

Chapter One—A Primer in Genetics

Introduction

“*Genetics*” is hard to miss in the United States today. Whether sometimes in the daily headlines or in a medical office, or in the decisions that a loved one has to make, we encounter genetics repeatedly. This familiarity, however, does not mean that the science behind it is well understood. The knowledge is so recent and the details so complex that many are tempted to give up on it. This is unfortunate because a working knowledge of the science behind the social challenges is within anyone’s reach. Further, this working grasp of the science and technology is not only a practical matter, but, more importantly, a moral one. Only this basic grasp will empower careful thinking and wise decision-making, whether for an individual or a society. This chapter then is designed to give the reader the working knowledge necessary to participate in conversations about the promises and the perils our culture faces in this age of biological control. Be patient as you read through this material. Such effort will pay dividends in getting a handle on the strange language of genetics. The task of this chapter will be achieved when the reader has a working grasp of the concepts of *gene*, *allele*, and the *Human Genome Project*, as well as a general understanding of how we can manipulate genes and make use of genetic knowledge.

What questions do you bring to this topic?

As we seek either factual explanation or meaningful understanding, we learn by posing questions and answering them. Often these questions are only vaguely present in one’s mental background, but they are there. Therefore, it helps greatly to identify some of these questions before beginning to read or discuss. Take a moment to identify two or three questions that you bring to the topic of genetics. In a group study, it is helpful to allow each person to share one of his or her questions. In a large group, or one with new participants, this can be the occasion to briefly introduce oneself.

Genetics 101

Genetics in its narrowest sense simply refers to the study of biological heredity and how genes effect the functioning and features of a living body. *Genetics* in its broadest sense serves as a catch phrase for the knowledge of how genes work, the impressive abilities it gives us, and the unprecedented challenges it poses. (This guide generally intends this second and broader meaning, except at certain places in this first chapter.) The center of this accumulating knowledge is the Human Genome Project (HGP), a three-billion-dollar federally funded science project whose purpose is to sequence, map, and understand the human *genome*. (A genome is the entire set of genes in any living creature.) The completion of the rough map of the human genome was announced on June 26, 2000, and is widely regarded as a milestone that marks the transformation

of the world of medicine. Just as dramatically, genetics will revolutionize a range of human endeavors—from bearing children to farming to how we understand what it means to be a human being. The reason genetics impacts human society so dramatically becomes clear when one understands what a gene is and how it works.

So what is a *gene*? Simply stated, a gene is a piece of chemical material (the chemical’s name is Deoxyribonucleic acid—DNA) that serves as: 1) the source of the instructions that build and maintain living bodies; and 2) the unit that passes along such information to succeeding generations. The promise and peril of genetics lie in the fact that we are dealing with these fundamental units, this foundation of present and future life. We will now examine each function of the gene as the route to a working knowledge of genetic science.



GENETICS!

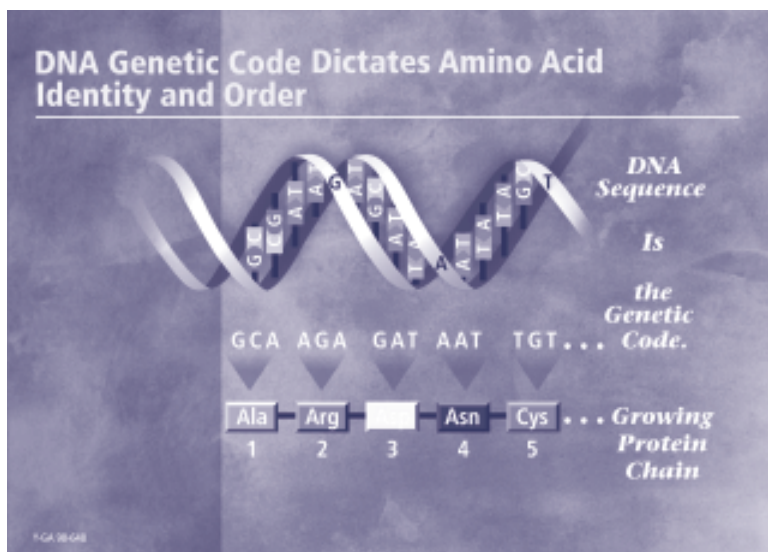
Where Do We Stand as Christians?

Genes: Instructions for Proteins

The nutrition label on packaged foods identifies carbohydrates, fats, and proteins as the main components of food. For our purposes, human bodies can also be divided into these categories. Carbohydrates function primarily as the body's energy source while fats are primarily the body's way to store excess energy. Proteins account for most of the remaining multitude of diverse tasks that structure and maintain the human body.

There are many types of proteins. Hemoglobin (the protein in blood that carries oxygen) is one example. Each hemoglobin molecule is tremendously complex, but its primary task is to carry a mere four oxygen molecules from the lungs to the rest of the body. Other well known proteins include antibodies, the immune system's soldiers. Another is collagen, the protein that gives elastic strength to cartilage and ligaments. Yet other proteins, called enzymes, act as catalysts in the thousands of biochemical pathways that give cells their function. The important point is not the names, but the recognition of the vast diversity and critical role that proteins play in our bodies.

Chemically, proteins are chains of amino acids linked together like beads on a necklace to form chains. In the human body, there are only about 20 different colored beads—that is, amino acids—but they are linked in a huge assortment of arrangements that form the multitude of proteins. These necklaces range from only a few to several thousand beads long. The order in which these beads are arranged (called the sequence) determines what protein is created and how it will function. The instructions for making these amino acids and their proper sequence are encoded in genes (refer to graphic). There are only four chemical units in this language of instruction: A (adenine), C (cytosine), G (guanine), and T (thymine). We might think of these as “letters” in the language of genetic instruction. The novel aspect of this language is that all words are exactly three letters long and are without space between them. Each three-letter word (called a codon) is an instruction for one of the 20 amino acids that make up any given protein. A six-word-long strand might read as AAT-CGT-ATG-CCT-TAT-GGA, and so on. Thus, we can think of each instruction for a protein (a gene) as a collection of these words that may range from a few to thousands of words. When the term “genetic sequence” is used, it refers to identifying these strands in their proper order.



DOE Human Genome Program

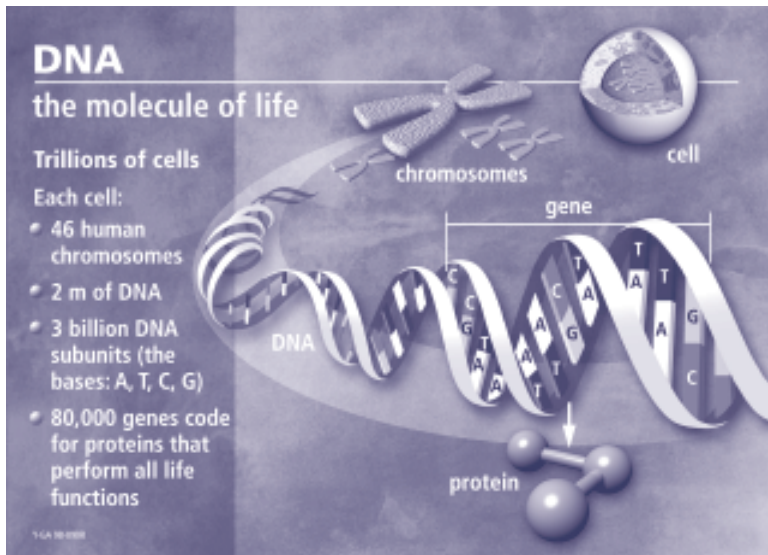
The U.S. Human Genome Project (in conjunction with a worldwide effort) began in 1990 as a 15-year effort coordinated by the U.S. Department of Energy and the National Institutes of Health.

Project goals are to:

- identify all the approximately 50,000 genes in human DNA,
- determine the sequence of the three billion chemical base pairs that make up human DNA,
- store this information in databases,
- develop tools for data analysis,
- transfer related technologies to the private sector, and
- address the ethical, legal, and social issues (ELSI) that may arise from the project.¹

The instructions for creating proteins are contained twice (but in reverse order) because they occur in a double structure that looks like a twisted rope ladder. This is called the *double helix* (refer to graphic). The chemical letters sit on the long bands (a different chemical substance) of the ladder's outer structure and form its rungs because each one connects with another letter on the opposite band. It is essential to note that a C will match up only with a G, and an A will match up only with a T to form these rungs (the matchings are called base pairs). In this way, each word and its exact sequence is present twice. This arrangement explains how DNA so readily duplicates its instructions. This ladder readily comes apart between the G-Cs and the A-Ts (chemically





called weak bonds) in a way that visually reminds one of a zipper. The presence of a complete set of instructions on each side of the ladder means that new chemical material can be joined to either side so that two duplicate sets of instructions will be created.

The collection of genes (called a genome and containing somewhere from fifty to seventy thousand genes) is found on 46 separate sets of these double helix structures. Each of these 46 is called a chromosome. These chromosomes are found within the nucleus of most human cells. When the time is right, special proteins uncoil the chromosomes, and the rungs of the ladder split at the point where the needed instructions for that cell are stored. The protein-building process then involves a series of messengers that copy the information from its source in the gene and

activate it for “expression” (the scientific term) in such a way that amino acids are linked together in sequences which, in turn, create proteins. These proteins then carry out their function, either within the cell or by traveling to target cells elsewhere in the body. In animals these functions range from creating ligaments, to carrying oxygen, to forming chemicals in the brain.

Although science still has much to learn about these processes, current knowledge about genes is sufficient to permit us to test, engineer, and duplicate these fundamental instructions of life. We will return to the implications of these abilities. At the moment, we should explore how genes are not just instructions for proteins, but also units of heredity.

Transmitting the Genetic Information through Reproduction

When thinking about genes as units of heredity, we will shift metaphors somewhat and think of genes as the kind of instructions we call recipes. In this analogy, genes are recipes passed on from generation to generation for “cooking up” living beings. The system is complex, but it functions much like parents passing on the family’s secret recipes. A critical component of this process is the variation or change that results, much like the newly combined set of recipes in the household of a newly married couple.

All living things are genetic at the basic level and share the need for some method of exchanging and varying the genetic information which is their heritage. Bees do this for flowers by the transfer of pollen. In mammals, the variation occurs when a sperm and an egg (called gametes), each containing a copy of recipes from the two different parents, combine to produce offspring with two non-identical copies of the genes.

Again, it helps to use the analogy of two sets of cookbooks, one from each parent. The cookbook in this analogy is the chromosome, which could be thought of as a collection of gene recipes. Most pages of those cookbooks, perhaps as high as 97 percent, contain gibberish (the scientific term is *nonsense*) that is of minimal importance or is left over from evolution. The roughly 50,000 functional genes are scattered among this gibberish and are hard to identify. Even with the HGP’s work, scientists will still need years to identify precisely these recipes. In the human genome, the 46 “cookbooks” or chromosomes are numbered by their size, #1 being the largest and #22 the smallest. There are two copies of each of these first 22 cookbooks. These duplicate copies of chromosomes have a special name, called autosomes. Forty-four of the 46 chromosomes are autosomes. The remaining two are special sex chromosomes, given labels X and Y rather than being numbered. If there is one copy of the X chromosome and one of a smaller version labeled Y, the body is male—refer to the picture of chromosomes called a *karyotype* on page 14. If both sex chromosomes in a particular human being are the large ones, labeled X, the body is female.



GENETICS!

Where Do We Stand as Christians?

The process of human sexual reproduction combines one copy of each of the 22 autosomes (cookbooks) and one sex chromosome from each parent, producing a child with 46 chromosomes, half from each parent. This regular reshuffling of the human (or any mammal's) gene pool creates *continuity with variation*. Additional alteration in the genes results from *mutation*. A mutation is a change in the DNA sequence due to chemicals, radiation, or copy errors. (We should note that mutations may occur at any time from conception onward as cells duplicate themselves.) The process of mutation is only vaguely understood, but its effects are clear. Inherited variation and mutation are the primary sources of genetic change, whether considered beneficial or harmful, and it is important to understand how this change occurs and how it effects organisms.

Understanding Genetic Change

Genes and Alleles

Two additional concepts can help us understand genetic change. The first is the difference between a gene and an allele. A *gene* is a sequence of DNA which encodes for a protein. *Alleles* are the variant forms of that gene found within a given population. They encode for that same protein, but with slight alterations. To return to the recipe analogy, we could think of a standard chocolate chip cookie recipe as a gene. Its allele would be the alteration of that recipe by a baker. Some of these alterations turn out to be flops, while others are hailed as improvements. For instance, the substitution of salt for one quarter of the recommended sugar would be an alteration making the cookie unpleasant to eat. The substitution of pure butter for margarine, on the other hand, would be considered a real treat. In genetics we call the first alteration a disease because it is harmful. In the other case, the alteration simply creates a difference that may be judged benign or beneficial. It is not always clear whether a genetic alteration represents abnormality or just diversity.

Dominant and Recessive

The second concept involves dominant vs. recessive genes. Recall that there are two copies of chromosomes 1 through 22 in each cell nucleus. Therefore, there are two copies (two alleles) of each gene on those chromosomes. In some cases, one abnormal allele is enough to cause trouble in a body despite the presence of the normal one. If so, the abnormal allele is called *dominant*. In other situations, the one good allele works well enough and the abnormal allele and its consequent condition, trait, or disease are termed *recessive*. For recessive conditions, the disease appears only if both alleles are abnormal. The person who has one normal and one abnormal allele of a recessive condition is called a carrier.

All humans carry about a half dozen lethal recessive alleles (from among their approximately 50,000 genes) that are hidden by the good copy. Every human then is a carrier of lethal diseases. These abnormal alleles do not cause problems unless that individual happens to mate with someone else carrying a lethal allele of the same gene. Incest and inbreeding are more likely to produce a match of two such recessive alleles due to the increased chance that both partners carry the same recessive allele.

Genetic Errors

Just about anything imaginable can and does go wrong in transmitting genetic information. Using the encyclopedic cookbook analogy, whole volumes may be missing or they may get put together incorrectly. Recipes don't get copied. Words get misspelled and letters get deleted. Nature is an excellent typist, but the genome's three billion base pairs are 200,000 times longer than this chapter. This genome is copied perhaps several trillion times from conception to death. Indeed, about 100 billion cell divisions are necessary each day just to replace cells lost to normal wear and tear. Mistakes are bound to occur, from conception onward, and some are lethal. In fact, it is estimated that 60-80 percent of all human conceptions die before birth, most within the first two weeks after conception, largely due to genetic errors. This phenomenon is called *fetal wastage*. In some cases, the embryo survives genetic abnormalities, but the individual will have many health problems, ranging from mild to severe.

For simplicity's sake, we can divide these errors into two major types. The first is chromosome errors. Sometimes whole or partial copies of chromosomes may be missing, joined incorrectly (called translocations), or have extra copies. Generally speaking, embryos with these errors do not survive to birth, but there are a few exceptions, the most widely known being Down's Syndrome. A child with Down's Syndrome has a third copy of chromosome #21 (see karyotype image on page 14), which is characterized by



slanting eyes, a large tongue, and mild to profound mental retardation. The second category of errors involve genes, either single or multiple ones (called multi-factorial syndromes), and there are several types of errors in each case. The following are representative examples and illustrate both the importance of alleles and how diseases can be either dominant or recessive.



DOE Human Genome Program

Single Point Deletions or Mutations

Cystic fibrosis is a recessive disease caused by the faulty production of a single protein that regulates the movement of chloride ions through cell membranes. This results in excessively thick and sticky mucus that encourages lung infections and digestive problems. The most common genetic error is an allele called delF508. This means that the 508th word in the recipe is missing. As a result, the protein is missing a single amino acid, labeled “F” for short. From a necklace 1,480 beads long, only a single bead is missing, but this tiny change leads to cystic fibrosis. While this delF508 allele is present in three-fourths of all children with cystic fibrosis, the other fourth is caused by various

other alleles. Despite the media’s use of the term, there is, therefore, no such thing as a “cystic fibrosis gene.” Rather, there is a gene for a particular lung cell membrane protein, and it has many variations, some of which cause cystic fibrosis. If both alleles (the particular copies of that gene in an individual) are delF508 or another harmful variation, then the child will have a disease called cystic fibrosis.

Even the misspelling (mutation) of a single letter in a single word can produce disease. In sickle cell anemia, the allele of a gene that codes for hemoglobin (the red oxygen carrying protein in the blood) contains a variation of the middle letter of the sixth word of the recipe (the middle base pair of the sixth codon of the gene). In this variation, a different amino acid is inserted into the protein as it is made. This variation of amino acid changes the solubility of the hemoglobin, which leads to symptoms such as severe joint pain, shortness of breath, increased infection, and anemia. These are all due to the effects of the impaired delivery of oxygen to tissues that need it for normal functions.

Multi-factorial Syndromes

Many syndromes and diseases are caused by more than one gene. News media often report the discovery of a “gene” that causes a common problem like alcoholism or Alzheimer’s disease. Yet a gene identified as the “cause” of early-onset Alzheimer’s accounts for only a small fraction of all Alzheimer’s cases. Science has yet to determine even what approximate combination of gene and environment account for these other cases.

Promise and Perplexity

With this basic knowledge in hand, it should begin to be clear why our new knowledge about genetics is so significant. Genetic knowledge answers many questions about how the world of living creatures works, about disease, plant reproduction, and many more. This knowledge then allows—in theory at least—human beings to manipulate these sets of basic instructions upon which living beings depend. This is awesome power. A convenient way to divide these powers is *diagnosis, engineering, and duplication* (cloning). We shall briefly expand on the promise and the perplexity that attends each.

Diagnosis, usually called genetic testing, can be broken down helpfully into several categories. These include: *Onset of life*, *adult-onset*, and *criminal or work place* testing. The most common form of genetic diagnosis involves the unborn or newly born. Currently, screens or tests are available for only a handful of possible, if significant, disorders. Hundreds of more tests, when developed, could be used since much (not all) of an individual’s genetic instructions are in place after conception. Testing at the onset of life also includes carrier testing. (These terms are explained in the chapter entitled *Genetic Testing at the Beginning of Life*—see page 26.)



GENETICS!

Where Do We Stand as Christians?

The testing of adults is possible to indicate future illness (Huntington's disease—see glossary for explanation) or, more commonly, the propensity for illness (for example, forms of cancer or heart disease). Such testing could be used in the workplace to identify those individuals, for instance, with a propensity to develop cancer in a toxic work environment. Finally, since each individual's genome has a genetic "fingerprint" (enough slight variations in base pairs to make it unique), a hair strand or bit of saliva from a crime scene can identify those who were present.

Genetic engineering is a term used in several ways. In this guide the definition is a broad one that means any process of manipulating the patterns of proteins in an organism by altering DNA sequences. This includes attempts to alter existing ones or to add new ones. The goals of such engineering range from medical to agricultural ones, but the common purpose is to change the way, amount, timing, and so forth, in which proteins are made.

A medical form of engineering is experimenting with the "correction" of disease-causing alleles by retrofitting (inserting back into place) non-harmful sequences for the harmful ones. One such experiment involves inserting non-cancerous genetic instructions into cancerous cells with the hope of replacing the cancer producing genetic sequence.

A major distinction in therapy is made between "correcting" somatic cells (body cells that will die with the individual) and altering germ cells (an individual's cells for sexual reproduction). Changes to germ cell alteration would be passed on to offspring. This kind of alteration obviously is more questionable because of the long term and unknown consequences.

Other forms of genetic engineering include efforts to insert foreign genetic material into a genome. Some instances alter only short segments of a genome; for example, the insertion of pest-resistant genes into soybean or corn seed. Other instances alter a genome dramatically by splicing it with significant pieces of foreign genetic material. In theory genetic engineering could be practiced on plants, animals, their embryos, and on humans who are indeed part of the animal kingdom. It is important to stress that much more has yet to be learned, but theoretical possibilities exist for large-scale alteration. In practice, most engineering thus far has focused on producing commercial products, such as new forms of seeds for farmers.

The widely discussed *cloning* of Dolly (sometimes called the "sheep heard round the world") represents an additional set of challenges. To clone means to reproduce the genome of a living organism, which then results in a nearly exact replica. The most commonly seen—and natural—form of cloning is that of identical twins: two individuals from one genome. The term "cloning" in public discussion is often used to indicate the reproduction of an adult genome, as in cloning a movie star's genome. Yet, it is important to distinguish, broadly speaking, three kinds of cloning: DNA (a gene or segment thereof), twin (as in splitting a cell or early stage embryo into multiples), and somatic nuclear transfer (the technique that produced Dolly).

The benefits of genetics for human endeavors, from medicine or agriculture, have been hinted at throughout this discussion. The difficult questions have also been just below the surface. What are the special dilemmas that arise when we know about incurable diseases before the birth of a child or before they occur in an adult? How shall we avoid discrimination based on genetic heritage? Is human behavior determined by our genes, just like hair color? Should we modify food sources? How much modification is safe? Should we engineer genes in a way that will have long-range impact, as in germ-line therapy or in the creation of new seed forms? Should we engineer "designer" children to fit parental desires? Who should regulate these practices, and how much? What should the church say in all of this? Questions such as these will be the concern in later chapters.

Discussion Starter

Whatever one's level of genetic knowledge, each of us approaches today's genetic developments with a set of preexisting judgements. These judgements are based on personal experience and values. They may be firm or quite malleable, but they exist. We might characterize the range of possible judgements in this way: a) unconditional acceptance; b) general approval; c) hesitant acceptance; d) critical engagement; e) charitable negation; f) resolute rejection. Of course, these categories are not precisely defined. Moreover, each person likely will find his or her view shifting a bit on the spectrum according to the specific purpose,



technology, or impact involved. Nevertheless, thinking about such categories can aid in gaining valuable self-understanding of where one stands. The end of this chapter is a good time to consider the initial judgment you bring to the study of genetics.

The question to reflect upon is: *Given what you know of genetics, which category on the spectrum best describes your judgment toward the potential benefits and dangers of genetics?* An awareness of this judgement will be significant in considering the various topics in subsequent chapters.

For Further Investigation

Genetic Testing & Screening: Critical Engagement at the Intersection of Faith and Science. Roger A. Willer, editor (Kirk House Publishers, Minneapolis, 1998) Copyright held by the Evangelical Lutheran Church in America. Several sections in *Genetics 101* above were adapted from the chapter by Kevin Powell, M.D., Ph.D. in this book. His chapter is an excellent place to seek additional explanation.

Several Web sites with excellent introductions to genetics are also available. The ones listed here include two government sites. (Inclusion on this list represents no recommendation of these sites over others that are available.)

www.ornl.gov/hgmis/project/info.html

www.ornl.gov/TechResources/Human_Genome/home.html

www.biology.about.com/science/genetics/cs/basicgenetics/index.htm

Citations

1. "Human Genome Project Information," The Human Genome Program of the U.S. Department of Energy, <www.ornl.gov/TechResources/Human_Genome/home.html>.