Chapter 9
DNA

Blueprint for the Future

There are some advantages of having a large population. For example, if one person in a billion is a truly exceptional scientific genius, it means that there are six of them in a world of 7 billion people and somewhere out there another one is being born every twelve to fifteen years. These people are the ones that have great insights that change the world for everyone else and now there are enough of them alive at any one time to work together or to compete for new discoveries. As the population of the world increases, so does the number of exceptionally brilliant scientists and so does the pace of discovery.

One of the areas that is benefiting from collaboration and new scientific discoveries is understanding our own biology. If you are a college freshman, more has been discovered about how our bodies work since you were born than was discovered in all of previous history and we are just getting started. In this unit, you will learn about these discoveries and how they are turning into technologies that affect your life and your future.

Why Do I Need to Know This?

Scientific knowledge and technological tools that can manipulate the basic blueprints of life present great opportunities and difficult choices that previous generations did not have. To deal with those choices when they come up, you need to think about them now to give yourself time to decide what to do. Some of the opportunities described in this chapter deal with feeding the two billion additional people that will be born in the next thirty years but there are risks to consider and this chapter will give you some background to make those choices. The areas described in this chapter are likely to be growth areas in the future in which you could find employment if you are well prepared in the life sciences and computer technology.

1 DNA—the Blueprints of Life

Learning Objectives

1. Describe the structure of a DNA molecule. [9.1.1]
2. Identify the molecules that comprise the base pairs and their possible combinations. [9.1.2]
3. Identify the number of amino acids, their function, and where people obtain them. [9.1.3]

4. Identify the role of a codon and how it relates to a byte of computer code. [9.1.4]
5. Identify the relationship between codons and genes and the function of genes. [9.1.5]
6. Identify the function of RNA. [9.1.6]
7. Identify the characteristics of human DNA including its width and the approximate number of genes. [9.1.7]
8. Describe how DNA can be used to identify individuals. [9.1.8]

This topic can be complicated and understanding can be lost in a flurry of scientific terms. The purpose of this section is to provide a framework of understanding. The student is encouraged to further their understanding of DNA and how it can be adapted for various purposes by taking classes in biology.

Structure of DNA

The structure of the strands of material that make up the chromosomes was not well understood until the mid-1950s when it was described as a double-helix. This was a milestone in understanding how chromosomes work. Now we know that chromosomes are made of DNA. DNA is an abbreviation of its chemical name—**D**eoxyribo**n**ucleaic **A**cid (DNA). The DNA molecules are like a computer program that contains the instructions for assembling all the molecules that make up all the cells in the human body. Since this discovery, scientists have been working to understand how this programming works which begins with the structure of the DNA molecule.

The strand of material that makes up a chromosome turned out to be a very long molecule with a complex shape. It is like a ladder that is twisted. The vertical side supports—the "rails" of the ladder—form spirals that wind around each other and the 'steps' of the ladder are made of two pieces that join in the middle, as shown in green in Figure 9.1.

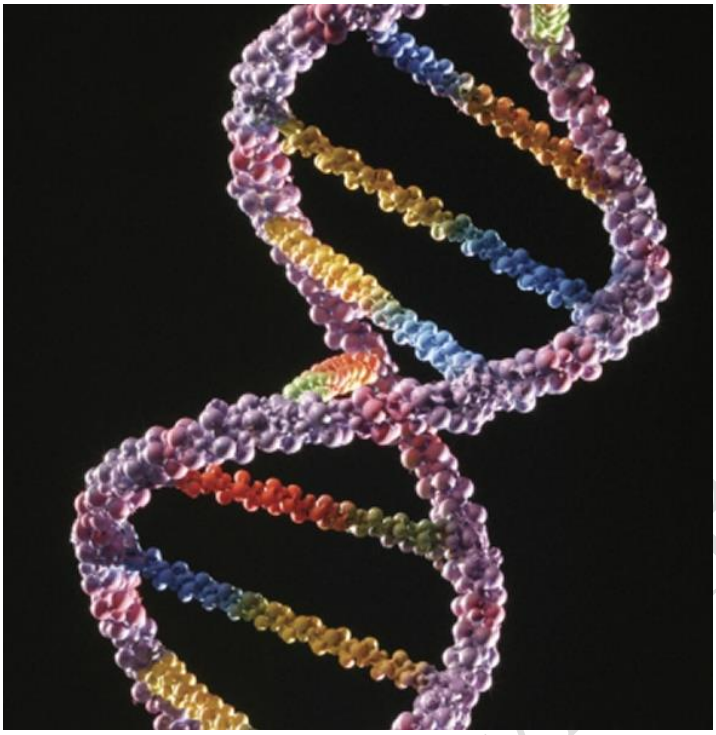

Figure 9.1. Cell nuclei and structure

The sides of the DNA molecule that make up the “rails” of the twisted ladder are made of two molecules that alternate. One of them is a phosphate molecule made of phosphorous and oxygen atoms and the other is a sugar molecule made of four carbon atoms and an oxygen atom in a five sided ring, as shown in Figure 9.2. The diagram of the sugar molecule is simplified. The carbon atoms are at the corners and extra hydrogen atoms aren’t shown. The two molecules connect through a molecule of carbon with two hydrogen atoms.

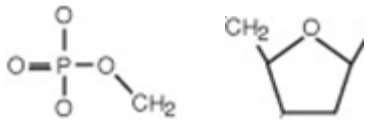

Figure 9.2. Building block molecules for the edges or "rails" of the DNA molecule ladder

These two molecules alternate to make up the “rail” on one side of the ladder. The “rail” on one side begins with the phosphate atom—called the 5 prime end— and ends with the sugar ring—called the 3 prime end. The “rail” on the other side begins with the sugar ring and ends with the phosphate molecule, as shown in Figure 9.3. The difference in the "rails" of the twisted ladder differentiates them and they can be thought of as left and right sides.

The “steps” of the ladder are made of only four different molecules called bases and they always come in pairs called base pairs. They connect between a sugar molecules on each side. One type of “step” is

the combination of cytosine and guanine as shown in Figure 9.3. The dotted lines between the cytosine and guanine indicate weak bonds that come apart easily. The other type of "step" in the DNA "ladder" is the combination of thymine and adenine as shown in Figure 9.3. The dotted lines between the thymine and adenine indicate weak bonds that come apart easily.

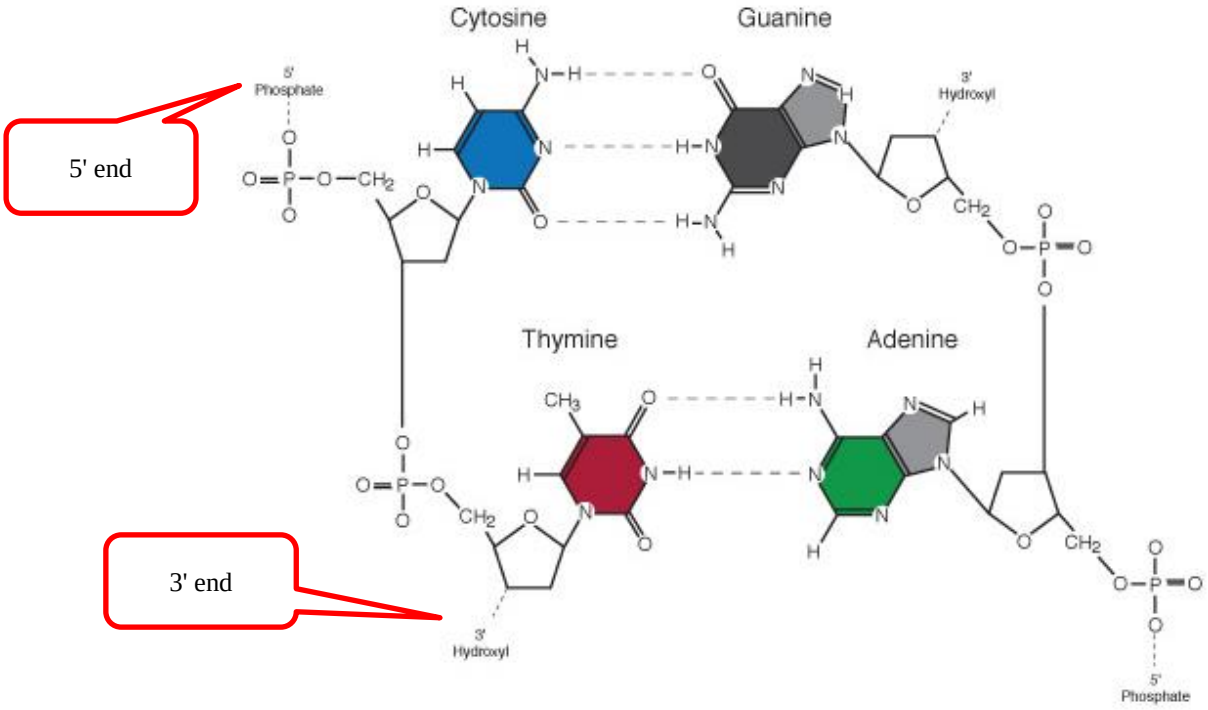

Figure 9.3. Base pairs in the DNA molecule

For convenience, these molecules are just referred to with single letters; G for guanine, C for cytosine, A for adenine, and T for thymine. Guanine and cytosine always pair together and so do adenine and thymine. Each step is represented by a pair of letters such as GC or CG depending on which side the molecules are on. Similarly, steps made of adenine and thymine can be referred to as either AT or TA. This convention allows the complex DNA molecule to be represented by a series of two-letter pairs that indicate the type of step, as shown in Figure 9.4. Scientists call these steps base pairs.

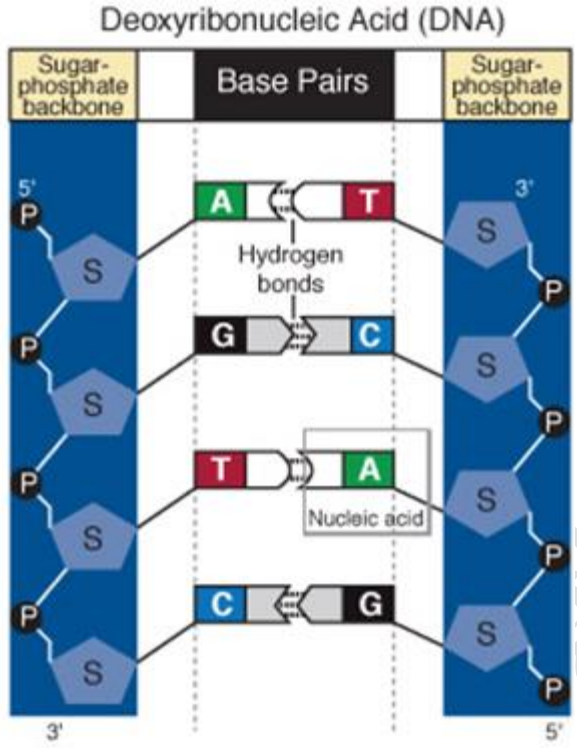

Figure 9.4.Diagram of base pairs in a DNA molecule

Proteins from Amino Acids

To understand the role of DNA we need to know a few more things about cells and how they function. Proteins are complex molecules that can control cell functions or make up the structures of the cells. For example, hemoglobin is a protein that transfers oxygen from the lungs to the cells and insulin is a protein that regulates the use of sugar. There are many different types of proteins. If we continue to use the metaphor of the DNA being like a programmed manufacturing machine, the proteins are the finished products. Proteins are assemblies of 20 basic building block molecules called amino acids listed in Figure 9.5. Humans get amino acids from the food they eat which supplies the raw materials for making proteins.

Amino Acid	Abbreviation
Alanine	Ala
Arginine	Arg
Asparagine	Asn
Aspartic acid	Asp
Cysteine	Cys
Glutamic acid	Glu
Glutamine	Gln
Glycine	Gly
Histidine	His
Isoleucine	Ile
Leucine	Leu

Lysine	Lys
Methionine	Met
Phenylalanine	Phe
Proline	Pro
Serine	Ser
Threonine	Thr
Tryptophan	Trp
Tyrosine	Tyr
Valine	Val

Figure 9.5. Twenty amino acids used as building blocks to make proteins

To create proteins, the DNA molecules need to contain directions for specifying any one of those 20 amino acids plus directions for how many of them are needed and in what order to assemble a protein like insulin or hemoglobin. Subsequent research has found that it takes three of the *steps* of the DNA *ladder* to specify one of the amino acids. Each step of the ladder can be one of four arrangements. If three of these steps are involved, there are 64 possible combinations (4x4x4) which is more than enough to assign each of the twenty amino acids a code using three base pairs. A group of three base pairs that identifies an amino acid is called a codon.

Digital computers employ programming languages that use a numbering system where each digit in a number has only two possible values—zero and one—and the each letter in the alphabet is represented by a group of eight digits called a byte. DNA is like a digital computer's programming language except that it uses a numbering system where each digit has four possible values—AT, TA, CG, GC—and each amino acid is represented by a group of three digits called a codon.

Genes

The DNA molecule is like a computer program that contains instructions for assembling proteins, when to turn the process on or off, and identifiers to mark the beginning and end of the instruction. A section of the DNA molecule as illustrated in Figure 9.6 that contains all of the instructions necessary for assembling a protein is called a gene.

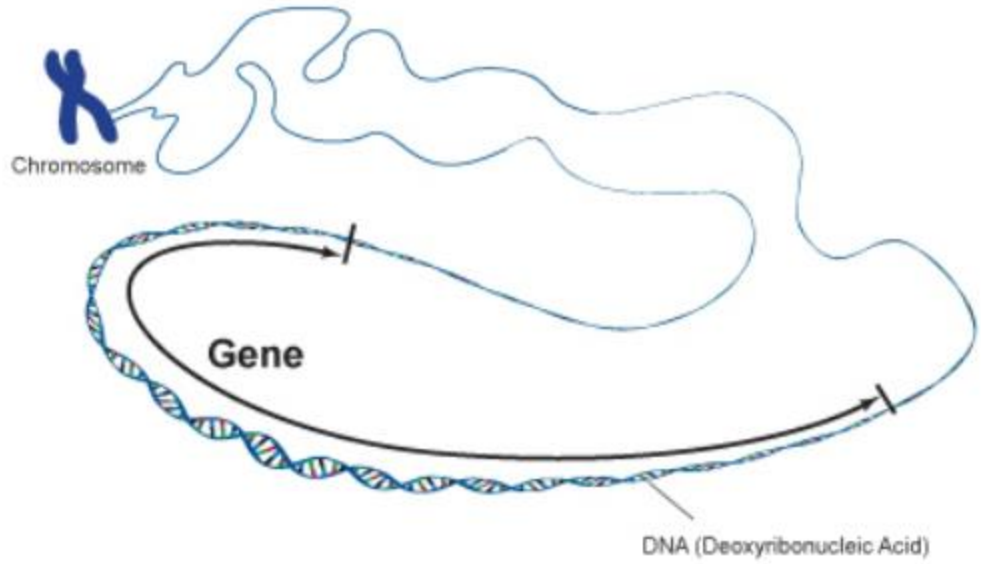

Figure 9.6. Genes contain the programming to create a protein molecule

A typical gene consists of thousands of base pairs. Each cell in our body contains a complete set of genes with all the necessary instructions for creating all of the different types of cells in our bodies. At some point in the development of an embryo, the cells take on specific functions and the genes that contain the code for other functions are turned off. Similarly, when we reach our full size, the genes that control growth reduce their activity to simply replace the cells that are lost. We do not know how this works but it is an area of intense research.

RNA

The DNA is the set of master instructions for assembling proteins. Part of the gene is a template that is used to make a new protein. The process of copying the template and then assembling a protein to match is done using another class of molecules called **R**ibo**n**ucleic **A**cid (RNA). The process works as follows:

- Messenger, mRNA, begins as a relatively short piece of the rail of a DNA molecule.
- The section of the DNA molecule that contains the code for a particular protein splits at the middle of each step, separating the AT and CG connections and spreads apart to make room for the mRNA.
- The mRNA, which is like a single rail of DNA, fits between the steps of the split DNA.
- The DNA and RNA are surrounded by a soup of available A, T, C, and G molecules. The RNA acts like the other side of the DNA ladder and attracts its own set of A, T, C, or G molecules that match up with one side of the DNA, as illustrated in Figure 9.7. This process of making a copy of part of the DNA molecule is called transcription.

- The mRNA molecule moves out of the DNA molecule. The two sides of the DNA molecule reattach. The mRNA molecule is like half a ladder.
- In the next stage, another molecule named transfer tRNA copies the code from the mRNA, uses it to select an amino acid, and then attaches the amino acid to the protein that is being assembled.
- When the process is complete, the RNA breaks down so its parts can be reused.

Figure 9.7.DNA splits and RNA copies a section of the gene to use as a template

Human DNA

Once it was discovered that DNA contained genes that controlled all of the functions of the cell, the obvious question was what part of each chromosome controlled what function? To answer this question, scientists started examining portions of the DNA molecule. They discovered that the task would be enormous.

The width of a human hair is about 100,000 nanometers (nanometers are one billionth of a meter) but the width of a DNA molecule is about 2 nanometers and base pairs are spaced about .34 nanometers apart. This is much too small to manipulate directly with the smallest tools. In the 1980s, the methods available for determining the base pairs in the DNA molecule used toxic chemicals that could break the molecule into segments, radioactive tracer elements, and ultra-thin gels. (Collins 2006) It would take a university research lab 18 months to determine the sequence of few hundred base pairs.

Many diseases are caused by dysfunctional genes. One of the most common in North America is cystic fibrosis (CF). After months of research, scientists were able to say that the dysfunctional gene that was responsible for CF was on chromosome 7 and they had narrowed it down to a segment that was 2 million

base-pairs long. Scientists invented new computerized search techniques but it still took four more years to finally identify the one base-pair that was different in people who had the disease. To make this discovery, two dozen teams around the world worked for ten years at a cost of $50 million. A cure hasn't been found yet, but now that they know where to look, they can test people to see who has the defective gene.

Like many research projects, they discovered useful information in addition to what they originally sought. They found that significant amounts of the DNA molecule do not have a discernable function. Mutations in those sections do not appear to cause any problems but differences are inherited. They also found that the definition of a gene was not as simple as they thought. One gene could create several similar proteins. (Collins 2006) When computer programmers write a code that performs a function which can be used by several different processes, they give it a name and store it where all the processes can use it. Apparently, DNA programming works in a similar fashion where some sections are used by more than one process. This makes it harder to identify a gene because some of the working parts might be stored at another location on the DNA molecule.

To decode human DNA would be a much bigger challenge. There are approximately 3 billion base pairs in human chromosomes that make up the complete instruction manual and templates for how to make a human—known as the human genome. The human genome project (HGP) was founded in 1990 by the U.S. National Institutes of Health in cooperation with the Wellcome Trust in London and labs in France, Germany, China, and Japan. Its logo is shown in Figure 9.8.

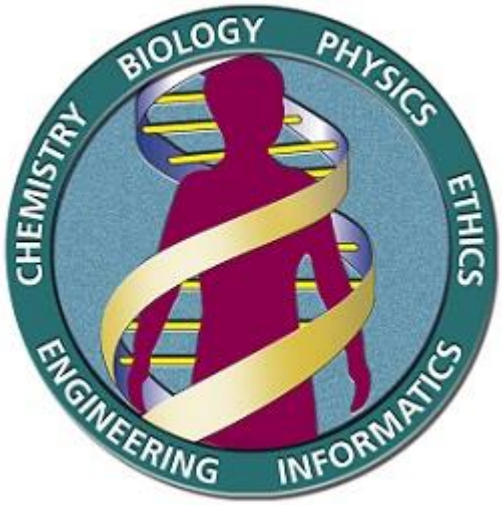

Figure 9.8.Logo of the Human Genome Project

It was expected to take 15 years and cost $3 billion to determine where the genes were located. The head of the project was James D. Watson who was one of the discoverers of the DNA structure.

One of the issues that arose early in the project was ownership of the information. Watson and most scientists thought the information should be public knowledge but the U.S. was allowing private companies who were doing similar research to patent the information. Many scientists were concerned that allowing private companies to claim ownership of the knowledge about the human genome would restrict development.

Proponents of patents argued that private companies could discover this information faster and cheaper. To illustrate this point, one of the private companies—Celera Genomics owned by Craig Venter—declared that it would pursue the same goal and would do it faster and for a fraction of the cost. (Stanford Encyclopedia of Philosophy 2008)

Advances in computer technology were greater than the teams expected and the competition between the public and private efforts spurred both of them to greater efforts. Instead of taking 15 years, they were able to meet their target of mapping more than 80% of the genome in only ten years. The achievement was announced jointly on June 26, 2000 by President Clinton and Prime Minister Blair. HGP announced that the project of identifying all of the genes in human DNA was completed in 2003. Two areas of the DNA are not done. The section at the waist of the DNA molecule—the centromere—is still unmapped and the ends of the DNA strands—telomeres—appear to be very repetitive and they are not well mapped. Scientists found that there are about 20,000 to 25,000 genes in the human genome. (Human Genome Project 2011)

Advances in computer and laboratory technologies have reduced the price of performing a DNA sequence dramatically. Instead of costing $3 billion dollars and taking fifteen years, it can now be done for less than $10,000 in a few days. Because of the lower price and faster processing, new studies can be done such as the one in which they mapped the DNA of one thousand people who were more than 100 years old to see if they had any special genes that would account for their long lives. (Smith 2010) [Link]

On May 20, 2010, researchers at the J. Craig Venter Institute announced that they used a computer to design a DNA molecule and then placed it into a living cell. (Venter 2010) The historic development had the following characteristics:

- Started with a digital code in a computer
- The chromosome was built from four bottles of chemicals (A,T, C, and G)
- Transplanted into a bacteria cell
- Bacteria became a new species of bacteria
- First self-replicating species designed by a computer
- The specie's website is encoded in the DNA molecule along with the names of its creators

This new field that combines molecular biology, statistics, and computer science is called

bioinformatics which might be a good career for a student who is good in all of those areas.

DNA Identification

The mutations that naturally occur become part of the DNA that is inherited. Because large sections of our chromosomes appear to be unused, mutations in those sections do not cause premature deaths or diseases but just accumulate. The result is that each of us has a collection of DNA mutations in the non-functioning sections of our chromosomes that is almost unique. The process of DNA identification has five steps, as shown in Figure 9.9.

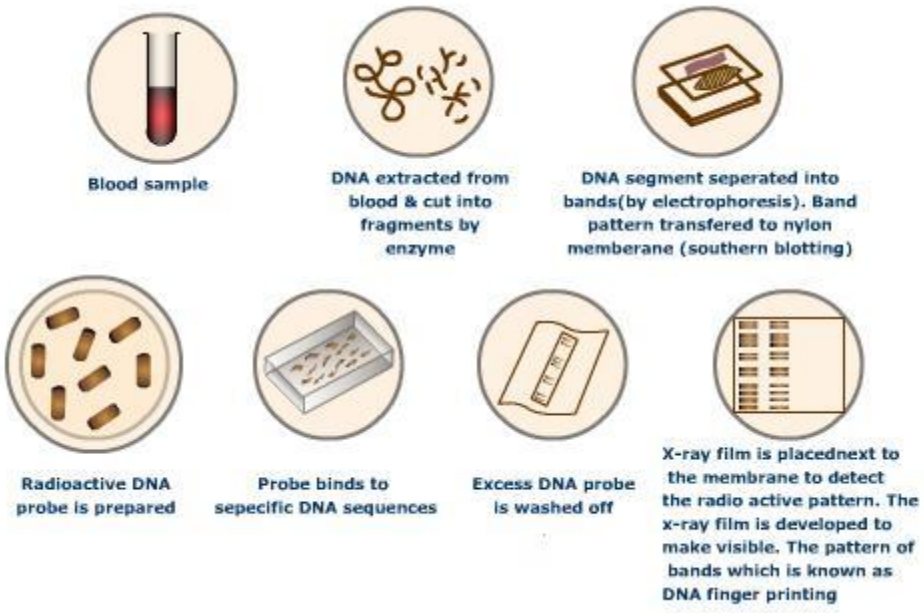

Figure 9.9.Using DNA for identification

To learn more about DNA techniques, you can sign up for a free course from the government at (President's DNA Initiative n.d.) [Link]

Because DNA can be obtained from any living cell, it is useful for identifying people. Because we inherit half of our chromosomes from each parent, DNA testing can be used to prove relationships such as paternity. Police and government agencies store DNA profile data for use in identifying suspects which can be a very useful tool. (DNA Profiling 2009) [Link]

Many people are concerned about the use of a DNA database by the government. Since April 2004, anyone age ten or above who is arrested in England or Wales can have their DNA and fingerprints taken without their consent. The information is retained by the police even if the charges are dropped or the person is acquitted. By May of 2007, the database had the DNA profiles of 105,000 children. The number of people

in the database is increasing by approximately 80,000 per year. The database in the UK has four million DNA profiles on record (6% of the population) and approximately one-quarter of these people have not been convicted of a crime. (Slack 2007) [Link]

Key Takeaways

- A DNA molecule is like a twisted ladder. The sides are made of alternating sugar and phosphate molecules. The steps of the ladder connect a phosphate molecule on one side to a sugar molecule on the other. [9.1.1]
- The four molecules that make up the base pairs are adenine, thymine, cytosine, and guanine. The pairs of molecules that make up the steps of the DNA ladder are represented by letters. They only occur in the following pairs; CG, GC, TA, or AT. [9.1.2]
- There are twenty (20) amino acid molecules. They are the building blocks of much larger molecules called proteins from which living organisms are made. Amino acids are part of the food people eat. [9.1.3]
- A codon is a group of three base pairs. Because each base pair can be one of four different pairs, a codon can have up to 64 possible combinations. A codon can be used to identify an amino acid. It is analogous to a byte of computer code that is used to identify each letter. [9.1.4]
- A gene is like a small computer program that uses codons to provide instructions for the assembly of a protein. [9.1.5]
- RNA has the ability to copy a section of the DNA molecule and use it like a template to assemble a protein. [9.1.6]
- A DNA molecule is 2 nanometers thick compared to 100,000 nanometers for a human hair. A human DNA molecule has about 2 million base pairs and about 20,000 genes. [9.1.7]
- Mutations in DNA can be inherited and they build up. The combination of mutations from each parent is almost unique and can be used to identify individuals and their relatives. [9.1.8]

2 DNA and Disease

Learning Objectives

1. Identify the characteristics of bacteria and the types of drugs that fight them. [9.2.1]
2. Identify the characteristics of viruses and the types of drugs that fight them. [9.2.2]
3. Identify the barriers that keep bacteria and viruses out of the body. [9.2.3]
4. Identify the processes of the innate immune system. [9.2.4]
5. Identify the processes of the adaptive immune system. [9.2.5]
6. Identify the viruses associated with the common cold, cervical cancer, chicken pox, and AIDS. [9.2.6]
7. Describe how immunity and vaccines work. [9.2.7]

8. Identify the characteristics of a retrovirus and why HIV is particularly dangerous. [9.2.8]

In this unit, we explore what scientists have discovered about the role of DNA in diseases and the technologies that have been developed to treat them.

Viruses and Bacteria

First, we need to distinguish between viruses and bacteria. Bacteria are complete cells that come in many varieties. Some of them are beneficial but others cause disease. The bacteria that cause disease reproduce rapidly and consume resources that are needed by our cells. Our bodies respond by trying to kill these cells with a variety of mechanisms that are collectively known as our immune system. Examples of diseases caused by bacteria are:

- Tetanus
- Typhoid fever
- Diphtheria
- Syphilis
- Cholera
- Leprosy
- Tuberculosis (see Figure 9.10)

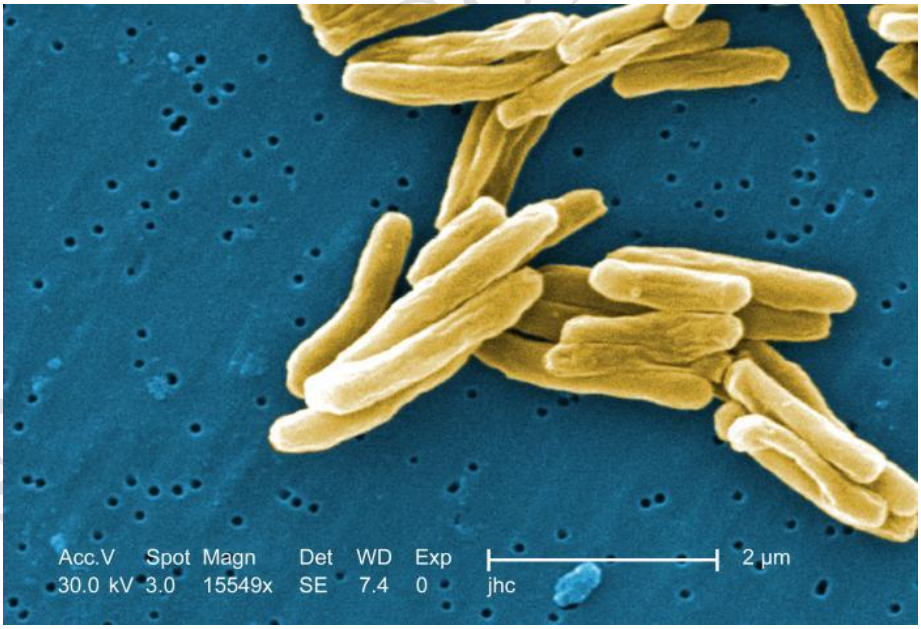

Figure 9.10. Tuberculosis bacteria, 2 micrometers long

Drugs such as penicillin or sulfa can kill bacteria and are called antibiotics. They kill bacteria by interrupting one of the processes that are necessary for life. Some harmful bacteria are always present but our normal immune system keeps them in check while other helpful bacteria perform valuable services such as

aiding our digestive systems. Many antibiotic drugs kill both types of bacteria which can cause problems unless the helpful bacteria are replaced.

There is another class of bodies that cause disease but which are smaller than cells and do not have the ability to reproduce on their own. Recall that normal cells in our bodies carry a set of instructions encoded into DNA molecules that are used by RNA molecules to construct proteins and control our bodies. Partial strands of DNA or RNA called viruses originate outside the cell but can enter a cell and make copies of themselves at the expense of normal cell activity—often killing the host cell—which makes the person sick.

A virus consists of a short strand of DNA or RNA encapsulated in a coating that helps it penetrate the cell. The coating is called the capsid. The DNA or RNA contains the code for duplicating the virus and its capsid coating. The capsid coating has many different shapes depending on the method used to get through the cell's outer wall. Some viruses are spherical like this computer simulation of a tobacco mosaic virus shown in Figure 9.11. Viruses are typically much smaller than bacteria. Because they are not alive, antibiotics that kill bacteria do not affect viruses.

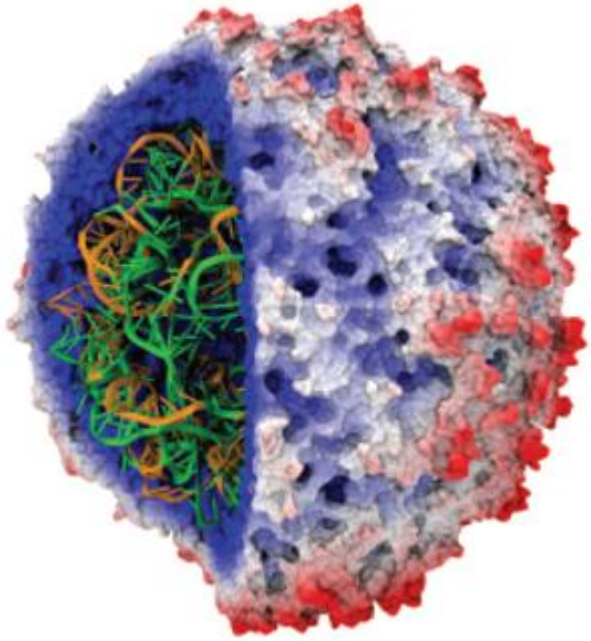

Figure 9.11.Rotavirus .07 micrometers across

Cells normally allow a variety of molecules to pass through their cell walls. The capsid (coating) of the virus mimics one of these molecules to gain entrance to the cell. Once inside the cell, the coating dissolves, releasing the DNA or RNA strand into the cell's reproductive environment. The DNA or RNA strand uses the amino acids present in the cell to make copies of itself and its capsid that pass out through the

cell membrane. This process may take over the reproductive processes of the cell until the cell dies from lack of needed proteins. Anti-viral drugs interrupt the process of passing through the healthy cell wall or strengthen the body's adaptive immune system so it can kill them more effectively.

A disease that causes immediate symptoms that require urgent care is acute. A disease that persists at a lower level for longer than three months without killing the host is called chronic. (Definition of Chronic disease 2004)

Approximately 250 viruses cause disease in humans. Examples of common diseases that are caused by viruses are shown in Figure 9.12 (Viruses That Cause Human Disease 2007)

Family	Virus	Disease
Adenovirus		Common cold
Bunyavirus	Hantaan	Kidney failure
	La Crosse	Encephalitis (brain infection)
	Sin Nombre	Lung syndrome
Calicivirus	Norwalk	Gastroenteritis (diarrhea, vomiting)
Coronavirus	Corona	Common cold
Filovirus	Ebola	Hemorrhagic fever
	Marburg	Hemorrhagic fever
Flavivirus	Hepatitis C (non-A, non-B)	Hepatitis
	Yellow fever	Hepatitis, hemorrhage
Hepadnavirus	Hepatitis B virus (HBV)	Hepatitis, liver carcinoma
Herpesvirus	Cytomegalovirus	Birth defects
	Epstein-Barr virus (EBV)	Mononucleosis, nasopharyngeal carcinoma
	Herpes simplex type 1	Cold sores
	Herpes simplex type 2	Genital lesions
	Human herpesvirus 8 (HHV8)	Kaposi's sarcoma
	Varicella-zoster	Chicken pox, shingles
Orthomyxovirus	Influenza types A and B	Flu
Papovavirus	Human papillomavirus (HPV)	Warts, cervical carcinoma
Picornavirus	Coxsackie virus	Myocarditis (heart muscle infection)
	Echovirus	Meningitis
	Hepatitis A	Infectious hepatitis
	Poliovirus	Poliomyelitis
	Rhinovirus	Common cold
Paramyxovirus	Measles	Measles
	Mumps	Mumps
	Parainfluenza	Common cold, ear infections
Parvovirus	B19	Fifth disease, chronic anemia
Poxvirus	Orthopoxvirus	Smallpox (eradicated)

Reovirus	Rotavirus	Diarrhea
Retrovirus	Human immunodeficiency virus (HIV) Human T-cell leukemia virus (HTLV-I)	Acquired immunodeficiency syndrome (AIDS) Adult T-cell leukemia, lymphoma, neurologic disease
Rhabdovirus	Rabies	Rabies
Togavirus	Eastern equine encephalomyelitis Rubella	Encephalitis Rubella, birth defects

Figure 9.12.Diseases caused by viruses

Human Defenses Against Bacteria and Viruses

There are several defense mechanisms that defend our bodies from viruses. Our skin is our first line of defense. It has an outer layer of dead cells that are not affected by exposure to bacteria or viruses.

Figure 9.13.Skin forms a barrier of dead cells to block bacteria and viruses

Where our body has to interact with our environment, other physical barriers are used. The linings of our air passages and lungs secrete mucus that traps particles. The mucus is expelled by coughing, sneezing, or transferred to the digestive tract. In the digestive tract, a strong acid in the stomach kills bacteria. In the intestines helpful bacteria like Escherichia coli (E. coli) compete for space and resources with infectious bacteria limiting the resources available. Our eyes are protected by tears that flush particles into the digestive tract.

When bacteria or viruses get past these barriers and the body recognizes them as foreign invaders, an all-purpose defense system goes into action called the innate immune system. The blood vessels in the area expand to bring more blood to the area causing it to redden. In the blood, there are cells that do not carry oxygen and do not appear red. These white blood cells (WBC) are attracted to any type of cell or virus that is not normally part of the body. They surround the bacteria or virus and excrete digestive chemicals to kill them which usually kills the white blood cells as well. The dead white cells accumulate as a yellow liquid commonly called pus. The mucus and tear barriers can increase their flow causing runny nose or itchy eyes. The body temperature might rise to create an environment in which some bacteria do not grow as well. If the immune system is triggered by foreign bodies that are not dangerous, it is called an allergic reaction.

Our bodies have a more specialized response that is tailored specifically to each type of bacteria or virus. This is called the adaptive immune system. The innate response system gives the body time to manufacture antibodies and killer T cells. Antibodies identify the foreign target by the presence of proteins or other molecules that do not belong on a normal cell. These proteins are called antigens because of their ability to trigger the formation of antibodies. There are two types of antibodies. The first type is called Immunoglobulin M (IgM) and it is produced for a few weeks during the infection. The presence of IgM antibodies indicates an acute infection. The second type is called Immunoglobulin G (IgG). IgG continues to be produced by the body after the infection. The antibodies are used to program the killer T cells to attack and kill cells that have the antigen (foreign protein). The IgG antibodies continue to be manufactured for many years. If the same bacteria or virus invades again, the body can start making appropriate killer T cells right away to defeat the infection before it becomes acute and we probably do not even notice it. At that point we say we are immune to a particular disease. (Immune System 2008)

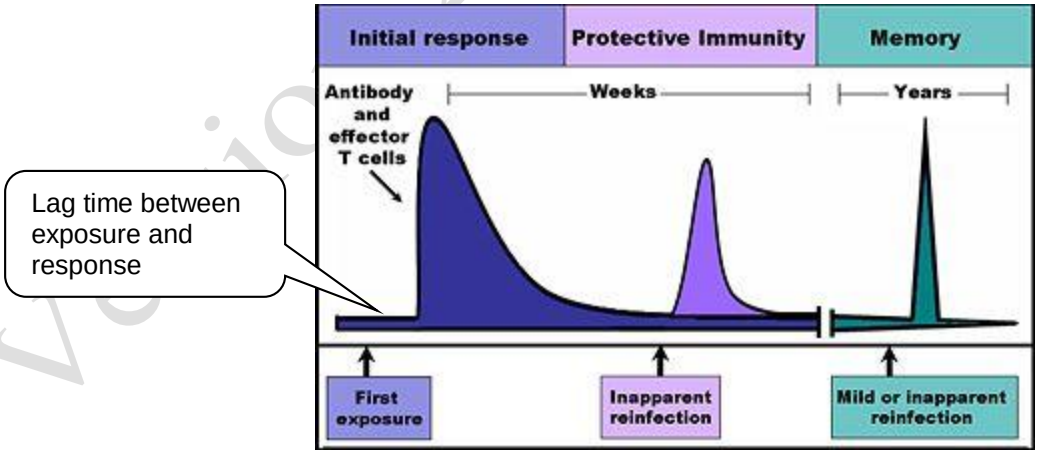

Figure 9.14. Adaptive immune system protects against future infections

Vaccines

It is possible to get the body to produce IgG antibodies by introducing the antigen that is related to the disease without giving the person the actual disease. Once the body produces the IgG antibody for a specific virus or bacteria, it is ready to respond quickly to the next infection. Common diseases for which there are vaccines are listed in Figure 9.15. (List of Vaccine-Preventable Diseases 2007) [Link]

Anthrax
Cervical Cancer (Human Papillomavirus)
Diphtheria
Haemophilus influenzae type b (Hib)
Hepatitis A
Hepatitis B
Influenza (Flu)
Japanese encephalitis (JE)
Lyme disease vaccine no longer available in the United States.
Measles
Meningococcal
Monkeypox (The smallpox vaccine is used for this disease.)
Mumps
Pertussis
Pneumococcal
Polio
Rabies
Rotavirus
Rubella
Shingles (Herpes Zoster)
Smallpox
Tetanus
Tuberculosis (TB)
Typhoid
Varicella (Chickenpox)
Yellow Fever

Figure 9.15.Diseases for which there are vaccines

There are some viruses that succeed in avoiding the immune system by mutating often—an example of which is the virus responsible for influenza. It mutates into forms that are different enough so that the IgG antibodies generated by the last infection are not triggered by the new version. This type of virus needs a different vaccine for each new mutation. Some mutations of the influenza virus are so different that few people have immunity, in which case it can affect more people. An outbreak of a disease that spreads rapidly to many people is an epidemic. If the disease spreads among people in many countries around the world, it is

called a pandemic.

Diseases are often overlooked in historical records but they often kill more people in wars than die in combat. Before science discovered that bacteria and viruses cause disease, little was done to protect against them and the conditions in which armies lived in the field were ideal for spreading disease. In the U.S. Civil War, twice as many men died from disease as from combat wounds. In World War I, about 20 million people were killed but another story is often overlooked. An unusual strain of influenza virus was first detected in Kansas in 1918 near a military base. Some of the soldiers caught the disease and then carried it with them to Europe where it killed more than 50 million people. (Barry 2004) A recent mutation of the influenza virus that spread in 2009 named H1N1 was similar to the virus of 1918 and caused great concern in 2009.

Retrovirus and HIV

There is a class of virus that has a different life cycle. A retrovirus injects an RNA strand into the cell that builds a strand of DNA. The virus splices the piece of DNA into one of the DNA strands that make up the cell's chromosomes. This permanently changes the cell's DNA and the viral section of DNA is reproduced each time the cell divides.

The Human Immunodeficiency Virus (HIV) is a retrovirus that is particularly dangerous because it attacks the cells that are part of the immune system. If the immune system is not working properly, people die of diseases from which they would normally recover. When the immune system is harmed by HIV, the condition is known as acquired immune deficiency syndrome (AIDS). HIV infection is a pandemic that has killed approximately 25 million people worldwide.

Fear of HIV infection prompted investment in research to find cures, treatments, and vaccines to fight the spread of HIV. As a result, there are several new drugs that are effective against viruses.

Key Takeaways

- Bacteria are complete cells with their own reproductive system and some of them can be killed by drugs called antibiotics. The antibiotics attack a structure like the cell wall or process like reproduction that is unique to the bacteria without killing many normal cells. [9.2.1]
- Viruses have relatively short strands of DNA or RNA that are enclosed in a capsid that can infiltrate into a cell and hijack its reproductive system to make more viruses. Drugs that fight viruses usually focus on the ability of the virus to pass into or out of healthy cells. [9.2.2]
- The barriers that keep out most bacteria and viruses are skin, tears, and mucus. [9.2.3]
- The innate immune system attacks unrecognized cells with white blood cells that enclose and digest the foreign cells. Blood vessels expand to increase blood flow in the area which causes swelling and redness. Mucus and tear production increases and so does body temperature.

[9.2.4]

- The adaptive immune system reacts to foreign proteins that are part of the bacteria or virus coating called antigens by designing antibodies for each antigen. There are two types of antibodies, IgM and IgG. The antibodies are used to manufacture killer T cells that destroy cells that have those proteins. [9.2.5]
- A few viruses and the diseases they cause: [9.2.6]
  - Common cold: Adenovirus
  - Cervical cancer: Papovavirus
  - Chicken Pox and shingles: Herpesvirus
  - AIDS: Retrovirus
- IgM antibodies do not last long but IgG antibodies persist for years which allow the body to respond faster the next time that particular bacteria or virus enters the body providing immunity to that disease. [9.2.7]
- A retrovirus goes beyond tricking healthy cells into making more viruses. It splices some of its DNA into the DNA of the cell so that it makes viruses and that trait is inherited when the cell divides. [9.2.8]

3 Cloning, Stem Cells, GMOs, and Aging

Learning Objectives

1. Identify the characteristics and uses of molecular cloning. [9.3.1]
2. Identify the characteristics and uses of cellular cloning. [9.3.2]
3. Identify the process of cloning a mammal. [9.3.3]
4. Identify the characteristics of embryonic and adult stem cells. [9.3.4]
5. Identify the processes of gene therapy and the role of retroviruses. [9.3.5]
6. Identify products of genetic manufacturing. [9.3.6]
7. Identify examples of transgenic plants and animals and their transplanted properties. [9.3.7]
8. Identify an example of a hypothesis of cell reproduction that might provide a cure for aging. [9.3.8]

Understanding the inner workings of cells and how DNA works provides opportunities to take part in the process and influence its outcomes. In this section, you will learn about methods that are used to change the blueprints of life and areas of ongoing research.

Cloning

Making identical copies is called cloning. Making copies of sections of the DNA molecule is called molecular cloning. This technology is used to make enough DNA to perform an identity match from a very small sample. It is also used to manufacture antibodies to fight disease. For example, if a person's immune

system needs help to fight a particular disease, antibodies for that disease, called monoclonal antibodies, can be cloned in large numbers outside the person's body and then injected to give their immune system a boost.

A culture of identical cells is useful for testing and research. For example, if you are comparing the effectiveness of five different antibiotics on a particular type of disease bacteria, you want to know that the samples of bacteria are exactly the same in each of the tests. To get identical samples, scientists clone the bacteria cells. If a cell divides into two cells, each of them is a clone because they have the same DNA (assuming no mutation occurred during cell division). To make sure they are all the same, a simple, low-tech method is used. Very small amounts of the cells are placed on the dish in separate areas and allowed to grow but kept separate. The groups of cells are examined to see if any of the groups grew from a single cell and are therefore clones of each other. When they find such a group, it is used to grow more cells that are all clones of each other. This process is called cellular cloning.

Cloning an entire organism is done by swapping the nucleus of an adult for the nucleus of a fertilized egg. When the egg is first fertilized, it has only one complete copy of DNA from which the entire organism is assembled. If the cell's DNA is removed and DNA from another organism is inserted, the organism can develop into a clone of the organism from which the DNA was obtained. Because the DNA is very small, the entire nucleus which contains the DNA is usually exchanged. In 1996, this procedure was used successfully for the first time on a mammal. The nucleus from a cell in an adult white-faced sheep was transferred to a fertilized egg from a black-faced sheep from which the nucleus had been removed. The result was a white-faced sheep named Dolly that had the same DNA as the white-faced sheep. the process is shown in Figure 9.16.

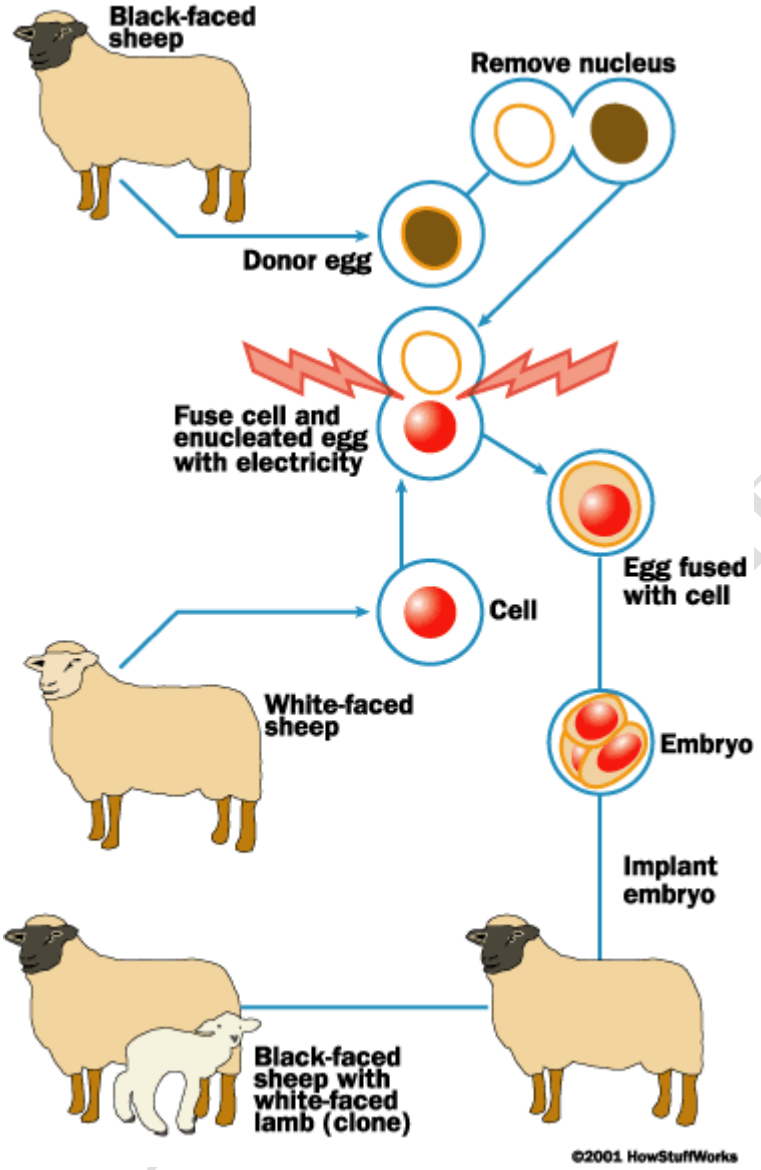

Figure 9.16.First cloned mammal

The success rate was low in this early experiment where 276 eggs were used to create one live sheep. (Cloning Fact Sheet 2006) [Link] Since Dolly, several other types of mammals have been cloned including cattle, horses, goats, rabbits, rats, and mice.

One of the things that has been learned from cloning animals is that there is more to it than simply replacing the nucleus. The animals often have health problems, cancers, and short lives. Studying clones provides evidence that there is more to our makeup than DNA. There are other factors that activate or deactivate genes. A study of identical human twins, which are naturally occurring clones, showed that they become more different as they age and that twins that are raised in different homes develop differences more rapidly. (Twin Data Highlight Genetic Changes 2005) [Link]

Stem Cells

The ability to make an entire organism from one set of chromosomes is amazing because there are hundreds of different types of cells in the human body. When the fertilized egg cell begins to grow and divide, these early cells eventually turn into many different types of cells from brain cells to toenails. If you imagine a tree, it shares a main stem (trunk) that separates into branches and then into a variety of parts like leaves, flowers, fruits, or nuts. If we think of the first embryo cells as the main stem, they divide into progressively more specialized cells. The cells at the beginning of the process from which all the others develop are called embryonic stem cells because the cells in the embryo are at the stem of the tree-like chart as shown in Figure 9/17. (Conan-Davies 2005)

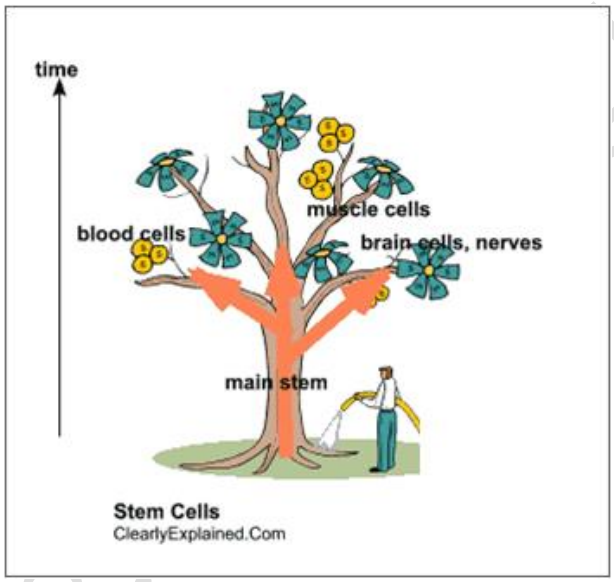

Figure 9.17.Embryonic stem cells can become any other type of cell

As the embryo develops into a fetus, embryonic stem cells differentiate into more specialized stem cells that create a class of cells like skin cells or liver cells. These adult stem cells are more limited in the type of cells they can become. Some adult stem cells remain capable of reproducing all the types of cells necessary to make a new organ. For example, a lizard can grow back an entire tail and a human can grow back large portions of the liver. We are all familiar with how our skin repairs a cut which is an example of regeneration. Most human adult stem cells are turned off when we reach adulthood and we cannot re-grow or repair most organs. For example, if the spinal column is severed, our bodies do not grow a new section to splice it back together. Scientists hope to discover the mechanism that turns this ability on and off in order to repair damaged organs.

Gene Therapy

It is one thing to know that a defective gene causes a disease but it is much harder to fix it. It is possible with the smallest of needles to remove and replace the nucleus of a cell but DNA strands are much too small for this type of microsurgery. To make changes to the DNA strands themselves requires a different type of tool. Recall that retroviruses are capable of using their RNA to make segments of DNA and splice them into a chromosome, as shown in Figure 9.18.

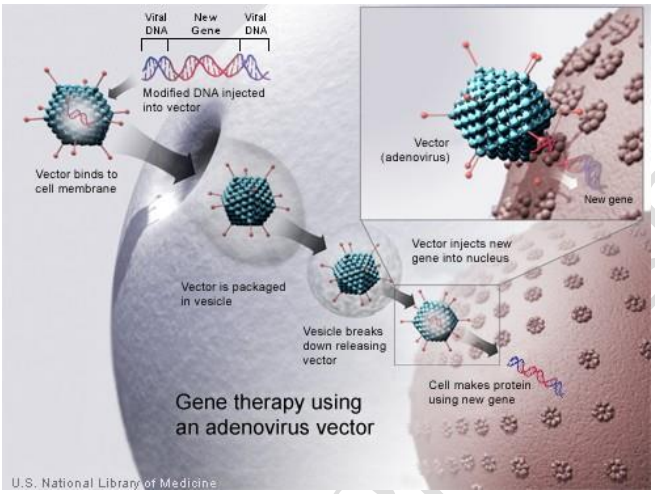

Figure 9.18.Retrovirus used to deliver DNA

This is just the type of tool that is needed. Scientists have modified retroviruses that can splice a healthy gene into a chromosome. When this method is successful, the new gene is part of the chromosome and it is duplicated when the cell divides.

Other viruses simply introduce their DNA into the cell where it is replicated but it is not spliced into the chromosome. If this method is used to provide functional DNA, it only lasts as long as that cell is alive because the functional DNA is not reproduced when the cell divides. This method is safer to use but must be repeated more often. Repairing or replacing defective DNA is called gene therapy.

Genetic Manufacturing

One of the hormones that humans use to regulate the metabolism of sugar is insulin. People whose bodies do not produce enough insulin are called diabetics. Supplementary amounts of insulin are injected periodically. Initially the only source of insulin was from slaughtered pigs or cattle. This type of insulin is not exactly the same as human insulin and it can trigger an innate immune response. Scientists modified E. Coli bacteria and spliced in a human gene that produces human insulin. The insulin is marketed under the trade name of Humalin. This method is much cheaper and because it is the same molecule as human insulin there are fewer

problems with allergic reactions. (Recombinant DNA Technology in the Synthesis of Human Insulin 1994) [Link]

One of the benign bacteria in the human intestine is E. coli and it has been studied extensively. It grows well outside the body and for these reasons it is often used for gene modification experiments. Scientists have announced a genetically modified strain of E. coli that can feed on sugar and produce isobutanol. (University of California 2008) [Link] This hydrocarbon is a better fuel than ethanol because it has more carbons per molecule which gives it a higher energy density (more miles per gallon). Recall from the discussion of organic chemistry that any carbon chain that ends with an oxygen-hydrogen pair is an alcohol and that butane is a hydrocarbon with four carbons. The molecule has the structure shown in Figure 9.19.

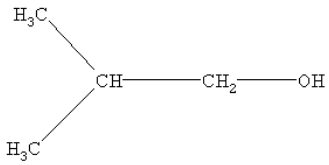

Figure 9.19. Isobutanol fuel from bacteria

Genetically Modified Organisms (GMOs)

In 1798, Thomas Malthus explained that population would increase exponentially if it is not limited by resources. In the 1960s, the Green Revolution produced far more food from the same land by using hybrid plants, fertilizer, and machines. This additional food allowed for more population growth. To make a hybrid, scientists find varieties of the same plant and crossbreed them to make a plant that has the best characteristics of both such as larger seeds or fruits that do not spoil as quickly.

Population is catching up with the increased productivity of the Green Revolution and new methods are sought that would increase food production. One of those methods is genetic modification. Genetic modification is similar to making hybrids but the genes come from other plants that would not ordinarily crossbreed. Such an organism is called a genetically modified organism (GMO).

Some plants like the redwood tree contain genes that produce chemicals called insecticides that kill insects. Scientists have transferred genes like these to several food crops to give them the same resistance to insects. Other plants have natural resistance to herbicides that kill most weeds. By transferring that gene into food crops, the field can be sprayed with the herbicide without harm to the food crop. Plants or animals that contain genes from other types of organisms with which they wouldn't ordinarily breed are called transgenic. In 2010, 148 million hectares (365 million acres) of transgenic crops were planted in 29 countries, as shown

in Figure 9.20. (Economist 2011) [Link]

Figure 9.20. Genetically modified crop in millions of hectares

The crops included herbicide and insect-resistant soybeans, cotton, canola, and alfalfa. Seeds for these plants can be patented and a large majority of the patents are held by Monsanto, Inc. Monsanto's control of food crops is a concern for many poor countries because they are losing their option to buy seeds from other companies that are being bought by Monsanto or forced out of business.

Similar techniques can be used on fish and mammals. A gene that makes coral phosphorescent was transferred to pet fish. The new type of fish glows in the dark and is trademarked ***GloFish***, as shown in Figure 9.21.

Figure 9.21. Genetically modified fish emit light

Animals have been altered to produce human proteins that are too complex for production in bacteria such as the anticoagulant—prevents blood clotting—ATryn. Researchers test the effect of certain genes by creating mice that do not have that gene.

Researchers have created the ability to produce hormones like insulin from bacteria and other animals but they can also produce other hormones like anabolic steroids and human growth hormone (HGH). Normally HGH is produced during childhood but stops when a person becomes an adult. By injecting growth hormones, athletes can grow larger as young adults, which is an advantage in some sports. Sporting organizations ban their use but the temptation is great for individuals who want to win.

Aging

The cells in young animals and humans reproduce effectively but as they age, the reproduction process begins to fail and the body shows signs of aging such as wrinkled skin, white hair, and less flexibility. The reasons for this are not fully known but research into the structure of DNA and what factors turn genes on and off have caused optimism that someday this condition may be avoided. One promising area of research is to determine why cells only divide correctly a certain number of times. It appears that this limitation is due to the part of the DNA molecule at the ends. (Alternity Healthcare 2010)

At the end of each chromosome is a region of DNA that consists of repetitive sections called telomeres as shown in Figure 9.22.

Figure 9.22. Telomeres

This region marks the end of the chromosome and prevents it from joining end-to-end with another chromosome during reproduction. Each time the cell divides, some of this region is used up and the section shortens. One hypothesis states that loss of telomeres is the cause of aging. When the chromosomes begin to run out of telomeres the cells do not divide accurately or often enough and the organs start to deteriorate or develop cancers. This hypothesis is supported by the observation that animals that are cloned from adult DNA usually do not live as long as animals that are bred the usual way.

Cells that stop dividing are called ***senescent*** cells. Researchers have found that senescent cells in mice secrete substances that cause the immune system to react which causes inflammation. A strain of mouse was bred in which the senescent cells could be killed selectively. The mice without the senescent cells did not show the normal effects of aging. (Wade 2011)

If this hypothesis is correct, it might be possible to restore the missing telomeres and find a cure for aging. It is possible that one of the areas of research into the causes of aging could discover a "cure" and it could happen about the time that world population is reaching the earth's carrying capacity.

Key Takeaways

- Making exact duplicates of molecules by cloning is used to increase the amount of DNA molecules to make enough to run tests. Antibodies for certain diseases can be reproduced in quantity and injected into a patient to make the adaptive immune response stronger. [9.3.1]
- Cloning cells to produce identical test subjects for studies of bacteria and other cells

eliminates a variable in the study. [9.3.2]

- Mammals can be cloned by transplanting the nucleus and DNA from an adult animal into a fertilized egg that has had its nucleus removed. [9.3.3]
- Embryonic stem cells can develop into any type of cell while adult stem cells can develop into cells of a certain organ. [9.3.4]
- Gene therapy either inserts functional DNA into cells or splices it into the cell's DNA so it can be inherited by subsequent cells when the cell divides. [9.3.5]
- By inserting genes into bacteria, they can produce useful human proteins like insulin, or even fuel like isobutanol. [9.3.6]
- Genes can be inserted into the DNA of plants to give them desirable properties such as the ability to produce insecticides or resist herbicides. Animals like goats can be altered to produce human proteins like the anticoagulant ATryn. Mice can be made that do not have a particular gene to study the effect and isolate the function of individual genes. Human growth hormone and anabolic steroids can be produced to increase size and strength. [9.3.7]
- Aging might be caused by running out of telomeres at the end of the DNA molecule which are used up each time the cell divides. Gene therapy might add telomeres to the end of the DNA molecules to stop the aging process. [9.3.8]

Key Terms

3' end

end of the DNA molecule that ends in a phosphate molecule

5' end

end of the DNA molecule that ends in a sugar molecule

Acquired Immune Deficiency Syndrome (AIDS)

educed effectiveness of the immune system due to HIV results in infections by diseases that would otherwise be prevented

acute

major symptoms that require immediate care

adaptive immune system

process of identifying foreign matter (antigens) on bacteria or viruses and designing antibodies that are used to make killer T cells to kill them

adenine

one of the four base molecules that make the cross links or base pairs in the DNA molecule

adult stem cells

cells that can develop into cells of a particular organ but not other organs

allergic reaction

response of the innate immune system to foreign bodies that are not dangerous such as pollen

amino acids

twenty basic building block molecules used to make proteins

antibiotics

drugs that kill certain bacteria without killing too many healthy cells

antibodies

molecules that are created in response to the presence of foreign proteins that are used to make killer T cells

anticoagulant

prevents blood clots

antigen

protein that is not normally present in the body

anabolic steroids

chemicals that cause increase or build-up

bases

one of four molecules in the DNA molecule; Cytosine, Guanine, Adenine, Thymine

base pairs

base molecules combine in only four ways; CG, GC, AT, TA

bioinformatics

combination of molecular biology, statistics, and computer information systems

byte

group of eight digits used to identify letters and numbers in digital computers

capsid

outer coating of a virus

cellular cloning

growing identical copies of a cell

chronic

problem that persists for longer periods of time

clones

organisms with the same DNA

codon

group of three base pairs that make a programing unit in a DNA molecule

cytosine

one of the four base molecules that make the cross links or base pairs in the DNA molecule

deoxyribonucleaic acid (DNA)

molecules that contain the blueprints for creating the rest of the organism

diabetic

person whose body does not make enough insulin

Escherichia coli (E. coli)

bacteria normally found in the human intestine

embryonic stem cells

cells that can turn into any other type of cell in the organism typically found in the embryo stage

epidemic

disease that spreads rapidly to many people

gene

section of DNA that performs a function

gene therapy

replacing defective genes with functional genes

genetically modified organisms (GMO)

living things whose DNA has been altered artificially

guanine

one of the four base molecules that make the cross links or base pairs in the DNA molecule

herbicides

kills plants

human genome

set of genes in DNA with instructions for making and operating a human

human genome project (HGP)

effort to map the human DNA to determine where the genes are and what they do

human growth hormone (HGH)

chemical that promotes growth during childhood

human immunodeficiency virus (HIV)

retrovirus that attacks cells that are part of the immune system

hybrid

plants or animals that are a combination of traits from other plants or animals

immune

the adaptive immune system has IgG antibodies present that can kill bacteria or viruses quickly to prevent disease

immune system

processes that protect the organism from bacteria and viruses

Immunoglobulin G (IgG)

antibody that is produced during an infection by a bacteria or virus that continues to be produced for years

Immunoglobulin M (IgM)

antibody that is produced during an infection by a bacteria or virus that persists in the body for a few weeks

innate immune system

responds to unknown foreign cells to protect the body

insecticide

kills insects

insulin

hormone that regulates sugar levels in the blood

isobutanol

organic fuel that is an alcohol of butane that can be made by genetically modified bacteria

killer T cells

cells that are designed to kill bacteria or viruses that have a particular protein

molecular cloning

making identical copies of sections of DNA

monoclonal antibodies

antibodies to a certain disease produced by cloning

pandemic

disease that spreads rapidly to many people across large regions

proteins

complex molecules that make up cell structures or perform particular functions like hemoglobin

pus

dead white blood cells and dead bacteria and viruses

retrovirus

type of virus that can splice its DNA into a cell's DNA

ribonucleic acid (RNA)

molecule used to transfer patterns from the DNA molecule that are used to assemble proteins

senescent

cells that have stopped dividing

telomeres

repetitive DNA at the end of chromosomes

thymine

one of the four base molecules that make the cross links or base pairs in the DNA molecule

transcription

copying a section of DNA

transgenic

organism with genes from another type of organism

virus

strands of DNA or RNA enclosed in an envelope of proteins that can take over the reproductive systems of other cells

white blood cells

part of the innate immune system, cells that engulf and digest foreign cells like bacteria or viruses

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