Know Your Biomarker

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

RET

MSI | MSS | NRAS | NTRK

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

Who should have RET biomarker testing?

While there are no current guidelines for RET testing in colorectal cancer, it should be considered in all patients with advanced or stage IV / metastatic colorectal cancer.

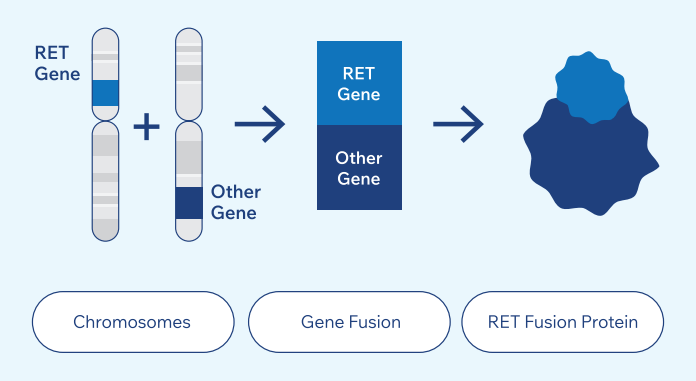
What is RET?

RET is a gene and protein involved in controlling cell growth and cell development.

Changes in the RET gene and protein can lead to several cancers, including about 3% of colorectal cancer, as well as non-small cell lung cancer, and several endocrine cancers. Genes, like RET, 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.

RET abnormality is also associated with Hirschsprung's disease, a non-cancer condition affecting the nerves of the intestine. Hirschsprung's disease is usually found in babies or young children.

RET fusion is a particular type of abnormality in which part of the RET gene breaks off and attaches to another gene.



Genes give the instructions for your cells to make proteins, and when RET gene fusion occurs, cells will make abnormal proteins called RET fusion proteins. Fusion proteins can cause cells to grow and survive when they shouldn't, leading to cancer.

Colorectal cancers with RET fusion are rare, making up about 1% of CRC, and they tend to have other common biomarker findings.

CRC with RET fusion

→ is more often located on the right side of the colon

→ more often has microsatellite instability (MSI-High, also known as dMMR)

→ more often has normal (wild-type, non-mutant) KRAS, NRAS, and BRAF genes.

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

How is RET tested? How are the results reported?

RET status is usually tested in a tumor cell biopsy sample. RET abnormalities can be detected with several laboratory methods, including

→ FISH (Fluorescence In Situ Hybridization): Uses fluorescent DNA pieces to see if there are changes in the RET gene in the tumor. This is especially useful for finding RET gene fusions.

→ NGS (Next-Generation Sequencing): A method used to read many DNA sequences at once to find gene changes. This can be used to find RET fusions or RET mutations.

If your RET gene has no changes, it may be reported as “RET negative”, “normal”, “wild-type”, “non-mutant”, or “no fusion detected”.

If your RET gene has a mutation, it will be reported as “mutant” or “RET positive”.

If your RET gene has a fusion, it will be reported as “RET fusion detected” or “RET positive”.

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

If your colorectal cancer does not have a RET abnormality (RET negative, RET wild-type, RET non-mutant, or no RET gene fusion detected)

→ Targeted therapy will be guided by other biomarkers.

→ Immunotherapy will be guided by other biomarker testing.

→ Treatment options also include traditional chemotherapy combinations.

If your colorectal cancer has a RET abnormality (RET positive, RET mutant, or RET gene fusion detected)

→ You may benefit from RET targeted therapy with a RET inhibitor drug. The RET inhibitor used in colorectal cancer patients is selpercatinib (Retevmo).

→ Immunotherapy will be guided by other biomarker testing.

→ Further targeted therapy options will be determined by other biomarker testing.

→ Treatment options also include traditional chemotherapy combinations.

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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.