Know Your Biomarker

RAF | CEA | ctDNA | DPYD | FAP | HER2 | KRAS | Lyn

HER2

MSI | MSS | NRAS | NTRK

K3CA | TMB | Tumor Location/Sidedness | UGT1A1 | P

Who should be tested for HER2?

If you have stage IV / metastatic colorectal cancer, you should be tested for HER2.

What is the HER2 biomarker?

HER2 (also known as ERBB2) is a gene that helps control cell growth and cell survival.

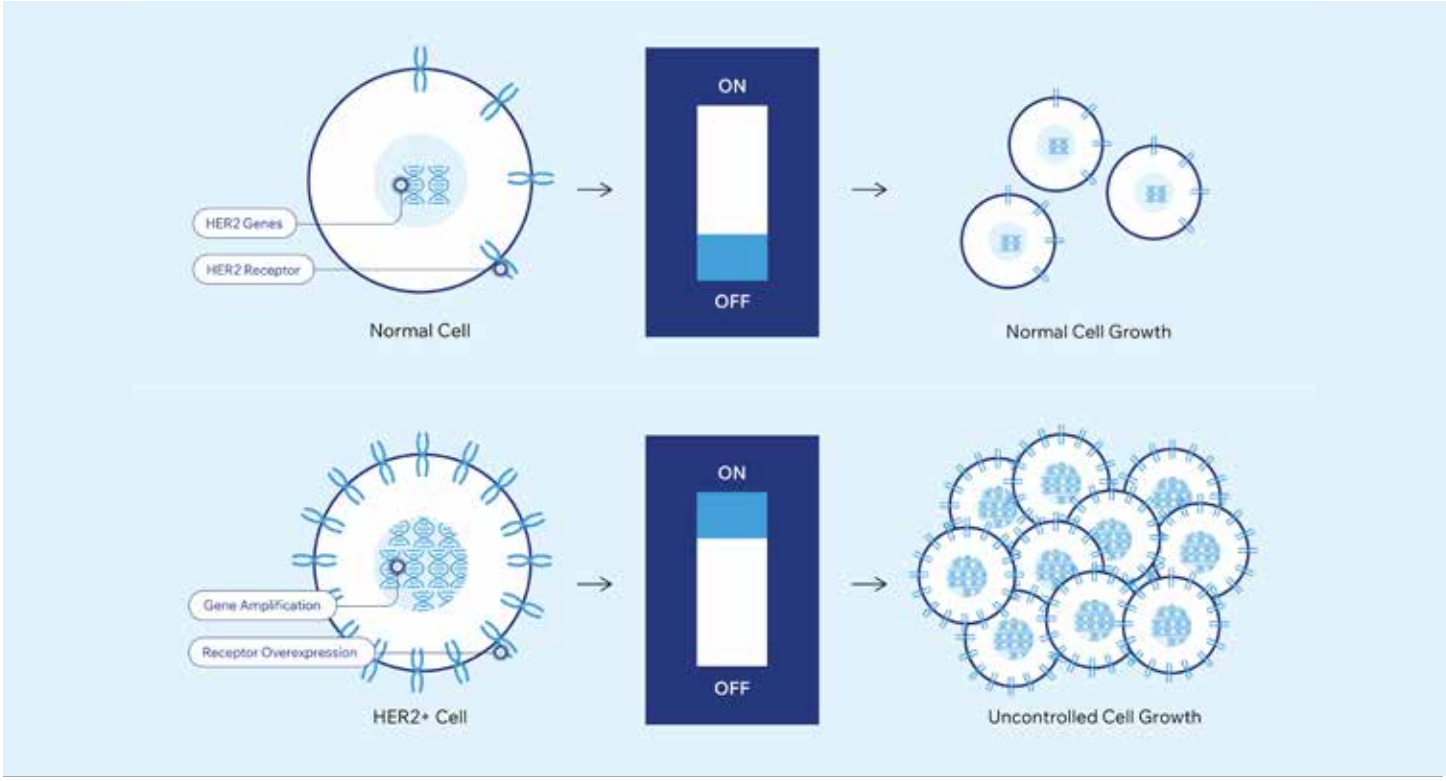
Genes, like HER2, that can cause normal cells to become cancer cells are called oncogenes. Oncogenes can act like an "on switch" for cancer. When the switch changes in the wrong way, it can make cells grow out of control.

In the case of HER2, the switch is turned "on" when there are either too many copies of the HER2 gene, called HER2 gene amplification, or too much HER2 protein being made, called HER2 protein or receptor overexpression.

The changes in HER2 that are related to colorectal cancer are not hereditary, meaning they are not passed from parents to children.

HER2 is important in several different types of cancer. You may have heard of it in connection to breast cancer, but that isn't the only HER- involved cancer. HER2 abnormalities are found in 20% of stomach cancers and 3-5% of all colorectal cancers (CRC). The percentage is higher in colorectal cancer without KRAS, NRAS, or BRAF mutations.

HER2 is a prognostic biomarker, meaning it gives information about the likely course of disease (prognosis). It is also a predictive biomarker that predicts whether a tumor will respond to specific targeted treatments like EGFR inhibitors or HER2 inhibitors.



How is the HER2 biomarker tested? How are results reported?

HER2 status is usually tested in a tumor sample, either from a biopsy or from tumor removed during surgery. HER2 status can be tested with several laboratory methods, including immunohistochemistry (IHC), fluorescence in situ hybridization (FISH), and next-generation sequencing (NGS). IHC is used to measure the amount of HER2 protein. FISH is used to find HER2 DNA that is abnormal in a specific way. And NGS is used to determine the pattern of HER2 DNA, looking for any kind of abnormality.

HER2 status may also be tested in a blood sample by looking at circulating tumor DNA (ctDNA) for HER2 gene abnormalities. This is also called a liquid biopsy.

HER2 results are reported as “negative” or “positive”. Negative means there is a normal amount of HER2, that is, no HER2 abnormality. Positive means there is a HER2 abnormality, either too many copies of the HER2 gene, or too much HER2 protein.

If testing is done by IHC, results may be given as a number, such as 0, 1+, 2+, or 3+, based on how much HER2 protein appears in the tumor sample. A report of 0 is HER2 negative. Reports of 1+ or 2+ are sometimes considered uncertain and may need another type of testing to confirm the cancer is HER2 positive. A report of 3+ is a certain HER2 positive result.

When tested by FISH or NGS, the report will just say either HER2 negative or HER2 positive.

How does my HER2 status impact my treatment?

If your colorectal cancer is HER2 negative

This means your cancer has a normal amount of HER2 gene copies or HER2 protein

→ Your treatment options will be determined by other aspects of your health and colorectal cancer, like other biomarker testing results, tumor location, and cancer stage.

→ These options may include traditional chemotherapy, targeted therapy (such as EGFR inhibitors), and immunotherapy based on the results of your other biomarker testing.

If your colorectal cancer is HER2 positive

This means your cancer has HER2 gene amplification or HER2 overexpression

→ Your treatment options include therapies that directly target HER2.

→ Combinations of HER2 inhibitors are often used.

→ The HER2 inhibitors used in colorectal cancer include trastuzumab (Herceptin), pertuzumab (Perteja), and tucatinib (Tukysa). They are also known as anti-HER2 drugs. Lapatinib (Tykerb) is a dual-targeted therapy. It is both a HER2 inhibitor and an EGFR inhibitor.

→ Fam-trastuzumab deruxtecan-nxki (Enhertu) is a combined HER2 inhibitor and conventional chemotherapy drug that is used in HER2 positive metastatic colorectal cancer (mCRC).

→ EGFR inhibitors (for example cetuximab or panitumumab) are less effective in colorectal cancer with HER2 amplification.

There are ongoing clinical trials for treatments that are more effective against colorectal cancers with HER2 abnormalities. Talk to your oncology team about whether you could benefit from a clinical trial.

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Biomarker testing can give you and your medical team valuable knowledge about your cancer and help guide your treatment choices. For more information about colorectal cancer biomarkers, please visit knowyourbiomarker.org and talk to your medical team.