Detection and Clinical Application of Tumor Markers





He Lingyuan 2025.12.26

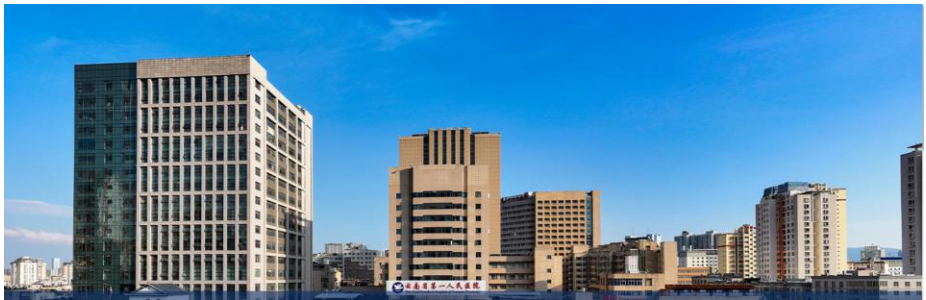
Personal introduction



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Quick questionnaire

How familiar are you with Tumor Markers? Please think about your current knowledge.



A. Very Familiar (I can name several markers and their clinical uses)

B. Somewhat Familiar (I’ ve heard of them and know a basic example)

C. A Little Familiar (I recognize the term but not the details)

D. Not Familiar (This is a new topic for me)

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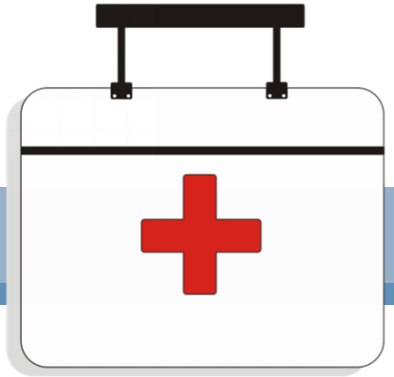
03 Combined Use of Tumor Markers

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01

Understanding Tumor Markers



The mere mention of cancer strikes terror into people's hearts

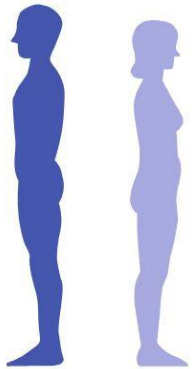




Global Cancer Statistics

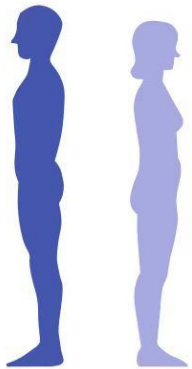
Estimated New Cases

Male			Female		
Prostate	313,780	30%	Breast	316,950	32%
Lung & bronchus	110,680	11%	Lung & bronchus	115,970	12%
Colon & rectum	82,460	8%	Colon & rectum	71,810	7%
Urinary bladder	65,080	6%	Uterine corpus	69,120	7%
Melanoma of the skin	60,550	6%	Melanoma of the skin	44,410	4%
Kidney & renal pelvis	52,410	5%	Non-Hodgkin lymphoma	35,210	4%
Non-Hodgkin lymphoma	45,140	4%	Pancreas	32,490	3%
Oral cavity & pharynx	42,500	4%	Thyroid	31,350	3%
Leukemia	38,720	4%	Kidney & renal pelvis	28,570	3%
Pancreas	34,950	3%	Leukemia	28,170	3%
All sites	**1,053,250**		**All sites**	**988,660**	



Estimated Deaths

Male			Female		
Lung & bronchus	64,190	20%	Lung & bronchus	60,540	21%
Prostate	35,770	11%	Breast	42,170	14%
Colon & rectum	28,900	9%	Pancreas	24,930	8%
Pancreas	27,050	8%	Colon & rectum	24,000	8%
Liver & intrahepatic bile duct	19,250	6%	Uterine corpus	13,860	5%
Leukemia	13,500	4%	Ovary	12,730	4%
Esophagus	12,940	4%	Liver & intrahepatic bile duct	10,840	4%
Urinary bladder	12,640	4%	Leukemia	10,040	3%
Non-Hodgkin lymphoma	11,060	3%	Non-Hodgkin lymphoma	8,330	3%
Brain & other nervous system	10,170	3%	Brain & other nervous system	8,160	3%
All sites	**323,900**		**All sites**	**294,220**	

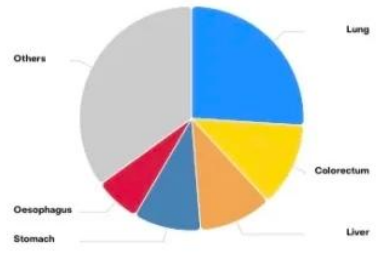


China Cancer Statistics

Number of new cases	Number of deaths	Number of prevalent cases (5-year)
4 824 703	2 574 176	10 968 974

Top 5 most frequent cancers**

Males

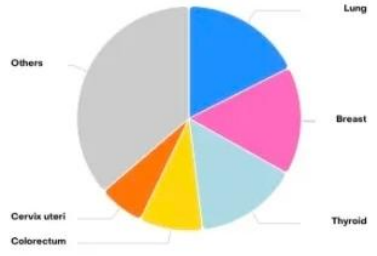


Total: 2 533 906

Rank	Cancer site	Number of cases	Percent
1st	Lung	658 722	26.0%
2nd	Colorectum	307 688	12.1%
3rd	Liver	267 898	10.6%
4th	Stomach	246 550	9.7%
5th	Oesophagus	167 472	6.6%
-	Others	885 576	34.9%

Number of new cases in 2022, males, all ages

Females

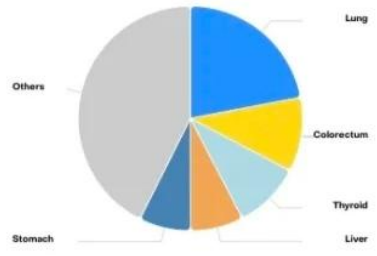


Total: 2 290 797

Rank	Cancer site	Number of cases	Percent
1st	Lung	401 862	17.5%
2nd	Breast	357 161	15.6%
3rd	Thyroid	341 211	14.9%
4th	Colorectum	209 418	9.1%
5th	Cervix uteri	150 659	6.6%
-	Others	830 486	36.3%

Number of new cases in 2022, females, all ages

Both sexes

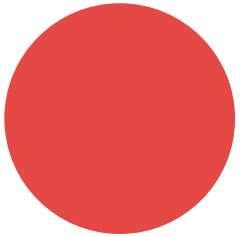


Total: 4 824 703

Rank	Cancer site	Number of cases	Percent
1st	Lung	1 060 584	22.0%
2nd	Colorectum	517 106	10.7%
3rd	Thyroid	466 118	9.7%
4th	Liver	367 657	7.6%
5th	Stomach	358 672	7.4%
-	Others	2 054 566	42.6%

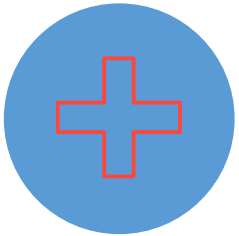
Number of new cases in 2022, both sexes, all ages

Definition and Purpose



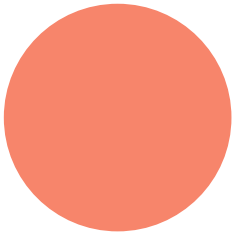
Biological indicators of cancer

Substances produced by cancer cells or host response (non-tumorous cells), detectable in bodily fluids, used for diagnosis and monitoring disease progression.



Clinical applications overview

Essential for screening high-risk groups, assessing treatment response, detecting recurrence, and providing prognostic information.



Limitations and challenges

No single marker is 100% specific; benign conditions can cause elevations； requiring careful interpretation.

Major Tumor Marker Categories

01 Protein kind of tumor markers

02 Carbohydrate antigen markers

03 Enzymes of tumor markers

04 Hormone kind of tumor markers

05 Other tumor markers

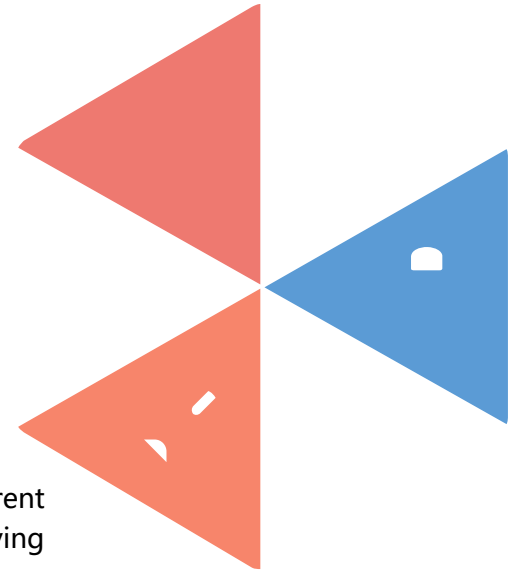
Historical Development

Early cancer detection attempts

First tumor marker (Bence Jones protein) discovered in 1846, leading to modern immunoassay techniques.

Technological advancements

From radioimmunoassays in 1960s to current high-sensitivity automated platforms improving detection.



Evolving clinical roles

Transition from diagnostic tools to comprehensive monitoring systems in oncology practice.

Tumor Markers Detection Process

Blood sampling



Centrifugation



Detection



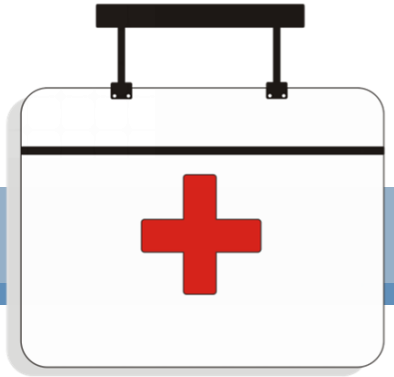
Laboratory test report





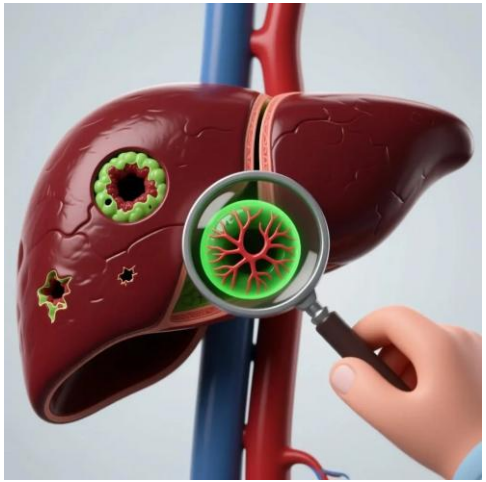
02

Major Marker Categories



Protein kind of tumor markers

1. AFP: Alpha-Fetoprotein



· Glycoprotein, 70 kDa

· Normal: <25 μg/L

· Elevated in:

Hepatocellular carcinoma (HCC)

Germ cell tumors (testis, ovary)

Benign liver diseases (cirrhosis, hepatitis)

· Not suitable for screening but useful for monitoring high-risk patients

Protein kind of tumor markers

2. CEA: Carcinoembryonic Antigen



· Glycoprotein, 180 kDa

· Normal: <5.0 µg/L

· Elevated in:

Colorectal cancer

Gastric, breast, lung cancers

Benign conditions (liver disease, smoking, inflammation)

· Used for prognosis and monitoring recurrence after surgery

Protein kind of tumor markers

3. B2GM： B2-Microglobulin



· Polypeptide, 11.8 kDa

· Normal: <2.5 mg/L

· Elevated in:

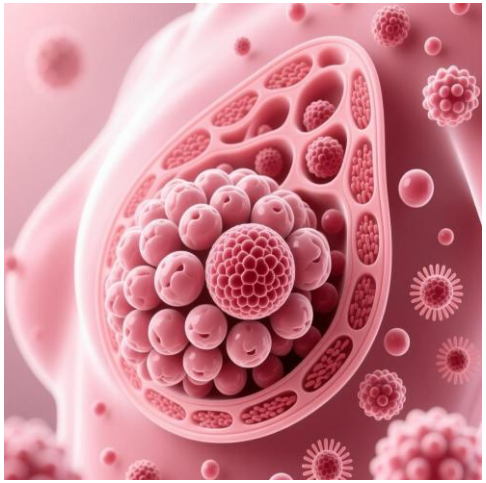
Myeloma, chronic lymphocytic leukemia(CLL), lymphomas

Non-cancerous conditions （Kidney disease, hepatitis）

· Used for prognosis evaluation

Carbohydrate antigen markers

1. CA15-3



· Carbohydrate antigen , 300 kDa

· Normal: <25 U/L

· Elevated in:

Breast cancer

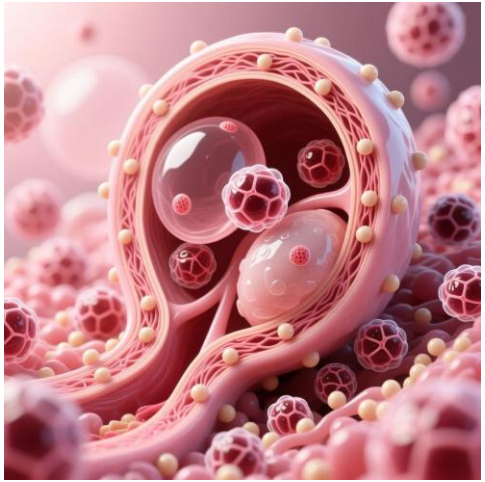
Ovarian, uterine, lung, gastric, pancreatic, hepatocellular cancers

Benign conditions (hepatic, pancreatic, rheumatic, and tuberculosis)

· Used for monitoring the disease course, not suited for screening or for diagnosis

Carbohydrate antigen markers

2. CA125



· Carbohydrate antigen , 200-500 kDa

· Normal: <35 U/L

· Elevated in:

Ovarian cancer

Breast, cervical, endometrial, pancreatic cancers

Benign conditions (acute adnexitis, external endometriosis, pelvic inflammatory, peritonitis, acute pancreatitis)

· Used for monitoring the disease course and treatment

Carbohydrate antigen markers

3. CA19-9/GICA (Gastrointestinal Cancer Antigen)



· Carbohydrate antigen , 36kDa

· Normal: <37 U/L

· Elevated in:

Pancreatic cancer

Hepatocellular, colorectal and gastric cancer

Benign conditions (cholecystitis, obstructive jaundice, chronic active hepatitis, liver cirrhosis, and primary biliary cirrhosis)

· Used for monitoring the disease course

Repeated determination are always better than single marker determination

Enzymes of tumor markers

1. PSA (Prostate-Spesific Antigen)



· Serine protease, 33 kDa

· Normal: t-PSA < 4.0 µg/L
f-PSA < 0.8 µg/L
f-PSA/t-PSA > 25%

· Elevated in:
Prostate cancer
Benign conditions (Prostate hyperplasia, prostatitis, prostate infarction)

· Used in: Prostate cancer screening (with DRE)
Monitoring the disease course after surgery/radiation

Enzymes of tumor markers

2. NSE (Neuron-Specific Enolase)



· Enzyme of glycolysis, 39 kDa for subunit

· Normal: <15 µg/L

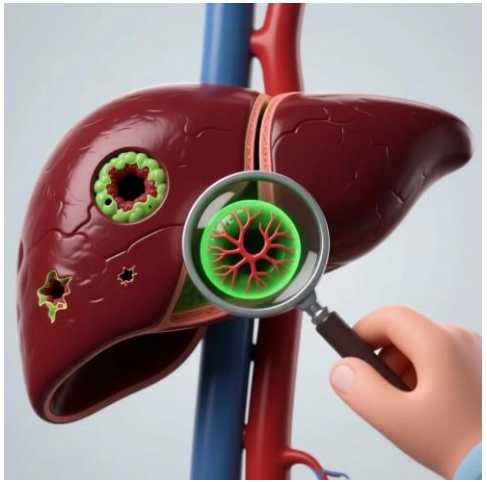
· Elevated in:

Lung cancer, especially in SCLC (small cell lung cancer)
Neuroblastoma
Benign conditions (Pulmonary, cerebral diseases)

· Used in: Monitoring the outcome of treatment and disease course

Enzymes of tumor markers

3. AFU (α-L-Fucosidase)



· Lysosomal enzyme, 200-220 kDa for subunit

· Normal: 234–414 μmol/L

· Elevated in:

Hepatocellular carcinoma (HCC)

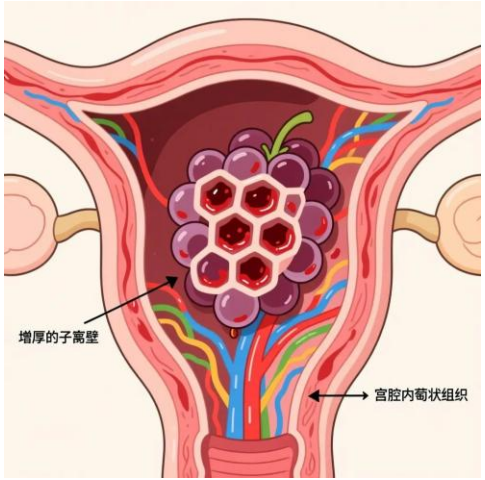
Metastatic liver cancer, breast or lung cancer

Benign conditions (liver cirrhosis)

· Used in: Monitoring the outcome of treatment and disease course

Hormone kind of tumor markers

1. HCG (Human Chorionic Gonadotropin)



· Glycoprotein, 36-42 kDa

· Normal: <5 U/L

· Elevated in:

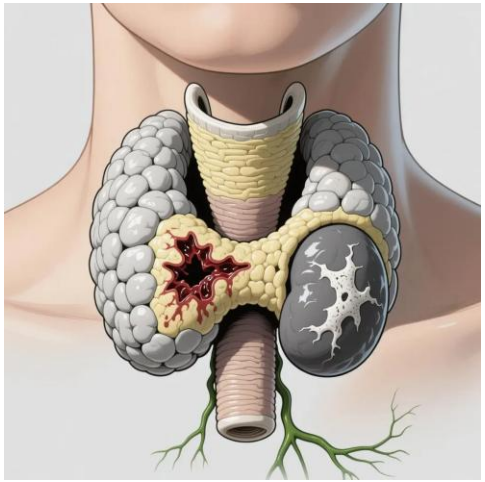
Gestational trophoblastic disease; Germ cell tumors

Pregnancy

· Used for prognosis evaluation

Hormone kind of tumor markers

2. CT (Calcitonin)



· Hormone, 36-42 kDa

· Normal: <100 ng/L

· Elevated in:

Medullary thyroid carcinoma (MTC)

Lung cancer , lukemia

· Used for detection of early cancer

Other tumor markers

Tumor marker	Reference Value	Related Tumor
CA50	<24kU/L	Pancreatic Cancer, Colon cancer, Gastric cancer
CA 72-4	<6 kU/L	Gastric cancer, Mucinous ovarian carcinoma
CA242	<20kU/L	Panereatic Cancer, Colon cancer, Gastric cancer
PAP	<2.0 pg/L	Prostate cancer
SCC	<1.5 pg/L	Cervical cancer, Squamous cell carcinoma of the lung
TPA	<80 U/L	Bladder cancer, Prostate cancer, Digestive tract tumor
CYFRA21-1	<3.3 pg/L	Non small cell lung cancer
Sialic acid	<1.8 mmol/L	Lung cancer, Gastric cancer, Melanoma

In-class Quiz



1. Which tumor marker is most commonly used for screening and monitoring prostate cancer?
   A. CA125
   B. PSA
   C. AFP
   D. CEA

2. The main clinical uses of tumor markers do NOT include which of the following?
   A. Definitive diagnosis of cancer
   B. Monitoring treatment response
   C. Assessing risk of cancer recurrence
   D. Screening high-risk populations

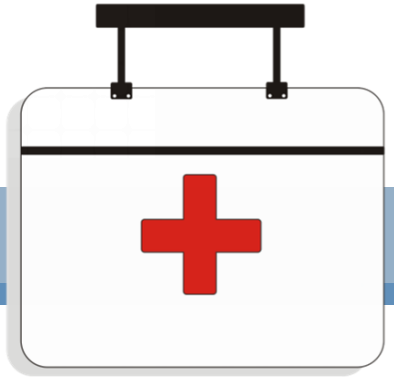
3. A significant elevation of Alpha-fetoprotein (AFP) is typically associated with which type of tumor?
   A. Breast cancer
   B. Liver cancer
   C. Colon cancer
   D. Lung cancer

4. Regarding the limitations of tumor markers, which statement is correct?
   A. They are highly specific and are not elevated in benign conditions.
   B. They are highly sensitive and can be used alone to diagnose cancer.
   C. They can be mildly elevated in certain inflammatory or benign diseases.
   D. They are elevated in the blood of all cancer patients.



03

Combined Use of Tumor Markers



Features of Ideal Tumor Markers

The ideal marker would be a "blood test" for cancer in which a positive result would occur only in patients with malignancy, one that would correlate with stage and response to treatment and that was easily and reproducibly measured.

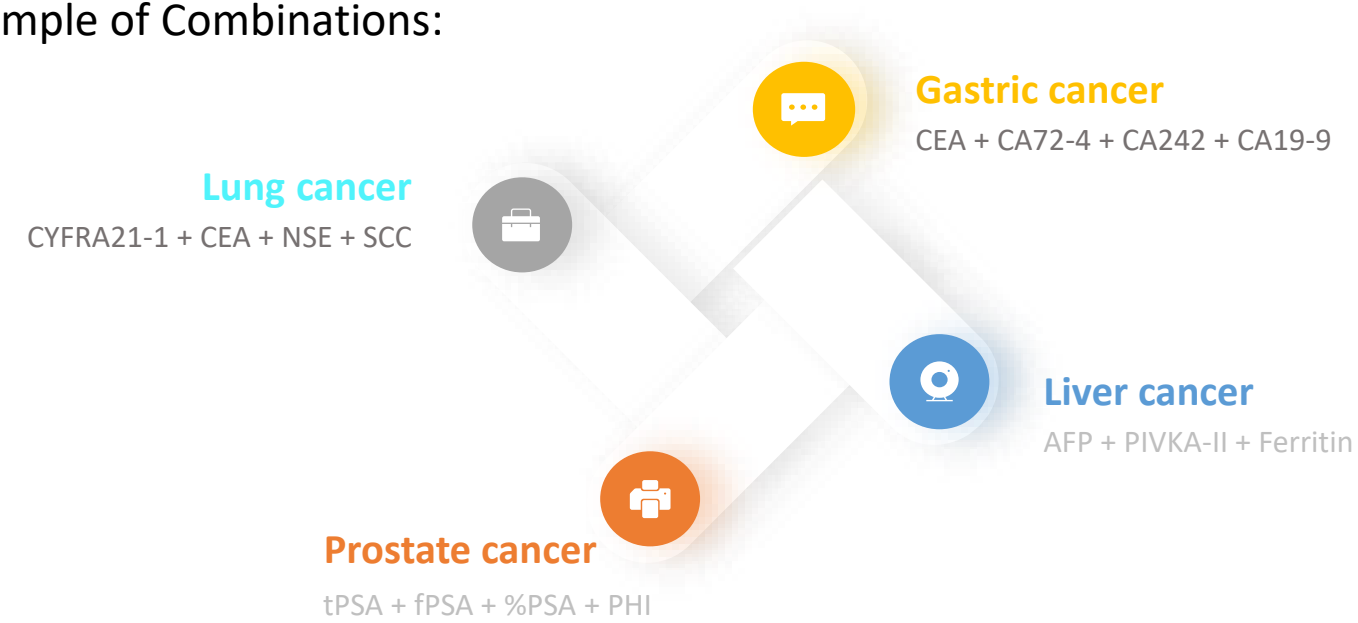
No tumor marker is now available which met this ideal 

Combined application of tumor markers 

Combined use of Tumor Markers

Combination improves sensitivity & specificity

Example of Combinations:



Matters needing attention



01 Tumor markers are not for screening in general population

02 Used for monitoring therapy & detecting recurrence

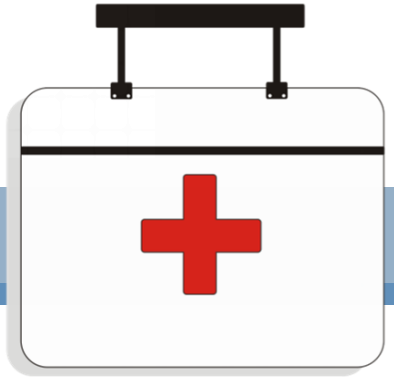
03 Always interpret in clinical context (imaging, symptoms, history)

04 Serial measurements > single measurement

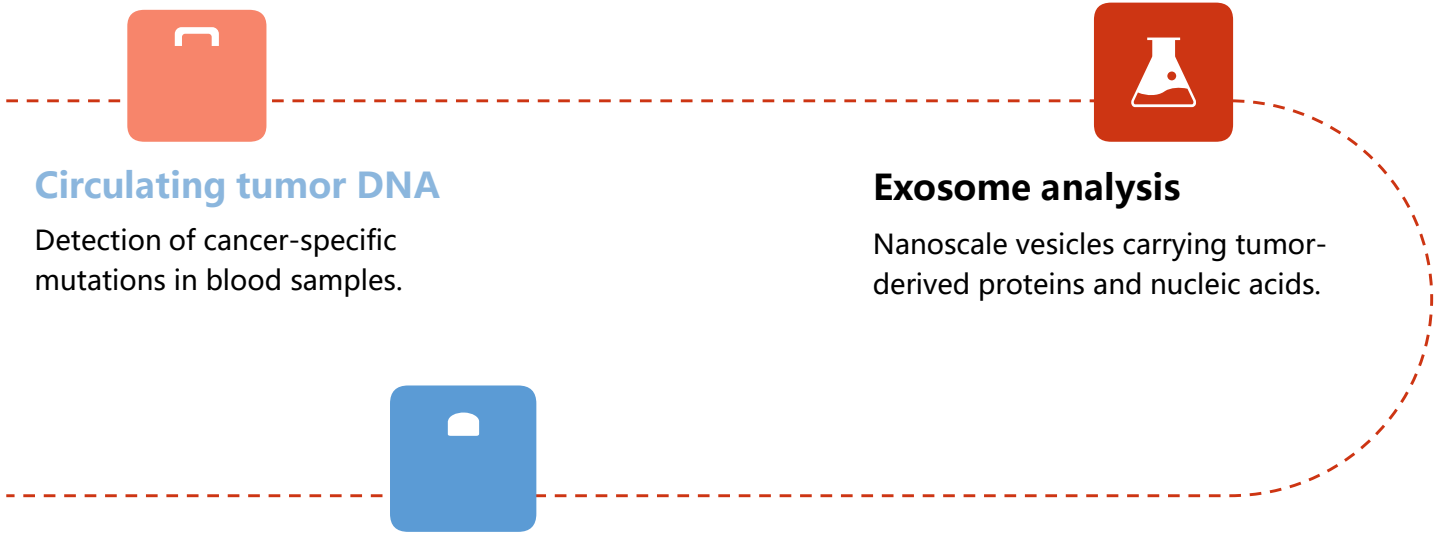


04

Advances and Innovations



Molecular Technologies



Circulating tumor DNA

Detection of cancer-specific mutations in blood samples.

Exosome analysis

Nanoscale vesicles carrying tumor-derived proteins and nucleic acids.

Proteomic profiling

Mass spectrometry approaches identifying novel marker patterns.

Future Directions

Emerging biomarker technologies

Liquid biopsies and circulating tumor DNA showing promise for non-invasive monitoring.



Personalized medicine approaches

Integration with genomic profiling enables tailored treatment strategies.

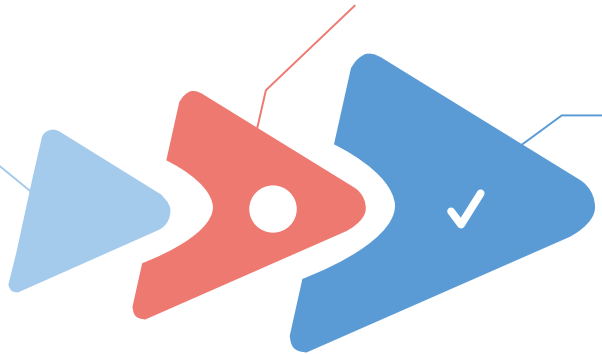
AI-assisted interpretation

Machine learning algorithms improving diagnostic accuracy through pattern recognition.

Precision Oncology

Companion diagnostics

Matching targeted therapies with specific biomarker profiles.



Resistance monitoring

Detecting emerging mutations during treatment courses.

Minimal residual disease

Ultra-sensitive assays for post-treatment surveillance.

Summary

- ✓ Tumor markers are valuable tools in oncology diagnostics & monitoring :
  AFP, CEA, β2MG, CA15-3, CA125, CA19-9, PSA, NSE, AFU, HCG, CT……
- ✓ Must understand their limitations:
  Not 100% specific or sensitive ; Can be elevated in benign conditions
- ✓ Combined use with imaging & clinical assessment is key

Case Study: The Use of CEA in Colorectal Cancer

Mr. Johnson, a 60-year-old man with a long-term smoking history, visited the doctor due to changes in bowel habits and bloody stools. A colonoscopy with biopsy confirmed Stage III colon adenocarcinoma. Before surgery, his Carcinoembryonic Antigen (CEA) level was 45 ng/mL. Six weeks after successful tumor resection surgery, his CEA level dropped to 5 ng/mL. During regular follow-up one year post-operation, his CEA level was found to have gradually increased again to 20 ng/mL.

1. What purpose of tumor marker use in cancer management is demonstrated by the significant pre-operative CEA elevation and its rapid drop after surgery?

2. What clinical scenario might the gradual rise in CEA level one year later suggest?

3. Can the elevated CEA level alone confirm cancer recurrence? Why or why not? What investigations should follow?



Case Study: The Use of CEA in Colorectal Cancer

Answers:

1. It demonstrates the use of CEA for monitoring treatment response (in this case, indicating successful surgical removal of the tumor mass).

2. It may suggest cancer recurrence or metastasis. A pattern of gradual rise is particularly concerning.

3. No, it cannot confirm recurrence alone. CEA elevation can also be caused by other factors like smoking or colitis. Imaging studies (e.g., CT, PET-CT) must be performed to locate possible recurrent or metastatic lesions, followed by pathological confirmation if needed.



Thank you



