Hello everybody, I hope y’all are striving through test week! Welcome to what is likely your final unit of genetics (or perhaps the end of your 3rd)! For those of you who have taken genetics lab, you will see a great deal of overlap.

Remember: the Tutoring Center offers free individual and group tutoring for this Genetics. Our Group Tutoring sessions will be Thursday from 5:15-6:15 PM at the Sid Rich basement, room 75! You can reserve a spot at https://baylor.edu/tutoring. I hope to see you there!

Keywords: Mutation, Mutagen, DNA Repair, Electrophoresis

**Topic of the Week: DNA Mutations and Repair** (18)

**DNA Mutation:** a change in DNA base sequence. May lead to genetic variation and diversity, but may also lead to genetic diseases, cell damage or cancer.

*note: DNA mutations are often used to investigate molecular (DNA/RNA/protein) function in lab (ex. Lac operon)*

- **Somatic:** mutation of a body cell that will not be passed to offspring
- **Germline:** mutation of gametes which will affect an organism’s offspring → genetic diseases

**Causes of Mutations:**
- **Spontaneous:** natural changes in DNA
  - **Strand Slippage:** multiple variations of a sequence occur on a DNA molecule. This could cause the DNA strand to slip and form a loop. The loop itself will give a short deletion. However, the location of the loop will determine the overall change to DNA
  - **Template Strand:** deletion mutation
  - **New Strand:** addition mutation

**Short video:** [https://www.youtube.com/watch?v=E18J1-LP4TU](https://www.youtube.com/watch?v=E18J1-LP4TU)

**Unequal Crossing Over:** misalignment of chromosomes in **Prophase I** of meiosis causes an **insertion** on one chromosome and a **deletion** on another (**indel**).

**Depurination:** removal of a purine (A or G) base from DNA by cleavage of the attachment to the 1’C. During replication, this location on the **template strand** can’t serve as a template, so the DNA-pol will synthesize an A nucleotide on the new strand. (right)

*All diagrams, tables and figures are the property of Benjamin A. Pierce; Genetics: A Conceptual Approach*
Induced: caused by a **mutagen** (something that is mutation-inducing)

**Base Analogs:** a molecule similar to a base that causes transition mutation

**Intercalating Agents:** molecules which intercalate (stick themselves between) the DNA helix; distorted DNA structure leads to **indels** → frameshift mutation

**Ethidium Bromide:** stain used to dye DNA in molecular bio because it intercalates DNA and gives off fluorescent red/purple color

**Radiation:** may change DNA sequence or helix/chromosomal structure

**Ionizing Radiation:** high energy rays penetrate tissue and damage DNA

**Non-ionizing Radiation:** causes bases to dimerizes, forming bulky lesions of DNA (ex. Thymidine dimers from UV radiation) → lesions prevent normal DNA replication

**Types of Mutations:**

**Base Substitution:** one base or type of base is substituted for another

**Transition:** Purine → Purine; Pyrimidine → Pyrimidine

**Transversion:** Purine → Pyrimidine; Pyrimidine → Purine

**Indels:** mutation that causes an insertion and a deletion

**Frameshift Mutation:** changes the entire reading frame; from mutation site downstream all other amino acids are affected

**In-Frame Mutation:** changes a particular amino acid without changing the reading frame; in multiples of 3

**Expanding Nucleotide Repeats (ENR):** when genes exist in many copies, DNA may exhibit *strand slippage* due to hairpin loops caused by complementarity. The number of copies of an ENR gene is directly correlated to how severe its effects are and how early it will onset.

**Anticipation:** Over generations, a particular **ENR** gene will get more and more severe and start sooner because of continued strand slippage

**Protein Mutations:**

**General:**

**Missense:** mutation results in coding for a **different** amino acid

**Silent:** changes in base(s) does **not** result in the change of amino acid due to the degeneracy of the code

**Nonsense:** turns an amino acid codon into a nonsense codon (**STOP**) → ends translation early!

**Specific:**

**Neutral:** change in protein sequence, but **no change** in protein function

**Loss of Function:** takes away a trait normally present (think of as recessive)

**Gain of Function:** gives a new trait **not normally** present (think of as dominant)

**Conditional:** a mutant phenotype that will **only** be expressed under a given [set of] condition(s).

**Lethal Mutation:** causes death in the organism which it affects

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Suppressor Mutations: a mutation that hides the effect of another → restores ‘wild type’

Intragenic: suppressor mutation is in the same gene as the mutation it is affecting
- May alter the original mutation to restore the original amino acid
- May cause a new mutation to give a new and functional amino acid

Intergenic: occurs in another gene affecting the translation of the mutant gene

Effect on Phenotype:
- Forward: normal phenotype to mutant phenotype
- Reverse: mutant phenotype to normal phenotype

DNA Repair:
- Direct repair: Converts altered base back to its original without removal (chemically changes altered base)
- Mismatch Repair: Mismatched bases cause a distorted lesion in the DNA which will be recognized by proteins
  - Lesion is excised by mismatch repair proteins and replace it with special polymerases and new nucleotides

Note: Damage to DNA repair mechanisms can cause diseases like Xeroderma pigmentosum or even cancer

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Highlight #1: Gel Electrophoresis (19.2)

Gel Electrophoresis (GE): Separation of DNA due to its mass (ie molecular weight)
- DNA moves down an electrophoresis gel due to its net negatively charged backbone

Gel: highly porous agarose gel allows DNA to pass through. The largest pieces will travel the furthest and the smallest pieces will travel the least far. DNA is dyed to visualize under UV light (above, right)
  - Cathode (-): the negatively charged pole will repel the DNA towards the anode
  - Anode (+): the negatively charged DNA will be attracted to the positive charge

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Week 11 Concept Check:

1. What is the word for a DNA mutation that would alter the sequence of amino acids in a protein but would not change the protein identity?
   a. Frameshift
   b. Neutral
   c. Silent
   d. Nonsense

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2. DNA of individuals who experienced high levels of radiation at the Chernobyl power plant disaster had severe damage to DNA and chromosomal structure. What type of radiation did they most likely encounter?
   a. Non-ionizing (UV)
   b. Neutral
   c. Slow
   d. Ionizing

3. A DNA molecule moves towards the ______ due to its ______ charge.
   a. Anode; negative
   b. Cathode; positive
   c. Anode; positive
   d. Cathode; negative

4. Bob’s family has a long running genetic disease caused by a single mutated protein. However, Bob does not display this. After a DNA sequence was done, it was found that the disease-causing gene was intact and mRNA was transcribed, but there was another mutation that prevented cap-binding protein from attaching it to a ribosome. What type of mutation does he have?
   a. A neutral mutation
   b. A frameshift mutation
   c. An intergenic suppressor mutation
   d. An intragenic suppressor mutation

5. DNA evidence is collected at a crime scene. The “target” DNA collected is compared to 4 other samples of DNA from suspects. Which DNA profile best matches the target?
   a. A
   b. B
   c. C
   d. D

6. A DNA transition mutation of the following coding sequence could not have resulted in which of the following amino acids?
   5’-ATG-3’
   a. Met (start)
   b. Val
   c. Thr
   d. Ile

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THINGS YOU MAY STRUGGLE WITH:

1. In unequal crossing over, there is no net gain or loss of genetic info; a larger part of a homolog is transferred to one chromosome and the smaller segment of the crossover is transferred to the other chromosome (an **indel**). The issue here in terms of change of DNA is twofold:
   a. The first is that a possible break in a gene could be initiated.
   b. The second is the **serial positioning effect**, where the actual order in which genes are expressed

2. ENR often includes specifically **tri-nucleotide repeats**, thus may be called expanding trinucleotide repeats. They are the same thing, but this is just specific to the number of repeats of a DNA within a given gene.

3. DNA fragment size can be determined by comparing it to a known “ladder.” A ladder is given by a company to show bands of DNA of specific size. Any band horizontal to a ladder band will be the same size.
   a. Exception to this: circular DNA can change shape as it supercoils, so it may travel “further” than DNA with same # of BPs should because it is very condensed

CONGRATS; You made it to the end of the resource! Again, group tutoring will be every Thursday from 5:15-6:30 PM. You can reserve a spot at [https://baylor.edu/tutoring](https://baylor.edu/tutoring). I hope to see you there!

Answers:

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