

Mutational Testing: The Breakdown

What is mutational testing?

The function of a cell is determined by that cell's DNA. DNA can be thought of as a blueprint for a cell. It controls all function of a cell including growth and cell reproduction.

DNA is grouped into sections called codons. Groups of codons form exons, which in turn are grouped as genes. There are two primary genes that are important to GIST, KIT and PDGFRA.

GIST cells may have an error, or mutation, in their DNA that causes them to become GIST. Mutational testing (also called genotyping) looks at the DNA of a sample of a GIST tumor to determine exactly where this error occurred. This is reported as a mutation.

KIT mutations are found on exons 8, 9, 11, 13, and 17. PDGFRA mutations can be found on exons 12, 14, and 18. Some GISTs do not show any known mutation; these are called wild-type. The most common mutations are KIT exon 9 and KIT exon 11. Wild-type GIST is more common in people diagnosed as children.

What does this mean for a GIST patient?

There are two basic reasons that genotyping is important to GIST patients. From a clinical perspective, a patient's mutation influences how they respond to different medications and treatments.

The exact mutation of a GIST cell determines the pattern of the disease. For instance, the primary tumors of people with KIT exon 9 mutations are generally found in the small bowel or colon. However, the primary tumors of people with KIT exon 11 mutations can be found anywhere in the gastrointestinal tract.

People with KIT exon 11 mutations respond better to treatment with Gleevec. They have a longer period of time before progression occurs after the start of treatment with Gleevec. There is clear evidence that people with exon 9 muta-

How to Arrange for Mutational Testing:


A growing number of institutions are developing the capacity to perform mutational testing for GIST patients. Ask your physician if his/her affiliated institution is amongst these. If not, ask if he/she will send the specimen to:

Dr. Christopher Corless
OHSU Dept. of Pathology (mailcode L471)
3181 SW Sam Jackson Park Rd
Portland, OR 97239
Tel. 503-494-6776
Email: corlessc@ohsu.edu
Website: www.heinrich-corless.net/kit.html

Requests for *KIT* and *PDGFRA* mutation screening must originate from a pathologist or treating physician. One paraffin block of the tumor (either biopsy or surgical specimen) or 15 unstained sections of the tumor should be sent to the address listed above. A copy of the original pathology report as well as the patient's insurance information must be included.

Please note that the testing may not be covered by your insurance policy. Check with your provider for details.

Fill out and carry this quick reference card in order to easily share your mutation information.



The Life Raft Group
Ensuring that no one has to face GIST alone.

GIST GENOTYPE CARD

Name: _____

Primary Tumor Location: _____

Mutation: _____

Details: _____

Blood Type: _____

tions respond better to higher doses of Gleevec. More studies are in progress on mutation and response to treatment. GIST patients should talk to their doctors about this.

The second reason that genotyping is important to GIST patients is "portability". Currently, this data is collected by a handful of doctors and studies. Due to privacy laws and other regulations, the different doctors and researchers cannot communicate this information to each other. Having this information on an easy to carry card means that the patient can overcome this barrier.

It is possible that someone who is showing resistance to treatment has developed a secondary mutation. This is a topic of significant scientific research. However, a single resistant GIST tumor can have multiple secondary mutations in different GIST cells. Due to this, testing for secondary mutations may not be useful in determining treatment approaches at this point.

How is mutational testing done?

A sample of a GIST tumor is sent to a lab. These samples are usually embedded in paraffin. Using organic solvents, the DNA is extracted from the paraffin. This DNA is then cop-

Definitions:

Exon: An exon is a sequence of DNA that contains the information required for a body to produce a specific protein.

KIT: The protein produced from the "c-kit" gene. This is one of the genes that potentially carries the mutation that causes GIST.

Mutation: A change in the genotype of a cell, often resulting in a change in function of the cell.

Mutational Testing: Also known as genotyping, examines a cell sample to determine its genetic make up.

PDGFRA: This is a protein that is closely related to GIST. The gene producing this protein is another potential location for a mutation that causes GIST to occur.

Proteins: Proteins are the fundamental components of all living cells. Each protein has a specific function in the body. A mutation may cause a change in a protein, leading to a change in behavior of a cell.

ied using a technology called polymerase chain reaction or PCR.

The copied DNA is then "sequenced" or read, piece by piece. Although this process is very time-consuming, new technologies are speeding up the process. Currently it can take up to four days to read a single exon. The entire process may take more than a month to complete.

Additional Resources:

View the following LRG webcasts at http://www.liferaftgroup.org/library_videos.html

Mutational Testing: Broken Down by Drs. Christopher Coreless and Michael Heinrich
"GIST" the Basics by Jerry Call, LRG Science Coordinator and Dr. David Josephy

Read more about GIST mutations at: http://www.liferaftgroup.org/mut_testing.html

In case of emergency, contact:

Name: _____

Cell: _____

Home: _____

Physician:

Name: _____

Number: _____

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