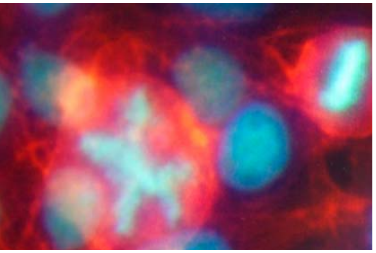
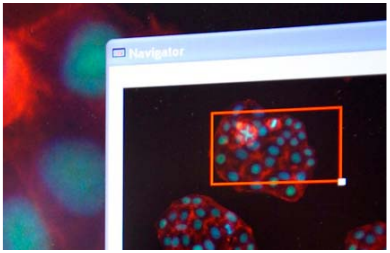
We Innovate Healthcare

Roche

Genetic Testing in **Research & Healthcare**

Genetic Testing in Research and Healthcare

Human genetic testing is a growing science. It is used to study genes in humans and signal early onset of disease.

Genetic testing is sometimes misunderstood. You may even hear things written or said about genetic testing that are not true.

Roche has created this brochure to clear up the facts about this important topic. We hope to help more people understand genetic testing.

There are three sections in this booklet:

"Some Facts about Genetics and Genetic Testing" answers a few basic questions and describes Roche's role in this important field.

"Issues to Think About" covers what genetic testing can mean to patients. It presents what researchers have learned about how some patients and patient groups view genetic testing.

"How Genetic Information Is Used" describes some of the uses of genetic information.

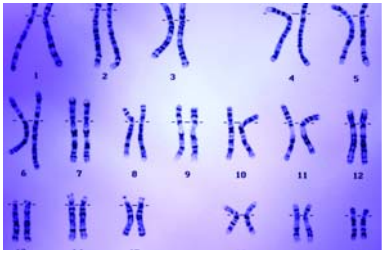
Some Facts about Genetics and Genetic Testing

What is a gene?

A gene is the basic unit of heredity. Genes play a role in the color of your eyes, the shape of your hands, and many other traits.

Genes are made up of a chemical called DNA (deoxyribonucleic acid). Strands of DNA are found in the nucleus of every cell of your body. Several genes can be found on a single strand of DNA.

DNA stands for deoxyribonucleic acid. DNA stores the information to make proteins, and it is what genes are made of.



DNA stores the information needed to make proteins, which are the basic building blocks of life. Proteins perform almost all the functions the body needs. These include forming hair, muscles, and skin; making energy; breaking down medicines; and fighting infections.

So, genes are made of DNA, which tells the body what proteins to make and when. The proteins, in turn, make the body grow, work, and react to change.

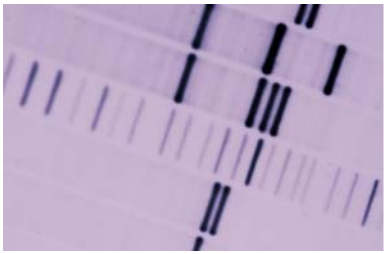
What is genetics?

Genetics is the study of the way certain traits, such as blue or brown eyes, are passed from parents to their children. This passing on of traits is called inheritance.

What is the human genome?

The human genome is the set of all biological information that you inherited from your parents. It is found in the nucleus of every cell of your body.

The complete human genome is contained in 23 pairs of chromosomes. Chromosomes are long strands of DNA, each containing many genes.



What is genetic testing?

Genetic testing can refer to several different things. In general, genetic testing is used to analyze human genes. We can analyze the parts of a person's genome that relate to their health or the health of their children.

Genetic testing can also refer to tests on the DNA of infectious agents. These agents may be found in humans or in the environment. The hepatitis B virus is an example of an infectious agent.

Finally, genetic testing also refers to using DNA to identify someone. Examples are tests for paternity (fatherhood) and for matching blood and hair found at a crime scene.

What are the medical uses of genetic tests?

Medical uses of genetic tests include finding inherited diseases, such as Huntington's disease and sickle cell anemia. People who have the genes for these disorders have a high risk of getting the disease. Therefore, tests may also be used as possible preventative measures for persons at risk.

Tests for some disorders are done when the mother is pregnant or soon after the baby is born. These include Fragile X Syndrome and Down syndrome. (Both these genetic disorders can cause mental retardation.)

Genetic testing is also used to advise prospective parents of the risk of having a baby with an inherited disease, such as cystic fibrosis. This type of testing is called carrier testing.

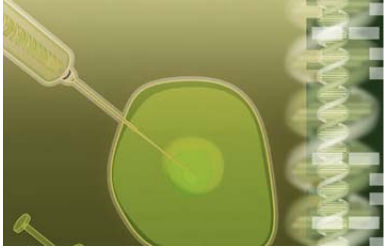
Newborns are also routinely screened for some inherited disorders that may keep them from using certain nutrients. These disorders can lead to severe disabilities if they aren't treated soon after birth. Examples of these disorders include phenylketonuria (PKU), hyperthyroidism and biotinidase deficiency.

Another example is a disorder that causes iron to build up in the body. It is called familial hemochromatosis. Iron build-up can be fatal. Members of families with a history of this disorder can now be tested for the genetic defect. If it is present, they can be followed closely to see if they develop the disease (not all do). If they do get symptoms, they can be treated.

In the future, genetic testing may be used even more to guide doctors and patients in designing the best treatments for each person enabling early treatment and prevention. For example, research is already underway to better understand how genes affect the way a person responds to medications.

What are the non-medical uses of genetic tests?

Genetic tests are commonly used to determine the identity of a person. They are used to identify accident victims. Police use them to test whether tissue (such as blood or hair) left at a crime scene matches up with the suspect's DNA. Genetic tests can also be used to determine paternity and other family relationships. These tests don't tell any other medical information about the person, though.



What is the impact of genetic testing within Roche?

Genetic testing is done in a laboratory, using cells gathered from inside the cheek or a blood sample. This is called diagnostic or molecular testing.

Roche is one of the world's leading providers of diagnostic tests. Roche is also a major global pharmaceutical company. These two strengths put Roche in an excellent position to improve healthcare by combining innovative testing, health information and treatments. Genetic tests are expected to help a great deal in Roche's efforts to deliver more personalized healthcare.

Roche pioneered a testing technique called the polymerase chain reaction (PCR). The PCR technique is used to copy very small amounts of genetic material in order to get amounts large enough to measure.

Roche has used PCR to develop many tools and products for genetic testing. Some of these products are used in clinical laboratories to find mutations linked to cystic fibrosis and other inherited disorders. Others are used to diagnose infectious diseases, such as hepatitis, HIV, (human immunodeficiency virus) and SARS (Severe Acute Respiratory Syndrome).

Roche's strategy also includes pharmacogenetic testing as part of our clinical trials. This enables us to combine testing with treatment. A good example of this approach is a new drug for breast cancer. This new medicine treats a very aggressive form of breast cancer found in 25-30% of all patients. In this form of cancer, there are many copies of a gene that cause high levels of a tumor growth factor protein, Her2. The drug disarms (neutralizes) the protein and kills cancer cells that carry it. The drug is very effective. But it will only work if the patient has this form of cancer. So doctors always run the Her2 test before prescribing the drug.

Issues to Think About

Are genetic tests only used when specific treatments are available?

Genetic tests can still be useful, even if there is no treatment or prevention strategy now. In fact, new diagnostic tools often come before new or improved treatments. For example, the development of the new cancer drug discussed above would not have been possible without the Her2 test.

Patient advocacy groups also support having the option of genetic testing. These groups feel that testing can be useful regardless of whether treatments or prevention are available. Genetic tests can help with family planning decisions. They may also help to improve a person's overall quality of life. For example, the European Genetics Alliances Network (EGAN) of patient and parent organizations for Genetic Services has this story: "A family had bought an apartment on the fourth floor of a building without an elevator. A short time later, their child developed a progressive paralyzing muscular distrophy. If the disease had been detected sooner, the family would have been able to find more suitable housing arrangements."

Some people and families want to know about their risk of getting a certain disease, while others may not. Researchers have measured how people handle this choice with respect to breast cancer. Over 80% of the women who were asked, said yes to taking part in the study. These women were given a genetic test for breast cancer. They also got genetic counseling. After counseling, they filled out a questionnaire. This study found no evidence that genetic counseling raises worry. In fact, levels of worry about developing breast cancer went down following genetic counseling. This was true regardless of what risk the women were told they had as a result of the test.

When might someone want to seek genetic counseling, and why?

For some rare diseases, if you have the genes for the disease, you are very likely to develop symptoms of the disease (Huntington's disease, cystic fibrosis, and hemophilia are examples of such diseases). Therefore, genetic testing can have a big impact on both the patient and their family. Patients and their families may feel stigmatized, or marked, by the test results. They may even find the information too hard to bear. In such cases, people may want to seek advice and to talk about the problem with a counselor or advocates at patient organizations who can provide advice and/or support. This doesn't just happen with genetic tests, but with all medical tests that may have a major impact on patients' lives (HIV testing and a biopsy for cancer are two good examples).

Genes also play a part in developing many so-called common complex diseases, but they are not the deciding factor. These diseases include heart (cardiovascular) disease, diabetes, and arthritis, among others. As science develops genetic tests for complex diseases, these tests may help to detect only one of many risk factors. Other possible risk factors, arising out of the environment and lifestyle, also play a role in the course of such diseases. In this way, genetic tests are much like other medical tests, such as those for blood pressure or cholesterol levels.

As with all medical tests, patients should ask their doctor as many questions as needed to understand their test results. In some cases, patients may want to speak with a genetic counselor.

Genetic counselors are involved in reviewing family histories, providing risk assessments, explaining inheritance patterns, discussing genetic testing options, and describing management and treatment alternatives. Those who see a genetic counselor may include pregnant women over the age of 35, those who are suspected of having a pregnancy affected with a genetic condition, individuals who are carriers of an inherited disorder, are themselves affected with a birth defect or inherited disorder, or have a family history of a birth defect or inherited disorder. Patients also may want to contact patient organizations that represent people with their disease or condition to ask for advice and support.

How Genetic Information Is Used

What if I don't want to be tested or know my test results?

Everyone has a basic right to make their own decisions about their healthcare. This includes deciding:

- whether they will have certain tests done, and
- whether they should be told the test results (This is often referred to as “the right to know” and “the right not to know”).

The best approach is to talk about these questions with a doctor. Decide what should happen with the test results before you take a genetic test.

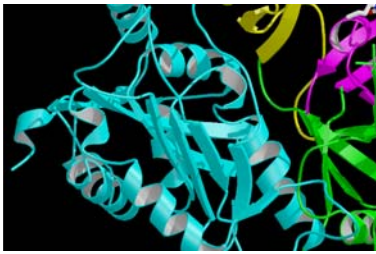
How are genetic test results protected?

Genetic information is protected the same way as any other personal medical information. That is, there are strict rules that control who may see the information and when. There are also national and even international laws to protect your privacy.

Why does Roche take blood samples for genetic testing in clinical trials? What happens to those blood samples?

As part of many of its clinical trials, Roche asks patients if they would like to give an extra blood sample for a genetic study. It’s up to the patient to decide if they want to give the extra blood sample or not. It’s important for patients to know that they can still take part in the clinical trial, whether or not they choose to be part of the genetic study.

The sample may be used to test whether certain gene variations can predict how a patient will respond to the medicine tested. The sample is only used for questions related to what is being studied in the clinical trial.



To protect privacy, information about the patient's identity is separated from blood samples at Roche. This process is called "anonymization." Anonymization assures that any information obtained from the blood sample cannot be tracked back to the patient. This also means that patients cannot receive any results from these genetic tests. Most of these tests are in the early stages of research, and scientists are not always sure how effective they are. So it makes sense not to keep patients' identities. Not even the researchers themselves know whose sample they are testing. And patients understand when they sign up for the extra study that they will not get any results back.

Has this type of research already led to practical uses?

Yes. For example, a drug commonly given to children with a certain type of leukemia is usually very successful. But about 1 in 300 children cannot break down this drug in their bodies because of a gene variation. As a result, these children can suffer serious, sometimes fatal, reactions to regular doses of the treatment. Now, a simple genetic test is routinely used to identify such children so that they can get a different dose.

Examples like this are the reason Roche is working to move genetic testing forward in research and development and in patient care.

Pharmaceuticals

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