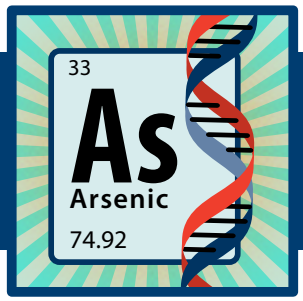
UNIT: DNA
LESSON 1: ARSENIC AND EPIGENETICS: A DNA STORY
Activity 1C: Epigenetic Word Map – Linking Vocabulary



TEXAS BIOMEDICAL RESEARCH INSTITUTE
HEALTH STARTS WITH SCIENCE

Objectives

The Student Will Be Able To:

1. Construct a word map of epigenetic vocabulary. **(Act. 1C)**
2. Interpret the correlation between epigenetic terminology. **(Act. 1C)**
3. Analyze the association of epigenetic concepts. **(Act. 1C)**
4. Analyze a reading passage by applying reading strategies. **(Act. 1C)**

Overview

BACKGROUND

Exploring Deoxyribonucleic Acid (DNA)

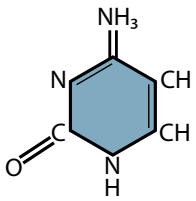
Our understanding of deoxyribonucleic acid (DNA) has changed over the decades from Miescher's 1869 discovery of nucleic acids to Leven's 1919 discovery of the three major components of a nucleotide (phosphate-sugar-base) to Chargaff's 1950 identification of hereditary units now known as ***genes*** to Franklin and Wilkins' X-ray crystallography images which laid the foundation for Watson and Crick's identification of the elegant double helix structure of DNA. These discoveries led to the 2003 decoding the entire ***human genome*** which has exponentially expanded our understanding of the complexities of DNA.

DNA Structure

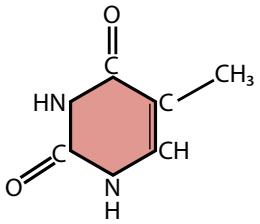
Individual DNA strands are made of ***nucleotides***. Each nucleotide consists of three molecules: a sugar, a phosphate group, and a nitrogen base. The sugar and phosphate make up the backbone of the DNA strand. The sugar is ***deoxyribose*** (dee-oxee-RYE-bose) which is the D in DNA. Each nucleotide has a nitrogen base attached to

Fig. 1

Pyrimidines

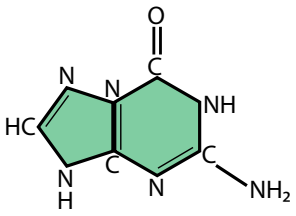


Cytosine
C

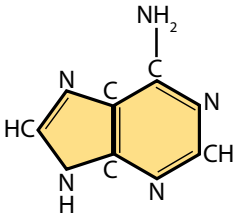


Thymine
T

Purines



Guanine
G



Adenine
A

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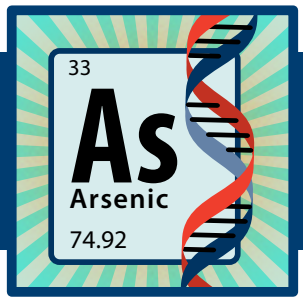
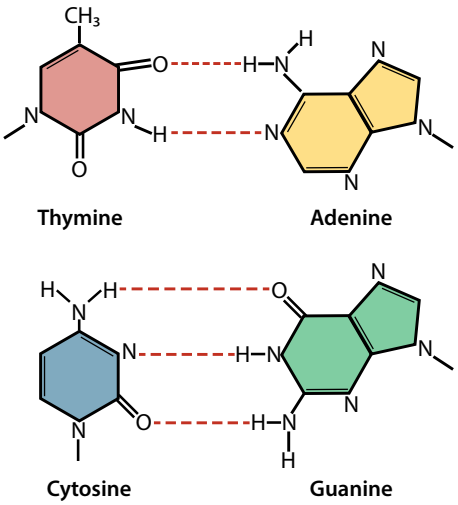


Fig. 2

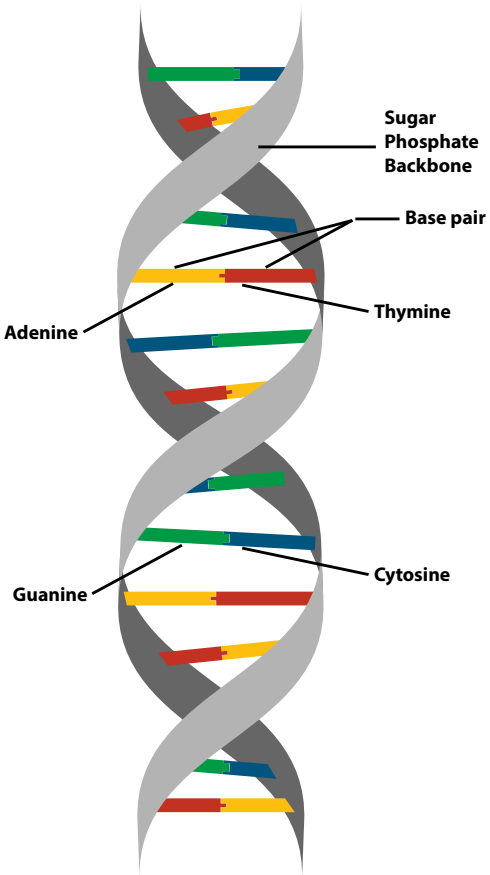


it: ***adenine (A), thymine (T), guanine (G), and cytosine (C)***. There are two types of nitrogen bases: ***purines*** (A & G) and ***pyrimidines*** (T and C). Purines consist of two carbon-nitrogen rings while pyrimidines only have one carbon-nitrogen ring (Fig. 1).

Atoms within each base share electrons to make a stable, neutrally charged molecule. However, not all atoms in each base share electrons equally. This causes ***polarity*** within the molecule, meaning parts of the molecule have a partial negative or positive charge. These opposite charges will attract oppositely charged polar molecules forming weak but important temporary bonds between bases. These are called ***hydrogen bonds*** (Fig. 2).

The hydrogen bonds pull one DNA strand toward a complimentary DNA strand. The bonded DNA strands twist into a double helix structure (Fig. 3).

Fig. 3



DNA
Deoxyribonucleic acid

The DNA contains ***genes***. Genes are formed by combinations of three nucleotides. These sets of three are referred to as ***codons***. The sequence of genes on the DNA determines an organism's ***genotype***. How a genotype is expressed, meaning how it shows up on a body, is known as the ***phenotype***.

Although the DNA strands are chemically bonded to each other, chemical bonds can break. Sometimes bonds which hold the nitrogen base to the sugar-phosphate backbone break and the nitrogen base can move and attach to other sugar-phosphate groups. It isn't just bases that can move. Entire nucleotides can move to different locations on the DNA strand. When bases or nucleotides move or change position, it can affect the genetic code.

DNA contains the genetic information, but that information needs to get from the DNA into the ***cytoplasm*** where cell structures interpret the information and express the gene. Sounds simple, but there is a BIG problem: DNA cannot get through the ***semipermeable membrane*** that surrounds the cell nucleus. How does the genetic code get out of the nucleus?

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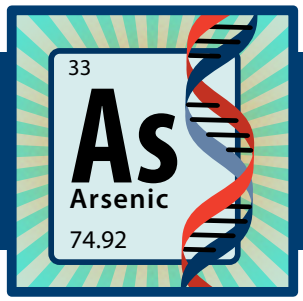
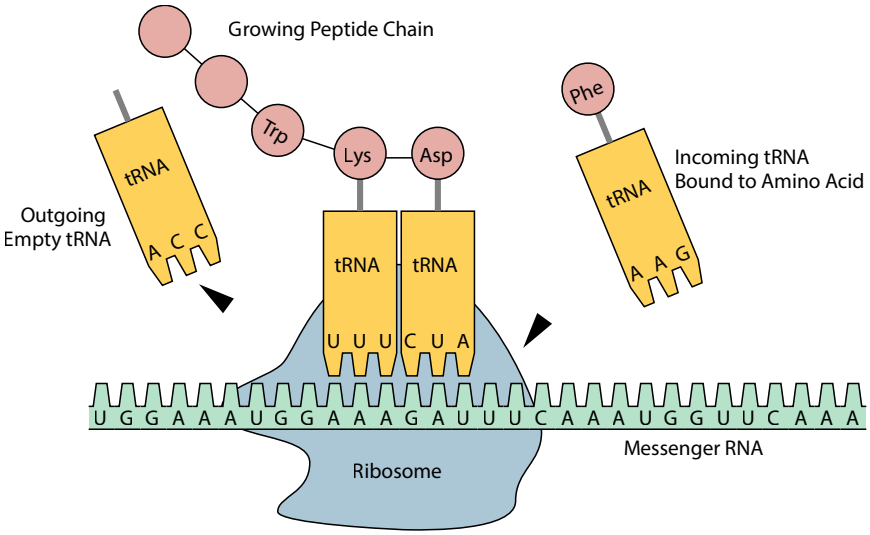


RNA to the Rescue!

Ribonucleic acid (RNA) is a single-stranded molecule made up of a sugar, phosphate group, and nitrogen base. Unlike double-stranded DNA which has deoxyribose as it's sugar, the single-stranded RNA's sugar is ***ribose*** (RYE-bose). During the process of DNA ***transcription***, small portions of the DNA molecule unwind, and hydrogen bonds between nitrogen bases are temporarily broken, exposing codons. The exposed DNA amino acids attract complementary bases, but these individual bases are attached to an RNA nucleotide. Like DNA, each individual RNA building block carries a base. Both DNA and RNA have adenine, guanine, and cytosine bases. But RNA does not have thymine. Instead, RNA has a different base: ***uracil (U)***. Uracil has a similar structure to thymine, so when DNA sections unwind and expose codons, complimentary RNA nucleotides line up with the DNA bases. But, instead of thymine (T) lining up with adenine (A), uracil (U) lines up across from adenine.

The single stranded RNA molecule is assembled as bonds form between adjacent phosphate/ribose molecules. The temporary hydrogen bonds between DNA and RNA bases break and a newly assembled single stranded RNA molecule is formed. The single-stranded RNA can pass through the semipermeable nuclear membrane and carry the genetic code into the cytoplasm.

There are many types of RNA molecules, each with a specialized task. Three types of RNA are engaged with interpreting the genetic code: ***transfer RNA*** (tRNA), ***ribosomal RNA*** (rRNA) and ***messenger RNA*** (mRNA). The mRNA carries the complimentary codon into the cytoplasm. Once in the cytoplasm, rRNA surrounds a strand of mRNA and travels down the mRNA strand like a roller coaster car glides on the tracks. As the rRNA moves along the mRNA strand, tRNA brings in amino acids which pair up with the codon on the mRNA. The amino acids form bonds with adjacent amino acids and form a ***peptide chain***. The resulting peptide chain is better known as a protein.



Peptide Synthesis

Source: Wikipedia, based on work by Boumphreyfr.

There are other forms of RNA. For example, there are long strands of RNA which do not code for any protein. Called long non-coding RNA (lncRNA), these lncRNA were called "junk RNA" and considered not important for metabolic processes. However, research is revealing lncRNA play an important role in activating and de-activating genes, affecting both the genotype and phenotype of an organism.

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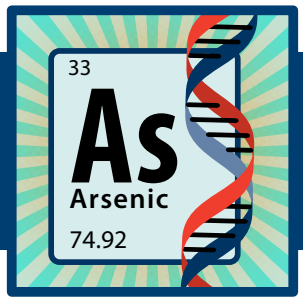


Assembling amino acids to form a protein is called protein synthesis. This is a complex metabolic process and at any point errors can be made. When dealing with complex systems, errors can happen.

MUTATIONS

Although ***microscopic*** or ***nanoscopic***, the processes which take place inside cells are extremely complex. The more complex a system, the higher the chance that mistakes can happen. Sometimes a nucleotide moves to another section of a DNA strand or is eliminated entirely from the strand. When these types of changes occur on DNA, a mutation results. During DNA transcription, mRNA transcribes the mutation and carries this "misinformation" out of the nucleus and into the cytoplasm. Most mutations are harmless, but some can have devasting results.

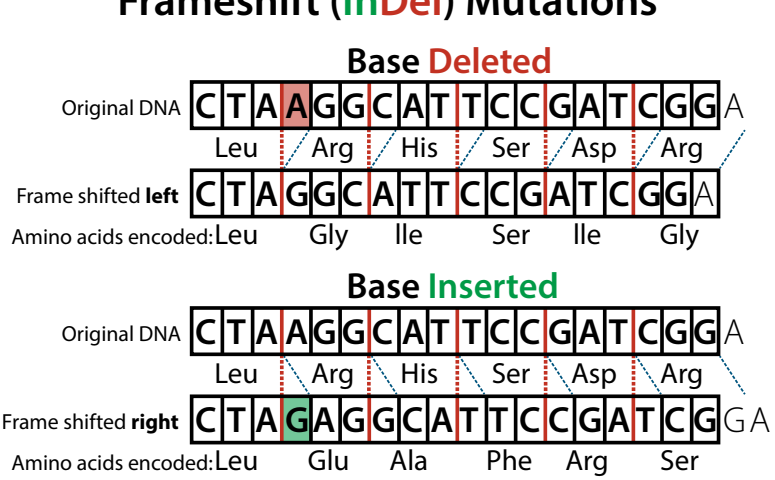
Types of Mutations

Point mutation: a change to a single nitrogen base. Generally, a point mutation is harmless. An example of a point mutation would be an error in pairing. Instead of an A-T pairing, an A-G pairing may result.

Frameshift mutation: These mutations are more serious and can even lead to deadly consequences. In a frameshift mutation, a single base is either deleted from a gene or an extra base is inserted into a gene. This causes a shift to the codon which impacts how the gene is interpreted by the single-stranded mRNA. The entire DNA codon is shifted and every codon from that point on is incorrect. When the mRNA reads the codon, mRNA reads an incorrect code and carries this incorrect code to rRNA. As rRNA "reads" the code, tRNA brings in the wrong amino acid, creating the wrong protein.

There are two types of frameshift mutations: ***insertions*** and ***deletions*** (Fig. 4). Each DNA codon codes for a specific amino acid. For example, DNA codon AGG (adenine, guanine, guanine) codes for the amino acid arginine. However, if the A is deleted, the DNA codon is read as GGC by mRNA. GGC is the code for glycine. This is an example of a ***deletion frameshift***. Using the same DNA codon, if a guanine base (G) is inserted into the DNA strand before the AGG, the codon changes. The mRNA now reads GAG (guanine, adenine, guanine) which is the code for the amino acid glutamine. This is an example of an insertion frameshift.

Fig. 4



Source: *Based on a graphic by Henry K. O'Norman.*

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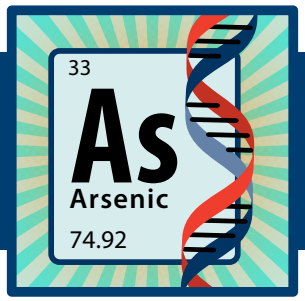

Frameshift mutations can cause ***hereditary diseases*** such as cystic fibrosis and Tay-Sachs disease. The mutation responsible for cystic fibrosis causes is a thickening of the fluids in the lungs, blocking airways and damaging lung tissue which prevents efficient oxygen/carbon dioxide exchange. This eventually leads to respiratory failure and death. Cystic fibrosis also increases risk of secondary infections as the thick fluid traps air-borne pathogens. These secondary infections, like pneumonia, can also be fatal. Tay-Sachs disease is caused by a mutation that prevents the production of an enzyme that helps break down fatty substances called gangliosides. The build up of gangliosides interferes with nerve function, resulting in siezures, paralysis, and death.

Both of these diseases are caused by different frameshift mutations. These diseases cause severe health issues which result in a decreased life span. Frameshift mutations can also lower resistance to various infectious diseases like TB or HIV, which puts individuals at risk without their knowledge. Although mutations in the genetic code are responsible for most inherited diseases, research is showing that the environment can also influence the genetic code.

EPIGENETICS

Epigenetics is the study of how changes in gene expression affects the phenotype which is the physical appearance of an individual, but does not change the DNA sequence. ***Gene expression*** refers to when genes are active or not active. Unlike genetic mutations where genes are rearranged, epigenetic changes affect when genes are "on" and "off". This changes how and when genes are expressed. When genes are turned off, necessary proteins may not be produced or when genes are turned on at the wrong time, proteins are produced not needed. Although the DNA itself is not changed, epigenetic changes in gene expression can be inherited from one generation to the next. Epigenetic changes can also be influenced by environmental factors such as diet, stress, and exposure to toxins, such as arsenic.

Because behaviors (diet, exercise) and environmental factors influence epigentic changes, epigenetic changes can occur throughout your life. Sometimes epigenetic changes can be reversed as behaviors are modified (quit smoking, increase exercise) or detrimental environmental factors (toxins, infectious diseases) are removed. Epigentic changes are passed on from one generation to another, affecting the health of offspring later in life, and can be passed down through multiple generations.

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