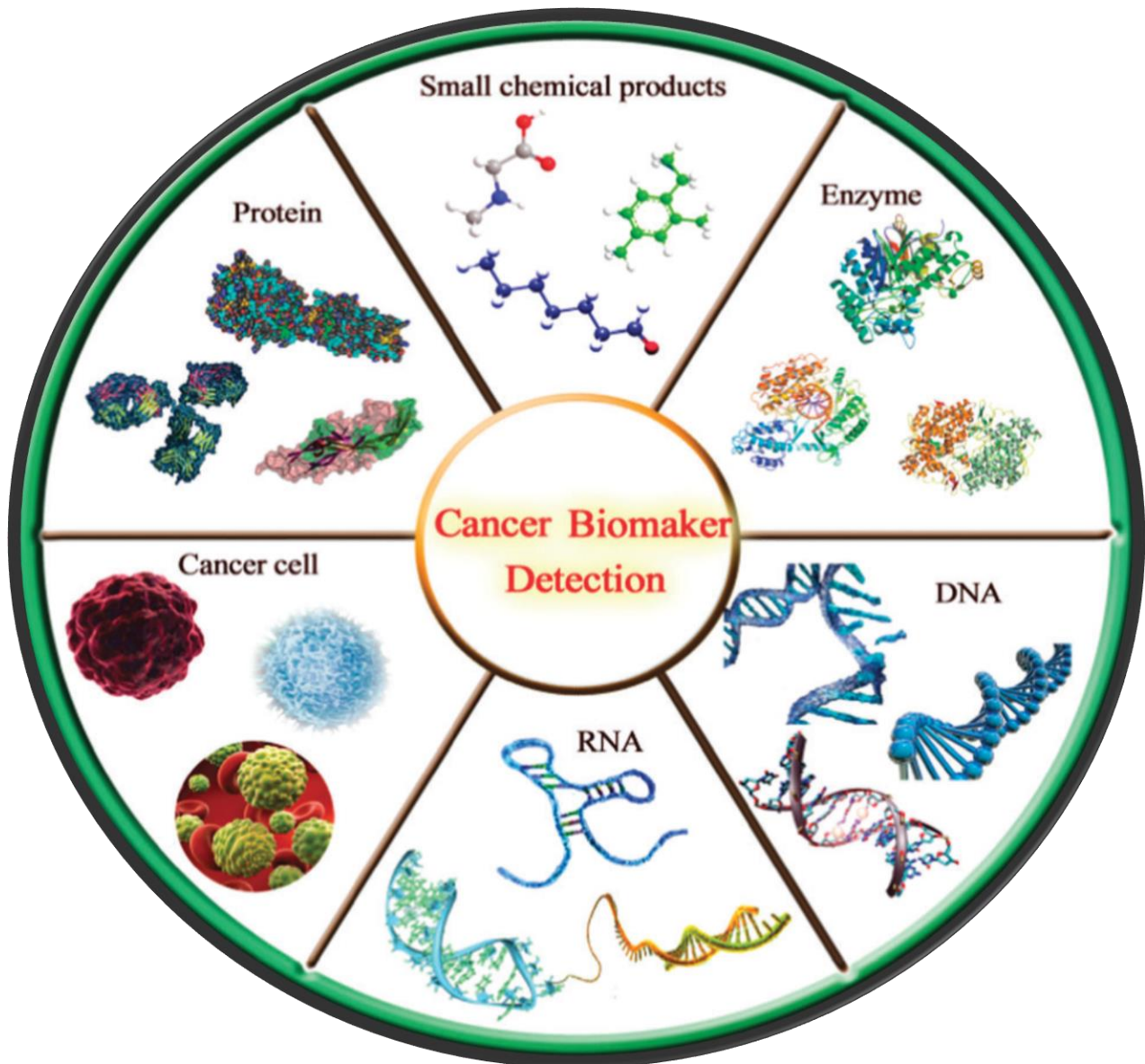


Fig. Schematic illustration of various cancer biomarkers.

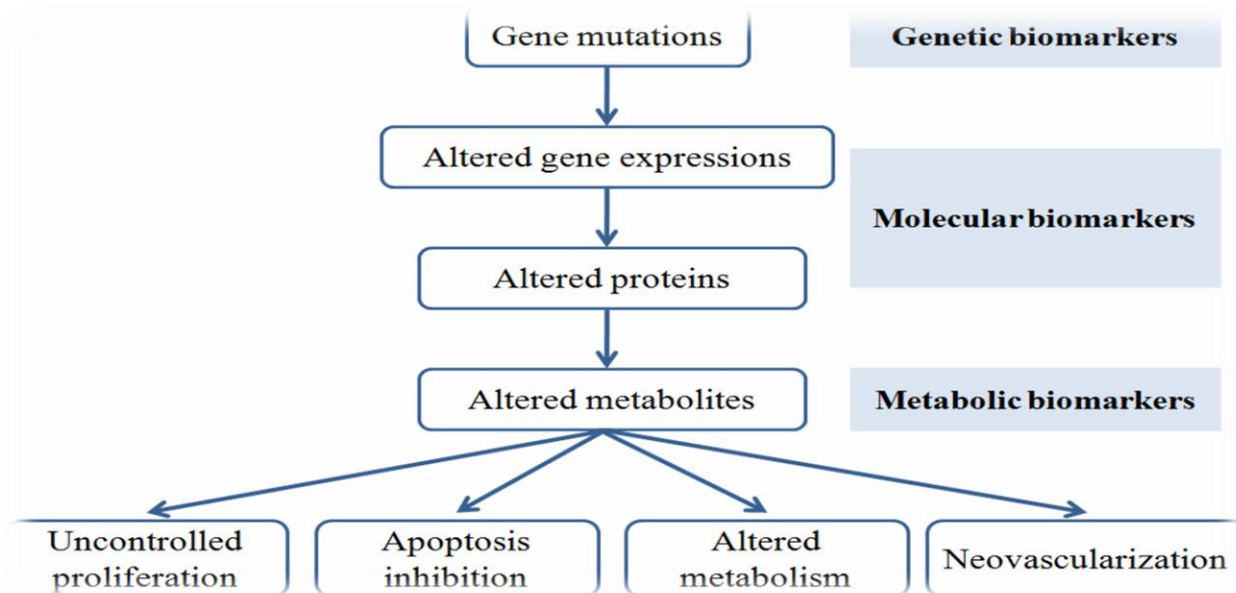
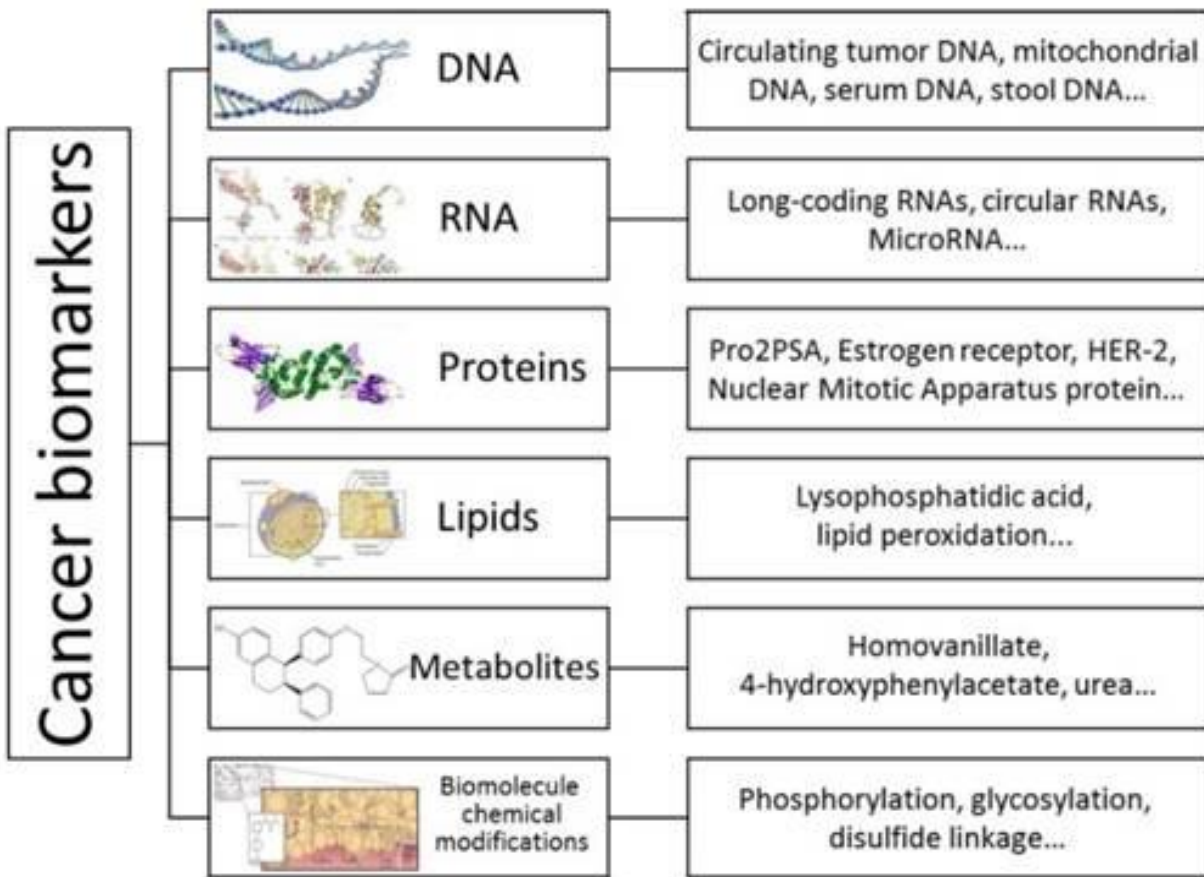


Fig. Identification of biomarkers in the process of carcinogenesis (Adapted from Bhatt AN, Mathur R, Farooque A, et al. *Cancer biomarkers – Current perspectives*. Indian J Med Res 132, August 2010, p. 130).

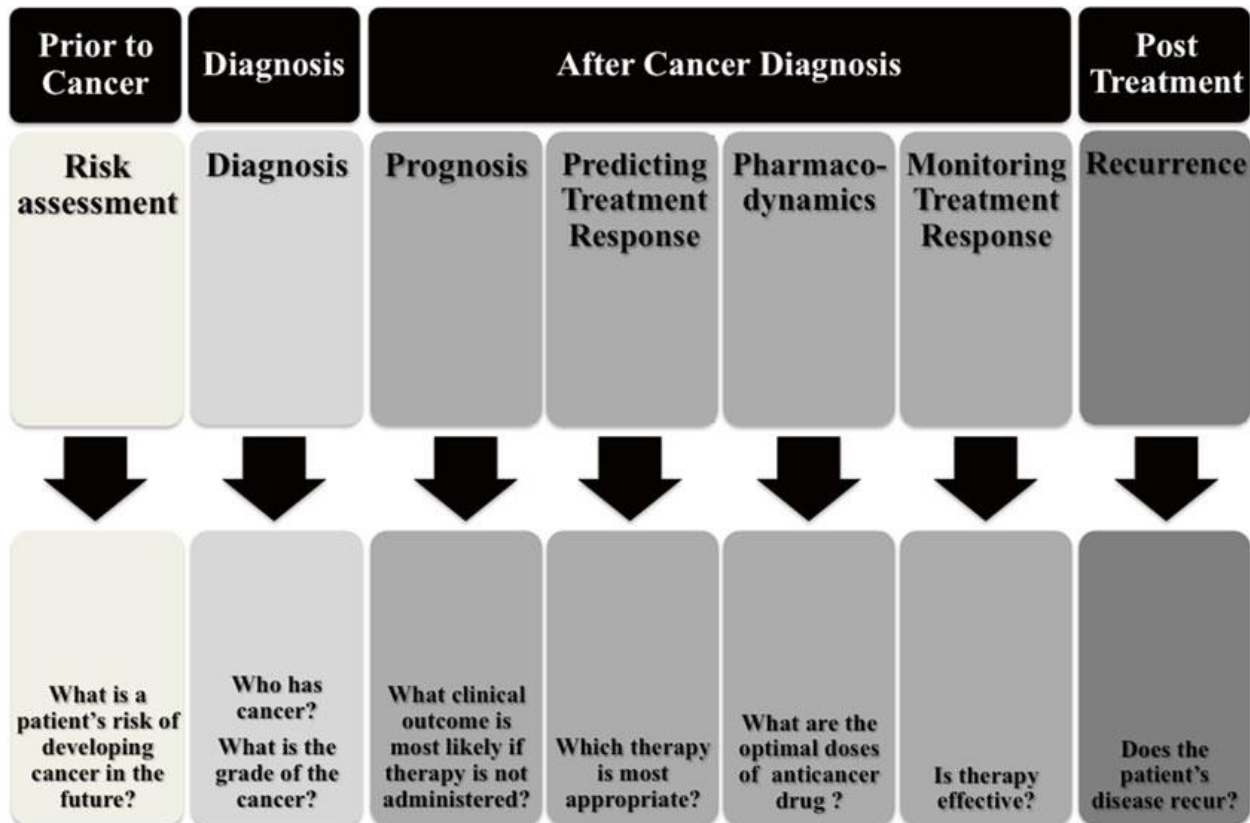


Fig. Potential fields of application of a cancer biomarker test

MECHANISMS OF BIOMARKER ELEVATION IN BIOLOGICAL FLUIDS:

Gene overexpression:

The protein encoded by a gene can be expressed in increased quantities as a result of:

- 1-increases in gene or chromosome copy number
- 2-increased transcriptional activity that result of imbalances between gene repressors and gene activators.
- 3-Epigenetic changes, such as DNA methylation
- 4- On a larger scale, chromosomal translocations can result in gene regulation by promoters that are sometimes enhanced by steroid.



-- Genomic microarrays represent a highly powerful technology for gene-expression studies.

Example of a putative biomarker is the protein human epididymal secretory protein 4 (HE4), which is overexpressed in ovarian carcinoma.

Increased protein secretion and shedding

20–25% of all proteins are secreted, aberrant secretion or shedding of membrane bound proteins with an extracellular domain (ECD) is another means by which molecules can be elevated in biological fluids.

Example of shedding of membrane proteins into fluids (and thus serving as a cancer biomarker) is HER2 (also known as ERBB2).

HER2 is a cell membrane surface-bound tyrosine kinase that is involved in cell growth and differentiation. Overexpression of this protein is associated with high risks of relapse and death from breast and ovarian cancers.

Angiogenesis, invasion and destruction of tissue architecture

Tissue invasion by the tumor might permit direct release of molecules into the interstitial fluid and subsequent delivery by the lymphatics into the blood.

For epithelial cancer types, the proteins must break through the basement membrane of the invading tumor before they appear in the blood.

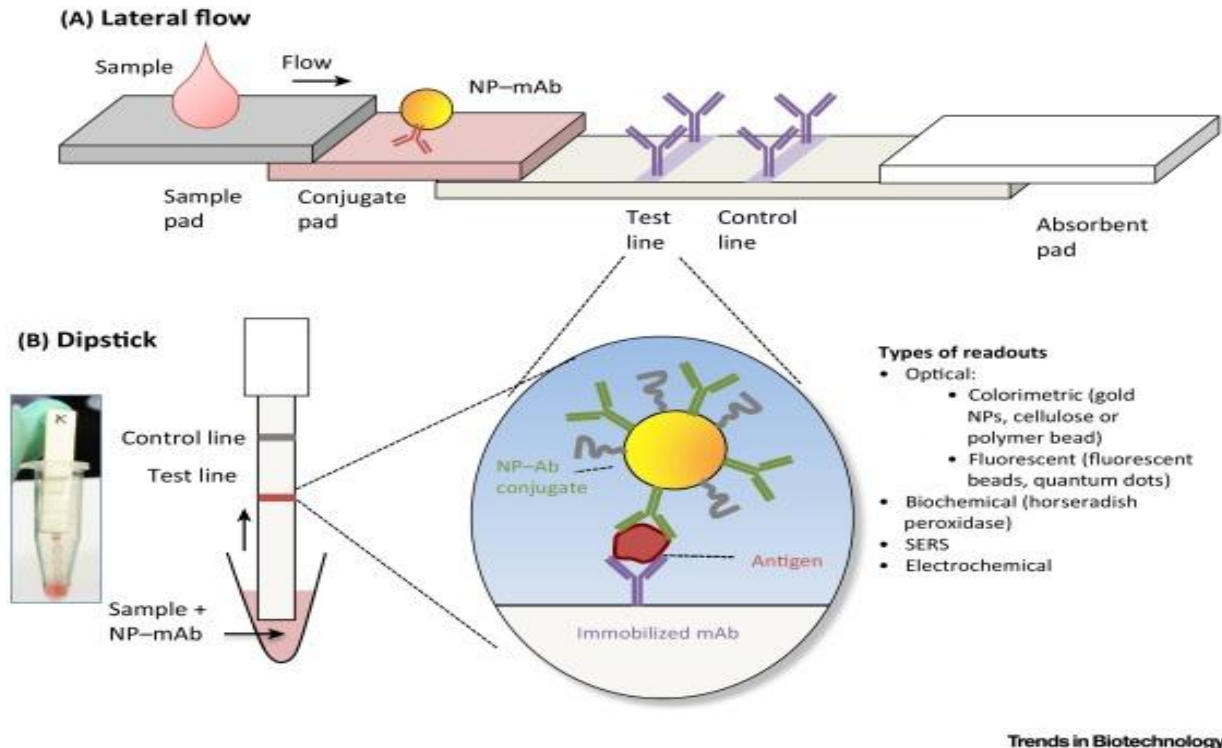
For example, PSA is abundantly expressed by prostatic columnar epithelial cells and secreted into the glandular lumen.

Point-of-Care (POC) for Cancer Detection:

Fast, reliable, and non-invasive diagnostic tools that can be used directly or by local physicians at the point-of-care. POC devices is sample application. Clinical specimens may include saliva, breast milk, urine, cerebrospinal fluid, stool, seminal plasma, amniotic fluid, or blood.

1. Lateral Flow Immunoassays:

incorporate antibodies to detect the presence of cancer biomarkers. provide a qualitative yes/no answer to the presence of a biomarker in a short period of time (usually minutes).



2. Circulating Tumor Cells

cancerous tumor can be detected when peripheral tumor cells are shed and subsequently leave the immediate area of the tumor. They then move through the blood stream or lymphatic system.

CELL SEARCH® is one of the first Food and Drug Administration (FDA) approved tests for the detection of CTCs in cancer patients.

3. Prostate Cancer

One widely known biomarker used in cancer diagnostics is prostate specific antigen (PSA).

PSA is a serine protease kallikrein protein produced by epithelial cells in the prostate.



It is detectable with the use of an antibody-based POC platform.

Pancreatic Cancer

Pancreatic cancer is one of the most aggressive and poorly diagnosed cancers,

Pancreatic cancer is associated with mutated genes such as the oncogene (KRAS) and the tumor suppressor gene (TP53).