**Study Plan: Episode 4—Reading the Code of Life**

1. Read the UNIT OVERVIEW presented in this Study Guide.
2. View the video "Reading the Code of Life."
3. Read UNIT OBJECTIVES and KEY CONCEPTS sections of this study guide.
4. View the video a second time, this time taking notes. Pay particular attention to topics identified by the UNIT OBJECTIVES or KEY CONCEPTS as significant.
5. Read Chapter Four in Microbes and Society, pages 58 – 86.
6. Return to the Unit Objectives and Key Concepts listed in this Study Guide. Do you feel you have achieved each objective? Review sections of the text or video pertinent to material you don't feel you have mastered.
7. Test your mastery of the material by answering the Review Questions at the end of this Study Guide.
8. Check your answers against the answer key; review material relating to any questions you missed.
9. Explore further! Retrieve from the library the articles listed in Suggested Further Reading that sound interesting.

**Unit Overview**

Directions for the synthesis of proteins, molecules that do the work of the cell and give it its structure, are stored in DNA. The information stored in DNA is organized into genes. Genes are transcribed into mRNA, a working copy of the gene that is subsequently translated into a protein. The arrangement or sequence of the nucleotide bases contained within a gene determines the structure of the protein for which it codes. The proteins are what end up operating the cell and providing structure for the cell.

A mutation is heritable change in the DNA sequence of an organism. Mutations produce genetic variability; genetic variability promotes species survival in a changing environment. Note, however, that beneficial mutations are very rare as compared to harmful mutations.

Among mutations important to bacteria are those which confer resistance to antibiotics. In the presence of an antibiotic, susceptible cells die and resistant mutants, now without competition, thrive; they reproduce and ultimately dominate the population. The rise in antibiotic resistance has become a public health concern. We cannot stop mutations in bacteria, which are common due to the rapid growth rate of the bacterial cells, but we can use antibiotics responsibly and look for new antibiotics.

As antibiotic-resistant bacteria emerge, the on-going discovery of novel antibiotic compounds becomes increasingly important. Many antibiotics, like penicillin, are produced by microorganisms. Certain microorganisms that live in soil produce diverse antibiotics, which they use to destroy neighboring bacterial who are competing for nutrients. Streptomycin and its derivatives, for example, block protein synthesis in target cells. Penicillin and its derivatives disrupt the formation of chemical bonds that hold bacterial cell walls together. Penicillin and its derivatives cause the cell wall to weaken until it ruptures.

The search for antibiotic-producers has traditionally been limited to screening organisms isolated from nature. Modern molecular techniques, however, have made it possible to isolate, directly from a particular source, the genetic material of organisms, which will not grow under laboratory conditions. Segments of recovered DNA are engineered into host organisms that thrive in "captivity"; the hosts are subsequently screened for gene expression.

Expression of a gene is subject to regulation, enabling cells to save energy by producing only the proteins they need. To encourage optimal antibiotic production in host cells, gene regulation must be well understood.

**ANTIBIOTIC RESISTANCE**

Antibiotics should be prescribed with restraint and care. Why? Besides performing their intended function, they commonly disrupt the balances among bacterial populations that normally compete for resources in the mammalian intestines and other locations on or within the body. Such disruptions lead to secondary infections by species normally held in check by superior competitors. The superior competitors are killed by the antibiotics, and the other microbes are then free to grow unchecked.

Worse yet, antibiotics have been overprescribed in the human population. Too frequently they have been used for simple infections that many individuals could have overcome successfully on their own. Disturbingly, many antibiotics have lost their punch. Over time, they did destroy the most susceptible cells of their target populations. But they also favored their replacement by more resistant cells. Millions of people around the world are now dying of tuberculosis, cholera, and other bacterial infections. Even vancomycin, held in reserve as "the antibiotic of last resort" is no longer effective against certain pathogenic strains of gut-inhabiting (or enteric) bacteria. In 1996 the World Health Organization announced that, in the race for supremacy, pathogens are sprinting ahead.

Since many antibiotics are produced my other microorganisms an intensive hunt is underway for new antibiotics. One such strategy is to collect soil-borne organisms in the Chernobyl area where a nuclear accident occurred (by scientists such as Jennie Hunter-Cevera and Yuri Gleba). The thought is that the radiation would increase the rate of mutation and the microorganisms might mutate and produce a new antibiotic to which there would be no resistance.

Another avenue that is being pursued is to clone the DNA from an environmental sample and try to produce the proteins from the cloned DNA (e.g. Julian Davies of TerraGen Diversity). This approach has potential when the organisms cannot be cultured because of a dependency upon communities that exist within the microbial world.

**Unit Objectives**

* Describe the structure of DNA and how it is replicated.
* Explain the two steps in gene expression: transcription and translation.
* Explain how gene expression is regulated
* Distinguish between a repressor and an inducer.
* Explain the difference between genotype and phenotype.
* Explain how the microbial genome changes by mutation and the relationship to antibiotic resistance

**Key Terms**

* Chromosome
* Codon
* Deoxyribonucleic acid (DNA)
* Exon
* Gene
* Intron
* Messenger RNA (mRNA)
* Nucleotide
* Promoter
* Repressor protein
* Ribonucleic acid (RNA)
* Ribosome
* Semi-conservative replication
* Transcription
* Transfer RNA (tRNA)
* Translation

**Key Concepts**

**STRUCTURE AND FUNCTION OF GENETIC MATERIAL**

The Structure of DNA (for pictures refer to your textbook)

* DNA is composed of deoxyribose (a sugar), a phosphate, and a nitrogenous (nitrogen -containing) base. Bases used in DNA are adenine (A), guanine (G), cytosine (C), and thymine (T).
* Deoxyribose and phosphate bond (through a strong **covalent bond**) to form long strands that wrap around a central core of bases, forming a double helix.
* A type of bond called a **hydrogen bond** (a type of attraction that forms between opposite partial electrical charges similar to what holds water molecules together in water) forms between the A-T and G-C bases, forming pairs that hold the two strands together. This is called base pairing and A is considered complementary to T and C is complementary to G (fit together like puzzle pieces not mirror images).
* The DNA molecule can be imagined as a ladder wrapped around a broom stick. Remove the broomstick and you've got the double coil of the DNA double helix. You may remember the pairing sequence A-T and C-G by the phrase, "AT Cottage Grove."

**DNA Replication**

* Replication is making a copy of a DNA molecule.
* Replication must occur prior to cell division
* Replication begins by breaking the A-T and C-G bonds within a short stretch of DNA (unzip), forming a bubble and exposing bases to pair with "free" nucleotides in the vicinity (dissolved in the cytoplasm of a bacterium or nucleus of a eukaryotic cell).
* The enzyme DNA polymerase facilitates the joining of the new nucleotides into a new DNA strand
* Each newly formed strand of DNA is complementary to the template (original strand).
* If the old unzipped strand was GCTTATGC the new one would be CGAATACG
* Replication begins at a genetically specified point on the chromosome called the origin.
* Replication forks travel simultaneously in opposite directions around the chromosome. When they meet at a point called the terminus, the two completed chromosomes separate.
* At the end of replication you get two uble-strands of DNA. Each double-strand of DNA is composed of one original strand and one newly-synthesized strand. This is what we call semi-conservative replication.

**Gene Expression**

Gene expression consists of two steps: transcription and translation. The end result is the production of a protein from the information encoded in the base sequence of the DNA

**Transcription**

* Transcription is the polymerization (construction or synthesis) of ribonucleotide building blocks into a molecule of RNA - either messenger RNA (mRNA), transfer RNA (tRNA), or ribosomal RNA (rRNA).
* RNA is much like DNA, but differs in:
* Its sugar (in RNA the sugar is ribose and in DNA it is deoxyribose)
* One of its nucleotides (the base, uracil (U), is used instead of thymine of DNA; uracil base pairs with adenine
* RNA is a single strand (not double as in DNA)
* RNA is one gene's worth, while DNA strands contain many genes - all the genes necessary for the cell to live.
* Transcription begins when the information in DNA is transcribed (rewritten) into RNA: C pairs with G and A pairs with U (uracil).
* Transcription begins near a site on the genome called a promoter. Here RNA polymerase (an enzyme) separates the two strands of the DNA "ladder", forming a bubble in the DNA. It stops at a place called the terminator. The mRNA transcript is released and the DNA bubble closes.

**Translation**

* Translation is the polymerization or assembly of amino acids into a protein.
* All three types of RNA molecules participate in translation, but mostly the mRNA and the tRNA seem to be highly active in the process.
* The language of DNA is read in groups of 3 bases (the three bases are called a triplet in the DNA and a codon in the mRNA); each group of three bases code in the RNA is deciphered into 1 amino acid (the language of proteins).
* mRNA carries the information that determines the order of amino acids in the protein.
* rRNA is a component of ribosomes, the site of translation. A ribosome is a very large molecule composed of rRNA and proteins. The ribosome is an enzyme complex – not an organelle as some sources indicate.
* tRNA carries the appropriate amino acids to the ribosome. Each tRNA has two active sites: the anti-codon site that recognizes a complementary or matching mRNA codon and a site that recognizes the corresponding amino acid.
* The specificity of codon-anticodon pairing determines the sequence of amino acids in a protein. The correspondence between codon and amino acid is called the genetic code.
* The genetic codes specifies 20 different amino acids
* Three of those codes actually tell the ribosome to stop translation.

**REGULATION OF GENE EXPRESSION**

* Gene expression is usually regulated by increasing or decreasing the rate of transcription or translation.
* Not all genes need to be expressed all the time (would use too much energy) so transcription is often regulated by regulatory proteins.
* Repressor proteins bind to the DNA and physically stop the RNA polymerase. Thus, transcription is stopped. Inducer proteins physically bind to repressors and change the ability of the repressors to block transcription and thus, transcription increases.
* *Inducible* enzymes are produced only when their substrate is abundant.
* *Repressible* enzymes are produced only when their product is scarce.
* *Constitutive* enzymes are always produced.
* *Irrepressible* students will be continuing with their study of biology, in spite of this sticky tangle of terms!

**CHANGES IN A CELL'S GENETIC INFORMATION** (mutations or genetic exchange)

**The Genome**

* The genome is the sum total of a cell's genetic information (DNA).
* The genome can change by mutation or by genetic exchange.
* Most of a prokaryote's genes are in its single, circular chromosome. Some are in small circular pieces of DNA called plasmids.
* Some plasmids have genes that encode resistance to antibiotics (called R plasmids).
* Most eukaryotes do not have plasmids; most of their genome is in chromosome pairs.
* *Genotype* is the genes that a cell contains. *Phenotype* is the outward expression of a cell's genes.

**Mutations**

* There are a variety of mutations that can occur. For example, a base-pair substitution mutation is the substitution of one base pair with another (also called a point mutation). What all mutations have in common is that they are inheritable to the daughter cells.
* Every time the chromosome is replicated, mistakes can occur and mutations result. The mutation rate is the number of mutations per cell per generation.
* Mutations occur more frequently in microbial populations than in eukaryotic populations because they divide so rapidly. Yet, the rate of mutation is still relatively low because the rate of mutation is estimated to be about 1 mutation every 100 million replications.
* Spontaneous mutations are relatively rare. Induced mutations can be caused by a variety of factors such as tobacco smoke, formaldehyde (chemical), radiation and UV light (physical).
* Many mutations are silent; they do not change the cell's phenotype.
* Lethal mutations result in the destruction of an essential gene product. This is the typical type of mutation.
* Beneficial mutations are extremely rare and when they occur they help the organism in a specific situation. Outside that situation the mutation may actually be detrimental. An example of this is flies that developed resistance to DDT survive the application of that pesticide. However, their growth rate is slower. If they are put into a situation where the pesticide is not used, they will be competing with faster growing, yet DDT-sensitive flies. They end up losing out in that situation.
* There are mechanisms that cells use to repair the DNA, which lowers the mutation rate. The DNA repair mechanism involves enzymes that replace wrong bases with the correct one.

**Review Questions**

**True/False**

1. By the process of translation, RNA makes DNA.
2. The three kinds of RNA are messenger, transfer, and ribosomal RNA.
3. Mutations occur rapidly in microbes because their enzymes make more mistakes when copying their DNA.
4. Both DNA and RNA are double-stranded molecules.

**Fill In**

1. The nucleotides of DNA consist of three parts; a deoxyribose, a phosphate and a \_\_\_\_\_\_\_\_\_\_\_ base.
2. The base pairs of DNA are united by \_\_\_\_\_\_\_\_\_\_\_\_\_bonding.
3. The type of RNA that carries the amino acid to the ribosome is \_\_\_\_\_\_\_\_\_\_\_\_\_.
4. The number of amino acids directed by the genetic code is \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.
5. In the DNA double helix the number of thymine bases always equals the number of \_\_\_\_\_\_\_\_\_\_\_.

**Multiple Choice**

1. During transcription of DNA, the sequence ATCG will order an mRNA base sequence of (remember uracil (U) replaces thymine (T) in RNA)
2. ATCG.
3. GCTA.
4. GCUA.
5. UAGC.
6. The function of tRNA is to
7. build the ribosome.
8. carry amino acids to the ribosome.
9. catalyze nucleotides.
10. transport nucleotides to the ribosome.
11. Select the correct description about the anti-codon.
12. It is found on tRNA.
13. it bases pairs with the codon on the mRNA.
14. It is composed of amino acids.
15. All of the above
16. Both “A” and “B”
17. The genome is the
18. signal for enzyme induction.
19. signal for enzyme repression.
20. sum total of all DNA in the cell.
21. sum total of all DNA and RNA in the cell.
22. Antibiotic resistance
23. allows bacteria to survive in antibiotics than used to kill them
24. is due to mutations
25. is a threat to public health
26. rapidly spreads though bacterial populations because they share genes
27. all are correct
28. Which one of the following comparisons between DNA and RNA is not correct?
29. DNA and RNA differ in the sugar they contain
30. DNA and RNA all contain A, C, and G but only RNA contains U
31. DNA is read 3 bases at time (triplets) and RNA is read 3 bases at a time (codon)
32. DNA and RNA are the same length

**Discussion Question**

1. Much of our knowledge about molecular genetics in humans developed from studying the genetics of microorganisms. What advantages do microorganisms offer for study? How can their genetics be applied to humans?
2. What song is the guitarist playing in the video when they focus on him?

**Answers**

**True/False**

1. F 2. T 3. F 4. F

**Fill In**

1. nitrogenous bases 2. hydrogen (or chemical) 3. tRNA 4. twenty 5. adenine

**Multiple Choice**

1. D 2. B 3. E 4.C 5.E 6. D

**Discussion**

1. Microorganisms are easier to cultivate and control than humans; they present fewer ethical problems. DNA structure, function and behavior are the same in all cells; the genetic code is universal. Many prokaryotic regulatory and repair processes are found in eukaryotic cells; many prokaryotic genes are found in eukaryotic cells. Yeasts can be used to study genetics mechanisms in eukaryotic cells.
2. This is an extra credit question and I am not going to answer the question.

**Suggested Readings**

Ames , B.W. 1979. Identifying environmental chemicals causing mutations and cancer. *Science* 204:587.

Drake, J.W. 1991. Spontaneous mutation. *Annual Reviews of Genetics.* 25:125-46. Freifelder, D. 1987. *Microbial Genetics.* Boston: Jones and Bartlett.

Glass, R.E. 1982. *Gene Function:* E. coli *and its heritable elements.* Berkeley: University of California Press.