Understanding Tumor Markers

CREATE AN ENVIRONMENT WHERE CANCER CANNOT THRIVE

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Tumor Markers Overview

WHAT ARE TUMOR MARKERS?

Tumor markers are substances that are produced by cancer or by other cells of the body in response to cancer or certain benign (noncancerous) conditions.

Most tumor markers are made by normal cells as well as by cancer cells; however, they are produced at much higher levels in cancerous conditions. These substances can be found in the blood, urine, stool, tumor tissue, or other tissues or bodily fluids of some patients with cancer.

Most tumor markers are proteins. However, more recently, patterns of gene expression and changes to DNA within tumor tissue specifically have also begun to be used as tumor markers.

Thus far, **more than 20 different tumor markers have been characterized** and are in clinical use. Some are associated with only one type of cancer, whereas others are associated with two or more cancer types. There is no "universal" tumor marker that can detect any type of cancer.

There are some limitations to the use of tumor markers. Sometimes, **non-cancerous conditions can cause the levels of certain tumor markers to increase.** Not everyone with a particular type of cancer will have a higher level of a tumor marker associated with that cancer. Moreover, **tumor markers have not been identified for every type of cancer.**

HOW ARE TUMOR MARKERS USED IN CANCER CARE?

To help detect, diagnose, and manage some types of cancer.
Although an elevated level of a tumor marker may suggest the presence of cancer, this alone is not enough to diagnose cancer. Therefore, measurements of tumor markers are usually combined with other tests, such as biopsies, to diagnose cancer.

Before treatment to help plan the appropriate therapy
In some types of cancer, the level of a tumor marker reflects the stage of the disease and/or the patient's prognosis.

During cancer therapy to assess treatment response
A decrease in the level of a tumor marker or a return to the marker's normal level may indicate that the cancer is responding to treatment, whereas no change or an increase may indicate that the cancer is not responding.

After treatment to check for recurrence

HOW ARE TUMOR MARKERS MEASURED?

Laboratory evaluation of a **sample of tumor tissue or bodily fluid**. If the tumor marker is being used to determine whether treatment is working or whether there is a recurrence, the marker's level will be measured in multiple samples taken over time.

TUMOR MARKERS CURRENTLY IN COMMON USE:

ALK gene rearrangements
Cancer Types:
Non-small cell lung cancer and anaplastic large cell lymphoma
Tissue Analyzed:
Tumor
Application:
To help determine treatment and prognosis

Alpha-fetoprotein (AFP)
Cancer Types:
Liver cancer and germ cell tumors
Tissue Analyzed:
Blood
Application:
To help diagnose liver cancer, follow response to treatment; assess stage, prognosis, and response to treatment of germ cell tumors

Beta-2-microglobulin (B2M)
Cancer Types:
Multiple myeloma, chronic lymphocytic leukemia, and some lymphomas
Tissue Analyzed:
Blood, urine, or cerebrospinal fluid
Application:
To help determine treatment and prognosis

Beta-human chorionic gonadotropin (Beta-hCG)
Cancer Types:
Choriocarcinoma and testicular cancer
Tissue Analyzed:
Urine or blood
Application:
To assess stage, prognosis, response to treatment

BCR-ABL fusion gene
Cancer Types:
Chronic myeloid leukemia
Tissue Analyzed:
Blood and/or bone marrow
Application:
To help determine treatment and prognosis

BRAF mutation V600E
Cancer Types:
Cutaneous melanoma and colorectal cancer
Tissue Analyzed:
Tumor
Application:
To help determine treatment and prognosis

CA15-3/CA27.29
Cancer Types:
Breast cancer
Tissue Analyzed:
Blood
Application:
To assess treatment efficacy or if disease has recurred

CA19-9
Cancer Types:
Pancreatic, gallbladder, bile duct, and gastric cancers
Tissue Analyzed:
Blood
Application:
To assess whether treatment is working

CA-125
Cancer Types:
Ovarian cancer
Tissue Analyzed:
Blood
Application:
To help in diagnosis, assessment of response to treatment, and evaluation of recurrence

Calcitonin
Cancer Types:
Medullary thyroid cancer
Tissue Analyzed:
Blood
Application:
To aid in diagnosis, check whether treatment is working, and assess recurrence

Carcinoembryonic antigen (CEA)
Cancer Types:
Colorectal cancer and breast cancer
Tissue Analyzed:
Blood
Application:
To check whether colorectal cancer has spread; look for breast cancer recurrence; assess response to treatment

CD20
Cancer Types:
Non-Hodgkin lymphoma
Tissue Analyzed:
Blood
Application:
To determine whether treatment with a targeted therapy is appropriate

Chromogranin A (CgA)

Cancer Types:
Neuroendocrine tumors
Tissue Analyzed:
Blood
Application:
To help in diagnosis, assessment of treatment response, and evaluation of recurrence

Chromosomes 3, 7, 17, and 9p21

Cancer Types:
Bladder cancer
Tissue Analyzed:
Urine
Application:
To help in monitoring for tumor recurrence

Cytokeratin fragments 21-1

Cancer Types:
Lung cancer
Tissue Analyzed:
Blood
Application:
To help in monitoring for recurrence

EGFR mutation analysis

Cancer Types:
Non-small cell lung cancer
Tissue Analyzed:
Tumor
Application:
To help determine treatment and prognosis

Estrogen receptor (ER)/progesterone receptor (PR)

Cancer Types:
Breast cancer
Tissue Analyzed:
Tumor
Application:
To determine whether treatment with hormonal therapy (such as tamoxifen) is appropriate

Fibrin/fibrinogen

Cancer Types:
Bladder cancer
Tissue Analyzed:
Urine
Application:
To monitor progression and response to treatment

HE4

Cancer Types:
Ovarian cancer
Tissue Analyzed:
Blood
Application:
To assess disease progression and monitor for recurrence

HER2/neu

Cancer Types:
Breast cancer, gastric cancer, and esophageal cancer
Tissue Analyzed:
Tumor
Application:
To determine whether treatment with trastuzumab is appropriate

Immunoglobulins

Cancer Types:
Multiple myeloma and Waldenström macroglobulinemia
Tissue Analyzed:
Blood and urine
Application:
To help diagnose disease, assess response to treatment, and look for recurrence

KIT

Cancer Types:
Gastrointestinal stromal tumor and mucosal melanoma
Tissue Analyzed:
Tumor
Application:
To help in diagnosing and determining treatment

KRAS mutation analysis

Cancer Types:
Colorectal cancer and non-small cell lung cancer **Tissue Analyzed:**
Tumor
Application:
To determine whether treatment with a particular type of targeted therapy is appropriate

LDH Lactate dehydrogenase

Cancer Types:
Germ cell tumors
Tissue Analyzed:
Blood
Application:
To assess stage, prognosis, and response to treatment

Nuclear matrix protein 22

Cancer Types:
Bladder cancer
Tissue Analyzed:
Urine
Application:
To monitor response to treatment

Prostate-specific antigen (PSA)

Cancer Types:
Prostate cancer
Tissue Analyzed:
Blood
Application:
To help in diagnosis, assess response to treatment, and look for recurrence

Thyroglobulin

Cancer Types:
Thyroid cancer
Tissue Analyzed:
Blood
Application:
To evaluate response to treatment and look for recurrence

Urokinase plasminogen activator (uPA) & plasminogen activator inhibitor (PAI-1)

Cancer Types:
Breast cancer
Tissue Analyzed:
Tumor
Application:
To determine aggressiveness of cancer and guide treatment

5-Protein signature (Ova1)

Cancer Types:
Ovarian cancer
Tissue Analyzed:
Blood
Application:
To pre-operatively assess pelvic mass for suspected ovarian cancer

21-Gene signature (Oncotype DX)

Cancer Types:
Breast cancer
Tissue Analyzed:
Tumor
Application:
To evaluate risk of recurrence

70-Gene signature (Mammaprint)

Cancer Types:
Breast cancer
Tissue Analyzed:
Tumor
Application:
To evaluate risk of recurrence

ENOX 2 (OncoBlot) Tumor Cell Surface Proteins

Cancer Types:
More than 26 cancer types identified
Tissue Analyzed:
Blood
Application:
Indicates presence of malignancy and organ site; Follow up to other tests (such as high PSA, abnormal mammogram, suspicious PET scan);
Recurrent cancer testing, Familial cancer testing, Testing after completion of cancer treatments

CAN TUMOR MARKERS BE USED IN CANCER SCREENING?

Because tumor markers can indicate response of a tumor to treatment and for prognosis, researchers have hoped that they might also be useful in screening to detect cancer early, before symptoms.

For a screening test to be useful, it needs very **high sensitivity** (ability to correctly identify people who have the disease) and **high specificity** (ability to correctly identify people who do *not* have the disease).

If a test is <u>highly sensitive,</u> it will identify most people with the disease—that is, it will result in very few false-negative results.

If a test is highly specific, only a small number of people will test positive for the disease who do not have it—it will result in very few false-positive results.

Although tumor markers are extremely useful in determining whether a tumor is responding to treatment or assessing whether it has recurred, **no tumor marker identified to date is sufficiently sensitive or specific to be used on its own to screen for cancer.**

For example, the prostate-specific antigen (PSA) test, which measures the level of PSA in the blood, is often used to screen men for prostate cancer. However, an increased PSA level can be caused by benign prostate conditions as well as by prostate cancer, and **most men with an elevated PSA level do not have prostate cancer.**

Initial results from two large randomized controlled trials, the NCI-conducted Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, or PLCO, and the European Randomized Study of Screening for Prostate Cancer, showed that **PSA testing at best leads to only a small reduction in the number of prostate cancer deaths**. Moreover, it is not clear whether the benefits of PSA screening outweigh the harms of follow-up diagnostic tests and treatments for cancers that in many cases would never have threatened a man's life.

Similarly, **CA-125**, a tumor marker that is sometimes elevated in the blood of women with ovarian cancer but can also be elevated in women with benign conditions, **is not sufficiently sensitive or specific to be** used together with transvaginal ultrasound to screen for ovarian cancer in women at average risk.

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Source: National Cancer Institute www.cancer.gov