



RAF	CEA	ctDNA	DPYD	FAP	HER2	KRAS	Lyr
c-MET				MSI	MSS	NRAS	NTR
3CA	TMB	Tumor Location/Sidedness				UGT1A1	R

## Who should have MET / c-MET biomarker testing?

All patients with stage IV / metastatic colorectal cancer (mCRC) should be tested for the c-MET (MET) biomarker.

## What is MET or c-MET?

MET is a gene that encodes a protein called c-MET. MET is the mesenchymal-epithelial transition factor gene, and the gene and the protein play a role in cell growth, cell survival, and cell migration.

Where there are abnormalities in the MET gene or in c-MET protein expression, it is called MET dysregulation. MET dysregulation includes:

- MET gene amplification – too many copies of the MET gene
- MET gene mutation – a change in the DNA sequence of the MET gene
- c-MET protein overexpression – too much of the c-MET protein is made

When MET dysregulation occurs, it can cause cancer by making cells grow and survive when they shouldn't. Genes, like MET, that can cause normal cells to become tumor cells are called oncogenes. MET dysregulation can also help cancer cells spread to other parts of the body, because of MET's role in cell migration. This is called tumor invasion (spread to nearby sites) and tumor metastasis (spread to distant sites in the body).

MET or c-MET dysregulation is important in colorectal cancer, occurring in 15-81% of these cancers across different studies. The changes in MET that are related to colorectal cancer are not hereditary, meaning they are not passed from parents to children.

## How is MET / c-MET tested? How are the results reported?

c-MET status is usually tested in a tumor cell biopsy sample. c-MET testing is usually performed on a sample of the primary tumor. c-MET status may also be tested in a blood sample by examining circulating tumor DNA (ctDNA) for MET gene changes. This is called a liquid biopsy. The MET gene can also be analyzed for mutations in tumor tissue.

c-MET status can be tested with several laboratory methods, including

- IHC (Immunohistochemistry): Uses special antibodies to detect the c-MET protein in the tumor tissue. A chemical makes the protein visible under a microscope.
- FISH (Fluorescence In Situ Hybridization): Uses fluorescent DNA pieces to see if there are changes in the MET gene in the tumor.
- NGS (Next-Generation Sequencing): A method to read many DNA sequences at once to find gene changes.

Your test report will differ based on the type of testing you had.

- If you had c-MET protein testing, such as IHC, your results may be reported as “normal” or “high”. Normal c-MET expression is sometimes reported as “c-MET negative”. High c-MET expression is sometimes reported as “c-MET positive”.
- If you had MET gene testing via FISH, your results may be reported as “negative” or “positive”. Negative means that there is no detected MET gene abnormality. Positive means that a MET gene change is present.
- If you had MET gene testing via next-generation sequencing (NGS), your result will be reported as “MET wild-type” or “MET mutant”. MET wild-type, sometimes abbreviated MET-WT, means there is no mutation in the MET gene. MET mutant means there is a mutation (abnormality) in the MET gene sequence.

### **What do my results mean for me? How do they impact my treatment?**

If your colorectal cancer has normal c-MET expression (c-MET negative), no MET gene amplification, or no MET gene mutation (wild-type)

- Targeted therapy will be guided by other biomarker testing results.
- Immunotherapy will be guided by other biomarker testing results.
- Treatment options also include traditional chemotherapy combinations.

If your colorectal cancer has high c-MET expression, MET gene amplification, or a MET gene mutation causing high c-MET expression (mutant)

- There are ongoing clinical trials for MET inhibitor treatments targeted to colorectal cancers with high c-MET expression or MET mutations. Talk to your healthcare team about whether you could benefit from a clinical trial.
- Immunotherapy will be guided by other biomarker testing results.
- Further targeted therapy options will be determined by other biomarkers.
- Treatment options also include traditional chemotherapy combinations.



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](https://knowyourbiomarker.org) and talk to your medical team.