The Advantages of Using Genetic Tests to Detect Genetic Diseases Early in an Effort to Improve Prognoses

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ABSTRACT: Although genetic testing is surrounded by controversy, various genetic tests can be used to detect the gene mutations which result in genetic diseases such as breast cancer, cystic fibrosis and sickle cell anemia. The structure and function of DNA is essential for heredity. Transcription and translation are the processes of making proteins from the DNA sequence. Some mutations develop during the transcription and translation process. Mutations can form in the DNA, causing genetic diseases. Common genetic diseases include breast cancer, cystic fibrosis, and sickle cell anemia. Genetic testing can be performed to detect genetic diseases early. There are several different types of genetic tests depending on the age of the patient. Tests include pre-natal diagnosis, carrier identification, late-onset testing, and identification testing. The uses of genetic testing differ for each different test. Even though genetic testing has many positives, there are limitations. There are many legal controversies that center around genetic testing. Genetic testing is also a new source of discrimination in the workplace. Laws have been established in an effort to end discrimination because of genetic tests.

KEY WORDS: Genetic Testing – Genetic Diseases – Gene Function – DNA

INTRODUCTION

One single glitch in a sequence of thousands can cause life threatening diseases. DNA controls every aspect of the body. If there is a mutation in the DNA a genetic disorder is likely to occur. A genetic disorder is a disease that is caused by a mutation in DNA. Common genetic diseases include cancer, cystic fibrosis, and sickle cell anemia. Genetic diseases can be tested for using genetic testing. Genetic testing is a test completed to find mutations in genes that are known to cause certain diseases. Testing can be done on fetuses, to test for physical and mental deformities, couples, to test for carrier genes, and adults, to test for mutations leading to disease. Genetic testing can lead to early detection and better prognoses. Like any test, genetic testing has its limitations. False negatives and false positives are rare, but there is a potential for error. There are also legal issues that accompany genetic testing. Genetic testing can be done to lead to early detection and a better prognosis. Although genetic testing is surrounded by controversy, various genetic tests can be used to detect the gene mutations which result in genetic diseases such as breast cancer, cystic fibrosis and sickle cell anemia.

GENE FUNCTION

Structure of DNA

The structure of DNA, seen here, is essential to its role in heredity. Through DNA, traits and sometimes diseases are passed from parent to child. The structure of DNA accounts for this. DNA has a backbone that consists of alternating sugar, deoxyribose, and a phosphate group. From the sugar stems a nitrogenous base which can either be thymine, adenine, cytosine, and guanine. The nitrogenous bases are bonded through...
hydrogen bonds to a matching nitrogenous base. For example, the thymine bases attach to the adenine bases and the cytosine bases to the guanine bases. Those nitrogenous bases are then attached to another sugar-phosphate backbone. The connection of the backbones form a double helix, which then spirals to form DNA. (Campbell, 2005).

**Function of DNA**

The function of DNA is gene expression. The first part of gene expression is transcription. Transcription is the process of making RNA from a DNA template. RNA is a copy of the DNA that is also made of sugar, specifically ribose, and nitrogenous bases. RNA is used to protect DNA. If the DNA were to go into the cytoplasm to make a protein, there is a chance of it getting mutated or damaged. If this happened to the DNA it would not reversible. However, if the RNA was to get damaged or mutated, another strand could be made using the DNA template. The second part of gene expression is translation. Translation is "the synthesis of a polypeptide [a protein] using the genetic information encoded in RNA." During this process a protein, made of a sequence of amino acids, is produced. (Campbell, 2005).

Transcription occurs in the nucleus of the cell. This process occurs when more of a protein is needed. A signal is sent to start transcription for a certain gene that corresponds with the needed protein. The section of DNA that is transcribed is called the transcription unit. Transcriptions begins with an enzyme, called RNA polymerase, separates the two strands of DNA. The sequence of DNA where the RNA polymerase attaches is called the promoter. The RNA polymerase moves along the DNA attaching together RNA nucleotides. The RNA nucleotides are attached in a specific order as it corresponds with the DNA template. This process continues and the strand of RNA, called mRNA, becomes longer until the RNA polymerase reaches the terminator. The terminator is a sequence in the DNA that signals to end transcription. The mRNA is then sent into the cytoplasm of the cell so translation can occur. The entire process can be seen in the image to the left. Transcription is done because the DNA cannot leave the nucleus to make proteins, but mRNA can. (Campbell, 2005).

Once in the cytoplasm, the process of translation begins. The strand of mRNA is then taken out of the nucleus to a ribosome. Once the mRNA enters the ribosome translation, seen above, begins. The mRNA enters the ribosome and the ribosome starts to read it. On the front end of the mRNA is a sequence of nucleotides that tells the ribosome when to start, called the start codon. The start codon is usually the sequence AUG. There is also a set

("Translation," 2007)
on the back end telling the ribosome when to stop. The nucleotides of mRNA are read by the tRNA in sets of three, called codons. On one side of the tRNA is an anticodon, which is a sequence of nucleotides that correspond with the codons. On the other side of the tRNA is an amino acid that goes with the anticodon/codon sequence. When the tRNA links with a codon the amino acid attaches to other amino acids from previous codons, making a protein. (Campbell, 2005).

**MUTATIONS IN DNA**

Mutations in DNA can lead to serious diseases. There are many different types of mutations in DNA. The effects of each mutation is different for each mutation.

**Types of Mutations**

The code in DNA can sometimes be altered. These alterations are called mutations. Two main types of DNA mutations are frame-shift and point mutations. Frame-shift mutation results from an insertion or deletion of one nucleotide (Toland, 2001). This causes the rest of the nucleotides to shift, causing the DNA to become meaningless (Toland, 2001). The DNA is now meaningless because the sets of three are now shifted, and therefore the codons are changed (Toland, 2001). When the codons are changed, a different amino acid made producing a different protein (Toland, 2001). An addition, or insertion, of one or more nitrogenous base is when extra nucleotides are added to the DNA (Toland, 2001). This mutation is an example of a frame-shift mutation. The mutation of DNA can be caused by the addition or deletion of one of the base chemicals in the DNA sequence (Mayo Clinic Staff, 2006). When DNA is deleted it can be a small section, maybe just one nucleotide, or an entire part of a chromosome (Toland, 2001). An example of this can be seen below. When a single base is changed the codon is also changed. When this happens the incorrect amino acid is added and therefore the incorrect protein is produced. There are various causes and effects of these mutations. The effects of the mutations can be something as minute as a change in eye color or as severe as a fatal (Toland, 2001).

![Deletion and Insertion](image)

(“Mutate a DNA sequence,” 2007).

**Effects of Mutations in DNA**

Genetic diseases can be caused by a variety of different factors. The main cause of genetic diseases is a mutation in DNA (Mayo Clinic Staff, 2006). When there is a mutation in the DNA, protein production is effected. When there is a mutation in the DNA, there is also a mutation in the copied RNA. Because of this the amino acid sequence is also mutated causing a mutated protein to be formed. When the protein is deformed or mutated it cannot perform the basic function needed for cell survival. When the cell cannot perform the basic function diseases occur. The mutated proteins are the reason most genetic diseases occur. (Campbell, 2005)

**Causes of Mutations**

Mutations can be acquired or inherited. Mutations in DNA can be caused by exposure to chemicals or radiation (Mayo Clinic Staff, 2006). Certain types of diseases are caused by over exposure to certain chemicals. For example lung cancer can be caused by overexposure to such chemicals as asbestos and tobacco. The exposure to chemicals can change genes inside of cells. Because the genes are changed, the copied RNA is also going to be changed. The changed RNA will then produce the wrong protein or a mutated protein because the sequence of nitrogenous bases was altered. These incorrect proteins cannot perform the basic functions needed for survival. Because the protein cannot perform its specific task, diseases occur. Acquired mutations can also
lead to inherited mutations in future generations. (“Understanding cancer,” 2007).

Inherited mutations are passed on from parents to children. An example of this is a daughter developing breast cancer, the same cancer that her mother had. This means that the daughter inherited the mutation for breast cancer from her mother. Some diseases become genetic because the parent will pass their acquired mutated DNA on to their child. (“Understanding cancer,” 2007).

**COMMON GENETIC DISEASES**

These causes of genetic diseases lead to many different genetic diseases. Some of the most common genetic diseases include breast cancer, cystic fibrosis, and sickle cell anemia.

**Breast Cancer**

Although cancer is viewed as a spontaneous or environmental disease, almost 10% of all cancers are genetic (“Human genetic,” 2007). Breast cancer is a common form of cancer found mostly in women. Symptoms of breast cancer are unique from any other type of cancer. When breast cancer starts to develop there are little to no symptoms. As the cancer starts to grow, the symptoms become more prominent. Symptoms include a lump or thickening in the breast or underarm, a change in the shape or size of the breast, discharge from the nipple, tenderness at the nipple, ridges in the skin of the breast, and a change in the way the skin of the breast feels. Other symptoms may arise in rare cases. These symptoms are caused by a mutation in just one gene. (“Human genetic,” 2007).

The genes that cause breast cancer are not entirely known. There are two genes that have been found to carry the mutation for breast cancer. The two genes that have been identified to carry mutations causing breast cancer are the BRCA1 gene and BRCA2 gene. BRCA1 and BRCA2 are "tumor suppressor genes." Tumor suppressor genes are genes that lower the chance of a cell turning into a tumor in a multicellular organism. When there is a mutation inside these genes cancer is likely to develop because the tumor cannot be suppressed. Ten percent of breast cancer cases are caused by inherited mutations in DNA. The other ninety percent of cases are the result of a mutation while the cell divides, which can be seen below. This is called a somatic mutation. BRCA1 and BRCA2 do not just hold the mutations for breast cancer. Mutations in BRCA1 and BRCA2 can also cause prostate and colon cancer. (Stewart, 2007).

Case studies have been completed using a new test called the MammaPrint test. The case studies were performed in an effort to find the genes that are more deadly than other genes that cause breast cancer. The MammaPrint test “uses microarray technology to measure the level of RNA expression of the 70 genes in a surgically removed breast tumor sample” (Stewart, 2007). Microarray technology allows for the study of many genes, or even the entire genome, at once. In the first section the 70-gene profile was found for 117 young breast cancer patients. This information was then used to identify a gene expression that coincided with lymph node negative patients, meaning the cancer has not spread in a short interval of time. This was called the 70-gene prognosis profile. The 70-gene prognosis profile was then used to evaluate the prognosis of 295 women with stage I or II breast cancer. This test resulted in 180 women being identified as having a “poor-prognosis signature,” meaning there is a good
chance the cancer will spread to the lymph nodes. These women have a 10-year survival of only 55%, compared to 10-year survival rate of 95% for the women had a “good-prognosis signature.” (Wachter, 2007).

Cystic Fibrosis

Cystic Fibrosis is a genetic disease that affects the mucus glands. Mucus is a substance that lines and protects the airways, digestive system, and reproductive system. In cystic fibrosis patients, the mucus is abnormally thick and sticky. When the mucus is like this, it starts to obstruct tube-like organs such as the esophagus, intestines, and reproductive system. This build up of mucus can cause respiratory problems, as well as chronic digestive problems. Cystic Fibrosis can also cause infertility because of the build up of mucus. (“Cystic fibrosis,” 2007).

Cystic Fibrosis is caused by a mutation in a certain gene, the CFTR (cystic fibrosis transmembrane conductance regulator) gene. The CFTR gene holds the code for making proteins which act as channels, seen to the right, that carry negatively charged ions out of the cell. The fluidity of mucus and water movement in tissues is controlled by the transport of the chloride ions. The flow of negatively charged ions, usually chloride ions, regulates the flow of water and helps control the consistency of mucus, sweat, saliva, tears, and digestive enzymes.

A mutation in the CFTR gene can cause abnormally thick mucus that can obstruct airways and glands. Most mutations only change a single amino acid in a sequence. The most common mutation is delta F508, a deletion of one amino acid. This altered channel breaks down and rarely can develop in the membrane to transport chloride.

For a child to have cystic fibrosis, it must inherit two abnormal genes (one from each parent). Each parent must be a carrier of this disease for their child to inherit the disease. The gene that causes cystic fibrosis has been identified, although it is not known exactly what abnormal nucleotide is the cause of it, however, it is known that it is more than one point shift mutation that causes this disease. Another disease that is caused by a point mutation is sickle cell anemia. (“Cystic fibrosis,” 2007).

Sickle Cell Anemia

Sickle Cell Anemia is a disease that affects red blood cells. Sickle cell has a variety of symptoms and severity. All symptoms are caused by the sickle shape of the red blood cells. The sickle shape of the blood cells causes the cells to block small vessels. Symptoms include hand-foot syndrome (a condition when small blood cells in hands and feet are blocked causing pain and swelling), anemia (shortage of red blood cells), fatigue, paleness, shortness of breath, severe pain in organs and joints, eye problems, jaundice (yellowing of the eyes and skin), and delayed growth and puberty. Sickle cell can also cause infections and spleen damage. (“Sickle cell,” 2005).

Sickle cell is caused by defective hemoglobin. Hemoglobin is the protein that carries the oxygen on the red blood cell. Red blood cells are supposed to be round and doughnut shaped. Hemoglobin’s purpose is to carry the oxygen on red blood cells to other parts of the body. In sickle cell, after the hemoglobin drops off the oxygen hemoglobin cluster together and form long rods that cause the red blood cells to become stiff and assume a sickle shape, seen on the next page. The difference between the shapes of the hemoglobin can be seen below. The sickle shape of the blood cells inhibit the cells from entering small veins. This can cause...
oxygen deprivation which can lead to damaged tissue and eventually organs.

Sickle cell is caused by a mutation in the HBB gene, which effects the structure hemoglobin. Only one point mutation is needed for sickle cell anemia to be developed. This mutation causes there to be one incorrect amino acid in the sequence that form the hemoglobin protein. This incorrect hemoglobin causes the sickle shape. For a child to inherit sickle cell anemia, both parents must carry the mutated gene. (“Sickle cell,” 2005).

Carrier identification is a test preformed on couples who are considering having children yet their families have a history of genetic disorders (“What is genetic,” n.d.). Carrier identification tests their DNA to find if they are both carriers for certain disorders and test the likelihood their child would have a certain diseases (“What is genetic,” n.d.). Carrier Identification commonly tests for diseases such as cystic fibrosis and sickle cell anemia (“What is genetic,” n.d.). To do this test a blood sample is used (“Genetic test,” 2007). The blood sample from each parent is taken and tested (“Genetic test,” 2007). If both parents are carriers there is a twenty-five percent chance the child will have the disease and a fifty percent chance the child will be a carrier of the disease (“Genetic test,” 2007). If only one parent is a carrier there is almost no chance that the child will have the disease and a fifty percent chance of the child being a carrier of the disease (“Genetic test,” 2007). Both examples can be seen below.

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Aa x Aa      AA x Aa
AA Aa
Aa aa
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Prenatal diagnosis is a test done on a fetus (“What is genetic,” n.d.). This test is usually preformed when there is a risk of the child being mentally retarded or physically disabled (“What is genetic,” n.d.). A common disease that Prenatal diagnosis tests for is down syndrome (“What is genetic,” n.d.). Prenatal diagnosis is done through amniocentesis, seen on the next page (“Genetic test,” 2007). Amniocentesis is a test done using the amniotic fluid, which is the fluid that surrounds the fetus in the uterus (“Genetic test,” 2007). The amniotic fluid contains cells that contain the genetic code of the fetus (“Genetic test,” 2007). A needle is inserted through the abdomen and into the uterus (“Genetic test,” 2007). Two tablespoons
of amniotic fluid are extracted ("Genetic test," 2007). The DNA is then extracted from the amniotic fluid and examined ("Genetic test," 2007).

Late-onset disorders can also be tested ("What is genetic," n.d.). These tests can indicate a susceptibility for the genetic disease but are not proving the disease will definitely or definitely not develop the disease because environmental factors often come into play ("What is genetic," n.d.). Diseases that this test is used for are cancer and heart disease. Late-onset testing is usually done using a blood sample ("Genetic test," 2007). Blood is taken and sent to the laboratory for testing ("Genetic test," 2007).

Uses of Genetic Testing

Just as there is a variety of different genetic tests, there is a variety of uses of genetic testing. Individuals can get tested if they have symptoms of a certain genetic disorder, there is a family history of genetic disease, or if they are worried about passing on a problem to their children ("What is genetic," n.d.). Genetic testing because of family history does not guarantee that the disease will or will not develop. Testing just determines an individual's "level of risk" of developing a certain disease. This test determines if there are gene mutations that can cause you to develop the disease. This alone will not determine if you definitely will develop the disease because environmental factors often increase the chances of having a disease. If this test comes back positive there are certain "preemptive measures" that can be taken. These include lifestyle changes and preventive surgeries. Another use of genetic testing is to confirm a diagnosis. Genetic testing can also show the doctor exactly where the mutation occurs and can help them make a treatment plan. Prenatal testing is common to test whether the child is at risk for certain diseases and deformities. Tests can also be performed on a newborn to test for genetic diseases. The final use of genetic testing is done on parents to see if they carry genes for a disease that can be passed on to their children. (Mayo Clinic Staff, 2006).

ADVANTAGES AND DISADVANTAGES OF GENETIC TESTS

Although there are many advantages to genetic testing, there are also limitations. Before testing is done, the limitations must be known. After testing is complete, a healthy lifestyle must be maintained. Many legal issues have been raised dealing with genetic testing.

Limitations

Although genetic testing can be a useful tool for many patients, there are some limitations. Like most medical tests, genetic testing is not 100% accurate. Genetic tests can fail to detect every mutation that cause certain disease. Some genetic diseases, like cystic fibrosis, are caused by hundreds of mutations to the DNA and the tests cannot always detect all of the mutations. Other diseases can be caused by a mutation in several different genes, therefore if one is not mutated it is not guaranteed that the others are perfect. A positive result does not mean the disease will definitely be developed. The positive result just means there is a mutation present that is associated with a specific disease. A positive result also does not tell the severity of the disease. Some genetic diseases go from mild to severe. Like the positive result, a negative result does guarantee that a disease will not be developed, it just means the known mutations is not present. Genes are also only one factor in developing diseases. Environmental influences can also effect
whether or not the disease is developed. Diseases usually occur from a gene mutation in combination with environmental factors. Genetic testing is also not financially feasible for everyone. Tests cost anywhere from $100 to several thousand dollars. (Mayo Clinic Staff, 2006).

Maintaining Health After Testing

After the tests are completed the patient must live a healthy lifestyle. Doing this can prevent the disease from being developed earlier. Even if the test came back negative the patient should still maintain a healthy lifestyle. Regular doctor visits should be made to make sure environmental factors do not cause the disease to develop. If the test is positive, the patient should monitor their health and be aware of the symptoms that may occur. The patient should also meet with the doctor regularly and devise a plan if possible. The patient should ask the doctor if there are any preventive measures that can be taken so the chance of developing the disease decreases. After a test comes back positive the patient should also see a mental health professional because the results are stressful. (Mayo Clinic Staff, 2006).

Legal Issues

Although genetic testing can be lifesaving, there are some associated legal issues with this new technology (Mayo Clinic Staff, 2006). Because the results of genetic tests are kept in medical records, there is the possibility that they will be seen by insurance companies (Mayo Clinic Staff, 2006). When you apply for disability or insurance the companies can request to see your medical records (Mayo Clinic Staff, 2006). If the company sees the results, there is a chance they will see it as a pre-existing condition and not cover the cost of treatment for the disease (Mayo Clinic Staff, 2006). In 1996, the Health Insurance Portability and Accountability Act was passed (“Genetic testing,” 2006). This act banned forms of discrimination based on genetic information in group health care plans, but this act does not include individual insurance plans (“Genetic testing,” 2006).

There is also a chance that the results from genetic testing will be a new source of discrimination in the work place (“Genetic testing,” 2006). In 1990 the Americans with Disabilities Act limited the use of genetic information in the work place (“Genetic testing,” 2006). The Lawrence Berkeley Laboratory went to court in attempts to evoke the protections of the Americans with Disabilities Act (“Genetic testing,” 2006). The case went to the 9th Circuit Court of Appeals but was soon rejected (“Genetic testing,” 2006). Because of this a law was signed in February of 2000 prohibiting the federal government from viewing genetic information while hiring (“Genetic testing,” 2006). It was the hopes of President Clinton that more laws like this will be passed to stop discrimination because of genetic information (“Genetic testing,” 2006).

CONCLUSION

Genetic testing can save lives through early detection. Genetic diseases are caused by mutations in DNA. Types of genetic diseases include cancer, cystic fibrosis, and sickle cell anemia. Tests for genetic diseases are done on all ages. Prenatal testing is preformed on infants to test for physical and mental deformities. Tests can be preformed on couples who are at risk for passing on a genetic disease to a future child. Genetic tests can also be done to test for a possible genetic disease for someone who is at risk for developing a genetic disease. Although genetic testing does have its advantage, there are limitations. These limitations include false positives, false negatives, and cost. After testing health should maintained to insure environmental factors do not contribute to earlier development of a disease. Legal issues also have to be considered with genetic diseases. Even though there are few disadvantages to genetic testing, it has the potential to save lives. The early detection that comes with genetic testing will increase the prognoses of the disease. Genetic testing is a new tool that could end the suffering of many patients with genetic diseases.

REFERENCES


