Hunting the Inheritance of Huntington's Disease MiniLab

Student FRQs

Cat# M3010

Version 073126



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This resource provides 3 total FRQs of the following types:

- Question 1: Interpreting and Evaluating Experimental Results (9 pts)
- Question 5: Analyze Model or Visual Representation of a Biological Concept or Process (4 pts) - 2 Q5s provided

Q1. Huntington's disease (HD) is an inherited progressive, neurodegenerative disorder that is caused when the neurons in the brain die. It was discovered to be caused by a mutation of a CAG trinucleotide repeat in the huntingtin gene (*HTT*). HD is inherited in a dominant manner.

Part A

Describe Mendel's law of segregation.

Researchers are using AMT-130 gene therapy to reduce the amount of mutant huntingtin protein. AMT-130 gene therapy introduces a modified virus carrying miRNA (microRNA) into patient's brains. The miRNA prevents both the disease causing (mHTT) and normal HTT proteins from being produced. Progression of HD is measured by the Unified Huntington's Disease Rating Scale (cUHDRS). Lower cUHDRS scores indicate there is more disease progression and functional impairment. As seen in figure 1, patients' cUHDRS scores were calculated 36 months after receiving AMT-130 therapy and were compared to control patients that did not receive AMT-130.

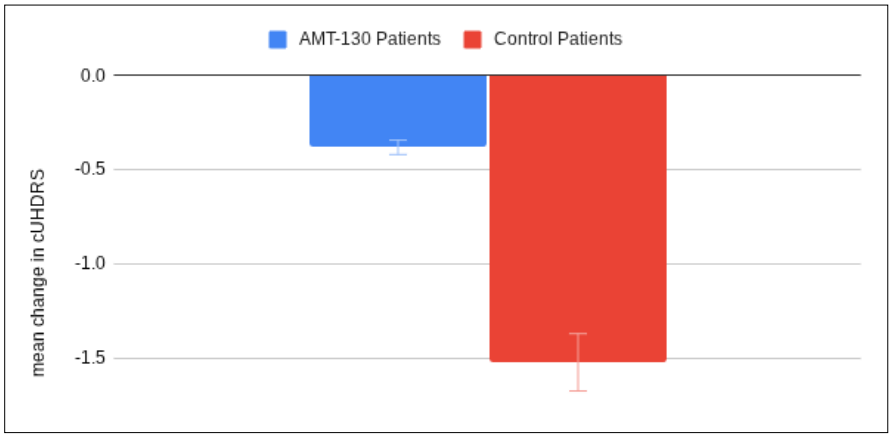


Figure 1: Mean change in CUHDRS 36 months after treatment with AMT-130 gene therapy (Error bars represent $\pm SE_{\bar{x}}$).

Part B:

i. **Identify** the independent variable in the researchers' experiment.

ii. **Describe** the effect of using AMT-130 gene therapy on patients cUHDRS scores.

iii. **Justify** why some patients were not given the AMT-130 gene therapy.

Q1 continued. The HD disease allele usually carries between 40 and 120 repeats of this CAG sequence creating an expanded allele and thus an elongated mutant protein. A different group of researchers claims that the sex chromosomes do not affect the age of disease onset. In a second experiment, these researchers looked at a genome-wide association study assessing the age of onset predicted by CAG length and the actual age of onset of motor symptoms (residual age of onset). A positive residual age of onset indicates an individual develops the first symptoms later than expected by their number of CAG repeats. The researchers then compared the residual age of onset to the patients' combination of sex chromosomes (Figure 2).

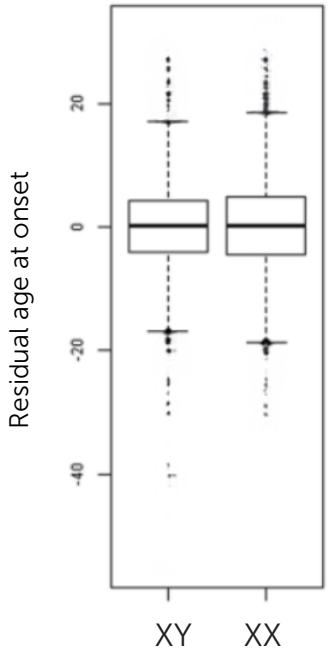


Figure 2: Residual age of onset in patients' with differing combinations of sex chromosomes.

Part C

i. **Identify** the dependent variable in the second experiment.

ii. **Calculate** the difference in the ranges of the residual age of onset for individuals with XY chromosomes and individuals with XX chromosomes.

iii. Based on the data in figure 2, **evaluate** the researchers claim that sex chromosomes do not affect the age of onset.

Q1 continued.

Part D

In a third experiment, scientists used the polymerase chain reaction (PCR) and gel electrophoresis to amplify and separate the DNA fragments. They then analyzed the results to determine how many CAG repeats individuals had. The following results show the huntingtin instability region including the 114 bp in the primers and the bases in the CAG repeats region of instability.

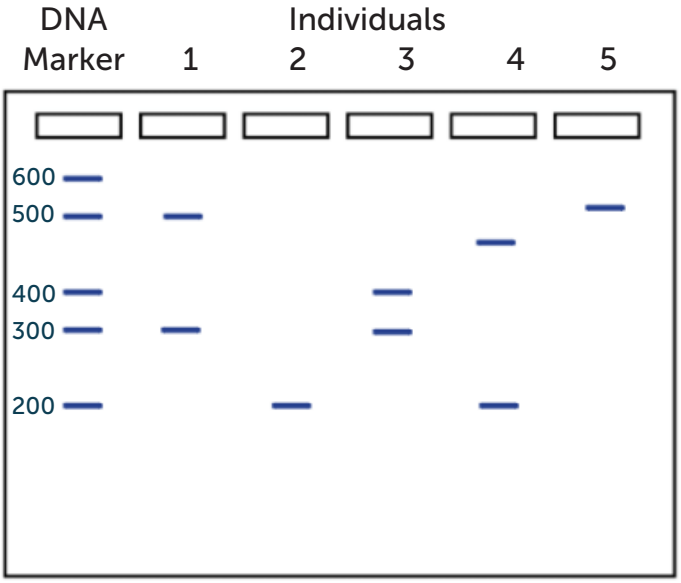


Figure 3: Gel electrophoresis results for CAG repeats and primers for five individuals. The DNA marker has the following number of base pairs: 200, 300, 400, 500, 600.

i. **Predict** all individuals that have at least one mutant gene that would cause Huntington's disease.

ii. **Justify** your prediction.

Q5. Huntington's disease (HD) is an inherited progressive, neurodegenerative disorder that is caused when the neurons (nerve cells) in the brain die. It was discovered to be caused by a mutation of a CAG trinucleotide repeat. While the normal allele of this gene carries between 10 and 35 copies of this CAG repeat, the disease allele carries between 40 and 120 repeats of this CAG sequence creating an expanded allele and thus an elongated mutant protein. The CAG trinucleotide repeat has been observed to exhibit dramatic instability when transmitted to subsequent generations once individuals have around 35 repeats. This means that the number of CAG repeats may increase from one generation to the next.

Part A

Describe the type of mutation displayed by the CAG trinucleotide repeat.

To investigate the inheritance pattern of HD, researchers studied a family and created the following pedigree (Figure 1).

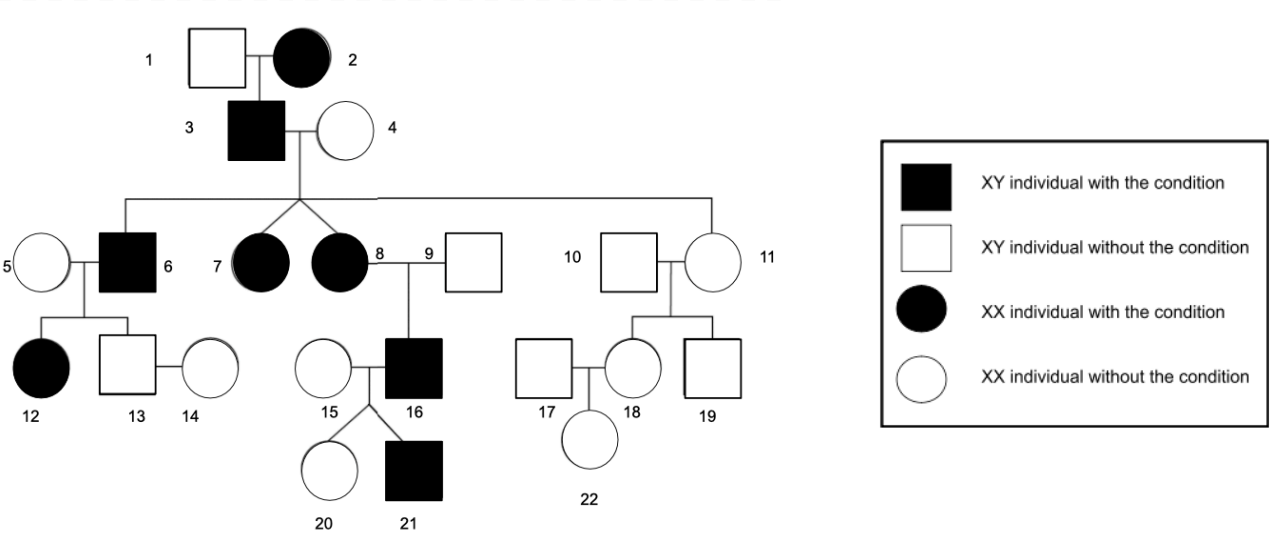


Figure 1. The phenotypes of five generations of a family with respect to HD. Individuals are numbered.

Part B

Explain how individual 11 does not have the condition but individual 3 does.

Part C

Using Figure 1, **identify** the type of inheritance pattern followed by Huntington's disease.

Part D

A student claims that individual 21 will have fewer repeats than individual 7. **Evaluate** their claim.

Alternate Q5. Huntington's disease (HD) is an inherited progressive, neurodegenerative disorder that is caused when the neurons (nerve cells) in the brain die. It was discovered that the disease has an autosomal dominant inheritance. HD is caused by a mutation of CAG trinucleotide repeats. While the normal allele of this gene carries between 10 and 35 copies of this CAG repeat, the disease allele usually carries between 40 and 120 repeats of this CAG sequence creating an expanded allele and thus an elongated mutant protein.

Part A

Identify the possible phenotypes of the offspring of a father that has 64 repeats on one allele and 22 repeats on the other allele and a mother that has 40 repeats on one allele and 8 on the other allele.

Scientists used the polymerase chain reaction (PCR) and gel electrophoresis to amplify and separate the DNA fragments. They then analyzed the results to determine how many CAG repeats individuals had. The following results show the huntingtin instability region including the 114 bp in the primers and the bases in the CAG repeats region of instability.

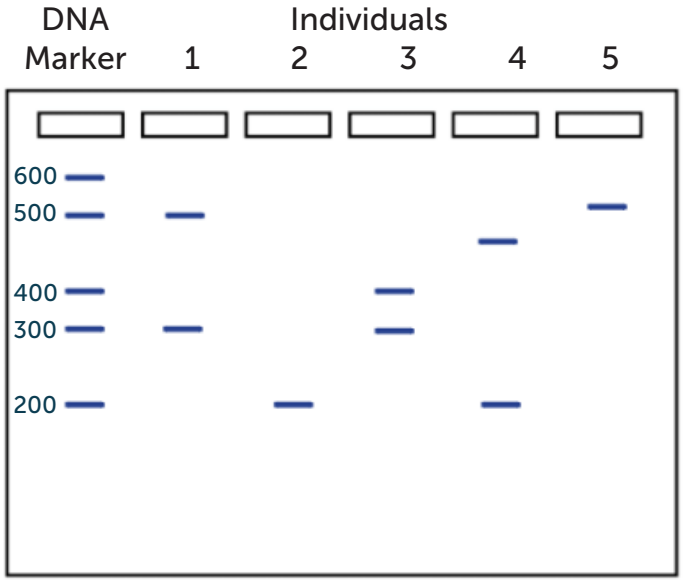


Figure 1: Gel electrophoresis results for CAG repeats and primers for five individuals. The DNA marker has the following number of base pairs: 200, 300, 400, 500, 600.

Part B

Explain how the DNA is able to be separated by the process of gel electrophoresis.

Part C

Determine which individuals have Huntington's disease.

Part D

Individual five only has one band of DNA shown. **Explain how** the researchers' electrophoresis results could still be accurate.

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