March 2017 | Members

Spotlight on Health

Colorectal Cancer

Tumor Mutation Testing

Cancer of the colon or rectum (colorectal cancer) is one of the most common types of cancer. If it is found very early, it can often be cured by surgery alone. If the cancer has already grown through the colon wall, treatment with drugs (chemotherapy) or radiation may be needed.

Unfortunately, colorectal cancer is often not found until it spreads to other parts of the body. When the cancer has spread far away, it is called advanced (or metastatic) cancer. This type of cancer is much more difficult to treat.

Newer treatments called "targeted" therapy drugs can help fight advanced colorectal cancer, but they don't work for everyone. This newsletter talks about how laboratory testing can help doctors choose targeted drugs that have the best chance of working.

Targeted Therapies for Advanced Colorectal Cancer

Standard chemotherapy is not very specific for cancer. It acts on all cells that divide rapidly. In contrast, targeted therapies act on specific "target proteins" in cells that cause cancer to grow and spread. For some patients with advanced colorectal cancer, targeted therapies can help even when standard chemotherapy does not. They can also be combined with standard chemotherapy.

What Are Mutations?

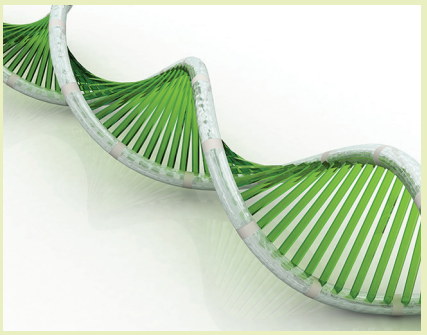
Mutations are changes in your genes. No one knows exactly what causes mutations, but your environment, diet, and age probably all play a role. Some mutations make cells grow faster than they should, live longer, or spread to other places in the body. These kinds of mutations are what cause most kinds of cancer.

Some mutations are important for another reason as well: they can cause targeted therapies to not work well. Others may make a drug work better. So, mutation testing is becoming an important part of choosing treatments for advanced disease.

How Testing for Mutations Can Help Choose Treatments

Some mutations are very common in colorectal cancer. For example, almost half of colorectal cancers have a mutation in the *KRAS* gene.[1,2] Many of these mutations cause some targeted therapies to not work.[1,3] Mutations in other genes, such as *NRAS*, *BRAF*, and *PIK3CA*, can also cause a targeted therapy not to work.

Testing cancers for these mutations can help the doctor choose the best treatment and know which drugs will probably not work. In fact, it's now recommended that all patients with advanced colorectal cancer be tested for mutations in certain genes.[3,4,5]



Additional Information

You can find more information about tumor mutation testing and targeted therapies at these Web sites:

- American Society of Clinical Oncology. cancer.net/navigating-cancer-care/cancer-basics/genetics/genetics-cancer
- Fight Colorectal Cancer. fightcolorectalcancer.org/fightcrc-fightit/biomarker-testing-for-colorectal-cancer/
- National Cancer Institute. cancer.gov/about-cancer/treatment/types/targeted-therapies/targeted-therapies-fact-sheet
- American Society of Clinical Oncology. cancer.net/navigating-cancer-care/how-cancer-treated/personalized-and-targeted-therapies/understanding-targeted-therapy

How the Laboratory Can Help

Quest Diagnostics offers tests for mutations in colorectal cancer. One test looks for mutations in just *KRAS*, *PIK3CA*, *BRAF*, and *NRAS*. However, new drugs are being developed all the time, and we are learning more about the effects mutations can have on treatment response. So, some physicians prefer to test cancers for mutations in more genes.

This is where a new tool, called IBM Watson® Genomics from Quest Diagnostics®, may help. It can look for mutations in many different genes.

For the test, the physician takes a small sample of a tumor after it has been removed during surgery. The laboratory tests the sample for mutations in 50 different genes. IBM Watson® then compares mutations in the tumor to known mutations and available treatments. (IBM Watson® is a high-tech supercomputer.) Quest medical experts review the results. The test report tells your doctor about:

- Any mutations found
- The roles those mutations play in cancer
- How those mutations might affect the choice of treatment
- Research studies (clinical trials) you and your doctor may want to consider taking part in

The doctor can then use the results to help you decide on the best treatment.

References

1. Semrad TJ, Kim EJ. Molecular testing to optimize therapeutic decision making in advanced colorectal cancer. *J Gastrointest Oncol*. 2016;7(Suppl 1): S11-20.
2. De Roock W, De Vriendt V, Normanno N, et al. *KRAS, BRAF, PIK3CA*, and *PTEN* mutations: implications for targeted therapies in metastatic colorectal cancer. *Lancet Oncol*. 2011;12:594-603.
3. Allegra CJ, Rumble RB, Hamilton SR, et al. Extended *RAS* Gene Mutation testing in metastatic colorectal carcinoma to predict response to anti-epidermal growth factor receptor monoclonal antibody therapy: American Society of Clinical Oncology Provisional Clinical Opinion Update 2015. *J Clin Oncol*. 2016;34:179-185.
4. National comprehensive cancer network clinical practice guidelines in oncology (NCCN Guidelines®). Colon cancer version 1.2017. nccn.org/. Updated November 23, 2016. Accessed December 20, 2016.
5. National comprehensive cancer network clinical practice guidelines in oncology (NCCN Guidelines®). Rectal cancer version 1.2017. nccn.org/. Updated November 23, 2016. Accessed December 20, 2016.