Genetic Disorders Lab

This lab is an opportunity for you to apply your knowledge of gene expression, mutations, and inheritance patterns to better understand genetic disorders. The information in this handout provides additional background on genetic disorders, genetic testing, and pharmacogenetics (a new field that merges genetics and drug development). In lab, you will choose and research a particular genetic disease with the ultimate goal of drawing connections between the symptoms of the disease and the genetic alteration associated with the disease. At the end of the lab period, you will have the opportunity to share your findings with your labmates and learn about the diseases chosen by others in your lab section.

LEARNING OBJECTIVES

- Apply your understanding of gene expression, mutations, and inheritance to understand genetic diseases.
- Draw connections between alterations in a gene and the symptoms observed in a genetic disorder associated with the altered gene.
- Describe the pattern of inheritance observed for a particular genetic disease.
- Understand challenges faced in studying, diagnosing, and treating genetic diseases, and the limits of genetic testing.
- Practice your oral presentation skills.

INTRODUCTION

The sections below were adapted from webpages put together by the National Human Genome Research Institute (NHGRI), whose focus is understanding the structure and function of the human genome and its role in health and disease. You are encouraged to explore the educational resources offered by the NHGRI (http://www.genome.gov/Education/) further if you are interested in learning more!

What Are Genetic Disorders

A genetic disorder is a disease caused in whole or in part by an abnormality in the DNA sequence. Genetic disorders can be caused by a mutation in one gene, by mutations in multiple genes, or by a combination of gene mutations and environmental factors. Damage to chromosomes, which can alter the structure of entire chromosomes or change the number of chromosomes, can also result in genetic disorders.

As we unlock the secrets of the human genome, we are learning that nearly all diseases have a genetic component. Some diseases are caused by mutations that are inherited from the parents and are present in an individual at birth. Other diseases are caused by acquired mutations in a gene or group of genes that occur during a person’s lifetime. These acquired mutations occur randomly or are caused by some environmental exposure (such as cigarette smoke). Many cancers are due to a combination of inherited and acquired mutations.

Genetic disorders typically involve the inheritance of a particular mutated disease-causing gene. The mutated gene is passed down through a family, and each generation has some potential to inherit the gene that causes the disease. Rarely, one of these diseases can occur spontaneously in a child when his/her parents do not have the disease gene, or there is no history of the disease in the family. This is due to a new mutation occurring in the egg or sperm that gave rise to that child.
Most genetic disorders, however, are caused by a combination of inherited mutations in multiple genes, often acting together with environmental factors. Examples of such diseases include many commonly occurring diseases, such as heart disease and diabetes.

Research on the human genome has shown that although many commonly occurring diseases are usually caused by inheritance of mutations in multiple genes at once, such common diseases can also be caused by rare hereditary mutations in a single gene. In these cases, gene mutations that cause, or strongly predispose, a person to these diseases often run in a family, and can significantly increase each family member’s risk of developing the disease. One example is breast cancer, where inheritance of a mutated BRCA1 or BRCA2 gene confers significant risk of developing the disease.

Geneticists group genetic disorders into three categories (see below). It is important to note that a particular disease may be able to be placed in more than one of these categories.

- **Monogenetic disorders** are caused by a mutation in a single gene. The mutation may be present on one or both chromosomes (one chromosome inherited from each parent). Monogenic disorders are relatively rare in comparison with more commonly occurring diseases. A major distinction among monogenic disorders is between “dominant” and “recessive” diseases. Dominant diseases are caused by the presence of the disease allele on just one of the two inherited parental chromosomes. Recessive diseases require the presence of the disease allele on both of the inherited parental chromosomes.

- **Multifactorial inheritance disorders** are caused by a combination of inherited variations in genes, often acting together with environmental factors. Heart disease, diabetes, and most cancers are examples of such disorders. Behaviors are also multifactorial, involving multiple genes that are affected by a variety of other factors. Researchers are learning more about the genetic contribution to behavioral disorders such as alcoholism, obesity, and mental illness.

- **Chromosome disorders** are caused by an excess or deficiency of the genes that are located on chromosomes, or by structural changes within chromosomes. Down syndrome, for example, is caused by an extra copy of chromosome 21, although no individual gene on the chromosome is abnormal. Prader-Willi syndrome, on the other hand, is caused by the absence or non-expression of a group of genes on chromosome 15. A specific form of blood cancer (chronic myeloid leukemia) can be caused by exchange of portions of two chromosomes that are NOT homologous (chromosomes 9 and 22). No chromosomal material is gained or lost, but a new, abnormal gene is formed that leads to formation of cancer.

**Genetic Testing**

Genetic testing uses laboratory methods to determine the sequences of particular genes. Genetic tests may be used to identify increased risks of health problems, to choose treatments, or to assess responses to treatments. Genetic tests can help to:

- Diagnose disease
- Identify gene changes that are responsible for an already diagnosed disease
- Determine the severity of a disease
- Guide doctors in deciding on the best medicine or treatment to use for certain individuals
- Identify gene changes that may increase the risk to develop a disease
- Identify gene changes that could be passed on to children
- Screen newborn babies for certain treatable conditions
Genetic test results can be hard to understand, however specialists like geneticists and genetic counselors can help explain what results might mean to an individual and their family. Because genetic testing tells you information about your DNA, which is shared with other family members, sometimes a genetic test result may have implications for blood relatives of the person tested.

There are various types of genetic tests, some of which are described below.

- **Diagnostic testing** is used to precisely identify the disease that is making a person ill. The results of a diagnostic test may help you make choices about how to treat or manage your health.

- **Predictive genetic tests** are used to identify gene changes that increase a person's likelihood of developing diseases. The results of these tests provide you with information about your risk of developing a specific disease. Such information may be useful in decisions about your lifestyle and healthcare.

- **Carrier testing** is used to find people who “carry” a gene allele that is associated with a disease. Carriers may show no signs of the disease; however, they have the ability to pass on the allele on to their children. This type of testing usually is offered to people who have a family history of a specific inherited disease or who belong to certain ethnic groups that have a higher risk of specific inherited diseases.

- **Research genetic testing** is used to learn more about the contributions of genes to health and to disease. Sometimes the results may not be directly helpful to participants, but they may benefit others by helping researchers expand their understanding of the human body, health, and disease.

Genetic testing may be beneficial whether the test identifies a mutation or not. For some people, test results serve as a relief, eliminating some of the uncertainty surrounding their health. These results may also help doctors make recommendations for treatment or monitoring, and give people more information for making decisions about their and their family's health, allowing them to take steps to lower his/her chance of developing a disease. For example, as the result of such a finding, someone could be screened earlier and more frequently for the disease and/or could make changes to health habits like diet and exercise. This information can also help people to make informed choices about their future, such as whether to have a baby. Genetic testing has a generally low risk of negatively affecting your physical health. However, it can be difficult financially or emotionally to find out your results. Learning that you or someone in your family has, or is at risk for, a disease can be scary. Some people can also feel guilty, angry, anxious, or depressed when they find out their results.

There are many reasons that people might get genetic testing. Doctors might suggest a genetic test if patients or their families have certain patterns of disease. The decision about whether to have genetic testing is complex, and it is essential to understand the limits of genetic testing in order to make an informed choice. Genetic testing cannot tell you everything about inherited diseases. As described earlier, most genetic diseases are the result of a combination of multiple gene alterations as well as environmental factors. Therefore, a positive result does not always mean you will develop a disease, and it is hard to predict how severe symptoms may be.

**Pharmacogenomics**

Pharmacogenomics uses information about a person's genetic makeup, or genome, to choose the drugs and drug doses that are likely to work best for that particular person. This new field combines the science of how drugs work, called pharmacology, with the science of the human genome, called genomics.
Until recently, drugs have been developed with the idea that each drug works pretty much the same in everybody. But genomic research has changed that “one size fits all” approach and opened the door to more personalized approaches to using and developing drugs. Depending on a person’s genetic makeup, some drugs may work more or less effectively than they do in other people. Likewise, some drugs may produce more or fewer side effects than in someone else. In the near future, doctors will be able to routinely use information about a person’s genetic makeup to choose those drugs and drug doses that offer the greatest chance of being effective.

Pharmacogenomics may also help save time and money. By using information about a person’s genetic makeup, doctors may be able to avoid the trial-and-error approach of giving various drugs until they find the right one. Using pharmacogenomics could help find the “best-fit” drug from the beginning.

Doctors are starting to use pharmacogenomic information to prescribe drugs, but such tests are routine for only a few health problems. However, given the field’s rapid growth, pharmacogenomics is soon expected to lead to better ways of using drugs to manage heart disease, cancer, asthma, depression, and many other common diseases. One current use of pharmacogenomics involves people infected with the human immunodeficiency virus (HIV). Before prescribing the antiviral drug abacavir (Ziagen), doctors now routinely test HIV-infected patients for a genetic variant that makes them more likely to have a bad reaction to the drug.

Until recently, drug developers usually used an approach that involved screening for chemicals that were effective for a broad range of people. Researchers are now using genomic information to find or design drugs aimed at subgroups of patients with specific genetic profiles. In addition, researchers are using pharmacogenomic tools to search for drugs that target specific cellular molecules and processes involved in disease.

LAB OUTLINE
I. Quiz
   To prepare for this quiz, read this handout and review your notes from your discussions of inheritance (genetics) in class.

II. Lab Discussion & Genetic Disease Selection

III. Genetic Disease Research

IV. Oral Presentations

REFERENCES
1 Adapted from: https://www.genome.gov/19016930
2 Adapted from: http://www.genome.gov/19516567
3 Adapted from: http://www.genome.gov/27530645