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The Amazing DNA Molecule: Its History, Structure and Function

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Introduction

This curriculum unit is intended for high school [college level or higher] biology students yet it can be modified to accommodate all learning backgrounds. Detailed lesson plans, which adhere to the CCI (Connecticut Competency Instrument) and state standards, will be included in this unit. It is intended that this unit be presented after both basic chemistry and the macromolecules of life have been thoroughly described and discussed since an understanding of these topics is essential for this unit to proceed as it is designed.

The purpose of this unit is to reveal the rich history in the race to discover the double helix, to exemplify the relationship between structure and function, to integrate the use of modern technology and to include a discussion of ethics into these topics. I have taken an interdisciplinary approach, and integrated science with history, mathematics, ethics and technology in an attempt to make the unit more exciting and learning more meaningful. Terms that need defining are bolded (usually just once) and can be found in Appendix A- the glossary.

Most of my students are familiar with the name DNA (deoxyribonucleic acid), yet many don't grasp the concept of what DNA actually is and what is does in the cells of our bodies. The ultimate goal of this unit is to bring forth marvel and respect and for this amazing DNA molecule as well as an understanding of its structure and function. Molecular biology is a branch of science that focuses on th pathway from DNA to the protein it codes for. The Central Dogma of molecular biology is that pathway: DNA -> messenger RNA -> protein. With this foundation, students will be better equipped to make sense of the modern technological advances in molecular biology and the implications they have on medicine and society. In addition, students will be empowered with the skills of critical and logical thinking which will be a tool they will use both inside and outside of the classroom.

Unit Objectives

To relate and cite history as it applies to scientific discovery.
To develop an understanding of the structure and function of DNA.
To examine and respond to the relationship of structure and function.
To manage and apply learning when examining technology and ethics.

To develop marvel and respect for this amazing DNA molecule.

Overview

This unit can be divided into five major sections: history, structure, function, technology and ethics. At times these sections overlap, yet overall it follows this order.

History

Although there were many individuals involved in the race for the double helix, this unit will focus on just a few of the key players directly involved in this discovery. The majority of the information presented in this history section came from my favorite source, The Eighth Day of Creation (#10) and from The Double Helix (#2).

-Erwin Chargaff-

American biochemist, working in New York at Columbia University

-Francis Crick-

English physicist, working in Cambridge at Cavendish Laboratory

-James Watson -

American biologist, working in Cambridge at Cavendish Laboratory

-Rosalind Franklin-

English chemist/crystallographer, working in London at King's College

-Maurice Wilkins-

English chemist/crystallographer, working in London at King's College

-Linus Pauling-

American Professor of Chemistry, working at CA Institute of Technology

Our story begins in 1950 when young James Watson journeyed to England to pursue research there. He was only twenty three when he left America, just after he earned his Ph. D. He knew phages (viruses that attack bacteria) and intended to continue his post-doctoral research in this area at the Cavendish Laboratory.

When Watson arrived in England, he met Francis Crick, a man in his early thirties pursuing his post-doctoral work. Crick was interested in proteins, and their structure, and he used a technique called x-ray crystallography to study proteins. Crick was reported to be very knowledgeable due to his voracious appetite for reading.

Upon meeting, the two quickly developed a sincere working relationship. They were able to compliment each other's research- Watson's background in biology was nicely balanced by Crick's background in physics. Neither were involved with DNA research when they met, and they never actually did any research directly with this molecule even though they are credited with the discovery of its structure.

At this point in time, the research showed that the genetic material was DNA, yet no one knew about the structure of this molecule. What was known was something called "Chargaff's Rules" which resulted from Chargaff's study of DNA from many different species. What he discovered was a ratio of nitrogenous bases. He noted that there were always approximately equal proportions of adenines to thymines as well as guanines to cytosines. It took some time before anyone realized the significance of this.

Many teams were interested in being the first to determine the structure of the DNA molecule. Linus Pauling proposed that it was a three chained helix, yet he never really did much research with DNA since he was already deeply involved in other areas of research. At this time he had a successful background in helical proteins. Many teams around the world were interested and involved with DNA, yet for our purposes we will note Maurice Wilkins and his team and King's College as the team that was most actively pursuing research in this area.

A new member joined Maurice Wilkins at King's College in 1951, Rosalind Franklin. She was under the assumption that she was given the DNA work upon her arrival to the King's College laboratory. She was the one to clean off the dusty files and equipment in order to perfect the technique of x-ray photographing a DNA molecule.

With so many individuals working with DNA in Europe, eventually Watson and Crick also became interested in this DNA molecule enigma. In fact, the two were eventually asked to back off since Wilkins' team had 'first dibs'.

For quite some time it was not clear if DNA was a helix, and if it was, how many strands it was composed of. Rosalind Franklin produced some fabulous x-ray photographs, yet even she did not realize how her photographs showed that DNA was a double helix. It took the ingenuity of the Watson-Crick team to make this clear.

Before Crick even saw these x-ray photographs, he heard about them from Watson. Watson attended a seminar where Rosalind Franklin presented her discoveries. She showed her photographs to the seminar attendees, and described other aspects of her DNA research. Watson returned to Crick's surprise without any notes from the seminar. Watson trusted his memory, but it failed him because he was only able to relate to his partner qualitative descriptions rather then exact quantitative descriptions. Some feel that if Crick attended the seminar, or if Watson took notes, they may have solved the puzzle sooner.

Crick's experience with x-ray diffraction by helical proteins made it much easier for him to decipher the information in the x-ray photograph of a DNA molecule. He was able to make mathematical calculations about bond angles and distance between atoms. Yet his initial calculations were off, even if only slightly and then he and Watson were asked by their cooperating supervisor to lay off DNA and get back to the work he had intended for them. And they did for about a year.

According to Judson, Rosalind Franklin was probably the only person still working with DNA during 1952. During this time she produced more and more photographs; yet she was still not ready to put faith in the idea of a helix. She kept detailed lab notes, and on several occasions she noted to herself that she did think that it could be a helix, or a double helix, yet she was cautious and conservative and kept these thoughts between herself and her notebook. In public she scrutinized the idea of it being a double helix. Some believe that she did not have the experience nor foresight that is required for pulling any and all data about structure from the x-ray crystallography photographs.

Maurice Wilkins initially gave Rosalind Franklin the green light to put all her efforts into DNA. When he requested that she share her findings, she put up the red light. She did not assume that this was a joint project, she believed it was hers. She and her research assistant worked diligently, perfecting the technique of isolating single fibers for x-ray crystallography and in doing so produced over 50 photographs of DNA in both its B and Z forms (Which by the way led to part of the reason Rosalind Franklin was not quick to adopt the double helix theory- the two structures gave two different photographs and it was yet to be known for sure that there were two forms of DNA.) This misunderstanding between Franklin and Wilkins quickly became a source of animosity.

Ultimately Watson and Crick resumed their quest and reentered the race. This time Crick actually saw the photographs taken by Franklin. Within weeks they were building models, trying to find a structure that conformed to the measurements Crick calculated from the x-ray photograph data. Within days, they found success- they figured it out!

In April 1953, Watson and Crick published their 2-page paper entitled: "Molecular Structure of Nucleic Acids: A Structure for Deoxynucleic Acids." The world was shocked, and they were too. The two made history, not only for discovering the structure of a DNA molecule, but also as two scientists who, although both extremely clever, won the race riding on the backs of others.

A Nobel Prize in Medicine or Physiology was awarded in December 1962 to Watson and Crick for the discovery of the DNA structure and to Maurice Wilkins for the x-ray photograph. Even though it was Rosalind Franklin who took the photograph, she died of cancer in 1958 year at age 37. I do not think it is presumptuous to assume that her developing cancer was directly job related, basing this on what we now know about exposure to x-rays and their link to mutations. It doesn't seem fair that Nobel Prize Laureates must be alive when presented the award. When you consider the relationship between and the situation with Franklin and Wilkins, one can clearly see an injustice to Franklin since it was her diligence and perseverance that produced the photographs.

Structure

The structure of DNA will ultimately be revealed as the history section ends. Chargaff's rules for base pairing and the x-ray diffraction photograph reinforces understanding of this molecule's structure. Constructing a DNA molecule will demonstrate its basic structure as well as provide a model for future discussion of DNA function.

It is worthy to note that there are several forms of DNA: B-DNA and Z-DNA are the two most important. Z-DNA is far less common than B-DNA. B-DNA is the double helix structure proposed by Watson and Crick and is the form DNA usually has in solution. This unit will focus only on the B form of DNA.

DNA, the hereditary material passed on from cell to cell, is a nucleic acid. A nucleic acid is a macromolecule that is composed of repeating nucleotides. There are two kinds of nucleic acids, DNA is one kind, RNA is the other.

A DNA molecule consists of a very long chain of repeating units. The repeating units are called nucleotides. A nucleotide has three components: a 5-carbon sugar (deoxyribose for DNA or ribose for RNA), a phosphate group (PO4) and a nitrogenous base (either a purine or a pyrimidine, which refer to the structure of the nitrogenous base- either two rings or one respectively). In a DNA molecule the four nitrogenous bases are adenine, thymine, guanine, and cytosine with the purines being adenine and guanine and the pyrimidines being thymine and cytosine. Adenine (purine) always bonds to thymine (pyrimidine) and guanine (purine) always bonds to cytosine (pyrimidine). [NOTE: to remember which is a purine and which is a pyrimidine- just recall that pyrimidine has a "Y" in its name and so do the two pyrimidine bases, thYmine and cYtosine] In an RNA molecule, thymine is not found, but the nitrogenous base uracil (a pyrimidine) is found and bonds with adenine during transcription.

The shape of a DNA molecule is like a ladder, twisted or coiled into a double helix. The rungs of our ladder would be the nitrogenous bases bonded to each other. The base pair adenine/thymine are held together as a rung of this ladder by two hydrogen bonds; the base pair guanine/cytosine are held together by three hydrogen bonds. The nitrogenous base pairs are bonded to a sugar phosphate backbone- a chain of alternating sugar and phosphate groups. A nitrogen from the nitrogenous base forms a covalent bond with the first carbon in a sugar molecule. The fifth carbon in the sugar molecule bonds with an oxygen from a phosphate ion. This same phosphate ion uses another oxygen to bond to the third carbon in another sugar molecule, and this repeated chain forms the backbone of a DNA strand. (See diagram #1 below.) But since DNA is double stranded, there are two sugar phosphate backbones. It is estimated that there are at least 3 billion base pairs on a human DNA molecule.

Diagram #1. A diagram of the sugar phosphate backbone of a DNA molecule. This diagram shows the linkage between a phosphate group and the deoxyribose sugar.

Function

Although DNA replication and cellular division are also important processes, this unit will explore protein synthesis. Students who can grasp the central dogma of molecular biology and the genetic code are those who are truly starting to make sense of this amazing molecule.

Let’s start with the nucleus. It is here where the DNA resides, and she never leaves her nucleus. So how does the information contained in DNA leave the nucleus? Her special messenger- RNA (m-RNA). Why does mRNA have to leave the nucleus? Because it needs the ribosomes to assist in protein synthesis. Also, the raw materials and other helpers needed to perform this process are found in the cytoplasm.

The base pairs in a DNA molecule are grouped into long chains called genes. Genes code for proteins therefore the hereditary information contained in DNA tells the cell how to make proteins. The language used by the nucleic acids is well understood by the cell and by molecular biologists and is known as the genetic code.

Imagine a gene about 300 base pairs long. Remember DNA structure- a double helix with nitrogenous base pairs hydrogen bonded to each other. Now think of the DNA molecule as a zipper, such as the one on a jacket. Open the zipper (molecule), and what you see are the two exposed metal sides (strands). The DNA molecule works just like that except where you use your hand to open the zipper, there is an enzyme that does the job for DNA. And just like you can zip your zipper back up, so can the DNA molecule! The RNA polymerase can move anywhere along the gene, opening and closing segments of DNA as needed.

The DNA strands are separated so that RNA can begin its job. RNA is the other type of nucleic acid, and has a few differences from DNA. First, it is single stranded. Second, its nucleotides do not contain the nitrogenous base thymine, but rather uracil. Third, its sugar is ribose; a sugar like DNA’s but with an oxygen bonded to the second carbon. Lastly, it leaves the nucleus. Similarities are that both contain nucleotides, and both follow same base pairing rules.

The nucleotides are grouped into threes, or triplets, called codons. Each codon codes for either a function (start, stop) or an amino acid. There are 20 different common amino acids which make all the proteins known to humans! Each of these amino acids has one or more codon. Therefore, the sequence of the nucleotides along the DNA specify the sequence of amino acids in the proteins.

Once DNA strands are separated, transcription can begin. Transcription is the transfer of information from DNA to mRNA. The way this occurs is as follows:

1. RNA polymerase separates the strands and will then help the messenger RNA assemble itself.
2. RNA polymerase knows when to begin once it finds the promoter and the start codon.
3. Following the base pairing rules, a complementary strand of messenger RNA is formed.
4. An mRNA strand continues to grow until it reaches a special terminator sequence on the DNA and the stop codon.
5. Transcription ends when RNA polymerase releases the newly synthesized strand of mRNA and itself leaves the DNA allowing it to “zip” back up.
6. Several copies of a gene can be transcribed simultaneously.

Once the messenger RNA transcript leaves the nucleus it heads for a ribosome. Now translation can begin. Briefly, translation is as follows:

1. Messenger RNA transcript arrives at ribosome.
2. Transfer RNA is responsible for bringing the amino acids into alignment to form the polypeptide.
3. Attached to one end of the transfer RNA is the amino acid, the other end is an anticodon, which is a complementary codon to the messenger RNA transcript.
4. Enzymes help couple each amino acid with its respective transfer RNA molecule and each transfer RNA molecule anticodon with messenger RNA codon.
5. The messenger RNA transcript is secured within a ribosome and will temporarily couple with the appropriate transfer RNA while it is being translated.
6. Once the transfer RNA is coupled with the messenger RNA, it transfers its attached amino acid to the chain which is growing as the as the messenger RNA strand is being read.
7. Termination of translation occurs when there is a stop codon, and water rather than an amino acid is added to the protein (peptide chain) which cleaves it.

Technology

Technology is a broad term for the application of science to achieve objectives. There are many different technological techniques and also many different technological projects. Many of these techniques are used by researchers from different scientific fields. For instance, Crick as a physicist and Franklin as a biochemist both used x-ray crystallography. It is important not to overlook the tools of a scientist and to recognize the implications of using these tools to increase understanding.

Since x-ray crystallography was integral in the discovery of the double helix, this unit will briefly explore this technique. X-ray crystallography is a method where an x-ray beam passes through a crystal of a particular substance. This causes the atoms of the crystal to deflect the x-rays in an orderly array. These diffracted x-rays can expose photographic film to produce a pattern of spots. These spots can be interpreted by crystallographers who use complicated mathematical equations to determine structural information. These spots can reveal information about the position of atoms in three-dimensional space.

To better understand this technique and to better understand Rosalind Franklin’s x-ray photograph one has to have an understanding of light and its properties. Light has been considered as both a wave and as a particle, or photon. Before this seminar I actually thought I knew what light was, and even now it is very challenging to

attempt to adequately describe it.

Electromagnetic energy, or radiation, is a form of energy released both naturally (sun), or it can be simulated (x-ray generator, light bulb, laser). This energy travels as a wave as does a pebble thrown in a puddle of water. These waves, as opposed to the water waves, are disturbances of electric and magnetic fields over a fixed position or time. Light induces a change in an electrical field. The energy contained in a photon is related to its wavelength. There is an inverse relationship, the shorter the wavelength, the greater the energy of each photon of that light. The order of light waves from longest wavelength to shortest is: Radiowaves, microwaves, infrared, visible light, ultraviolet, x-rays, gamma rays and cosmic rays. Therefore, the least energy is found in radiowaves and the most in cosmic rays.

Atoms of a molecule are arranged in a specific order, which is what distinguishes different molecules from one another. This order of atoms can be detected with a technique such as x-ray crystallography. As stated, light induces a change in an electrical field. Electrons are the particles of an atom that are negatively charged are those particles that will be affected by light.

Let's now adopt an analogy, to assist our understanding. Most individuals have a CD player, and many discs for it to play. Each CD contains a spiral track that holds the audio information. This spiral track is detected by a laser beam in your CD player. Each disc has a unique spiral track grating pattern that consists of different length elevated areas (pits) separated by flat areas (land). Ultimately, the laser (Light Amplification by the Stimulated Emission of Radiation) will pass over this pattern, making sound due to the pattern of the distances between the pits and land.

The wavelength of the laser is important. In order for the CD player to read this pattern, it must be able to detect the distances between the pits and land. The distance between two objects is best resolved with light that has a wavelength close to the length of the distance between two objects.

A CD is an example of an artificial or commercially made grating, but nature produces some, although they don't play music. Nature's gratings are the arrays of regularly spaced atoms that exist in a crystalline substance. A crystal of DNA would contain atoms that are separated from each other by distances that are much smaller than the wavelengths of lasers. Where as the laser could read the distance between the pits and land of a CD, the distance between the atoms ("pits") and the space in between adjacent atoms ("land") must be read with light that has a much smaller wavelength. X-rays are the source of light that must be used to detect these distances since their wavelength (approximately 0.5 x 10-10m) is closest to the distance between adjacent atoms.

When an x-ray beam is passed through a crystal of DNA, a diffraction pattern results. The angle of diffraction will tell us the distance between the repeating units. The x-rays are bombarding the molecule, but it is the electrons of the atoms and the electrons that are emitted by a heated filament in an x-ray tube that are interacting.

The planes of the molecule that have a lot of electron density are those that produce the distinct scattering pattern when bombarded by x-rays. This complicated arrangement of diffracted spots detected in a photograph is due to the three-dimensional structure of the molecule. Looking at Franklin's x-ray diffraction photograph of a DNA molecule, one can see an "X" with dark bands at its top and bottom. The two arms of the "X" are not solid, rather they are spaced bands which indicates a repeated pattern. These are produced because of areas of electron density. The vertical axis of a strand of DNA does not touch as many points on the molecule as would an axis tilted to the right or left of the vertical axis. The dark areas at the top and

bottom of the “X” result from the scattering of the electrons from the nucleotide base pairs.

Mathematical formulas are used to make calculations from the raw data. An x-ray crystallographer will be able to determine the distance between adjacent atoms using these formulas and measurements of the angles shown in the x-ray photographs. Thereafter, they can begin to generate a model for structure which is based on the actual raw data.

This is just one of many different techniques that uses light to determine composition and/or structure of molecules. There are also many other techniques and protocols for manipulating DNA. Recombinant DNA technology has swept the planet and so many biotechnological industries are profiting from the work of bacteria! The Human Genome Project has been in effect for quite some time, and has taken on the task of sequencing all estimated 3 billion nucleotide pairs of human DNA. Any and all data is being logged in with a gene bank, and credit and patents are granted when appropriate. Soon we will know the identity of every gene in our genome, and this will lead to all new technologies for genetic enhancement and engineering. Then will come the quest to determine what the function is of all these genes. Genetic screening has been available for years, yet now there will be much more to screen for.

Ethics

Because research can be very competitive, one can not exclude a discussion of ethics. The race for the double helix clearly calls for a discussion of ethics.

Rosalind Franklin was a young female doctorate, working in the 1950s in a male dominated field. She was isolated, and collaborated with no one. She was criticized for being passive, and lacking insight. Others tell a story of a woman who was misled into thinking she had independence and control over her research. They describe a bitter relationship between her and Maurice Wilkins- the man who ultimately received the Noble prize for her photograph. Is this fair?

We can also look at Watson and Crick, the two whose name is credited with the discovery of the double helix. But these two men didn’t do any of the laboratory experiments with this molecule. Do these men deserve that credit? Many believe that they do, because after all it was their insight that figured it all out. Yet what about the others whose name is unfamiliar even though their collaboration in that discovery was essential.

The Human Genome Project can be approached in many ways. Is this project going to reach its projections for sequencing the genome of a man from Albany, NY by next summer? What will be done with this information, and what implications might it have? How long before a project to determine the function of each of these genes, and when might that be completed? There are also companies that are patenting the genes they discover, and these companies are independent of the National Project that is federally funded. What does it mean to have a patent on a gene?

In addition, questions such as the following could be addressed: Does advancing technology bring forth benefits for all of society? Where is technology headed? Do you like the direction that it is heading? What technologies have improved our existence? What are the benefits of genetic screening? What are the benefits of genetic cloning?

Educational Strategies

I am an advocate of the Multiple Intelligences Theory, which is based on the idea that all individuals possess many different types of intelligences, and each of these can be better developed over time with practice. The most recognized seven would be: linguistic intelligence, logical-mathematical intelligence, spatial intelligence, bodily-kinesthetic intelligence, musical intelligence, interpersonal intelligence and intrapersonal intelligence. Strategies that incorporate energy spent exercising each of these areas will be the goal of this, and I imagine, every unit.

The ideas behind developing each of our many intelligences are numerous. For one, practice makes perfect. Well, maybe not exactly- but that adage gets the point across. If students get practice in each of these areas, in time they will be able to better identify where they are strong and where they are weak. Second, practice can only increase logical thinking skills which are critical to effective problem solving both inside and outside of the classroom. Lastly, identification of strength in an area that a student didn't think she/he was strong will bring forth further confidence in the student that will assist in more than just problem solving.

In addition, students learn in different ways. Some may be visual learners while others are auditory learners while still others are emotional learners. Ultimately all types of learners would be satisfied if lesson plans are of a diverse, multifaceted nature.

Effective teaching strategies that would be conducive for learning while also engaging one/some/all of these intelligences and the different types of learning styles could be some of the following:

-Lessons that focus less on lecture and more on activities.
-Activities with some sort of movement/motion are included.
-Assessments are of many type, ie. written, verbal, illustrated, performed.
-Composing lyrics to sing over well-known song or rap (see Appendix G).
-Group Activities and cooperative learning.
-Journal activities where students reflect thoughts and ideas.
-Written assignments could include poems, stories, research papers.
-Verbal assignments could include oral presentation or performance.
-Illustrated assignments could include drawings, models, posters or games.
-Performed assignments could be directed activity or a dance or song.

Lesson One: Introducing the History.

This lesson is the introduction to the unit- the historical background.

Because of the difficulty in reproducing certain types of graphics, this lesson will not include reproduced pictures of the key players, rather it will direct you to where you can obtain them in appendix. Ideally, a copy of a picture of each key player (Erwin Chargaff, Linus Pauling, James Watson, Francis Crick, Rosalind Franklin, and Maurice Wilkins) will be presented with this lesson. These pictures can be placed on cards, or if so inclined, pencils to make them puppets in your charade. This visualization of the players will not only assist our visual learners, it will also be conducive to reinforced learning.

In addition, many other reproduced pictures would be helpful in this lesson. Maybe some sort of slide show or powerpoint presentation is within your boundaries. At any rate, these reproduced items are suggested:

1. picture of the key players listed above
2. copy of the x-ray diffraction photograph
3. diagram of the method of x-ray crystallography
4. picture of Watson and Crick next to their DNA molecule model
5. picture of Nobel Prize being awarded for the DNA structure discovery
6. copy of the Watson and Crick journal article published in April 1953
7. diagram or model of a DNA molecule

Objectives:

-Students will be able to name and discuss the key players in the discovery of the structure of the DNA molecule.
-Students will be able to discover and recognize scientific contributions of the key players discussed.
-Students will be able to develop and organize scientific history in relationship to national/world history.
-Students will be able to formulate values that integrate and manage their learning.

Introduction:

This lesson can be initiated with an open-ended question- “Can anyone think of some sort of discovery that was made that had monumental implications for all of society?”

All responses must be recognized and responded to. Ideally students will think of major events like the atom bomb, landing on the moon, incandescent light bulb... and maybe even someone will state the discovery of DNA. Ultimately, this discovery will be described as one which did, and still does, have monumental implications for society.

Content:

1. A brief look into history of the 1940s and 1950s.
2. An introduction to the key players in the race to discover the double helix.
3. Explanation of major events that led to the publication of the DNA model.
4. Watson and Crick published paper.
5. Nobel prize awarded in 1962.

Methods and procedure:

1. Initiate lesson with above question.
2. Try to place student responses on time line handout.
3. Review and examine few key historical events that occurred both before and after the 1953 publication.
4. Illustrate the key players, and introduce them.
5. Relate the story of the race, distinguishing the fact that pure research can be very competitive, and because of this, many key players are seldom heard of or credited for their work in major discoveries.

Closure:

This lesson can also be closed with an open-ended question: “Which opinion would you support, a or b?”

a. If research wasn't competitive, we would not have great discoveries.
b. If research wasn't competitive, we would have more great discoveries.

Resources and materials:

reproduction of pictures/diagrams/drawings mentioned above and the means to display/distribute them (Appendix C will have list of where to find the resources suggested for this lesson.);
historical time line handout (Appendix B)

Assignment:

The closure question about opinion a or b can be further assigned as a homework essay for their journal. A scoring rubric must be given first outlining what elements are important to cover while writing the essay.

Lesson 2: Protein Synthesis

This lesson is an activity where function of DNA and the genetic code are explored. This lesson relates the structure of DNA to its integral function of protein synthesis.

Objectives:

-Students will be able to design a gene which codes for a polypeptide chain.
-Students will be able to manipulate and set-up a polypeptide.
-Students will be able to apply learning and employ the genetic code.

Introduction:

This lesson can be initiated with a question: "Can anyone give me an example of a protein?" The brainstormed ideas should be written on the board. Each student could be required to give some sort of response. The teacher would distinguish proteins from other macromolecules.

Content:

1. Review of proteins, amino acids, and dehydration synthesis.
2. Review of transcription, translation and the genetic code.
3. Make a small protein using labeled cutouts of amino acids, color coded for chemical property.

4. Design the gene that coded for your small protein.

Methods and Procedure:

1. Initiate lesson with above question, validating all brainstormed responses.
2. Review all content.
3. Provide students will pre cutout amino acids. Each amino acid would be a part of a large lock and key model, that will fit together only after you cleave (cut) off one hydrogen from one amino group and and oxygen and hydrogen from the carboxyl group of another amino acid. For instance:

H - [ISOLEUCINE] - OH H - [GLUTAMIC ACID] - OH

To form a peptide bond between the two will remove the OH from isoleucine and the H from glutamic acid. One water molecule has been removed and one bond has been formed.
4. Each student will form a small protein that is 15 amino acids long.
5. Once the protein is made, students will work backwards to determine the segment of DNA that coded for this protein, and then will be required to design the piece of complementary messenger RNA.

Closure:

This lesson can be closed with a statement about how essential proteins are to the cell. There are tens of thousands of proteins, each coded for by an individual's DNA. Point out how mutations in DNA can affect the proteins made. Point out how the redundancy in the genetic code allows a little room for this. Lastly point out how good nutrition is also key since the proteins you eat provide you with the amino acids your body needs. Our bodies can make only 12 amino acids, the other 8 we must ingest.

Resources and Materials:

You (or student) will need to make the different amino acid cutouts, enough for 15 per student. Ideally these will be color coded to represent chemical property. In addition, tape and surface paper will be needed.

In Appendix D you will find the genetic code and in Appendix E you will find a list of the 20 common amino acids and their chemical property.

Assignment:

In addition to having to design the gene and the mRNA complement, students should report how many water molecules they produced and how many peptide bonds were formed and attempt to predict any chemical property of their protein.

Lesson Three: Mutations

This lesson is an independent activity where students will determine mutations in sequences of DNA by comparing them with the data given.

Mutations in DNA can be very harmful. Some mutations are congential, meaning you have them at birth because you inherited them. Others can be brought on by some sort of environmental stress. For instance, the UV rays in sunlight directly affect DNA, and can cause it to mutate. Smoking can cause normal cells to turn cancerous, yet the way it does that has yet to be figured out. Mutations will lead to the production of inappropriate proteins that can no longer serve the function they are needed for. Other mutations can be tolerated due to the degeneracy of the genetic code.

Objectives:

-Students will be able to review the codons of the genetic code.
-Students will be able to identify which mutations are functional and which are not.
-Students will be able to integrate the direct link between structure and function.

Introduction:

This lesson can be initiated with a statement about good mutations. Mutations in DNA has led to the vast diversity among all of us. Mutations in DNA can occur during meiosis, or formation of the gametes due to the chromosomes crossing over eachother.

Content:

1. Review codons, and how they code for amino acids.
2. Describe mutations, and how to detect them.

Methods and Procedure:

1. Initiate lesson and describe mutations.
2. Model example of how to find a mutation.
3. Students will work independently on mutation worksheet.

Closure:

This lesson can be closed with a statement about the link between environmental stress and mutation. Describe why UV rays can be so harmful. The ozone layer blocks out these harmful rays, yet with the depletion of this layer, more of these rays are striking us down here on earth. What can be done to decrease your risk from these harmful rays?

Resources and Materials:

In Appendix F you will find the mutations worksheet, which is one way to present this lesson's objectives.

Assignment:

Students could have a journal assignment where they are to respond to a question such as: A friend of yours likes to tan in the sun and in tanning salons. This person does not know about DNA and mutations. What might you tell this person?

APPENDIX A

Glossary of Bold Terms

adenine: a nitrogenous base that is a purine; bonds to thymine

amino acid: basic subunit of proteins; there are 20 amino acids; composed of a central carbon atom bonded to a hydrogen, an amino group, a carboxyl group and a side chain

anticodon: a sequence of three bases of a transfer RNA molecule that pairs with the complementary three nucleotide codon of an mRNA molecule during protein synthesis

atoms: the smallest particle of a chemical element

base pair rules: purines and pyrimidines bond with each other; A-T and C-G

B form of DNA: the form of DNA that is most common; right hand turn of double helix; the form of DNA with the structure as that proposed by Watson and Crick

biotechnology: the use of living organisms or their components to do tasks

Central Dogma of Molecular Biology: transcription of DNA to RNA and the translation of RNA into protein; forms the backbone of molecular biology

codon: a three nucleotide sequence of DNA or mRNA that specifies a particular amino acid

complementary: refers to strand of DNA or mRNA that is formed from a template strand; follows base pairing rules

cytosine: a nitrogenous base that is a pyrimidine; bonds with guanine

dehydration synthesis: a type of reaction where two molecules are bonded together by the removal of water

deoxyribose: a five carbon sugar found in DNA; differs from ribose since it is missing one oxygen atom

DNA (deoxyribonucleic acid): the nucleic acid found in the cells of an organism; the hereditary material passed on during reproduction

double helix: refers to the double stranded model of DNA where two parallel strands are bonded, and twist 360o

enzymes: protein catalysts that are necessary for most of the chemical reactions that occur in cells

genes: a sequence of nucleotides in DNA that codes for a particular tRNA, mRNA or protein; distinct unit of hereditary material found on chromosomes

genetic code: the 64 possible combinations that code for amino acids; deciphered by the mid 1960s

guanine: a nitrogenous base that is a purine; bonds with cytosine

helix: spiraled curve or coiled curve

Human Genome Project: a worldwide endeavor to decipher the identity of all human genes; initiated by the Department of Energy and the National Institutes of Health in 1987 to understand the basis of human hereditary

macromolecule: term for a very large molecule made of of chains of repeating units

messenger RNA (mRNA): the type of RNA that carries the code for a protein from DNA to the ribosome where it is translated

nitrogenous bases: part of nucleotide; two families- purines (A,G) and pyrimidines (T, C, and U)

nucleic acid: macromolecules that are composed of nucleotides; DNA and RNA

nucleotide: the base units of nucleic acids; each contains a sugar, a phosphate group and one of four nitrogenous bases

nucleus: in a eukaryotic cell; a large membrane enclosed organelle that contains the cells's DNA

peptide bond: the bond formed between two amino acids by dehydration synthesis

phosphate group: a part of a nucleotide; a negatively charged polyatomic ion with one phosphorus bonded to four oxygens

polypeptide: a chain of amino acids joined by a peptide bond

promoter: a specific sequence of nucleotides that signals the beginning of transcription

proteins: organic compounds consisting of one or more chains of amino acids; contain nitrogen as well as carbon, hydrogen and oxygen

protein synthesis: is the process by which proteins are produced. Three generalized stages include initiation (mRNA finds ribosome), elongation (amino acids are added to growing polypeptide chain, and termination (water cleaves protein from mRNA and ribosome complex

purine: a five membered ring fused to a pyrimidine like ring; adenine and guanine

pyrimidine: a six membered ring make up of carbon and nitrogen; thymine, cytosine, and uracil

Recombinant DNA technology: A set of techniques for combining genes in the lab and transferring this recombinant DNA to others cells where it may be expressed

ribose: a five carbon sugar found in RNA

ribosome: cell organelles that are the site of protein synthesis

RNA (ribonucleic acid): The nucleic acid that is transcribed from DNA

RNA polymerase: an enzyme that links together the growing chain of nucleotides in an RNA molecule

terminator sequence: sequence of nucleotides that ends the transcript

thymine: a nitrogenous base that is a pyrimidine; bond to adenine

transcript: refers to the mRNA transcript transcribed from DNA

transcription: the copying of a genetic message from a strand of DNA to a molecule of RNA

transfer RNA (tRNA): the type of RNA that carries a particular amino acid; anticodon that is complementary to mRNA codon

translation: the process where information coded in DNA is used for the assembly of a particular amino acid sequence

x-ray crystallography: a method where an x-ray beam passes through a crystal of a particular substance which

causes the atoms of the crystal to deflect the x-rays in an orderly array. These diffracted x-rays can expose photographic film to produce a pattern of spots.

Z form of DNA: an alternate form of DNA where the molecule is a left-handed double helix that is longer and thinner than B DNA; has a zig zag appearance

APPENDIX B

Time line Handout

This time line allows room for adding in the events the lesson will highlight. The other information is provided to help make connections and to integrate as much history as possible.

1945 First atomic bomb dropped on Japan; WWII ends

1946 Stalin delivers speech which declares Cold War

1947 Jackie Robinson becomes 1st black man to play major league baseball; Truman Doctrine

1948 Truman elected president

1949 NATO (North Atlantic Treaty Organization) established

1950 Korean War begins

1951

1952 Eisenhower elected president; US tests first hydrogen bomb

1953

1954 Brown vs. Board of Education

1955 Montgomery bus boycott; first McDonalds in IL

1956 Elvis Presly's "Heartbreak Hotel" is number one

1957 Civil Rights Act to give blacks the right to vote; first nuclear power plant opened in PA

1958 Fidel Castro in Cuba

1959 one third of all Americans reside in the suburbs; Castro overthrows Batista

1960 Birth control pills made available

1961 Rachel Carlson, Silent Spring

1962

1963 John F. Kennedy assassinated

APPENDIX C

Sources for pictures/diagrams reference

(lesson plan one)

The page numbers are listed for reference #2 (The Double Helix); the other reference #10 (The Eighth Day of Creation) has a section in the book with many photos but these pages are not numbered. Photos/diagrams which can be found there will be marked with an [*]

1. picture of Erwin Chargaff *
2. picture of Linus Pauling *, pg 37
3. picture of James Waston *, pg 5, 120, 139, 221
4. picture of Francis Crick *, pg 5, 11, 221
5. picture of Rosalind Franklin *, pg 71
6. picture of Maurice Wilkins *, pg 19
7. copy of Rosalind Franklin's x-ray diffraction photograph *, pg 168
8. diagram of the method of x-ray crystallography
9. picture of Watson and Crick standing next to their model of DNA *, pg 215
10. picture of Nobel Prize being awarded to Watson, Crick and Wilkins *
11. copy of journal article published in April 1953 (reference #1)
12. diagram or model of a DNA molecule pg 206, any of the listed references

APPENDIX D

The Genetic Code

The genetic code is redundant. That is there are 64 possible combinations of the 4 different bases yet there are only 20 common amino acids. More than one codon will code for the same amino acid or function. This redundancy in the code is often called degeneracy.

Each codon is a segment of DNA. DNA is transcribed by RNA polymerase into messenger RNA, therefore sometimes you may see a genetic code where uracil (U) is substituted for thymine (T). Although this code presented uses the four DNA nitrogenous bases (A, C, G, and T), please note that it could be considered more appropriate to use the four RNA nitrogenous bases (A, C, G, and U) since the messenger RNA transcript is what is being decoded during translation.

	(1st base)				
	A	C	G	T	
(2nd)					(3rd)
A	AAA Lys	CAA Gln	GAA Glu	TAA stop	A
	AAC Asn	CAC His	GAC Asp	TAC Tyr	C
	AAG Lys	CAG Gln	GAG Glu	TAG stop	G
	AAT Asn	CAT His	GAT Asp	TAT Tyr	T
C	ACA Thr	CCA Pro	GCA Ala	TCA Ser	A
	ACC Thr	CCC Pro	GCC Ala	TCC Ser	C
	ACG Thr	CCG Pro	GCG Ala	TCG Ser	G
	ACT Thr	CCT Pro	GCT Ala	TCT Ser	T
G	AGA Arg	CGA Arg	GGA Gly	TGA stop	A
	AGC Ser	CGC Arg	GGC Gly	TGC Cys	C
	AGG Arg	CGG Arg	GGG Gly	TGG Trp	G
	AGT Ser	CGT Arg	GGT Gly	TGT Cys	T
T	ATA Ile	CTA Leu	GTA Val	TTA Leu	A
	ATC Ile	CTC Leu	GTC Val	TTC Phe	C
	ATG*Met	CTG Leu	GTG Val	TTG Leu	G
	ATT Ile	CTT Leu	GTT Val	TTT Phe	T

*ATG will code for either START if at the beginning of transcript or for Met if inside the transcript

APPENDIX E

The 20 Common Amino Acids

Proteins, like nucleic acids, are classified as macromolecules; which means they are long chains (polymers) of repeating units (monomers). A process called dehydration synthesis links the monomers together to form the large molecule, or polymer. The protein would represent the large molecule, or polymer, and the 20 common amino acids represent the basic subunits, or monomers, of proteins. When amino acids are adjacent, and lined

up in a particular arrangement, dehydration synthesis will occur. Water will be removed and a peptide bond will form between the two amino acids. Generally small chains of amino acids are called polypeptide chains where as long chains of amino acids are called proteins.

Proteins are essential for the functions of the cell. They are used for structural support (collagen and elastin), transport (hemoglobin), signaling between cells (insulin and other hormones), defense (antibodies), movement (actin and myosin) and as enzymes. A human has tens of thousands of different kinds of protein, each with a specific structure of amino acids and function as determined by the sequence of nucleotides in DNA.

Each amino acid has four partners covalently bonded to a central carbon atom. Three of these partners will always be a hydrogen atom (H), a carboxyl group (COOH) and an amino group (NH2). The fourth partner is the side chain, usually shown as -R. The differences in the atoms of the side chain is what makes each amino acid unique.

Amino Acid Name	Abbreviation	chemical property
glycine	Gly	non-polar
alanine	Ala	non-polar
valine	Val	non-polar
leucine	Leu	non-polar
isoleucine	Ile	non-polar
methionine	Met	non-polar
phenylalanine	Phe	non-polar
tryptophan	Trp	non-polar
proline	Pro	non-polar
serine	Ser	polar
threonine	Thr	polar
cysteine	Cys	polar
tyrosine	Tyr	polar
asparagine	Asp	polar
glutamine	Gln	polar
aspartic acid	Asp	acidic
glutamic acid	Glu	acidic
lysine	Lys	basic
arginine	Arg	basic
histadine	His	basic

APPENDIX F

Mutations Worksheet

Remember, each strand of DNA must be transcribed into its mRNA transcript. You may use T rather than U for ease, but remember that in the cell, mRNA uses uracil to bond with adenine. Use the genetic code to determine your answers.

Since the code is degenerate, it tolerates some mutations. For the following, identify the start codon, and then number the codons with number one being the first after the start codon. With each question you will be given some background. Identify each example under each question as either normal, or give the codon number with a mutation, and the amino acid this mutation codes for.

1. A base-pair substitution is the replacement of a nucleotide pair with another. This can either cause a change in the protein, or it may not due to the degeneracy of the code. The following is the sequence of amino acids in a protein. Which of the following strands of DNA would code for this protein? If it can not, identify the mutation, and the consequent amino acid.

Lys = Phe = Gly = Ala = Leu = Stop

a. A T A T T A C T T C A A A C C G C G T A A C A T T

b. A T A T T A C T T T A A A C C A C G T A A C A T T

c. A T A T T A C T T C A A A T C G C G T A A C A T T

d. A T A T T A C A T C A A A C C G C G T A A C A T T

2. You are a genetic counselor, and just received the results back from the DNA testing you sent out for. Two weeks ago you obtained blood samples from five members of a family that wanted to know if they had sickle-cell anemia. They all exhibit some form of anemia, but they want to know if it is sickle-cell to determine if they will pass it on to their future children. From the blood samples they isolated the gene that codes for the production of hemoglobin. Normal hemoglobin differs from sickle-cell hemoglobin in that valine is inserted into the protein where glutamic acid should be. This difference cause the cells to change shape, resembling crescent moons or sickles, and render them incapable of carrying oxygen. Which of the following samples have a mutation that causes the sickle-cell anemia disorder?

normal hemoglobin: Val = His = Leu = Thr = Pro = Glu = Glu = Lys ....

a. T A C C A T G T G A A T T G G G G T C T C C T T T T T

b. T A C C A A G T A G A A T G A G G C C T T C T C T T C

c. T A C C A A G T A G A A T G A G G C C A A C T C T T C

d. T A C C A A G T A G A A T G A G G C C A T C T T T T C

e. T A C C A C G T G A A T T G G G G T C T C C T T T T T

APPENDIX G

Examples for Modeling Composition of Lyrics for Song

*Sung to the Song of “Row, Row, Row Your Boat”

DNA is great, an amazing molecule

for our bodies to have live we need this mighty tool.

If we think about, the way it works all day

it never leaves the nucleus and this is what it’d say:

Oh I am so great, because of me you live

proteins, enzymes, hormones too- all these things I give.

But I’m not so great, since I can’t do it all

I tell the others what to do, my part might seem quite small

First there’s RNA, to write down my cute code

polymerase helps, I bid good bye, they leave my dense abode.

R N A heads for a special ribosome

for a bit the two are joined, they make a happy home.

Now it’s time to translate this genetic note

better be careful, for it must precisely be a quote.

They need a little help to get this job done right

quickly transfer RNA comes bouncing into sight

Each tRNA brings a special package

soon to be part of a protein but for right now it’s an amino acid.

Each triplet is a word that orders what to do

now tell me would this all get done if it were up to you?!

*Sung to the Song of “Twinkle, Twinkle Little Star”

Crick and Watson were the first

biochemistry can be nursed.

For the two were on the trail

but their data came by mail.

Then one day in 53

they knew what the structure be.

Now you wonder how could they

get the structure of DNA.

They viewed a special photograph

they did math and they did laugh

Rosalind Franklin took that pic

which gave the prize to Watson and Crick.

Annotated Student Reading List

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1. Watson, James D. and Francis H. Crick. “Molecular Structure of Nucleic Acids: A Structure for Deoxynucleic Acids.” Nature 171 (1953): 737-738 -A short succinct paper by Watson and Crick that give their proposal for the structure of DNA. 2. Watson, James D., The Double Helix. New York: Macmillan Publishing Co., 1968., 1-232 pp -Great photographs and an excellent source of information on the race to discover the double helix. But remember, it is written by Watson so it is pretty subjective. 3. Micklos, David A., and Greg H. Freyer. DNA Science: A First Course in Recombinant DNA Technology. Cold Spring Harbor, New York: Cold Spring Harbor Lab Press, 1990., 1-477 pp -A lot of detail, yet also a lot of great diagrams and illustrations of recombinant DNA technology. Would be a great reference if resources were available for cloning projects. 4. Watson, James D., et. al. Molecular

Biology of the Gene (4th edition). Menlow Park CA: The Benjamin/Cummings Publishing Company, 1987., 1-1163 pp + index -Excellent diagrams of DNA models. It also contains a lot of details about genetics and replication, topics that could follow this unit. 5. Alberts, Bruce, et. al. Molecular Biology of the Cell (3rd edition). New York: Garland Publishing Inc., 1994., 1-1294 pp + glossary + index -A nice place to review structures of eukaryotic and prokaryotic cells. When describing protein synthesis, one talks of different organelles within the cells. This book contains some fabulous electron micrographs and diagrams/drawings of these structures.

Annotated Teacher Bibliography

*same list as above but with these additions. 6. Weaver, Robert F. and Philip W. Hedrick. Genetics. Iowa: Wm. C. Brown Publishers, 1989., 1-576 + glossary + index -It is an older book where genetics is concerned, but still a good one. This takes an in depth look at the molecular basis of inheritance. It also discusses many genetic disorders, and genetic screening- topics one could slip into this unit. 7. Cutnell, John D. and Kenneth W. Johnson. Physics. New York: John Wiley & Sons, 1989., 1-903 pp + index -If you need conversion factors, formulas or information, this is your source. In addition, it contains lots of details about the electromagnetic spectrum, if you can get through it. 8. Cohen, Jon. “The Culture of Credit.” Science Vol 268 #5218 (1995): 1706-1711 -This article discusses scientific credit, those who earned it and those who didn’t. This could be a great article to promote an open ended writing assignment that ties in the loss of credit on Rosalind Franklin’s behalf with the same occurring with more recent scientists. Great discussion of ethics in science. 9. Watson, James D., et. al. Recombinant DNA (2nd edition). New York: WH Freeman & Co., Scientific American Book, 1992., 1-626 pp -Watson takes an in depth look at biotechnology and recombinant DNA technology. As good as [3] but with many more details. 10. Judson, Horace Freeland. The Eighth Day of Creation. New York: Simon and Schuster., 1979 -I think this was my favorite reference to read. He describes the rich history in the double helix race and it is written with an objective viewpoint. In addition, there are so many great photographs.

Materials for Classroom Use.

This unit does not offer materials outside of the reading list of resources. It does however, provide in the lessons and the appendices the materials that would facilitate effectively teaching this unit.