GENETIC TESTING: WHAT DOES IT REALLY TELL YOU?

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What is genetic counseling?

• **communication process**
  • address individual concerns relating to development / transmission of a hereditary condition
  • strong communicative and supportive element so that those who seek information are able to reach their own fully informed decisions without undue pressure or stress
Definitions:

- A cell
- Chromosomes: 23 pairs
- The chromosome is made up of genes
- The genes consist of DNA which is made up of four chemical letters
Children get half of their genes from each parent
Cancer Arises From DNA Mutations in Cells

- First mutation
- Second mutation
- Third mutation
- Further mutations
- Uncontrolled cell growth
So, not all DNA mutations come from my parents?
Somatic mutations
- Occur in *nongermline* tissues
- Cannot be inherited

Germline mutations
- Present in egg or sperm
- Can be inherited
- Cause cancer family syndrome

Mutation in tumor only
(for example, breast)

Mutation in egg or sperm

All cells affected in offspring

Nonheritable

Heritable
Benign versus deleterious

The more you like yourself, the less you are like anyone else, which makes you unique.

Walt Disney
DNA ANALYSIS
HEREDITARY CANCER RISK ASSESSMENT
Who Needs Genetic Assessment?

• Individuals with cancer diagnosed at a younger than average age
• Individuals with more than one kind of cancer
• Individuals with cancer who have a family history of related cancers
• Individuals with a known mutation in a family member
How can genetic testing be helpful?

• Most syndromes have risks for more than one type of cancer
• Knowing you have a mutation may impact your treatment decisions
• If you have a mutation, you may need screening that is different than other people
Questions to ask *before* testing?

- Will this affect my treatment?
- What is the chance that I have a mutation?

![Family tree diagrams](image)
Questions to ask *before* testing?

- What are the possible test results?
- What do the different test results mean for me and my family?
  - Positive, negative, variant of uncertain significance
You have a mutation, now what?

- Impact on treatment?
- Does my family need the information?
- Support groups available?
- Any other screenings that I need?
What if I *don’t* have a mutation?

- Impact on treatment?
- Could it still be inherited?
  - What does it mean for my family?
- Additional genetic testing?
- Is there research I can participate in?
53 year old
Breast cancer diagnosed at 45 years
Second breast cancer diagnosed at 52 years
BRCA1 and BRCA2 testing normal
Thyroid cancer: 33 yrs
Two paternal aunts with breast cancer in their 50’s.
Could it still be hereditary?
Maybe it’s something else? Can we figure it out?
Testing options

- Single gene testing
- Testing of genes with guidelines
- Multigene panel testing
Multigene panel testing

- Technology has progressed to the point that some of the ways we can test genes have changed.
- Cost of testing multiple genes is roughly equivalent to previous methods of testing one gene.
Advantages of multigene tests

- We now know that the “familiar” genes (e.g. BRCA) do not account for all genetic cancers
- Some rare syndromes have multiple genes associated with them
  - Easier and faster to test a panel of associated genes than to test genes sequentially
MORE IS BETTER. PANEL TESTING FOR EVERYONE!!

LET'S DO THIS!
Informed Decision Making Is Key
Disadvantages of multigene tests

- Some of the genes being tested are not well described in terms of their risks of cancers
- Many of the genes have no recommendations for follow up or surveillance
- The chance of finding a variant of unknown significance (VUS) is high
Variants of Unknown Significance

• A VUS is a change in the common sequence of DNA.
• A variant is NOT an indication of harmful mutation—brown eyes and blue eyes are different genetic sequences.
• Genetic variation is common.
• Most VUS do not have clinical implications.
  • Need to interpret in the context of personal and family history.
Genetic Testing Options

High risk
- Medical management guidelines
- Risk of other cancers

Moderate risk
- Medical management guidelines
- Risk of other cancers

Preliminary evidence

Uncertainty
Overview of multi-gene testing

- The recent introduction of multi-gene testing for hereditary forms of cancer has rapidly altered the clinical approach to testing at-risk patients and their families. Based on next-generation sequencing technology, these tests simultaneously analyze a set of genes that are associated with a specific family cancer phenotype or multiple phenotypes.
- Patients who have a personal or family history suggestive of a single inherited cancer syndrome are most appropriately managed by genetic testing for that specific syndrome. When more than one gene can explain an inherited cancer syndrome, than multi-gene testing, may be more efficient and/or cost-effective.
- There is also a role for multi-gene testing in individuals who have tested negative (indeterminate) for a single syndrome, but whose personal or family history remains strongly suggestive of an inherited susceptibility.

As commercially available tests differ in the specific genes analyzed (as well as classification of variants and many other factors), choosing the specific laboratory and test panel is important.

- Multi-gene testing can include “intermediate” penetrant (moderate-risk) genes. For many of these genes, there are limited data on the degree of cancer risk and there are no clear guidelines on risk management for carriers of mutations. **Not all genes included on available multi-gene tests are necessarily clinically actionable.** As is the case with high-risk genes, it is possible that the risks associated with moderate-risk genes may not be entirely due to that gene alone, but may be influenced by gene/gene or gene/environment interactions. Therefore, it may be difficult to use a known mutation alone to assign risk for relatives. In many cases the information from testing for moderate penetrance genes does not change risk management compared to that based on family history alone.
- There is an increased likelihood of finding variants of unknown significance when testing for mutations in multiple genes.
- It is for these and other reasons that multigene testing is ideally offered in the context of professional genetic expertise for pre- and post-test counseling.
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The patient had a different hereditary cancer syndrome that accounted for her breast and thyroid cancers. Testing was then an option for her family members.
COMMON QUESTIONS ABOUT GENETIC TESTING
Can genetic testing impact my health insurance?

- Genetic information can’t be used as a pre-existing condition for people who do not have cancer for health insurance or employment.
- Current laws do not apply to long-term care or life insurance
Why did my doctor do a genetic test on my tumor?

Tumors are tested for genetic changes because this information can help us treat your cancer.

The genetic changes in your tumor don’t usually mean anything about the genes in your other organs, but as we begin to test tumors for multiple genes, some of these may have implications for hereditary syndromes.
If I didn’t inherit the mutation in my family, can I still get cancer?

Yes.

*General population risks (usually) apply
*Follow screening recommendations
*Live a healthy lifestyle
If there is no family history of cancer does it mean mine is not inherited?

Not necessarily.

* Small families or not enough members of the “correct” gender.
* New mutation
Issues to consider

• Understand the reason for testing, and the associated risks, benefits, and limitations of the test

• Understand what test results mean before testing positive, negative or uncertain variant

• Obtain a copy of your test results
KEEP CALM
AND
CALL A
GENETIC COUNSELOR
THANK YOU!

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