A Primer on Genetics Research

with the STRONG HEART STUDY as an Example
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**Genetics Terms**

**Amino acids** – The chemical building blocks that are joined to form a protein.

**Chromosome** – Found in the nucleus of a cell. Humans have 23 pairs of chromosomes. The genes are located on the chromosomes.

**Deoxyribonucleic acid (DNA)** – The carrier of genetic information in cells. It is composed of 2 chains wound in a double helix.

**Family tree** – The ancestral history of an individual; a chart showing their relatives: parents, grandparents, children, grandchildren, aunts, uncles, nieces, nephews, and cousins.

**First degree relatives** – A person's mother, father, brothers, sisters, and children.

**Gene** – A particular segment of DNA molecule that determines a hereditary trait.

**Gene expression** – The level of activity of the products of a gene. Variation in the level of gene expression leads to variation in traits between individuals.

**Genome** – The total genetic information contained across all the chromosomes of an organism. The human genome contains between 30,000 and 40,000 genes.

**Genotype** – The genetic makeup of an individual. It can refer to all genes or to a specific gene.

**Heritability** – The proportion of genetic contribution to the expression of a trait.

**Linkage analysis** – Genetic analyses using family data to identify the location of a gene or genes influencing a trait. This is done by looking for consistent patterns of inheritance between the trait and the genes of related individuals.

**Linkage map** – A scale representation of a chromosome showing the relative position of its known genes.

**Phenotype** – The appearance or characteristics of an individual, which is dependent on the individual’s genetic makeup, for example, height, weight, cholesterol level, blood pressure.
Polymorphism – A variation within a gene.

Protein – A compound made of amino acids linked together in a particular order determined by a gene's DNA sequence. Proteins perform many functions in the cell.

Ribonucleic acid (RNA) – A product of the DNA sequence of a gene. Used as the pattern for making a protein.

Segregation – The inheritance of a particular variation of a gene from generation to generation through a family tree.

Siblings – A person’s brothers or sisters who are biologically related. Individuals who are the biological offspring of the same mother and father are considered full siblings while those who share only one biological parent are considered half siblings.

Trait – Any characteristic. May be genetically determined.
BACKGROUND

The STRONG HEART STUDY is a unique and valuable resource to help in improving our understanding of the mechanisms and risk factors (both genetic and environmental) that contribute to a variety of common diseases such as heart disease, high blood pressure, and diabetes. Understanding the causes and finding preventions for these diseases is a significant public health concern not only for STRONG HEART STUDY participants but for all people. Work done in the STRONG HEART STUDY, as well as in other similar studies, has shown that a person’s genetic make-up has a significant effect on their risk for developing these diseases. However, in the majority of cases it is not genetics alone, but the interplay of genes and environment that ultimately leads to the development of the disease. It has often been said that genetics loads the gun but the environment pulls the trigger.

We cannot change the genes we inherit but we can make decisions about the environments to which they are exposed, for example smoking and/or eating a high fat diet. The search to identify the specific genes contributing to disease risk is a slow difficult process with many steps. It is somewhat like looking for a specific person by first determining that they are in Alaska (i.e., there is a genetic effect), then in a particular village (i.e., which chromosome), then the specific house (i.e., which gene), and finally in which room they can be found (i.e., the specific variation in the gene causing the effect). An explanation is below.
COLLECTING FAMILY INFORMATION

The first step in identifying genes that contribute to disease risk is to collect extensive family data. This was done by STRONG HEART STUDY field staff who were community members; they visited the households of our participants and got information about the people living in each household and their relatives. From this information, they constructed family trees. An example of a small family tree is shown below. In a family tree diagram, males are represented by squares [□] and females by circles [○]. Individuals who are no longer living are represented by a diagonal line through a square or circle [∅].

A marriage is represented by a horizontal line (a marriage line) joining a square and a circle.

[□]—[○]

A sibship, which is a group of brothers and sisters who share the same two parents, is represented by another horizontal line, the sibship line, with vertical lines dropping from it to the squares and circles that represent each of the siblings.

[○] [□] [○] [□]

A vertical line dropping from the marriage line to the sibship line joins the parents and their children. The diagram below represents a woman, her husband who is no longer living, and their four children, two daughters and two sons.

[□]—[○]

[○] [□] [○] [□]
Family tree diagrams can be extended to include additional relatives. The family tree below shows a three-generation family with the grandparents in the top generation. The grandparents have four children, and each of the children is (or was) married. The daughter on the left has four children, one of her brothers has three children and the other brother has four. Her sister has been married twice. She has three children (full siblings to each other) by her first husband and one (half sibling to other three children) by her second.

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   |       |       |
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   +---+---+---+---+
       |   |   |   |
       |   |   |   |
       |   |   |   |
       +-------+
```

Additional information also can be included on the family tree. Dates of birth, etc. are often written below the symbol representing each family member. Symbols may also be shaded or filled in to represent particular characteristics of individuals in such a way that they are easy to pick out in the diagram.

**FINDING EVIDENCE OF GENETIC CONTRIBUTION**

The second step is doing analyses to determine if there is evidence of genetic contribution in general. In the STRONG HEART STUDY, our initial analyses have shown a significant genetic contribution to variation in a wide range of traits associated with risk for heart disease and diabetes. Some of these traits are heart function, overweight, and levels of cholesterol, triglyceride and blood pressure. These studies showed a genetic contribution to the disease risk factors we are interested in. They did not identify the specific genes involved.

**FINDING POSSIBLE LOCATION OF GENE ON CHROMOSOME**

The third step in identifying genes that contribute to disease risk is doing analyses to find general areas on the chromosomes that might contain contributing genes. We have identified several chromosomal regions that show evidence of containing genes influencing a variety of traits related to cardiovascular disease and related complications.
ANALYZING SPECIFIC GENES

The fourth step is testing specific genes within the identified chromosomal region to determine if they are in fact the contributing genes. We are now doing this testing.

IDENTIFYING VARIATIONS IN SPECIFIC GENES

The final step is to identify what variations in these specific genes are affecting the risk for developing these diseases. We will do this testing later in the study. We have made a lot of progress but there is much work left to be done.

BENEFITS

It is difficult to know what benefits our participants will get from the study because biomedical technology continues to advance rapidly. At a minimum, identifying the specific genes that contribute to increasing risk for these diseases could be used to help identify people who may be at greatest risk. It could also help to identify the types of environments people at risk particularly need to avoid or minimize. The information may also help to identify which types of interventions might be best for a particular individual, such as which could be the most effective prescription drug (personalized medication) for that individual. Certainly one outcome, but the one probably the farthest down the line in most cases, is that identifying specific genes could lead to the development of new medications and treatments. The STRONG HEART STUDY researchers will do all that we can to make this study beneficial to our participants.