NIH NATIONAL CANCER INSTITUTE

# Tumor Markers

## What are tumor markers?

A tumor marker is anything present in or produced by cancer cells or other cells of the body in response to cancer or certain benign (noncancerous) conditions that provides information about a cancer, such as how aggressive it is, whether it can be treated with a targeted therapy, or whether it is responding to treatment.

Tumor markers have traditionally been proteins or other substances that are made by both normal and cancer cells but at higher amounts by cancer cells. These can be found in the blood, urine, stool, tumors, or other tissues or bodily fluids of some patients with cancer. Increasingly, however, genomic markers such as tumor gene mutations, patterns of tumor gene expression, and nongenetic changes in tumor DNA, are being used as tumor markers.

Many 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 multiple different cancer types. No “universal” tumor marker has been found that can reveal the presence of any type of cancer.

## How are tumor markers used in cancer care?

There are two main types of tumor markers that have different uses in cancer care: circulating tumor markers and tumor tissue markers.

**Circulating tumor markers** can be found in the blood, urine, stool, or other bodily fluids of some patients with cancer. Circulating tumor markers are used to:

- estimate prognosis
- detect cancer that remains after treatment (residual disease) or that has returned after treatment
- assess the response to treatment
- monitor whether a cancer has become resistant to treatment

Although an elevated level of a circulating tumor marker may suggest the presence of cancer, this alone is not enough to diagnose cancer. For example, noncancerous conditions can sometimes cause the levels of certain tumor markers to increase. In addition, not everyone with a particular type of cancer will have a higher level of a tumor marker associated with that cancer. Therefore, measurements of circulating tumor markers are usually combined with the results of other tests, such as biopsies or imaging, to diagnose cancer.

Tumor markers may also be measured periodically during cancer therapy. For example, a decrease in the level of a circulating tumor marker may indicate that the cancer is responding to treatment, whereas an increasing or unchanged level may indicate that the cancer is not responding.

Circulating tumor markers may also be measured after treatment has ended to check for recurrence (the return of cancer).

Examples of commonly used circulating tumor markers include calcitonin (measured in blood), which is used to assess treatment response, screen for recurrence, and estimate prognosis in medullary thyroid cancer; CA-125 (measured in blood), to monitor how well cancer treatments are working and if cancer has come back in ovarian cancer; and beta-2-microglobulin (measured in blood, urine, or cerebrospinal fluid), to estimate prognosis and follow response to treatment for multiple myeloma, chronic lymphocytic leukemia, and some lymphomas.

**Tumor tissue markers** are found in the actual tumors themselves, typically in a sample of the tumor that is removed during a biopsy. Tumor tissue markers are used to:

- diagnose, stage, and/or classify cancer
- estimate prognosis
- select an appropriate treatment (eg, treatment with a targeted therapy)

In some types of cancer, the level of a tumor marker reflects the stage (extent) of the disease and/or the patient's prognosis (likely outcome or course of disease). An example is alpha-fetoprotein, which is measured in blood to assess stage, estimate prognosis, and follow response to treatment of germ cell tumors. More information about cancer staging is available on the Staging page.

Tumor markers may be measured before treatment to help doctors plan the appropriate therapy. For example, some tests, called companion diagnostics, which have been developed alongside their respective targeted therapy drug, are used to determine whether treatment with a particular targeted therapy is appropriate. Some of these tests measure how much of the tumor marker is present; others detect the presence of a specific marker, such as a gene mutation.

Some tumor tissue markers are targets for specific targeted therapies. However, not all targets of targeted therapies are tumor markers that are tested in patients. More information about therapies that are designed to interfere with specific targets involved in cancer cell growth and survival is available in the Targeted Cancer Therapies fact sheet.

Examples of commonly used tumor tissue markers include estrogen receptor and progesterone receptor (breast cancer), used to determine whether treatment with hormone therapy and some targeted therapies is appropriate; *EGFR* gene mutation analysis (non-small cell lung cancer), to help determine treatment and estimate prognosis; and PD-L1 (many cancer types), to determine whether treatment with a type of targeted therapy called an immune checkpoint inhibitor is appropriate.

## How are tumor markers measured?

A doctor takes a sample of tumor tissue or bodily fluid and sends it to a laboratory, where various methods are used to measure the level or presence (or absence) of the tumor marker.

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 at different times during and after treatment. Usually "serial measurements," which show how the level of a marker is changing over time, are more meaningful than a single measurement.

Some markers, such as the presence or absence of a particular genetic alteration that makes a tumor a candidate for treatment with a specific targeted therapy, do not themselves change over time. However, the proportion of tumor cells that have that alteration may change during and after treatment.

## Does NCI have guidelines for the use of tumor markers?

NCI does not have guidelines for the use of tumor markers. However, some national and international organizations have guidelines for the use of tumor markers for some types of cancer:

- The American Society of Clinical Oncology (ASCO) has developed and published clinical practice guidelines on a variety of topics, including tumor markers for breast cancer, colorectal cancer, lung cancer, and others.
- The National Academy of Clinical Biochemistry publishes laboratory medicine practice guidelines, including Use of Tumor Markers in Clinical Practice: Quality Requirements, which focuses on the appropriate use of tumor markers for specific cancers.

## What tumor markers are currently being used, and for which cancer types?

A number of tumor markers are currently being used for a wide range of cancer types. See the list of tumor markers in common use for more information. Although most of these can be tested in laboratories that meet standards set by the Clinical Laboratory Improvement Amendments, some cannot be and may therefore be considered experimental.

## Can tumor markers be used in cancer screening?

Because tumor markers can be used to predict the response of a tumor to treatment and for prognosis, researchers have hoped that they might also be useful in screening tests that aim to detect cancer early, before there are any symptoms.

However, although tumor markers are extremely useful for determining whether a tumor is responding to treatment or assessing whether it has recurred, no tumor marker identified to date is sufficiently sensitive (that is, able to correctly identify people who have the disease) or specific (that is, able to correctly identify people who do not have the disease) to screen for cancer.

For example, until recently, the prostate-specific antigen (PSA) test, which measures the level of PSA in the blood, was used routinely 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. Because results from clinical trials showed that PSA testing leads at best to only a small reduction in the number of prostate cancer deaths and can lead to overdiagnosis and overtreatment, the PSA test is no longer recommended for routine screening. Now it is often used to monitor men with a history of prostate cancer to see if their cancer has come back. See the PSA Test fact sheet for more information.

## What research is under way to develop more accurate tumor markers?

Cancer researchers are turning to proteomics (the study of protein structure, function, and patterns of expression) and proteogenomics (the integration of proteomics with genomics and gene expression analysis, or transcriptomics) with the hope of developing novel biomarkers that can be used to identify cancer in its early stages, to predict the effectiveness of treatment, and to predict the chance of cancer recurrence.

Liquid biopsies, a new approach to studying tumors in which bits of tumor material—including DNA and other molecules as well as whole cells—that are released from tumors are analyzed in bodily fluids such as blood or urine, may yield additional new biomarkers. As of May 2019, FDA has approved one liquid biopsy test: the cobas® EGFR Mutation Test for the detection of *EGFR* gene mutations in circulating tumor DNA of patients with lung cancer. FDA is prioritizing its review of several new liquid biopsy tests (e.g., Foundation One® Liquid, Guardant360®, Signatera™), for which it has granted breakthrough and expedited access pathway designations.

More information on NCI's role in supporting research on novel tools and methods for diagnosing cancer is available on the Cancer Diagnosis Research page.

### Selected References


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2. Andriole G, Crawford E, Grubb R, et al. Mortality results from a randomized prostate-cancer screening trial. *New England Journal of Medicine* 2009; 360(13):1310–1319. [PubMed Abstract]
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### Related Resources

Prostate-Specific Antigen (PSA) Test
Targeted Cancer Therapies
Tumor DNA Sequencing in Cancer Treatment
Tumor Markers in Common Use
Understanding Cancer Prognosis
Understanding Laboratory Tests

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