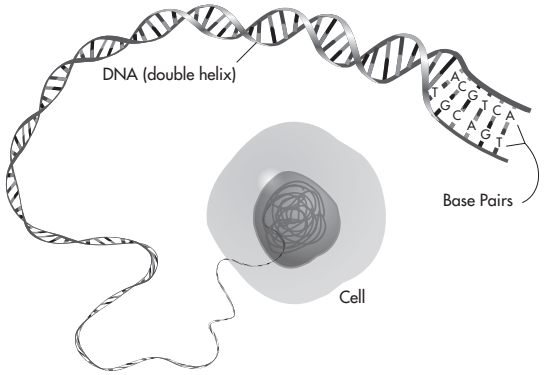


Figure 1.1: The double-helical DNA information molecule, the "instruction book" of all living things, here shown spilling out of the nucleus of a cell. The information content of DNA is specified by the order of the chemical bases (A, C, G, or T). Each of the two strands carries the complete information, since A always pairs with T, and C always pairs with G.

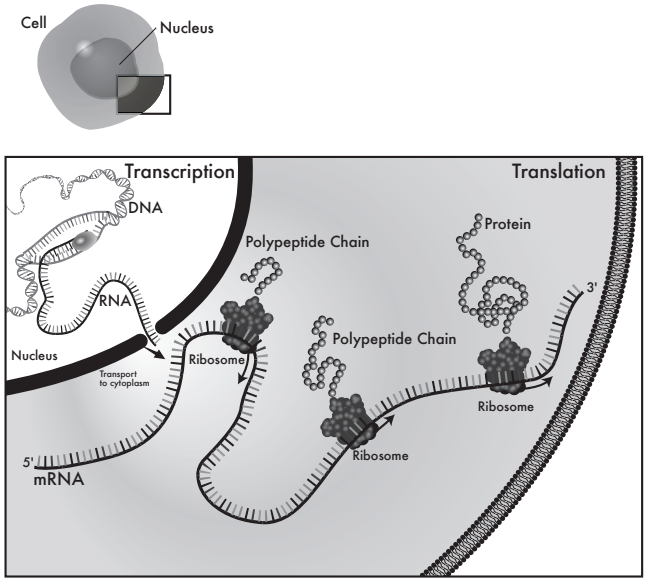


Figure 1.2: The "basic dogma of molecular biology": DNA codes for messenger RNA (called transcription, takes place in the nucleus), which then codes for protein (called translation, carried out by ribosomes in the cytoplasm).

Normal	DNA	HAS	ALL	YOU	CAN	ASK	FOR
Missense	DNA	HAS	ALL	LOU	CAN	ASK	FOR
Nonsense	DNA	HAS	ALL	YOU	STOP		
Frameshift	DNA	HAS	ALY	OUC	ANA	SKF	OR

Figure 1.3: Translation from RNA to protein occurs using a word length of three letters. Mistakes in the DNA genome lead to mistakes in messenger RNA, which then lead to mistakes of various types in the protein.

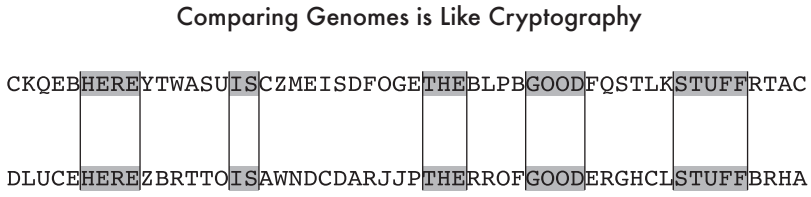


Figure 1.4: Comparing genomes from different organisms is a powerful method to identify the parts that are most functionally important, as these will have been the most constrained during the process of evolution.

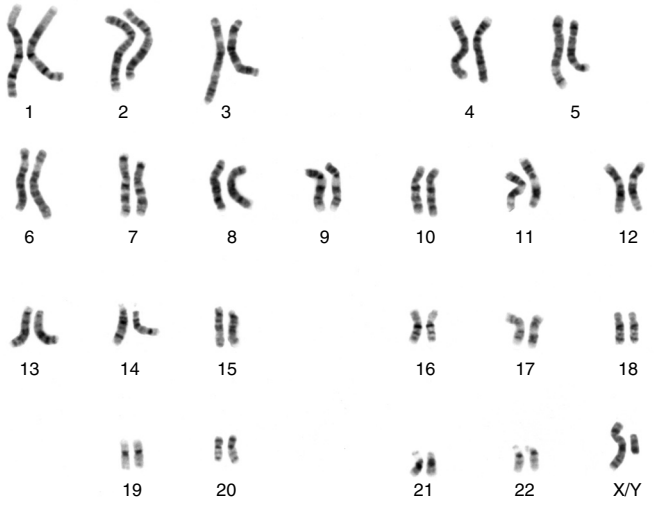


Figure 2.1: The chromosomes of a single cell from a normal human male. A female would have two X chromosomes instead of an X and a Y.

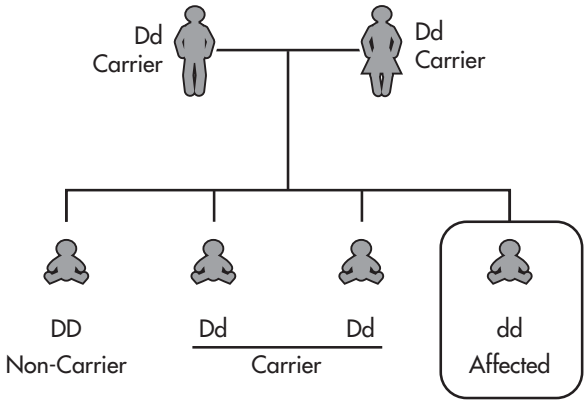


Figure 2.2: Recessive inheritance, as occurs in cystic fibrosis and sickle-cell anemia. "D" is the normal copy of the gene, "d" is the abnormal copy.

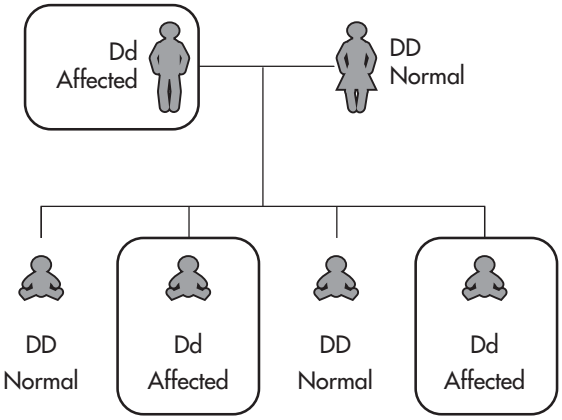


Figure 2.3: Dominant inheritance, as occurs in Huntington disease.

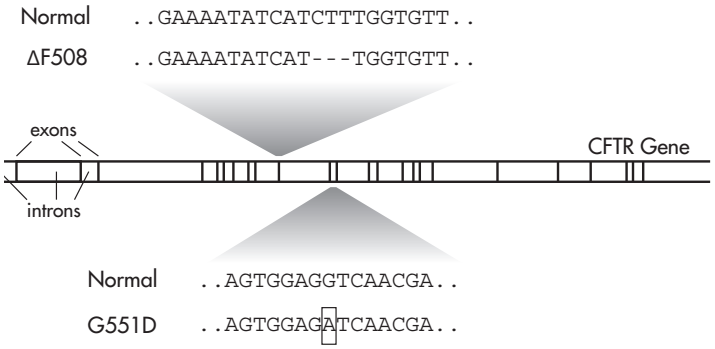


Figure 2.4: A diagram of the *CFTR* gene. This gene normally codes for a protein that transports salt and water across cell membranes in various organs. But if both copies of the gene are misspelled with mutations such as ΔF508 (a deletion of CTT) or G551D (a substitution of A for G), the result is cystic fibrosis.

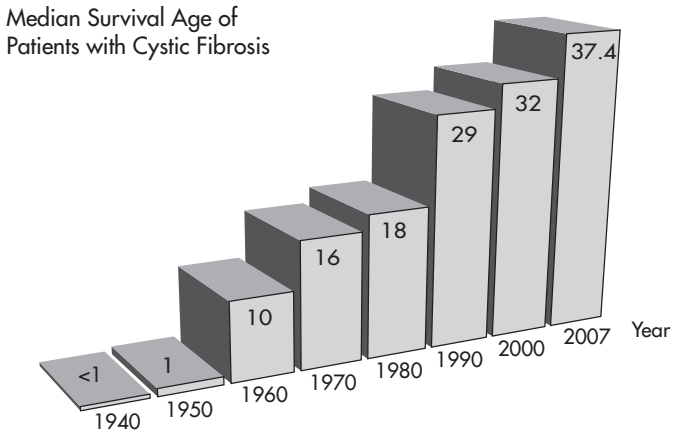


Figure 2.5: Medical research has led to dramatic improvement in survival for individuals with cystic fibrosis.

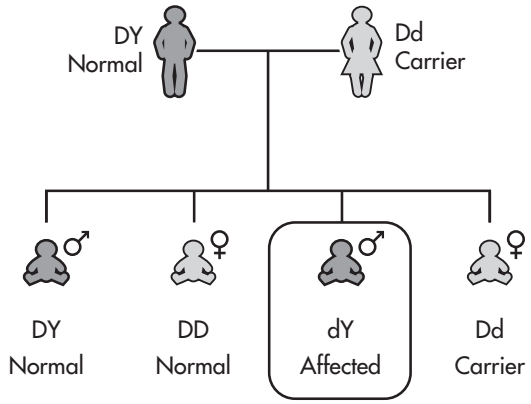


Figure 2.6: X-linked inheritance, where generally only males, with their single X chromosome, are affected. "D" is the normal copy of the gene, "d" is the abnormal copy.

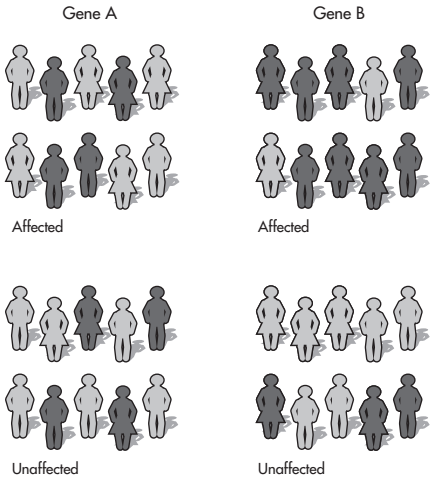


Figure 3.1: Finding the genetic glitches associated with risk of disease requires identification of variations in DNA that appear more commonly in affected than unaffected persons. Here gene B looks as if it might harbor an important risk factor, whereas gene A doesn't seem to be involved.

2000 letters of the DNA code

The boxes mark three common variants (SNPs).

But it turns out they are closely correlated:
C at SNP 1 is always found with A at SNP 2 and G at SNP 3.

Figure 3.2: Two thousand letters of the DNA code (showing just one strand).

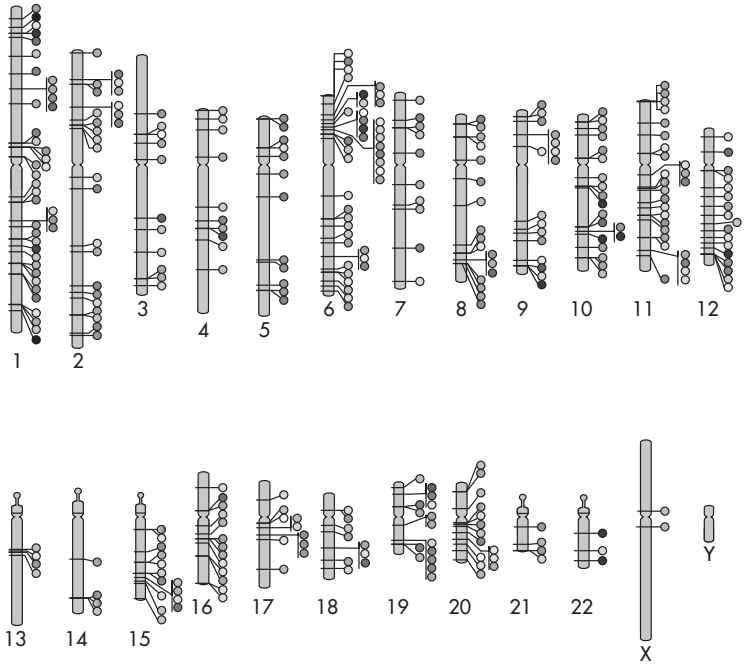


Figure 3.3: New findings about genetic risk factors for disease. Each symbol represents a newly discovered variant that predisposes to one of several dozen human conditions that are common in the population. This diagram would have had only seven entries in 2002.

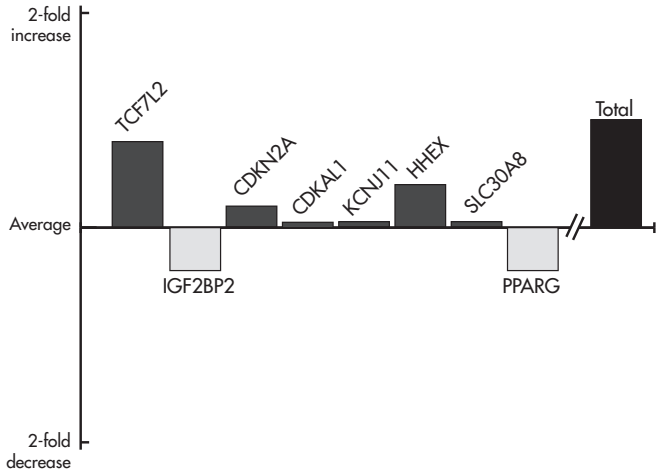


Figure 3.4: A typical graphic display of the results of genetic testing of an individual test for risk of type 2 diabetes. Eight different gene variants have been tested; each provides a risk that is higher (*TCF7L2*, *CDKN2A*, *HHEX*), lower (*IGF2BP2*, *PPARG*), or the same (*CDKAL1*, *KCNJ11*, *SLC30A8*) as an average person. The total risk for this person is elevated by a factor of 1.5.

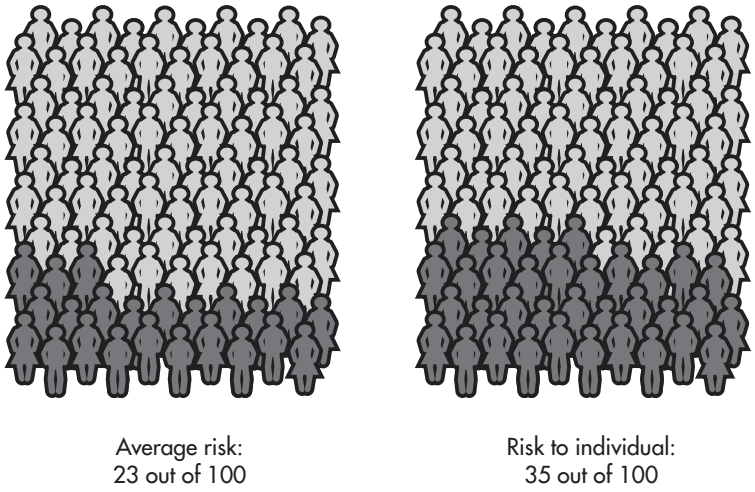


Figure 3.5: Another way of showing the 1.5-fold elevated diabetes risk for the person whose genetic test results were shown in Figure 3.4.

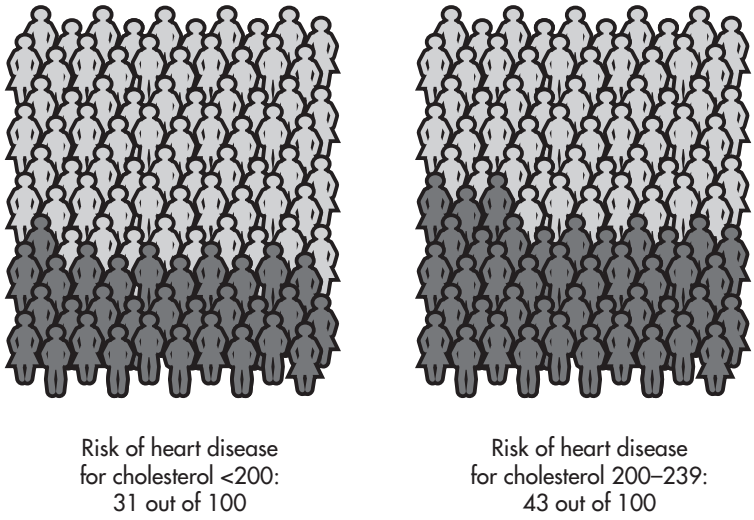


Figure 3.6: Cholesterol is a widely accepted risk factor for heart attack. Note that the increased statistical risk associated with a cholesterol level in the 200–239 range is similar to the diabetes genetic risk depicted in Figure 3.5.

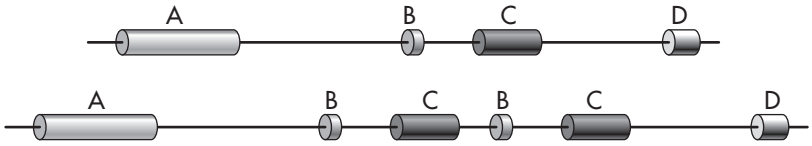


Figure 3.7: A copy number variant (CNV). The individual with the arrangement at the top has just one copy of genes A, B, C, and D. The individual at the bottom has an extra copy of genes B and C. Such CNVs are common in the human population, and may account for some of the "dark matter of the genome."

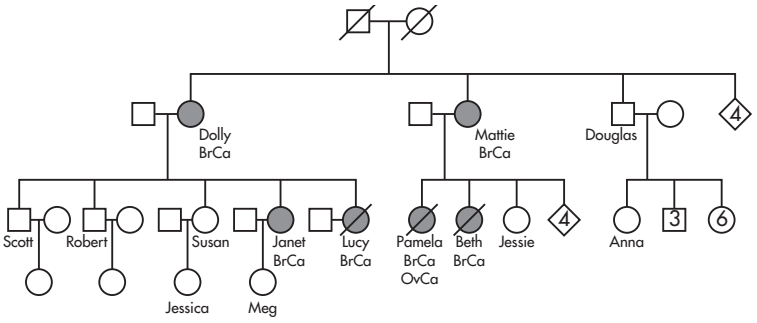
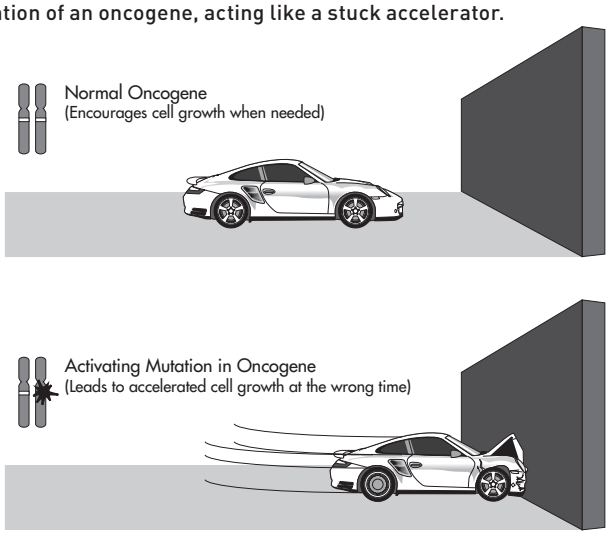


Figure 4.1: The pedigree of the Michigan family, showing many women affected with breast and ovarian cancer. Squares denote males, circles are females.

(A) Activation of an oncogene, acting like a stuck accelerator.



(B) Inactivation of a tumor suppressor gene, resulting in failure of the brakes.

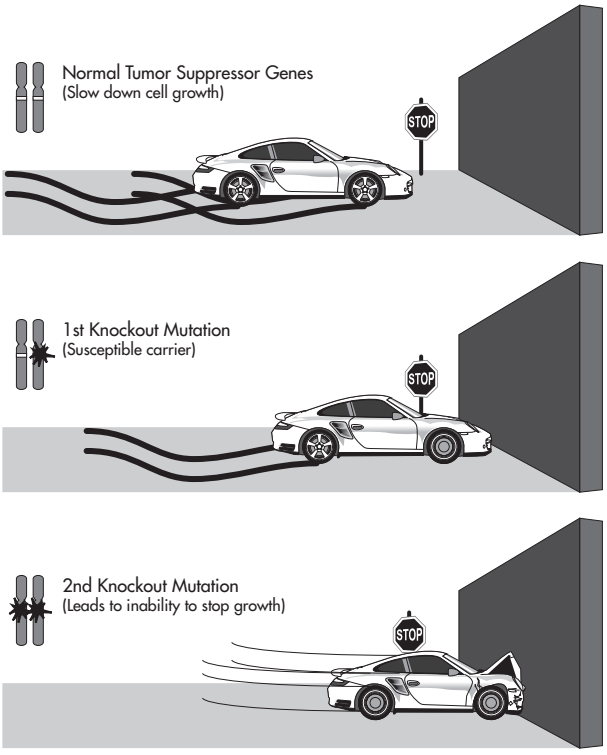


Figure 4.2: Mutations in specific genes can cause cells to grow out of control.

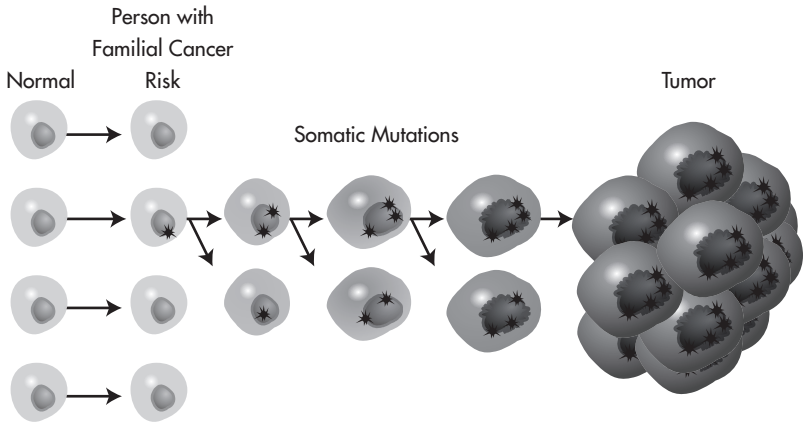


Figure 4.3: Cancer is a multistep process, requiring an accumulation of mutations before a frank malignancy occurs.

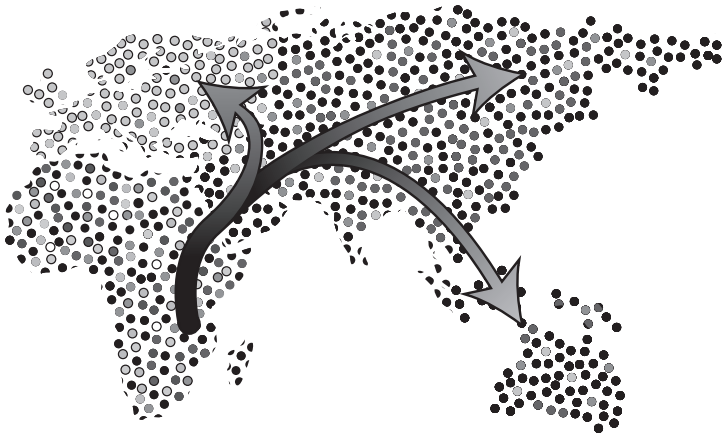


Figure 5.1: Schematic of the flow of human genetic variation out of Africa over the last 30,000 years. The greatest degree of variation still exists in Africa, with subsets of that having been carried by groups that populated Europe and Asia.

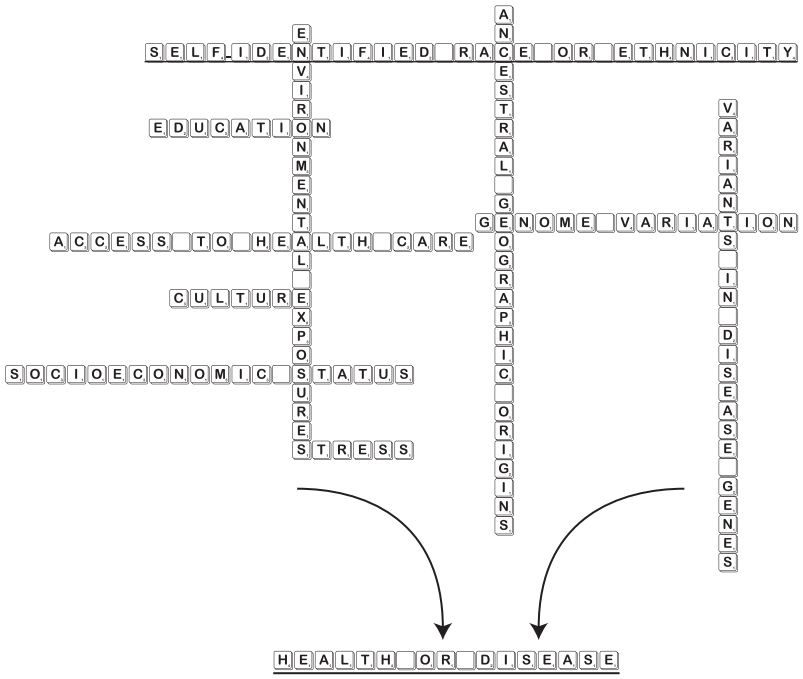


Figure 5.2: A graphic depiction of the complex connections between self-identified race and health.

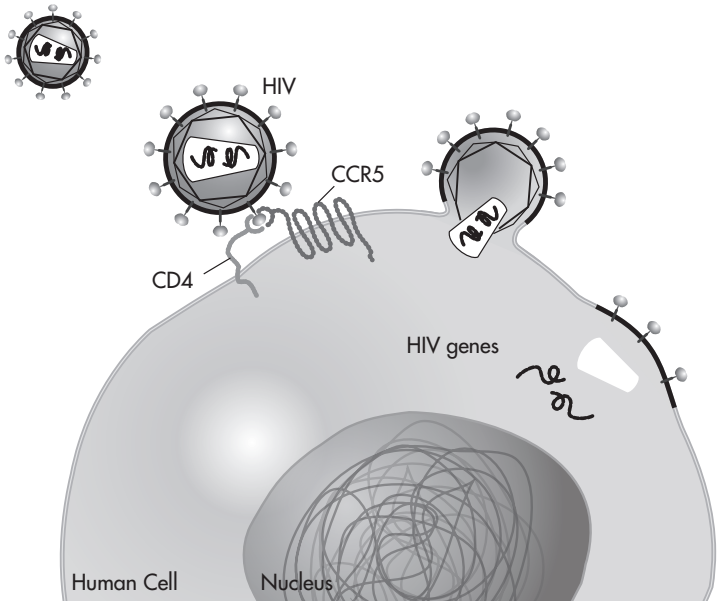


Figure 6.1: The diabolically clever AIDS virus (HIV) docks to the normal immune cell surface proteins CD4 and CCR5, and then gains access to the cell. It goes on to make many copies of itself, destroying the cell in the process. For an eye-catching animated simulation of these steps, see www.boehringer-ingelheim.com/hiv/art/art_videos.htm.

Figure 7.1: Enzymatic steps involved in the metabolism of alcohol.

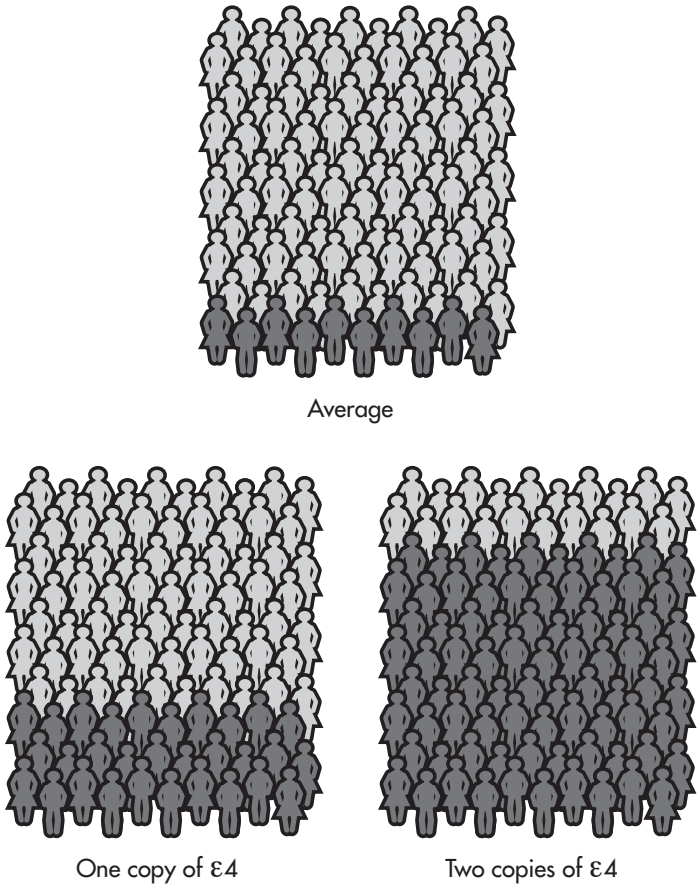


Figure 8.1: Risk of Alzheimer's disease by age 85, depending on *APOE* genotype.

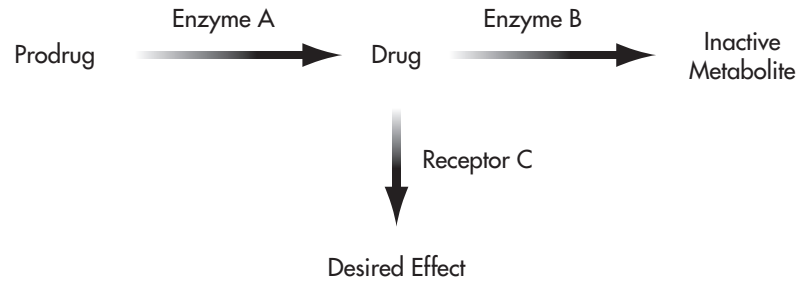


Figure 9.1: The potency of a drug can depend on enzymes needed to activate it (A) or degrade it (B), or on the way in which it binds to its receptor (C).

Table 9.1—Examples of Commonly Prescribed Drugs

Generic Name	**Trade Name**	**Purpose or Target**
atorvastatin	Lipitor	Lower cholesterol
clopidogrel	Plavix	Avoid clotting
esomeprazale	Nexium	Reflux
imatinib	Gleevec	Leukemia
levofloxacin	Levaquin	Infection
paroxetine	Paxil	Anxiety, depression
sildenafil	Viagra	Erectile dysfunction
trastuzumab	Herceptin	Breast cancer

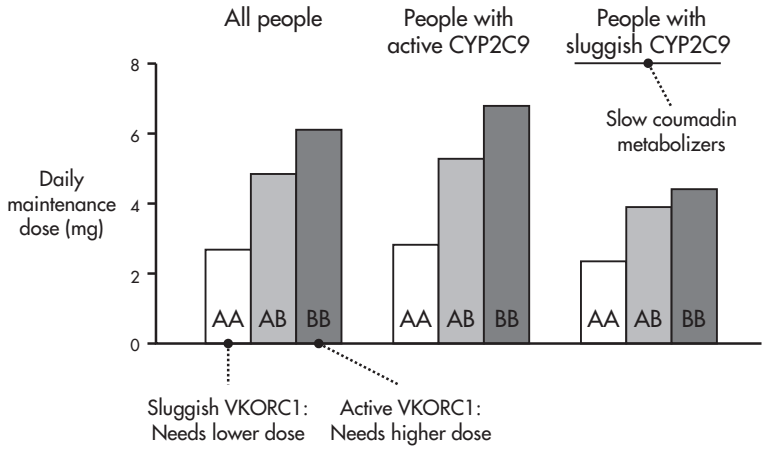


Figure 9.2: Variants in the *CYP2C9* and *VKORC1* genes play a substantial role in determining the optimum maintenance dose of coumadin. The *VKORC1* gene has two different forms: the A form is less active, the B form more active. Individuals are either AA, AB, or BB. (Data taken from M. Rieder, et al. *New England Journal of Medicine* 352 [2005]: 2285–93.)

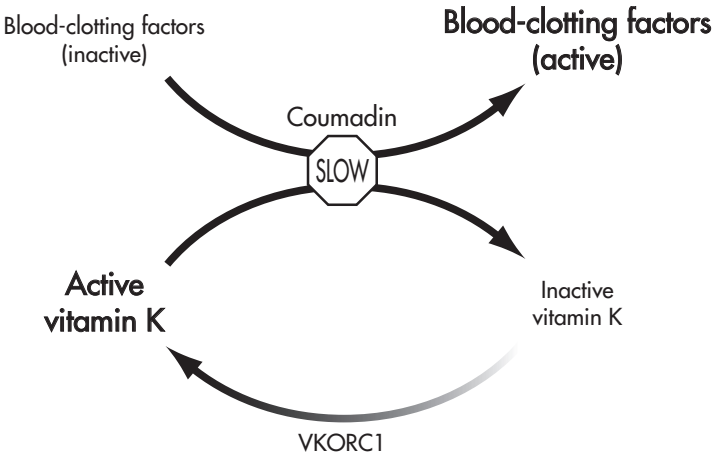


Figure 9.3: Vitamin K is critical for activating a number of blood-clotting factors; coumadin blocks that step. But vitamin K itself needs to be reactivated after each use, and that is carried out by the enzyme VKORC1. Individuals with sluggish VKORC1 will thus need less coumadin to achieve a particular level of blood thinning.

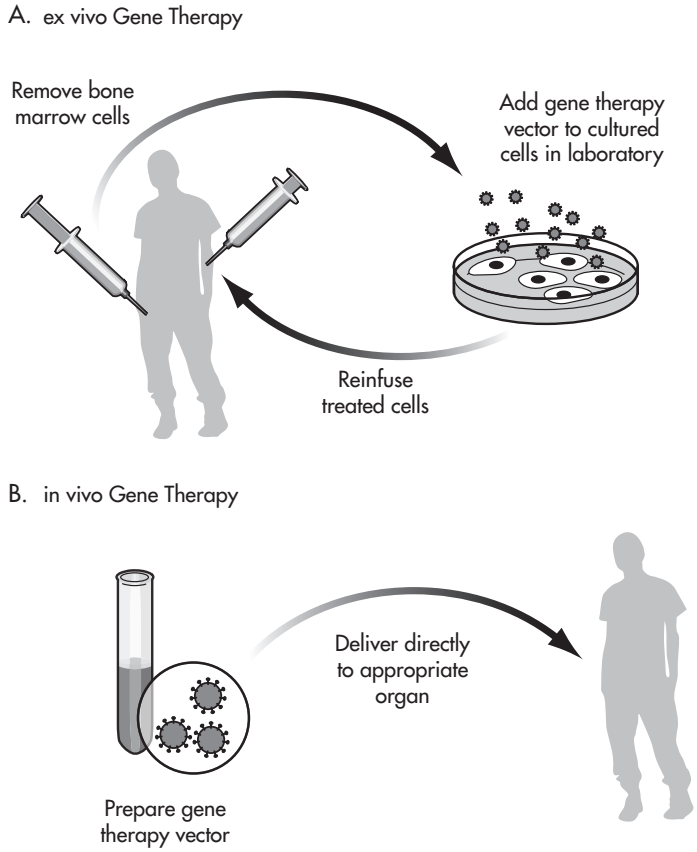


Figure 10.1: *Ex vivo* and *in vivo* approaches to gene therapy.

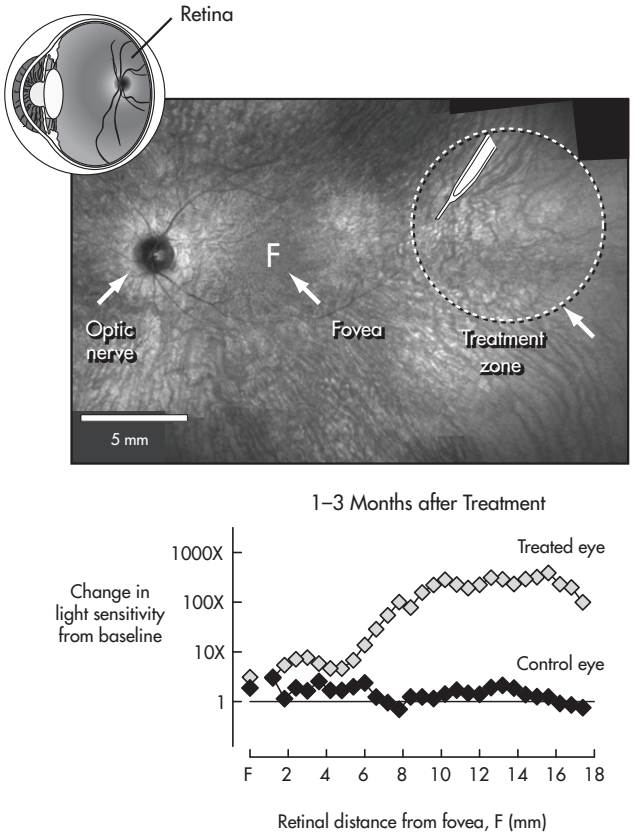


Figure 10.2: Dramatic improvement in Dale Turner's vision is apparent after gene therapy for his visual disorder. The area of the retina treated is marked by the dashed circle in the photograph of the back of Dale's eye. The graph shows a more than hundredfold improvement in visual acuity in the treated eye.

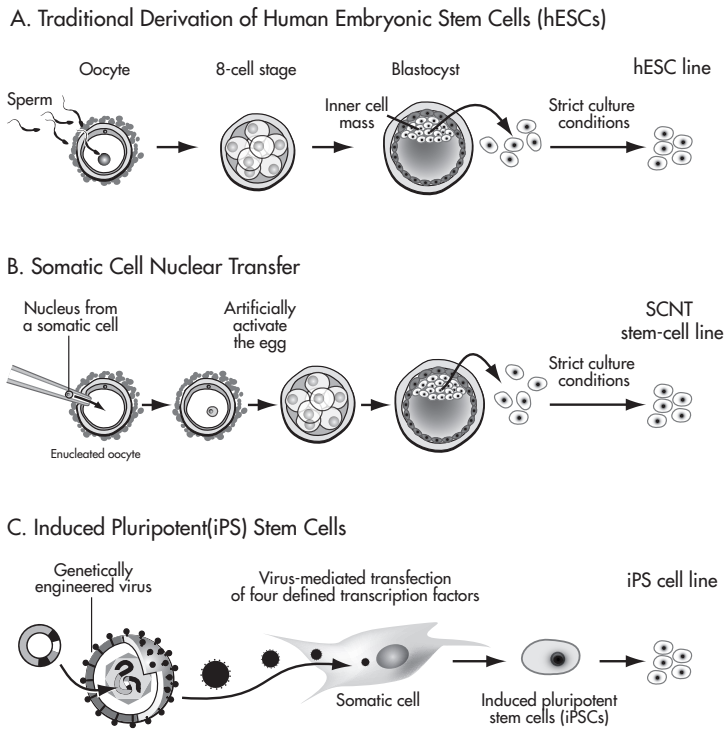


Figure 10.3: Three different types of human stem cells, created in very different ways.

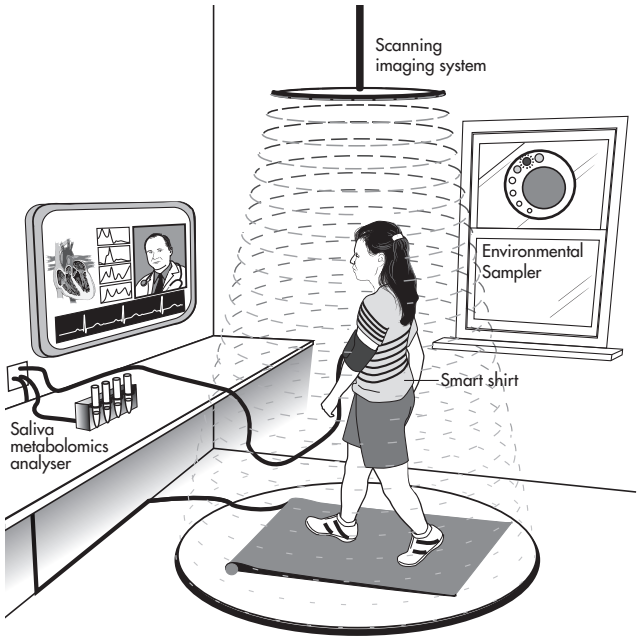


Figure 10.4: The home health station of the future, equipped with a monitor for recording body parameters; a saliva cup to monitor body metabolites and the oral microbiome; an exercise station that allows imaging of the person at rest and during exercise; and an environmental sampler for the indoor and outdoor air.

Glossary

(Excerpted fom the public "Talking Glossary of Genetic Tems,"
available from the National Human Genome Research Institute at
http://genome.gov/glossary.cfm.)

ACGT: Refers to the four types of bases in a DNA molecule. The letters are abbreviations for the chemical names: adenine, cytosine, guanine, and thymine. A DNA molecule consists of two strands wound around each other. The strands are held together by bonds between the bases. A pairs with T, and C pairs with G. The sequence of bases in a portion of a DNA molecule, called a gene, carries the instructions needed to assemble a protein.

Allele: One of two or more versions of a gene. An individual inherits two alleles for each gene: one allele from each parent. If the two alleles are the same, the individual is said to be homozygous for that gene. If the alleles are different, then the individual is heterozygous for that gene. Although the term "allele" was originally used to describe variation among genes, today it also can refer to variation among non-coding DNA sequences.

Amino Acids: A set of 20 different small molecules used to build proteins. Proteins consist of one or more chains of amino acids called polypeptides. The sequence of the amino acid chain causes the polypeptide to fold into a shape that is biologically active. The amino acid sequences of proteins are encoded in the genes.

Base Pair: Two chemical bases bonded to each other, forming a "rung" of the DNA "ladder." The DNA molecule consists of two strands that wind around each other like a twisted ladder. Each strand has a backbone made of alternating sugar (deoxyribose) and phosphate groups. Attached to each sugar is one of four bases A, T, C, or G. The two strands are held together by bonds between the bases (A forms a base pair with T, and C forms a base pair with G).

***BRCA1*/*BRCA2*:** The first two genes found to be associated with inherited forms of breast cancer. In healthy people, both genes play roles as tumor suppressors—that is, they help regulate cell division. When these genes are rendered inactive owing to mutation, uncontrolled cell growth results, leading to the cancer. Women with mutations in either gene have a much higher risk for developing breast and ovarian cancer than women with normal versions of the genes.

Carrier: An individual who carries and may pass on a genetic mutation associated with a disease but does not display symptoms of that disease. Carriers are associated with diseases inherited as recessive traits. In order to have the disease, an individual must have inherited mutated alleles from both parents. An individual having one normal allele and one mutated allele is a carrier and does not have the disease. Two carriers may produce children with the disease.

Carrier Screening: A type of genetic screening performed on people who display no symptoms of a recessive genetic disorder but may be at risk for passing it on to their children. A carrier for a genetic disorder has inherited one normal and one abnormal allele for a gene associated with the disorder. A child must inherit two abnormal alleles in order for symptoms to appear.

Chromosome: An organized package of DNA found in the nucleus of the cell. Different organisms have different numbers of chromosomes. Humans have 23 pairs of chromosomes: 22 pairs of numbered chromosomes called autosomes, and one pair of sex chromosomes (X and Y). Each parent contributes one chromosome to each pair so that offspring get half of their chromosomes from the mother and half from the father.

Cloning: A process for making identical copies of an organism, cell, or DNA sequence. Molecular cloning is a process by which scientists amplify a desired DNA sequence. The sequence of interest is isolated, inserted into another DNA molecule, called a vector, and introduced into a suitable host cell. Each time the host cell divides, it replicates the foreign DNA sequence along with its own DNA. Cloning also can refer to asexual reproduction.

Cytoplasm: The gelatinous liquid that fills the inside of a cell. It is composed of water, salts, and various organic molecules. Some intracellular organelles, such as the nucleus and mitochondria, are enclosed by membranes that separate them from the cytoplasm.

Deletion: A type of mutation involving the loss of genetic material. A deletion mutation can be small, involving a single missing DNA base pair, or large, involving a piece of a chromosome.

Diploid: See Haploid.

DNA (deoxyribonucleic acid): The chemical name for the molecule that carries genetic instructions in all living things. The DNA molecule consists of two strands that wind around each other in a double helix. Each strand has a backbone made of alternating sugar (deoxyribose) and phosphate groups. Attached to each sugar is one of four bases: A, T, C, or G. The two strands are held together by bonds between the bases (A bonds with T, and C bonds with G). The sequence of the bases along the backbones serves as instructions for assembling protein and RNA molecules.

DNA sequencing: A laboratory technique for determining the exact sequence of bases (A, T, C, and G) in a DNA molecule. The DNA base sequence carries the information the cell needs to assemble RNA and protein molecules. Therefore, information about DNA sequence is important to scientists investigating the functions of genes. The technology of DNA sequencing was made faster and less expensive as a part of the Human Genome Project.

Enzyme: A biological catalyst. An enzyme is almost always a protein. It speeds up the rate of a specific chemical reaction in the cell. The enzyme is not destroyed during the reaction and is used over and over. A cell contains thousands of different types of enzyme molecules, each specific for a different chemical reaction.

Exon: A portion of a gene that codes for amino acids. In the cells of plants and animals, most gene sequences are broken up by one or more DNA sequences called introns. The parts of the gene sequence that are expressed in the protein are called exons (because they are expressed), whereas the parts of the gene sequence that are not expressed in the protein are called introns (because they come in between the exons).

Founder effect: Refers to the reduction in genetic variation that results when a small subset of a large population is used to establish a new colony. The new population may be different from the original population, in terms of both its genotypes and its phenotypes.

Frameshift mutation: A type of mutation involving the insertion or deletion of a DNA sequence, where the number of base pairs is not divisible by three. "Divisible by three" is important because the cell reads a gene in groups of three bases. Each group of three bases corresponds to one of the 20 different amino acids used to build a protein. If a mutation disrupts this reading frame, then the entire DNA sequence following the mutation will be read incorrectly.

Fraternal twins: see Identical twins.

Gene: The basic physical unit of inheritance. Genes are passed from parents to offspring and contain the information needed to specify traits. Genes are arranged, one after another, on structures called chromosomes. A chromosome contains a single long DNA molecule, only a portion of which corresponds to a single gene. Humans have approximately 20,000 protein-coding genes arranged on their chromosomes.

Gene mapping: The process of establishing the locations of genes on the chromosomes. Early gene maps used linkage analysis. The closer two genes are to each other on the chromosome, the more likely it is that they will be inherited together. By following inheritance patterns, the relative positions of genes can be determined. More recently, scientists have used recombinant-DNA techniques to establish the actual physical locations of genes on the chromosomes.

Gene therapy: An experimental technique for treating disease by altering the patient's genetic material. Most often, gene therapy works by introducing a healthy copy of a defective gene into the patient's cells.

Genetic drift: A mechanism of evolution. It refers to random fluctuations in the frequencies of alleles from generation to generation due to chance events. Genetic drift can cause traits to either become prominent in or to disappear from a population. The effects of genetic drift are most pronounced in small populations.

Genetic engineering: The process of using recombinant-DNA technology to alter the genetic makeup of an organism. Traditionally, humans have manipulated genomes indirectly by controlling breeding and selecting offspring with desired traits. Genetic engineering involves the direct manipulation of one or more genes. Most often, a gene from another species is added to an organism's genome to give it a desired phenotype.

Genetic marker: A DNA sequence with a known physical location on a chromosome. Genetic markers can help link an inherited disease with the responsible gene. Segments of DNA close to each other on a chromosome tend to be inherited together. Genetic markers are used to track the inheritance of a nearby gene that has not yet been identified, but whose approximate location is known. The genetic marker itself may be a part of a gene or may have no known function.

Genetic screening: The process of testing a population for a genetic disease in order to identify a subgroup of people who either have the disease or have the potential to pass it on to their offspring.

Genetic testing: The use of a laboratory test to look for genetic variations associated with a disease. The results of a genetic test can be used to confirm or rule out a suspected genetic disease or to determine the likelihood that a person will pass on a mutation to his or her offspring. Genetic testing may be performed prenatally or after birth. Ideally, a person who undergoes a genetic test discusses the meaning of the test and its results with a genetic counselor.

Genome: The entire set of genetic instructions found in a cell. In humans, the genome consists of 23 pairs of chromosomes found in the nucleus as well as a small chromosome found in the cells' mitochondria. These chromosomes, taken together, contain approximately 3.1 billion bases of DNA sequence.

Haploid: Refers to a cell or an organism having a single set of chromosomes. Organisms that reproduce asexually are said to be haploid. Sexually reproducing organisms are said to be diploid (having two sets of chromosomes: one from each parent). Only their egg and sperm cells are haploid.

Haplotype: A set of DNA variations (or polymorphisms) that tend to be inherited together. A haplotype can be a combination of alleles or a set of single nucleotide polymorphisms (SNPs) found on the same chromosome. Information about haplotypes is collected by the International HapMap Project and is used to investigate the influence of genes on disease.

HapMap: An international project that seeks to relate variations in human DNA sequences with genes associated with health. A haplotype is a set of DNA variations (or polymorphisms) that tend to be inherited together. A haplotype can be a combination of alleles or a set of single nucleotide polymorphisms (SNPs) found on the same chromosome. The HapMap describes common patterns of genetic variation among people.

Identical twins: Also called monozygotic twins. They result from the fertilization of a single egg that splits very soon afterward. Identical twins share all their genes and are always of the same sex. In contrast, fraternal twins result from the fertilization of two separate eggs during the same pregnancy. They share half of their genes, just like any other siblings. Fraternal twins may be of the same or different sexes.

Intron: A portion of a gene that does not code for amino acids. In the cells of plants and animals, most gene sequences are broken up by one or more introns. The parts of the gene sequence that are expressed in the protein are called exons (because they are expressed), whereas the parts of the gene sequence that are not expressed in the protein are called introns (because they come in between the exons).

Karyotype: An individual's collection of chromosomes. The term also refers to a laboratory technique that produces a photograph of an individual's chromosomes. The karyotype is used to look for abnormal numbers or structures of chromosomes.

Messenger RNA (mRNA): A single-strand RNA molecule that is complementary to one of the DNA strands of a gene. The mRNA is an RNA version of the gene that leaves the cell nucleus and moves to the cytoplasm where proteins are made. During protein synthesis, an organelle called a ribosome moves along the mRNA, reads its base sequence, and uses the genetic code to translate each 3-base triplet into its corresponding amino acid.

Mutation: A change in a DNA sequence. Mutations can result from DNA copying mistakes made during cell division, from exposure to ionizing radiation, exposure to chemicals called mutagens, or infection by viruses. Germ line mutations occur in the eggs and sperm and can be passed on to offspring, whereas somatic mutations occur in body cells and are not passed on.

Non-coding DNA: DNA sequences that do not code for amino acids. Most non-coding DNA lies between genes on the chromosome and is of unknown function. Other non-coding DNA, called introns, is found within genes. Some non-coding DNA plays a role in the regulation of gene expression.

Nucleic acid: An important class of macromolecules found in all cells and viruses. The functions of nucleic acids have to do with the storage and expression of genetic information. Deoxyribonucleic acid (DNA) encodes the information the cell needs to make proteins. A related type of nucleic acid, ribonucleic acid (RNA), carries information to the cytoplasm to participate in protein synthesis.

Oncogene: A mutated gene that contributes to the development of a cancer. In their normal, unmutated state, onocgenes are called proto-oncogenes, and they play roles in the regulation of cell division. Oncogenes work like putting your foot down on the accelerator of a car, pushing a cell to divide.

Pharmacogenomics: A branch of pharmacology that is concerned with using data about DNA and amino acid sequence to inform drug development and testing. An important application of pharmacogenomics is correlating individual genetic variation with drug responses.

Polygenic trait: A trait whose phenotype is influenced by more than one gene. Traits that display a continuous distribution, such as height or skin color, are polygenic. The inheritance of polygenic traits does not show the phenotypic ratios characteristic

of Mendelian inheritance, although each of the genes contributing to the trait is inherited as described by Mendel. Many polygenic traits are also influenced by the environment and are called multifactorial.

Protein: An important class of molecules found in all living cells. A protein is composed of one or more long chains of amino acids; the sequence is a translation of the DNA sequence of the gene that encodes that protein. Proteins play a variety of roles in the cell, including structural (cytoskeleton), mechanical (muscle), biochemical (enzymes), and cell signaling (hormones). Proteins are also an essential part of the diet.

Race: In common parlance, a group of people who share a set of visible characteristics such as skin color, facial features, and hair texture, as well as a sense of identity. Although these visible traits are influenced by genes, the vast majority of genetic variation exists within racial groups and not between them. For this reason, many scientists believe that race is more accurately described as a social construct, not a biological one.

Recessive: Refers to a relationship between two versions of a gene. Individuals receive one version of a gene, called an allele, from each parent. In the case of a recessive genetic disorder, an individual must inherit two copies of a mutated allele in order for the disease to be present.

Recombinant DNA: A technology that uses enzymes to cut and paste together DNA sequences of interest. The recombined DNA sequence can be placed into vehicles called vectors that ferry the DNA into a suitable host cell, where it can be copied or expressed.

Retrovirus: A type of virus that uses RNA as its genetic material. When a retrovirus infects a cell, it makes a DNA copy of its genome that is inserted into the DNA of the host cell. There are various different retroviruses that cause human diseases, including AIDS.

RNA (ribonucleic acid): A molecule similar to DNA. Unlike DNA, RNA is a single strand. An RNA strand has a backbone made of alternating sugar (ribose) and phosphate groups. Attached to each sugar is one of four bases: A, U, C, or G. Different types of RNA exist in the cell: messenger RNA, ribosomal RNA, and transfer RNA. More recently, some small RNAs have been found to be involved in regulating gene expression.

Stem cell: A type of cell with the potential to form many of the different cell types found in the body. When stem cells divide, they can form more stem cells, or other cells that perform specialized functions. Embryonic stem cells are pluripotent and have the potential to form a complete individual, whereas adult stem cells are multipotent and can form only certain types of specialized cells. Stem cells continue to divide as long as the individual remains alive.

Telomere: An end of a chromosome. Telomeres are made of repetitive sequences of non-coding DNA that protect the chromosome from damage. Each time a cell divides, the telomeres become shorter unless a repair enzyme called telomerase is present. Eventually, the telomeres become so short that the cell can no longer divide.

Transgenic: Having one or more DNA sequences from another species, introduced by artificial means. Animals usually are made transgenic by having a small sequence of foreign DNA injected into a fertilized egg or developing embryo. Transgenic plants can be made by introducing foreign DNA into a variety of different tissues.

Tumor suppressor gene: A gene whose normal function is to direct the production of a protein that is part of the system that slow down cell division. The tumor suppressor protein plays a role in keeping cell division in check. When mutated, a tumor suppressor gene is unable to do its job. As a result, uncontrolled cell growth may occur, contributing to the development of a cancer.

Variant: A spelling difference in DNA.

Vector: Any vehicle (often a virus or a plasmid) that is used to ferry a desired DNA sequence into a host cell as part of a molecular cloning procedure. Depending on the purpose of the cloning procedure, the vector may assist in multiplying, isolating, or expressing the foreign DNA insert.

Virus: An infectious agent that occupies a place near the boundary between the living and the nonliving. A virus is a particle much smaller than a bacterial cell. It consists of a small genome of either DNA or RNA surrounded by a protein coat. Viruses enter host cells and hijack the enzymes and materials of the host cells to make more copies of themselves. Viruses cause a wide variety of diseases in plants and animals, including AIDS.

X chromosome: One of two sex chromosomes. Humans and most mammals have two sex chromosomes: the X and the Y. Females have two X chromosomes in their cells; males have an X and a Y chromosome in their cells. Egg cells all contain an X chromosome; sperm cells may contain an X or a Y chromosome. This arrangement means that during fertilization, it is the male that determines the sex of the offspring.

X-linked, or sex-linked: Term used for a trait whose gene is located on the X chromosome. Humans, and most mammals, have two sex chromosomes: the X and the Y. In a sex-linked disease, it is usually males that are affected because they have a single copy of the X chromosome that carries the mutation. In females, the effect of the mutation may be masked by the second, healthy copy of the X chromosome.

Y chromosome: One of two sex chromosomes. Humans and most mammals have two sex chromosomes: the X and the Y. Females have two X chromosomes in their cells; males have an X and a Y chromosome in their cells. Egg cells all contain an X chromosome; sperm cells may contain an X or a Y chromosome. This arrangement means that during fertilization, it is the male that determines the sex of the offspring.

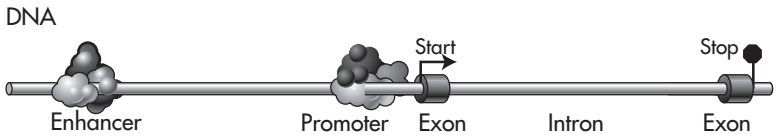


Figure B.1: A simplified cartoon of gene structure and function. The gene, made up of DNA, is transcribed into RNA beginning at a "start" signal. The DNA sequences just upstream of that, making up the "promoter," serve as recognition sites for RNA polymerase and a variety of other transcription factors, signaling the cell that this gene should be actively transcribed. Other DNA "enhancer" signals located some distance away often aid in this process. The initial RNA copy extends across the entire gene, but the introns are subsequently spliced out in the process of RNA maturation.

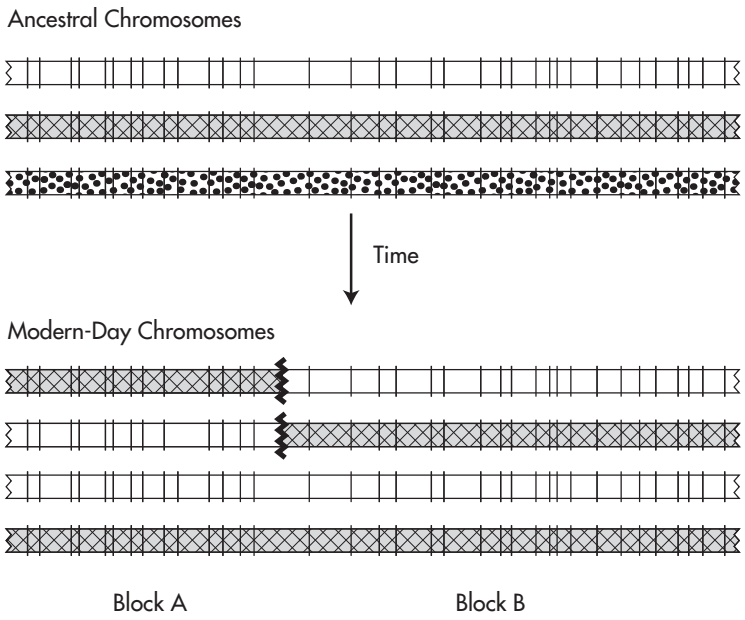


Figure B.2: The SNPs in the human genome tend to travel in neighborhoods, or "blocks." All humans are derived from a small group of about 10,000 ancestors. Three homologous segments of chromosomes that were present in these common ancestors are shown at the top; each vertical tick mark represents a SNP. Over the last 5,000 generations, the third ancestral type (stippled) was lost, but the other two were transmitted to modern times. In some copies (the bottom two), these segments appear identical to the ancestral versions, but in other copies a "hot spot" of recombination has allowed a crossover to generate two new chromosomal types. The SNPs within blocks A and B will remain tightly correlated with each other, but the correlation between SNPs in block A and block B will be limited by the presence of such crossovers. The HapMap project defined the boundaries of these blocks for selected European, Asian, and African populations.

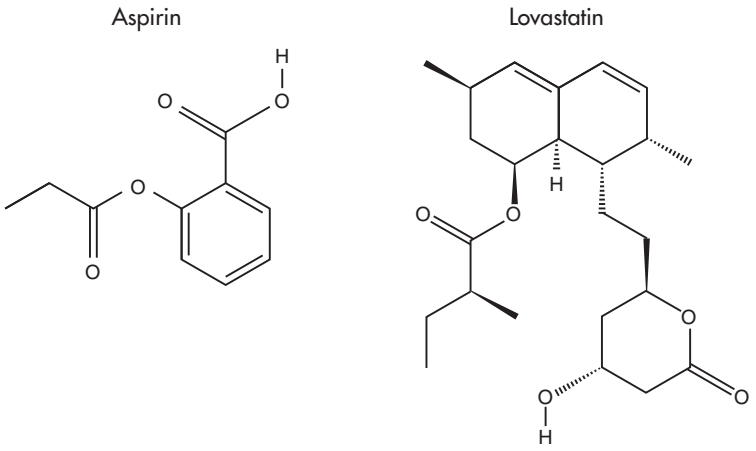


Figure D.1: The molecular structures of two common drugs: aspirin and lovastatin. These standard chemical drawings involve some shorthand conventions that are familiar to chemists—a carbon atom is inferred to be located at all the apexes of each structure, hydrogen atoms are left out in most instances, single lines indicate a chemical bond, and double lines indicate a double bond.

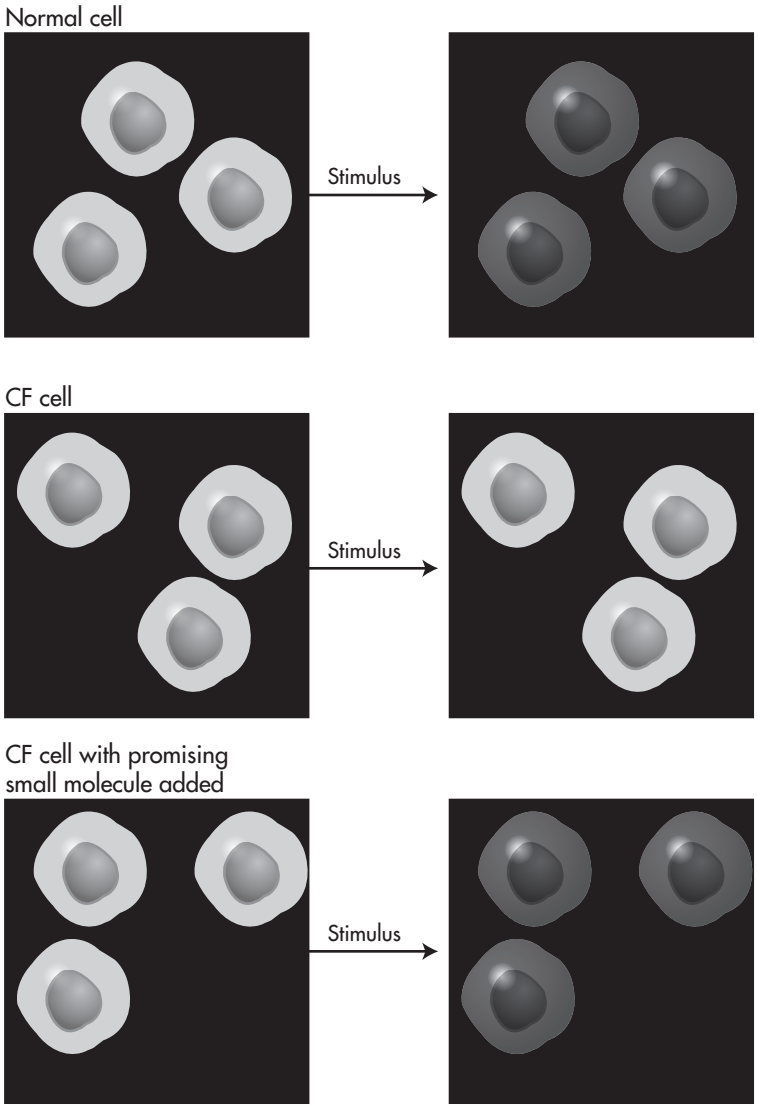


Figure D.2: A fluorescent assay for compounds that might be beneficial in cystic fibrosis (CF). To begin with, cells are loaded up with a fluorescent dye that senses the presence of chloride ions. Then a stimulus is delivered that normally opens the CFTR chloride channel, causing chloride to flow out, and reducing the fluorescent signal inside the cell (top panel). Lacking functional CFTR, a CF cell will remain brightly fluorescent even after the stimulus (middle panel). If a small molecule capable of activating the channel is present, however, the fluorescent signal will fade from the cell after the stimulus (bottom panel). Millions of compounds were tested to find a few that had this property.

Services Provided by Direct-to-Consumer Genetics Companies Offering Broad-Spectrum Testing

(as of May 2009)

DISEASES

Condition	23andMe[1]	deCODE	Navigenics
Abdominal aortic aneurysm	(+)	+	+
Alzheimer's disease		+	+
Asthma	(+)	+	
Atrial fibrillation	(+)	+	+
Basal cell carcinoma	(+)	+	
Bladder cancer	(+)	+	
Celiac disease	+	+	+
Chronic lymphocytic leukemia	(+)	+	
Colorectal cancer	(+)	+	+
Crohn's disease	+	+	+
Essential tremor	(+)	+	
Exfoliation glaucoma	(+)	+	+
Gallstones	(+)	+	
Gout	(+)	+	
Graves' disease			+
Heart attack	(+)	+	+
Intracranial aneurysm	(+)	+	+
Lung cancer	(+)	+	+
Lupus	(+)		+
Macular degeneration	+	+	+
Melanoma	(+)		+
Multiple sclerosis	(+)		+
Obesity	(+)	+	+
Osteoarthritis			+
Parkinson's disease	+		
Peripheral arterial disease	(+)	+	
Prostate cancer	+	+	+
Psoriasis	+	+	+
Restless legs syndrome	(+)	+	+
Rheumatoid arthritis	+	+	+

Sarcoidosis			+
Stomach cancer	(+)		+
Thyroid cancer		+	
Type 1 diabetes	+	+	
Type 2 diabetes	+	+	+
Ulcerative colitis	(+)	+	
Venous thromboembolism	+	+	+

TRAITS

Trait	23andMe[1]	deCODE	Navigenics
Alcohol flush reaction	+	+	
Ancestry	+	+	
Bitter taste perception	+	+	
Earwax type	+		
Eye color	+		
HIV/AIDS resistance (CCR5)	+		
Lactose intolerance	+	+	+
Malaria resistance (Duffy)	+		
Male pattern baldness	(+)	+	
Muscle performance	+		
Nicotine dependence	(+)	+	
Non-ABO blood groups	+		
Norovirus resistance	+		

DRUG SENSITIVITY

Drug	23andMe[2]	deCODE	Navigenics
Clopidogrel (Plavix)	+		
Coumadin (Warfarin)	+	+	

CARRIER STATE

Disease	Carrier at Risk?	23andMe	deCODE	Navigenics
Alpha–1-antitrypsin deficiency	Only smokers	+		
BRCA1/*BRCA2*	Yes[3]	Selected[4]		
Bloom's syndrome	No	+		
Cystic fibrosis	No	ΔF508[5]		
G6PD deficiency	Yes[6]	+		
Glycogen storage disease Ia	No	+		
Hemochromatosis	No	+	+[7]	
Sickle-cell Anemia	No	+		

1. For 23andMe, conditions and traits marked (+) are classified as "Research Reports": that is, the company believes no consensus about the significance of a genetic test result has been reached yet. DeCODE does not make this distinction. In addition to the entries shown in this table, 23andMe reports on 35 conditions and 18 traits in the "Research Reports" category, for which neither deCODE nor Navigenics reports results.
2. 23andMe includes three additional predictions of drug sensitivity in the "Research Reports" category, for which deCODE does not report results.
3. Women with *BRCA1/2* mutations are at high risk for breast and ovarian cancer; men are at slightly increased risk for prostate, pancreatic, and male breast cancer (see Chapter 3).
4. Test only detects three *BRCA1/2* mutations that are more common in Ashkenazi Jews. A negative test therefore does not rule out the possibility of other mutations in *BRCA1/2*.
5. Test only detects the ΔF508 mutation in *CFTR* (see Chapter 2), so a negative test does not rule out the possibility of being a CF carrier.
6. Generally, only male G6PD carriers are at risk for hemolytic anemia after fava beans or certain drugs, since the gene is on the X chromosome.
7. deCODE detects hemochromatosis carriers, but doesn't report them as such.