# PRECISELY YOU

Not an actual patient.

# BIOMARKER TESTING

## and Its Role in Your Metastatic Breast Cancer Journey

Precision Medicine

# Introduction

If you are hearing about biomarkers for the first time, you may wonder how biomarkers affect your care and what to do next. Here is some background information to help you get started.

## Why Are Biomarkers Important?

- Biomarkers provide clues about how your cancer works, including its strengths and weaknesses. Testing for biomarkers helps your doctors predict how your cancer may behave and understand how likely (or unlikely) it is that a specific treatment might work for you[1-4]
- Recent scientific advances have increased the number of actionable biomarkers. This means doctors can now personalize long-term treatment plans in a new way[5]

**No two breast cancers are the same**. Biomarker testing helps your care team get key information to make treatment decisions *precisely for you*[1,3,4,6,7]

## What Is a Biomarker?

- A **biomarker** is a substance that can be found in tissues or blood that signals a normal or abnormal process, or a condition or disease that helps your doctors make decisions about your care[8,9]

- A biomarker can be a change in DNA (mutations), RNA, or protein[8,9]

To learn more about biomarkers go to page 24

## Which Biomarkers Should I Be Tested for?

- All patients with breast cancer should be tested for their **hormone receptor (HR)** status (determined by testing for ER and PR) and HER2 to determine subtype[2,10,11,12]
- Breast cancer subtypes[11,12]:

**HR-positive/HER2-negative**

**HR-positive/HER2-positive**

**Triple-negative**
(HR-negative/HER2-negative)

**HR-negative/HER2-positive**

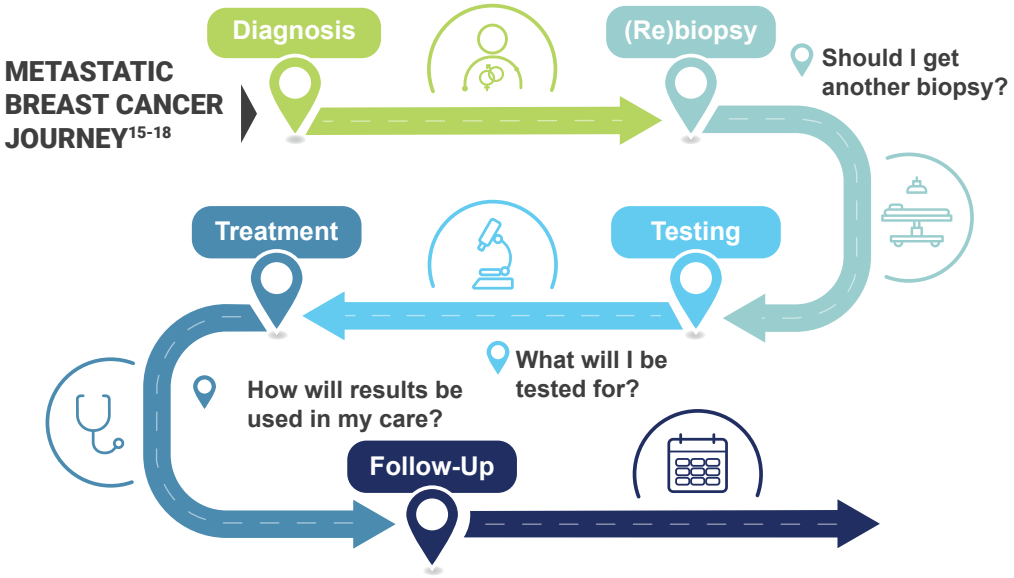
**Your doctor may recommend more biomarker testing for you based on your breast cancer subtype and stage**[2,10,13,14]

To learn more about additional biomarker testing, please go to page 10

ER, estrogen receptor; HER2, human epidermal growth receptor 2; PR, progesterone receptor.

## When Will I Be Tested for Biomarkers?

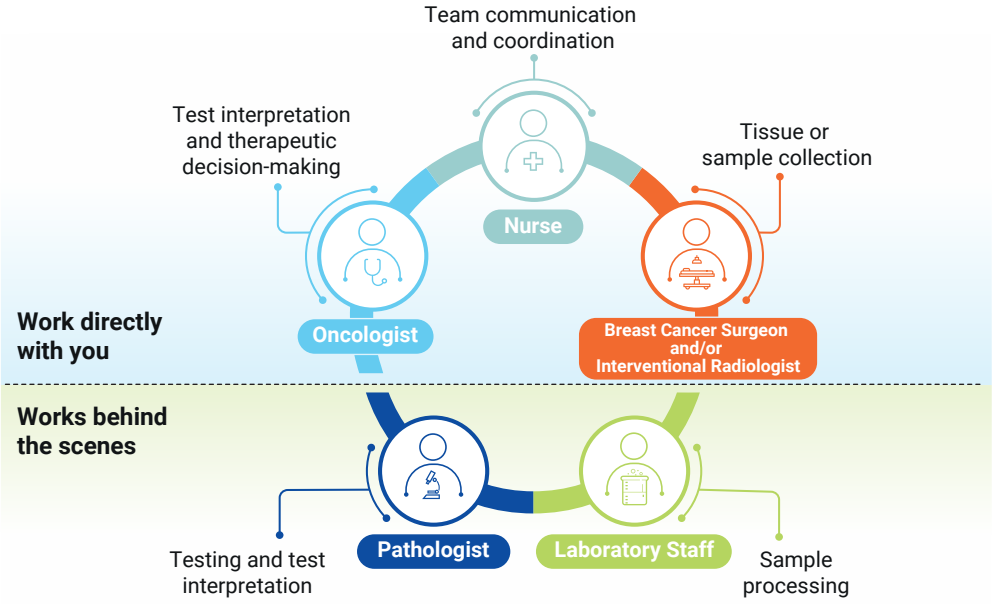
All breast cancer journeys are unique, but most have similar steps. Biomarker testing typically occurs before treatment initiation[2,3]




## Who Is Involved in Biomarker Testing?

Biomarker testing requires input from different specialties, so your care team includes a multidisciplinary team made up of professionals who specialize in different areas. These experts work together to get you the best care, even if you never meet them[15,16,19]

## Some Members of Your Care Team That Help You Get Biomarker Testing



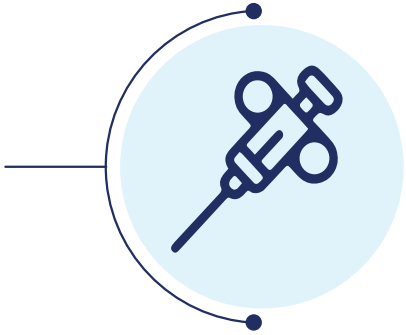

## Questions for Your Care Team

If I have questions about biomarker testing, who should I ask?

Are there resources that can help support me, like financial assistance programs, or financial counselors who can help me understand my insurance coverage?

## What Is the First Step in Biomarker Testing?

- Biomarker testing starts with a biopsy to remove tumor tissue or blood from your body[6]
- If surgery is part of your treatment plan, then biomarker testing may be conducted on the extracted tumor tissue[6]



- In other situations, a separate procedure using the least invasive method possible will be used to obtain a tissue biopsy sample or a liquid biopsy sample for biomarker testing[6]

## What Is a Liquid Biopsy? How Is That Different From a Tissue Biopsy?

- A liquid biopsy is a blood sample that is used to measure tumor cells and tumor DNA in the blood[20,21]
- A tissue biopsy is a sample of tumor tissue that can also be used to test for biomarkers[20,21]

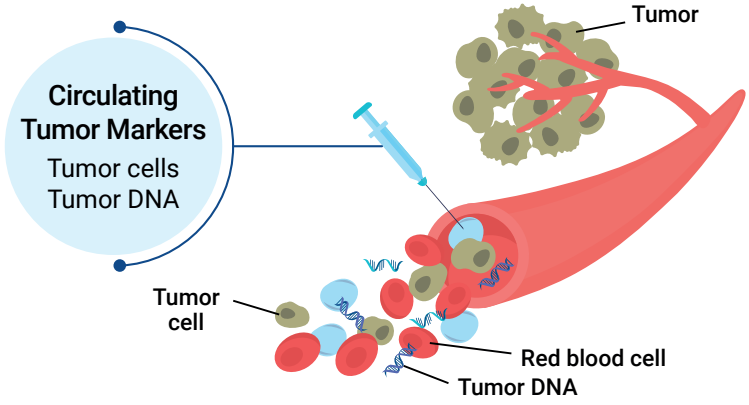



Image adapted with permission from Qi Z et al. *J Cancer*. 2018;9(18):3417-3426.[22]

- Your doctor may recommend a liquid biopsy if a tissue biopsy is not possible. They may also recommend a liquid biopsy to monitor for disease progression or recurrence later on[20,21]
- Importantly, liquid biopsies can have a high false negative rate, which means it may not identify biomarkers in your cancer. If you have a negative result with a liquid biopsy, ask your care team if tissue testing is right for you[20,21]

**To learn more about biopsies, please go to page 30**

**Any decision to undergo a biopsy and/or test for biomarkers should be made together by you and your care team.[8]**

## What if I Already Had a Biopsy? Do I Need to Have Another One?

- Even if you received biomarker testing at initial diagnosis, you may need a second biopsy (also called a **rebiopsy**) after your cancer has progressed for additional biomarker testing[6]
- In breast cancer, some biomarkers and even breast cancer subtype can change over time[22-27]
  - Cancers get new mutations, and some of these mutations may cause resistance to a particular therapy[22,26,27]

**To learn more about how cancer changes over time, please go to page 31**

**Rebiopsy and additional biomarker testing can help your care team know if your cancer has changed and may provide new information for treatment planning[6,28,29]**

## Questions for Your Care Team

Do I need another biopsy? Why or why not?

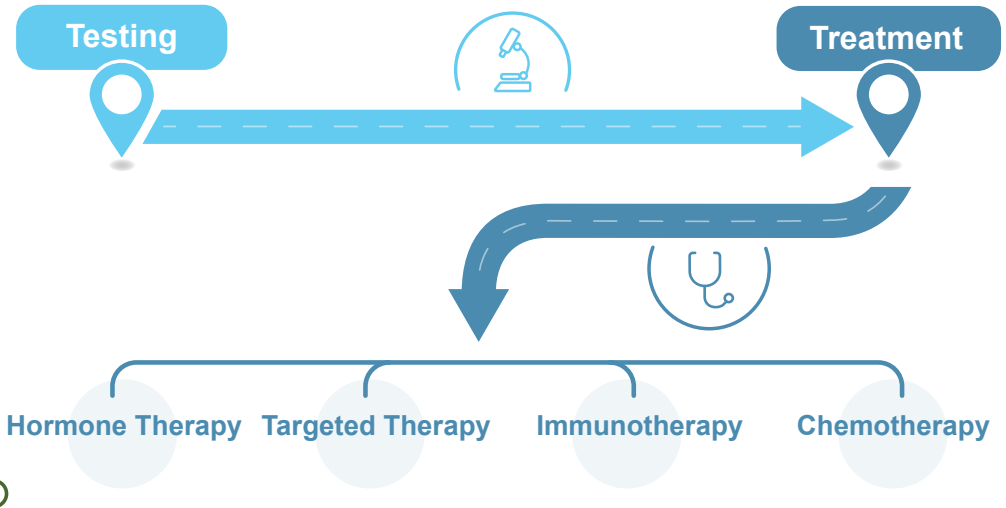
What type of biopsy should I get? Why?

How much will these procedures cost?

Will insurance pay for these procedures?

## How Will Biomarker Tests Be Used in My Care?

- Some biomarkers are called **predictive biomarkers**. These biomarkers help your doctor understand how likely you are to respond or not respond to a particular therapy[30]
  - If your test shows that your breast cancer has a predictive biomarker, your doctor may recommend you get a particular therapy, such as hormone therapy, targeted therapy, immunotherapy, or chemotherapy[2-4,10,13,14]




**Any decisions about biomarker testing and treatment options should be made together by you and your care team[8]**

**These decisions depend on several factors, including your type and stage of cancer, availability of tissue, your current treatment plan, and your overall health[8]**

## Which Biomarkers Should I Be Tested for?

- All patients with breast cancer should be tested for their **hormone receptor (HR)** status (determined by testing for ER and PR) and **HER2** to determine subtype[2,10,11,12]
- Because your breast cancer subtype can change if your cancer has progressed, it is important that you are tested for your subtype again: this information will determine if you are a candidate for some therapies[14,23-26,31]
- Your breast cancer subtype and stage will also determine if you should have additional biomarker testing[13,14]

**To learn more about how cancers can change, please go to page 30**

- To make a personalized, long-term treatment plan for your metastatic breast cancer, you may have additional biomarker testing for biomarkers common in breast cancer, rare biomarkers seen in all solid tumors, and biomarkers for immunotherapies.[14,32,33]
- Your doctors will make testing recommendations based on your breast cancer subtype and stage[14,32]

| | Biomarkers with an FDA-approved therapy for breast cancer or solid tumors | Breast cancer patients with this biomarker |
|---|---|---|
| **Common biomarkers in breast cancer** | *PIK3CA* | 36%[35] |
| | *ESR1* | 20-40%[36,b] |
| | *gBRCA1* or *gBRCA2* | 5%[37] |
| **Rare biomarkers in solid tumors**[34] | *NTRK* fusions[a] | 0.18%[38] |
| | *RET* fusions[a] | 0.15%[39] |
| | *BRAF* V600[a] | 0.17%[40] |
| **Immunotherapy biomarkers**[15,34,a] | PD-L1 | 20%[41] |
| | TMB[a] | 1.3%[42] |
| | MSI[a] | 1.5%[43] |

[a]Biomarker is actionable in all solid tumors.
[b]Prevalence specific to metastatic breast cancer following failure on aromatase inhibition.

**Depending on your breast cancer subtype, additional biomarker testing for biomarkers with an FDA-approved therapy may unlock more treatment options specifically for you**[32,33]

**To learn more about these biomarkers, please go to page 16**

## Questions for Your Care Team

What is my breast cancer subtype? What other biomarkers will you test for?

When will I learn my biomarker test results, and how will they be communicated to me?

Are there any limitations of the testing I'm receiving?

How much will these tests cost? Will insurance pay for these tests?

## What Happens After Biomarker Testing?

Your care team will be there to support you

Your **oncologist** will discuss test results with you and use biomarker test results to make treatment decisions[16]

A **radiation oncologist** will administer radiation therapy if part of your treatment plan[1,44]

Your **oncologist**, **nurse practitioner**, and **nurse** will oversee your overall treatment progress, help monitor symptoms and side effects, and adjust your treatment plan as needed[16]

A **pharmacist** will assist with providing prescription medications ordered by your oncologist[45]

## What Treatment Options Will Be Available to Me?

Your doctor will use your test results to determine if you are a good candidate for a particular therapy, such as hormone therapy, targeted therapy, immunotherapy, or conventional chemotherapy[13,14]

# How Do These Therapies Work?

## Hormone Therapy

- **Hormone therapy**, also known as endocrine therapy (ET), is used for the subtypes of breast cancers that are sensitive to hormones because they are found to have the following biomarkers[1,10]:

> **Estrogen receptor (ER)**

> **Progesterone receptor (PR)**

- There are several different types of hormone therapy. The most common types of hormone therapy work by blocking hormones from attaching to receptors on cancer cells or by decreasing your body's production of hormones[1,46]
- After treatment with a hormone therapy, some cancers develop resistance to this type of therapy. This means that the cancer may be less likely to respond to hormone therapy in the future. If your cancer has progressed after treatment with a hormone therapy, your doctor may recommend additional biomarker testing to help determine your next treatment[23,31]

**To learn more about how cancers can develop resistance to specific therapies, please go to page 30**

## Targeted Therapy

- **Targeted therapy** is a type of treatment that is designed to "target" and attack cancer cells only and have less impact on normal cells[1]
  - These drugs can either stop cancer cells from growing or carry chemicals to the cancer cells to kill them[1]
  - Some targeted therapies specifically target cancers that have developed resistance to other therapies[31]

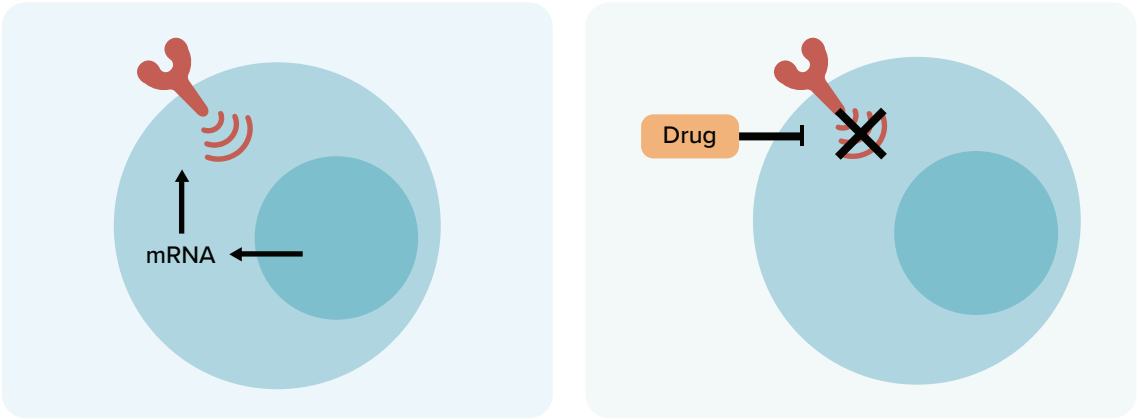



Image adapted with permission from Camidge DR et al. *Nat Rev Clin Oncol.* 2019;16(6):341-355.[47]

**Targeted therapies are designed with a better understanding of how cancer works and behaves[47]**

**To learn more about how targeted therapies are designed, please go to page 26**

- Biomarkers that show if you may be a good candidate for a targeted therapy include[2,14,31,32,34,46]:

**HER2 expression**

***BRCA1/2* mutation**

***PIK3CA* mutation**

***ESR1* mutation**

***RET* fusions**

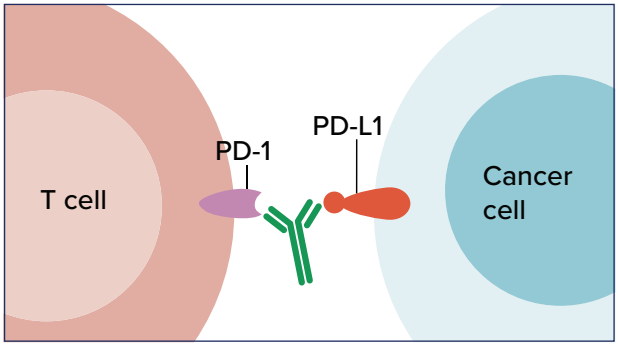
***BRAF* V600E mutations**

***NTRK 1/2/3* fusions**

- Other predictive biomarkers for targeted therapies, like Ki-67, show how quickly the cancer cells are dividing. This can help determine if you are eligible for a specific class of targeted therapy that stops cell division[13]
  - These biomarkers can be highly variable[13]

## Immunotherapy

- **Immunotherapy** is a treatment that uses your own immune system to recognize and destroy cancer cells[1,46]
  - Unlike chemotherapy which kills all dividing cells, immunotherapy can lead to hyperactivation of the immune system, which can result in autoimmune-like toxicities[1,46]




- Another group of predictive biomarkers is used to identify patients who may benefit from an immunotherapy. These biomarkers are more variable than driver alterations[14]
- Biomarkers for immunotherapy include[14]:

**PD-L1 expression**

**Tumor mutation burden (TMB)**

**Microsatellite instability (MSI)**

PD-L1, programmed death-ligand 1.

## Conventional Chemotherapy

- **Conventional chemotherapy** is a type of anticancer drug that kills all cells that divide quickly
  - This means that it kills cancer cells but can also kill normal cells, like hair cells or cells in your stomach[1]

- In the metastatic setting, chemotherapy may be used to slow down the cancer if it is growing quickly and impacting other organs, like the liver or lungs. It is also used to treat HR-positive metastatic breast cancer if the cancer stops responding to endocrine therapy[48]

**Based on your breast cancer subtype or other predictive biomarkers, you may be eligible for specific treatment options**[3,4,13,14]

**It is important that you are tested for all predictive biomarkers for your breast cancer stage. Knowing your biomarker status can help your care team choose the best treatment option for you**[3,4,13,14]

**Any decision to test for biomarkers, which tests to use, and treatment decisions should be made together by you and your care team**[8]

## Are There Any Additional Resources I Should Know About?

**There are multiple online resources full of information and support for patients like you. Some resources are listed below.**

If you need help navigating patient resources, information, and programs, Susan G. Komen offers a free helpline you can find at: **https://www.komen.org/support-resources/breast-cancer-helpline/**

If you'd like to connect to other cancer patients who may have the same biomarker status as you, join a biomarker group at: **https://biomarkercollaborative.org/**

To learn more about personalized medicine in cancer and other diseases, visit: **https://www.personalizedmedicinecoalition.org/personalized-medicine-101/**

This list of resources is not exhaustive. The above websites are independently operated and not managed by Novartis Pharmaceuticals Corporation. Novartis assumes no responsibility for the content on the sites.

## Questions for Your Care Team

What are my test results? What do these results mean?

| | Biomarkers with an FDA-approved therapy for breast cancer or solid tumors | My Result |
|---|---|---|
| Biomarkers that determine breast cancer subtype[11] | ER | |
| | PR | |
| | HER2 | |
| Current subtype | | |
| Common biomarkers in breast cancer[35-37] | *PIK3CA* | |
| | *ESR1* | |
| | *gBRCA1* or *gBRCA2* | |
| Rare biomarkers in solid tumors[34] | *NTRK* fusions[a] | |
| | *RET* fusions[a] | |
| | *BRAF* V600[a] | |
| Immunotherapy biomarkers[14,34,a] | PD-L1 | |
| | TMB[a] | |
| | MSI[a] | |

[a]Biomarker is actionable in all solid tumors.

How can I get a copy of my biomarker test results?

How will the biomarker test results affect my treatment plan? Are there any specific therapies that can be used to treat my breast cancer?

Will I need additional biomarker testing in the future? If so, when?

What next steps should I take?

## NOTES

# Introduction

Biomarkers and biomarker testing are complex. This section will help you understand some of the science behind biomarkers and how your care team might conduct biomarker testing.

## Biomarkers and Precision Medicine

- Major scientific breakthroughs over the last two decades led to the **explosion of new biomarkers and biomarker testing**. These new biomarkers are fundamental to precision, or personalized medicine[33,49]
  - Before precision medicine, cancer was treated with a "one-size-fits-all" approach. All breast cancer patients received similar treatment plans[49]
  - With precision medicine, treatment can be tailored for each individual patient with breast cancer[33]
- There are different types of biomarkers that doctors use to understand your cancer, including your **diagnosis** (type of cancer), **prognosis** (how your cancer may behave over time), **predicting** how you may respond to specific therapies, and monitoring your response[15]

**Precision medicine uses biomarkers to aid in the diagnosis, prognosis, or treatment of breast cancer[33]**

## Types of Biomarkers

| | | | |
|---|---|---|---|
| **Before diagnosis** | **Risk biomarkers** | → | Identify patients at greater risk for certain diseases[30] |
| | **Diagnostic biomarkers** | → | Help identify your disease and subtypes[30] |
| **Before treatment** | **Prognostic biomarkers** | → | Provide information on expected clinical outcomes[30] |
| | **Predictive biomarkers** | → | Provide information on expected treatment response[30] |
| | **Actionable predictive biomarkers** | → | Predictive biomarkers with an associated FDA-approved therapy[50] |
| **On therapy** | **Monitoring biomarkers** | → | Are used to monitor disease recurrence, progression, and whether the treatment is working[30] |

## Biomarkers Used in Breast Cancer

- The biomarkers most commonly used to help guide treatment decisions and optimize your care are **prognostic biomarkers**, **predictive biomarkers**, and **risk or susceptibility biomarkers**[30,50]

**Importantly, a biomarker can have multiple uses at once. A biomarker can be a risk, prognostic and predictive biomarker at the same time[33]**

## Key Scientific Discoveries that Led to the Development of New Biomarkers, New Therapies, and Precision Medicine

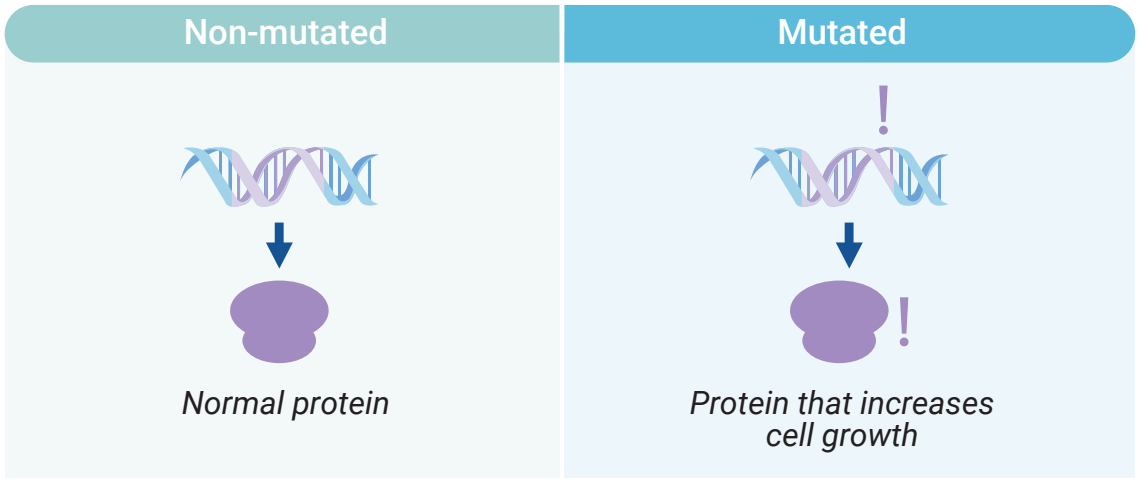
Scientists and doctors have spent decades trying to understand cancer. While there is still a lot to learn, our improved understanding of how cancers occur and how cancers change has impacted treatment for patients like you[49]

## How Cancer Occurs

Cancer is a genetic disease, which means it occurs because of a mutation, or change, in your DNA[51]

Mutations are normal and responsible for all of the diversity we see in the world. However, in cancer, some of these mutations cause the cell to grow and duplicate uncontrollably[51]

- Some mutations in cancer are called **driver alterations**[47]
  - Driver alterations are changes to your genes that may increase growth or survival of cancer cells in your body[47]




**Some targeted therapies are specifically designed to stop the growth of cancer cells with a specific driver alteration**[47]

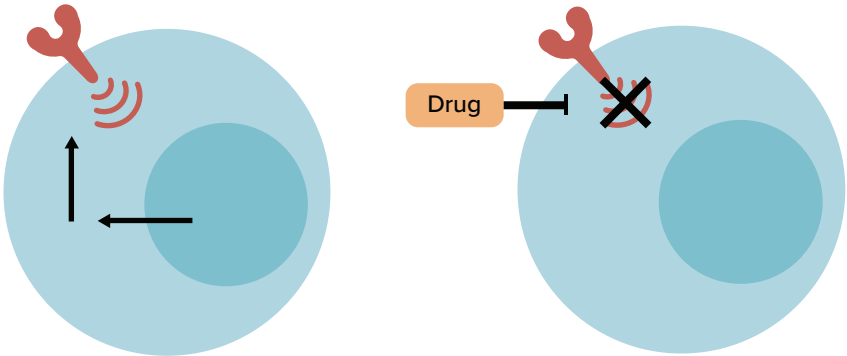



Image adapted with permission from Camidge DR et al. *Nat Rev Clin Oncol.* 2019;16(6):341-355.[47]

Some mutations that cause cancer are inherited while others are not[51,52]

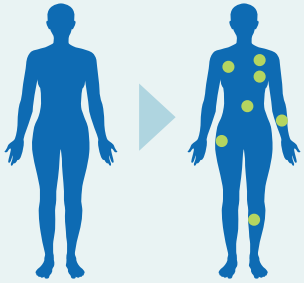
- Inherited mutations may also be called germline mutations

### Inherited Mutations

- Less common
- Exist in every cell in your body

### Noninherited Mutations

- More common
- Only in some cells in your body



In **breast cancer**, **1 in 10** women are positive for an inherited mutation[53]

**Most people with breast cancer do not have an inherited mutation.[52] If your doctor identifies a mutation in your cancer that can be treated with a targeted therapy, it does not necessarily mean that your family is at greater risk for developing cancer[14,34,53]**

You may be more likely to have an inherited mutation that causes cancer if[53]:

You are under 50 when you are first diagnosed with breast cancer

You have at least one close blood relative who:

- Was first diagnosed with breast cancer before they turned 50
- Had ovarian, pancreatic, or high-risk prostate cancer
- Had male breast cancer

You have at least 3 diagnoses of breast and/or prostate cancer on the same side of the family

You have Ashkenazi Jewish ancestry

If you are more likely to have an inherited mutation that causes cancer, your doctor may recommend genetic testing for an inherited mutation[53]

- A genetic counselor will help you understand the results from this test. The genetic counselor will also work with you and your family to determine if your family wants to be tested

**People with inherited mutations can take steps to reduce their personal risk of developing cancer[53]**

# How Cancer Changes

- Unlike other cells, cancer cells are genetically unstable. This means that they continue to get mutations over time[54]

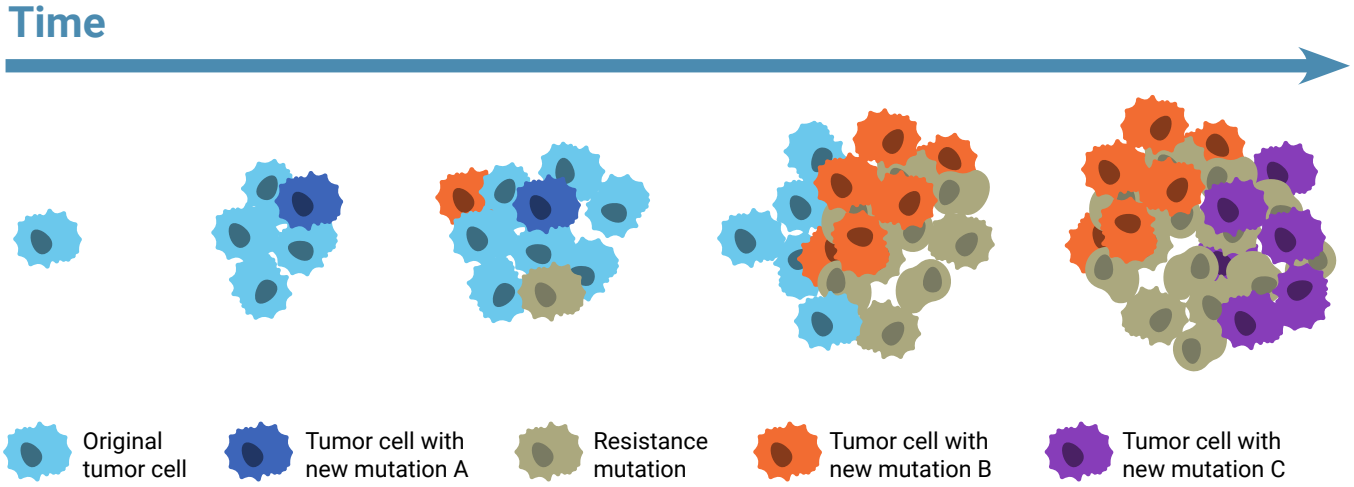



Image adapted with permission from Black JRM and McGranahan N. *Nat Rev Cancer.* 21(6):379-392. doi: 10.1038/s41568-021-00336-2[54]

- Some, but not all, of these mutations develop during your cancer treatment and cause your cancer to continue to grow and survive even though you are receiving treatment that kills cancer cells. These mutations are called resistance markers[27,28]

**Recently, some targeted therapies have been developed that specifically target resistance markers. Testing for biomarkers after progression is important to determine if you are eligible for one of these new therapies[23,31]**

- After your cancer **metastasizes**, or moves, to different parts of your body, it will continue to change and have more mutations. So, the mutations at one metastatic site may share some of the mutations at a different metastatic site. At the same time, it may have mutations that are unique to that tumor[27,55,56]

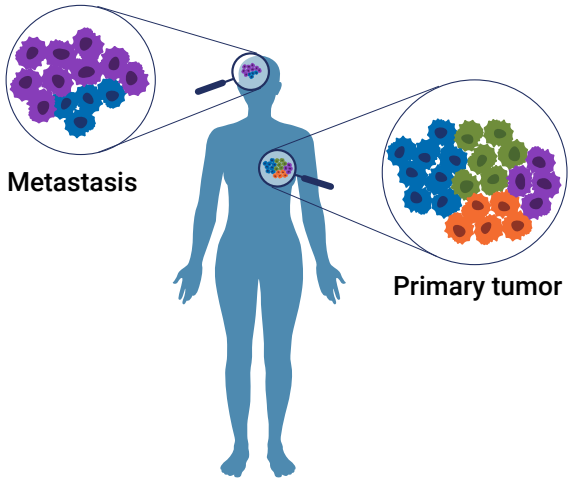



Image adapted with permission from Kashyap A et al. *Trends Biotechnol.* 2022;40(6):647-676. doi: 10.1016/j.tibtech.2021.11.006[56]

**Because tumor cells and tumor DNA from all metastatic sites appear in the blood, liquid biopsies can give your care team a better understanding of *all* mutations involved in your cancer[5,20,21]**

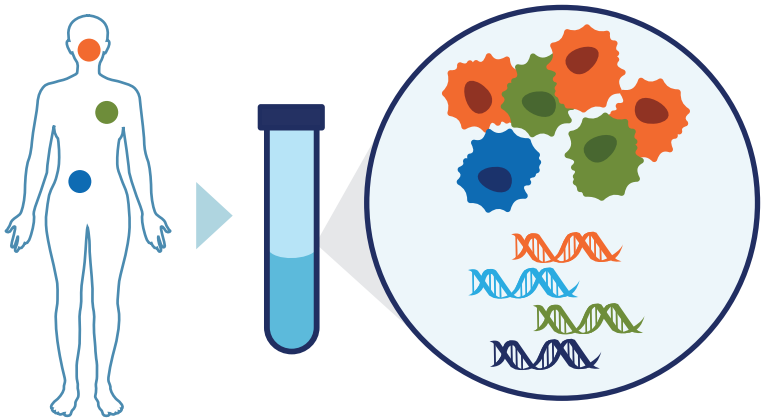


Image adapted with permission from Gilson P et al. *Cancers (Basel)*. 2022;14(6):1384. doi:10.3390.cancers14061384[57]

# Summary

Understanding how cancer works and how it changes has helped create new and better treatment options for patients like you. As scientists and doctors continue to learn more about cancer, the number of biomarkers and treatment options may continue to grow[10,13,14,49]

Ask your doctor about biomarker testing to see if you may be a good candidate for the newest therapies

## Glossary

**Biomarker:** A biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker can be a change in DNA (mutations), RNA, or protein. Biomarkers may be helpful for understanding the nature of disease, predicting health outcomes, and planning treatments[1]

**Biomarker testing:** One or more tests using various techniques to identify the presence or absence of biomarkers[1]

**Biopsy:** A procedure to remove a piece of tissue or a sample of cells from your body so that it can be tested in a laboratory[1]

**Breast cancer stage:** Refers to how advanced your breast cancer is based on the size of your tumor and whether it has spread to other locations (metastasized). Breast cancer staging will help your oncologist determine your chance of survival and the best course of treatment[1,13,14]

**Chemotherapy:** A type of treatment using drugs that kills cancer cells[1]

**Driver alterations:** Changes to your genes that may promote growth or survival of cancer cells in your body[58]

**Hormone therapy:** A treatment for breast cancer that is sensitive to hormones[1]

**Immunotherapy:** A type of cancer therapy that uses substances to stimulate or suppress the immune system to help the body fight cancer, infection, and other diseases[1]

**Interventional radiologist:** A medical doctor who is specially trained to use minimally invasive image-guided procedures to diagnose and treat diseases[59]

**Liquid biopsy:** Uses blood, saliva, or urine to investigate the presence of tumor cells or DNA shed from the primary tumor[1]

**Metastatic breast cancer:** Breast cancer that has spread from the original tumor location through the blood or lymph system to other locations in the body[1]

**Oncologist:** A medical practitioner qualified to diagnose and treat cancer[1]

**Pathologist:** A doctor who identifies diseases, and/or the presence of biomarkers, by studying cells and tissues under a microscope or with other equipment[1]

**Predictive biomarker:** A biomarker that may provide information on expected treatment response[30]

**Primary tumor:** The original, or first, group of cancer cells in the body[1]

**Prognosis:** The likely outcome or course of a disease; the chance of recovery or recurrence[1]

**Prognostic biomarker:** A biomarker that may provide information on expected health outcomes[30]

**Recurrence:** The return of cancer after a period of it not being detectable[1]

**Risk biomarker:** A biomarker used to identify patients at greater risk for developing cancer[30]

**Targeted therapy:** A type of treatment that uses drugs to attack specific types of cancer cells with less harm to normal cells. Some targeted therapies block the action of certain enzymes, proteins, or other molecules involved in the growth of cancer cells[1]

# References


**1.** NCI Dictionary of Cancer Terms. Accessed October 16, 2023. https://www.cancer.gov/publications/dictionaries/cancer-terms **2.** Wolff A et al. *J Clin Oncol*. 2013;31(31):3997-4013. doi: 10.1200/JCO.2013.50.9984 **3.** Van Poznak C et al. *J Clin Oncol*. 2015;33(24):2695-2704. doi: 10.1200/JCO.2015.61.1459 **4.** Harris L et al. *J Clin Oncol*. 2016;34(10):1134-1150. doi: 10.1200/JCO.2015.65.2289 **5.** Crimini E et al. *Cancer Treat Rev*. 2021;98:102223. doi: 10.1016/j.ctrv.2021.102223 **6.** Lungevity Foundation. Biomarker Testing. Accessed October 16, 2023. https://www.lungevity.org/sites/default/files/request-materials/biomarker-testing-booklet-081121.pdf **7.** Harbeck N et al. *Nat Rev Dis Primers*. 2019;5(1):66. doi: 10.1038/s41572-019-0111-2 **8.** Lungevity Foundation. Why Should I Talk to My Doctor About Comprehensive Biomarker Testing? Accessed October 16, 2023. https://lungevity.canto.com/direct/document/mh82qbv8fd7ileu3vjcc2pjc75/N2TClH1HMCd1h8WukUqWk2oiqY/original?content-type=application%2Fpdf&name=BiomarkerBrochure%28rev11-21%29.pdf **9.** What are biomarkers? Accessed October 16, 2023. https://www.mycancer.com/resource3,s/what-are-biomarkers/ **10.** Harris L et al. *J Clin Oncol*. 2007;25(33):5287-5312. doi: 10.1200/JCO.2007.14.2364 **11.** Howlader N et al. *Cancer Epidemiol Biomarkers Prev*. 2018;27(6):619-626. doi: 10.1158/1055-9965.EPI-17-0627 **12.** Kohler B et al. *J Natl Cancer Inst*. 2015;107(6):djv048. doi: 10.1093/jnci/djv048 **13.** Andre F et al. *J Clin Oncol*. 2022;40(16):1816-1837. doi: 10.1200/JCO.22.00069 **14.** Henry NL et al. *J Clin Oncol*. 2022;40(27):3205-3221. doi: 10.1200/JCO.22.01063 **15.** Cree IA et al. *J Clin Pathol*. 2014;67(11):923-931. doi: 10.1136/jclinpath-2014-202404 **16.** De Las Casas LE, Hicks DG. *Am J Clin Pathol*. 2021;155(6):781-792. doi: 10.1093/ajcp/aqaa212 **17.** Ciria-Suarez L et al. *PLoS ONE*. 2021;16(9):e0257680. doi: 10.1371/journal.pone.0257680 **18.** Riggio AI et al. *Br J Cancer*. 2021;124:13-26. doi: 10.1038/s41416-020-01161-4 **19.** Saini KS et al. *Ann Oncol*. 2012;23(4):853-859. doi: 10.1093/annonc/mdr352 **20.** Rolfo C et al. *J Thorac Oncol*. 2021;16(10):1647-1662. doi: 10.1016/j.jtho.2021.06.017 **21**. Merker JD et al. *J Clin Oncol*. 2018;36(16):1631-1641. doi: 10.1200/JCO.2017.76.8671 **22**. Qi Z et al. *J Cancer*. 2018;9(18):3417-3426 **23.** Zundelevich A et al. *Breast Cancer Res*. 2020;22(1):16. doi:10.1186/s13058-020-1246-5 **24.**Thompson AM et al. *Breast Cancer Res*. 2010;12(6):R92. doi: 10.1186/bcr2771 **25.** Schrijver WAME et al. *J Natl Cancer Inst*. 2018;110(6):568-580. doi: 10.1093/jnci/djx273 **26.** Arthur LM et al. *Breast Cancer Res Treat*. 2014;147(1):211-219. doi: 10.1007/s10549-014-3080-x **27.** Angus L et al. *Nat Genet*. 2019;51(10):1450-1458. doi: 10.1038/s41588-019-0507-7 **28.** Greaves M, Maley CC. *Nature*. 2012;481(7381):306-313. doi: 10.1038/nature10762 **29.** Tung N et al. *J Clin Oncol*. 2016;34(13):1460-1468. doi: 10.1200/JCO.2015.65.0747 **30.** Califf RM. *Exp Biol Med (Maywood)*. 2018;243:213-221. doi: 10.1177/1535370217750088 **31.** Burstein HR et al. *J Clin Oncol*. 2023;41(18):3423-3425. doi: 10.1200/JCO.23.00638 **32.** Clark AS et al. *JCO Oncol Pract.* 2022;18(12):830-832. doi: 10.1200/OP.22.00506 **33.** Chakravarty D et al. *J Clin Oncol*. 2022;40(11):1231-1258. doi: 10.1200/JCO.21.02767 **34.** Tateo V et al. *Pharmaceuticals (Basel)*. 2023;16(4):614. doi: 10.3390/ph16040614 **35.** Martínez-Sáez O et al. *Breast Cancer Res*. 2020;22(1):45. doi: 10.1186/s13058-020-01284-9 **36.** Brett JO et al. *Breast Cancer Res*. 2021;23(1):85. doi: 10.1186/s13058-021-04162-3 **37.** Kurian AW et al. *Cancer Epidemiol Biomarkers Prev*. 2009;18(4):1084-1091. doi: 10.1158/1055-9965.EPI-08-1090 **38.** Okamura R et al. *JCO Precis Oncol*. 2018;2018:PO.18.00183. doi: 10.1200/PO.18.00183 **39.** Paratala BS et al. *Nat Commun.* 2018;9(1)4821. doi: 10.1038/s41467-018-07341-4 **40.** Owsley J et al. *Exp Biol Med (Maywood).* 2021;246(1):31-39. doi: 10.1177/1535370220959657 **41.** Guo H et al. *Breast Cancer Res*. 2020;22(1):69. doi: 10.1186/s13058-020-01303-9 **42.** Kang Y-J et al. *Sci Rep*. 2022;12(1):20495. doi: 10.1038/s41598-022-23319-1 **43.** Bonneville R et al. *JCO Precis Oncol*. 2017;2017:PO.17.00073. doi: 10.1200/PO.17.00073 **44.** Valentini V et al. *Mol Oncol.* 2020;14(7):1431-1441. doi: 10.1002/1878-0261.12712 **45.** Mackler E et al. *J Oncol Pract*. 2019;15(4):e346-355. doi: 10.1200/JOP.18.00581 **46.** Schick J et al. *Breast Cancer (Auckl).* 2021;15:1-19. doi: 10.1177/1178223421995854 **47.** Camidge DR et al. *Nat Rev Clin Oncol*. 2019;16(6):341-355. doi: 10.1038/s41571-019-0173-9 **48.** Moy B et al. *J Clin Oncol*. 2021;39:3938-3958. doi: 10.1200/JCO.21.01374 **49.** Falzone L et al. *Front Pharmacol*. 2018;9:1300. doi: 10.3389/fphar.2018.01300 **50.** Vidwans SJ et al. *Oncoscience.* 2014;1(10):614-623. doi: 10.18632/oncoscience.90 **51.** Loewe L. *Nature Education*. 2008;1(1):113 **52.** Tomasetti C, Li L, Vogelstein B. *Science.* 2017;355(6331):1330-1334. doi: 10.1126/science.aaf9011 **53.** Tung et al. *J Clin Oncol.* 2021;39(31):3415-3418. doi: 10.1200/JCO.21.01761 **54.** Black JRM and McGranahan N. *Nat Rev Cancer*. 21(6):379-392. doi:10.1038/s41568-021-00336-2 **55.** Yates et al. *Cancer Cell*. 2017;32:169-184. doi: https://doi.org/10.1016/j.ccell.2017.07.005 **56.** Kashyap A et al. *Trends Biotechnol*. 2022;40(6):647-676. doi: 10.1016/j.tibtech.2021.11.006 **57.** Gilson P et al. *Cancers (Basel).* 2022;14(6):1384. doi:10.3390.cancers14061384 **58.** Sanchez-Vega F et al. *Cell.* 2018;173(2):321-337. doi: 10.1016/j.cell.2018.03.035 **59.** Johns Hopkins. What is Vascular and Interventional Radiology. Accessed October 16, 2023. https://www.hopkinsmedicine.org/interventional-radiology/what_is_IR.html

# Summary

Comprehensive biomarker testing should be an ongoing part of your breast cancer journey and the treatment discussions with your health care team[8]

Knowing your breast cancer subtype and other additional biomarkers can help determine your eligibility for certain treatment options[2-4,10,13,14]

Understanding the purpose of biomarker testing and knowing the right questions to ask may help you and your care team achieve the best possible health outcomes[2-4,8]

NOVARTIS

**Novartis Pharmaceuticals Corporation**
East Hanover, New Jersey 07936-1080



4/24

414044