

RAF	CEA	ctDNA	DPYD	FAP	HER2	KRAS	Lyr
ctDNA: Circulating Tumor DNA						NRAS	NTRI
K3CA	TMB	Tumor Location/Sidedness				UGT1A1	F

Who should be tested for ctDNA?

There are no standardized recommendations for ctDNA testing in colorectal cancer (bowel cancer). Talk to your medical team about whether ctDNA testing could be useful for you. ctDNA analysis may be used in testing for other biomarkers when tumor (tumour) tissue is unavailable.

What is ctDNA?

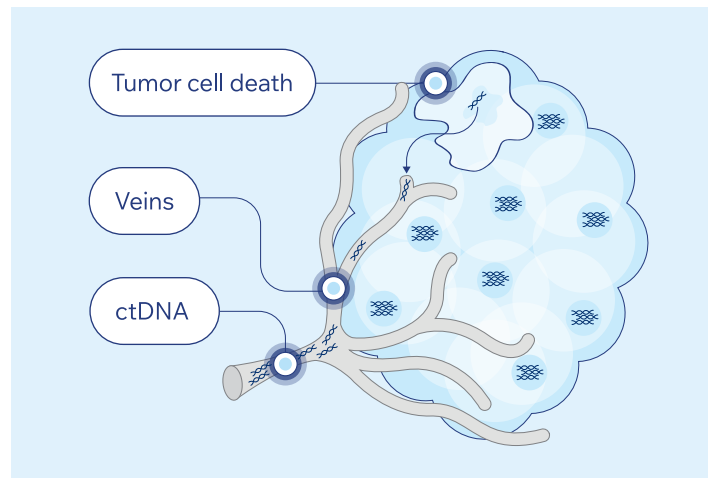
Circulating tumor DNA (ctDNA) is fragmented DNA from your tumor cells found in the blood. When tumor cells die, they release ctDNA into the bloodstream. Blood can be tested for the presence of ctDNA, and the ctDNA in blood can be isolated and tested for mutations.

Testing of ctDNA can be used to

- Identify residual colorectal cancer cells after surgery
- Determine recurrence risk after surgery
- Monitor for recurrence (the return of cancer after successful treatment)
- Predict treatment response in metastatic CRC
- Determine biomarker status (also called molecular profiling)
- Identify a change in biomarker status
- Find tumor mutations that cause a treatment to stop working (also called acquired resistance)

Testing for the presence of ctDNA in your blood can provide information about whether you have any remaining cancer cells (minimal residual disease, MRD) after surgery for Stage II or Stage III CRC, or a recurrence after treatment. In the setting of Stage IV / metastatic CRC (mCRC), measurement of the amount of ctDNA in blood before and during treatment can predict response to chemotherapy and immunotherapy. A decreasing ctDNA level during treatment predicts a good response to therapy, while an increasing level of ctDNA during treatment predicts treatment failure and disease progression.

ctDNA mutation testing, also known as ctDNA molecular profiling, can be used to get information about biomarker status. It is used when there is not enough tumor tissue available for tissue-based testing, when fast results are needed, or when it is suspected that there has been a change in biomarker status in the time since a tissue sample was analyzed (temporal heterogeneity). Microsatellite stability and instability (MSS / MSI), tumor mutational burden (TMB), as well as KRAS mutations, NRAS mutations, BRAF mutations, NTRK fusion, and HER2 amplification can all be examined in ctDNA.



How is ctDNA tested? How are the results reported?

ctDNA is tested in a blood sample. This is called a liquid biopsy. Some tests also use a tissue biopsy sample to create a personalized ctDNA blood test or to compare ctDNA to DNA taken directly from your tumor tissue. The result reported will depend on the goal and type of ctDNA testing.

If ctDNA is being used to look for minimal residual disease (MRD) after surgery, or to monitor for cancer recurrence, the result may be reported as “positive, ctDNA detected” or as “negative, ctDNA not detected”.

If ctDNA amount is measured to check treatment response in metastatic CRC, the numerical amount will be reported. Often, a percent decrease or increase since the pre-treatment measurement will be included.

If ctDNA testing is being used for biomarker testing (molecular profiling), either as the main biomarker profiling method or as a study of changes in biomarker status, your results will be reported like they would be for those tests if they were performed on tissue. For example, ctDNA testing of KRAS would be reported “KRAS wild-type” or “KRAS mutant”. And ctDNA testing of tumor mutational burden (TMB) would be reported as “TMB-Low” or “TMB-High”.

For more information about how ctDNA molecular profiling results are reported, please refer to the fact sheet of the specific biomarker tested (for example, KRAS, TMB, or HER2).

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

When ctDNA testing is used after surgery to determine recurrence risk and look for minimal residual disease (MRD)

- If your ctDNA test result is positive after surgery for Stage II or Stage III colorectal cancer, your risk of recurrence is high. Your medical team may start or increase adjuvant therapy (treatment intensification).
- If your ctDNA test result is negative after surgery for Stage II or Stage III colorectal cancer, your medical team may reduce your adjuvant treatment (treatment de-escalation).

Adjuvant therapy is treatment (for example, chemotherapy or targeted therapy) given after the main treatment (surgery) to treat any remaining cancer cells and prevent recurrence.



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.

When ctDNA testing is used to monitor for recurrence after completing CRC treatment

- If your ctDNA test result is positive after completing treatment, your medical team will order imaging (for example PET/CT scan or MRI scan) to look for recurrent cancer. If imaging does not find a recurrence, another type of imaging may be used.
- If your ctDNA test result is negative after completing treatment, you do not have a detectable recurrence. Your medical team will continue to monitor you.

When ctDNA testing is used for biomarker testing (molecular profiling)

- The impact of your results will depend on the biomarkers tested.

For information about the meaning and impact of your ctDNA biomarker testing results, please refer to the fact sheets of the specific biomarkers tested (for example, KRAS, TMB, or HER2).

When ctDNA is used to find mutations causing your tumor to develop resistance to targeted therapy

- Tumor DNA can change over time, and mutations may occur in genes, like KRAS and NRAS, that lead to resistance to targeted treatment with EGFR inhibitors.
- A tumor that was once resistant to EGFR inhibitors may lose that resistance after stopping the drug.
- A change in the biomarker status of your tumor may lead to a change in treatment.