DRAFT - Chromosome Connections Kit©: Constructing Punnett Squares

Student Activity Guide

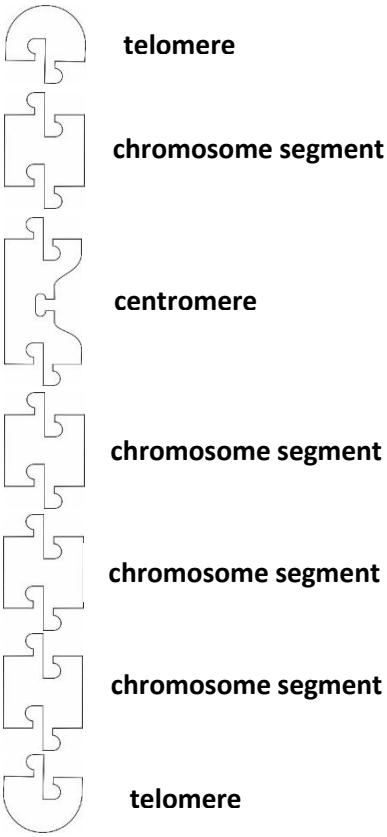
The probability of the genetic traits of offspring from a cross between individuals of known genetic composition can be determined using **Punnett squares** as a predictive tool.

Modes of Inheritance: Sickle Cell Disease - An Example of Recessive Inheritance

Introduction: **Sickle cell disease** is a **recessively inherited condition** due to a single point mutation in the gene for beta-globin protein found on chromosome 11. The mutation results in a beta-globin protein change from the amino acid glutamic acid to valine. People with the condition have atypical hemoglobin molecules which can distort red blood cells into a sickle shape. Painful episodes can occur when the sickled red blood cells get stuck in the capillaries depriving tissues and organs of oxygen-rich blood.

Constructing Chromosomes with Gene Sequences

Step 1: Use the red chromosome pieces to assemble a model of maternal chromosome 11. Human chromosome 11 is classified as a submetacentric chromosome with its centromere slightly above center making the p arm of the chromosome shorter than the q arm. We suggest the configuration shown below.



The beta-globin gene is located in the p arm (top section) of the chromosome.

Step 2: Use the red nucleotides to assemble the portion of a normal beta-globin DNA gene sequence shown below:

3' G G A C T C C T C 5'

5' C C T G A G G A G 3'

Step 3: Use the insert pieces to assemble a maternal chromosome with the beta-globin gene DNA sequence in place. See photograph below.

Note – insert improved photos of chromosomes with gene sequences inserted.

Step 4: Similarly, assemble the blue chromosome pieces to model paternal chromosome 11.

Step 5: Use the blue nucleotides to assemble the sickle cell disease beta-globin DNA gene sequence shown below:

3’ G G A C A C C T C 5’

5’ C C T G T G G A G 3’

Step 6: Use the insert pieces to assemble a paternal chromosome with the beta-globin gene DNA sequence in place. See photograph below.

Answer Part 3 questions 1 - 4.

The Genetic Codon Chart©

	U	C	A	G	
U	UUU → Phe F	UCU → Ser S	UAU → Tyr Y	UGU → Cys C	U
	UUC → Phe F	UCC → Ser S	UAC → Tyr Y	UGC → Cys C	C
	UUA → Leu L	UCA → Ser S	UAA → Stop	UGA → Stop	A
	UUG → Leu L	UCG → Ser S	UAG → Stop	UGG → Trp W	G
C	CUU → Leu L	CCU → Pro P	CAU → His H	CGU → Arg R	U
	CUC → Leu L	CCC → Pro P	CAC → His H	CGC → Arg R	C
	CUA → Leu L	CCA → Pro P	CAA → Gln Q	CGA → Arg R	A
	CUG → Leu L	CCG → Pro P	CAG → Gln Q	CGG → Arg R	G
A	AUU → Ile I	ACU → Thr T	AAU → Asn N	AGU → Ser S	U
	AUC → Ile I	ACC → Thr T	AAC → Asn N	AGC → Ser S	C
	AUA → Ile I	ACA → Thr T	AAA → Lys K	AGA → Arg R	A
	AUG → Met M	ACG → Thr T	AAG → Lys K	AGG → Arg R	G
G	GUU → Val V	GCU → Ala A	GAU → Asp D	GGU → Gly G	U
	GUC → Val V	GCC → Ala A	GAC → Asp D	GGC → Gly G	C
	GUA → Val V	GCA → Ala A	GAA → Glu E	GGA → Gly G	A
	GUG → Val V	GCG → Ala A	GAG → Glu E	GGG → Gly G	G

Amino Acid Properties

Translation Start Codon · Translation Stop Codon · Hydrophobic / Non-polar · Hydrophilic / Polar · Negative Charge · Positive Charge · Cysteine

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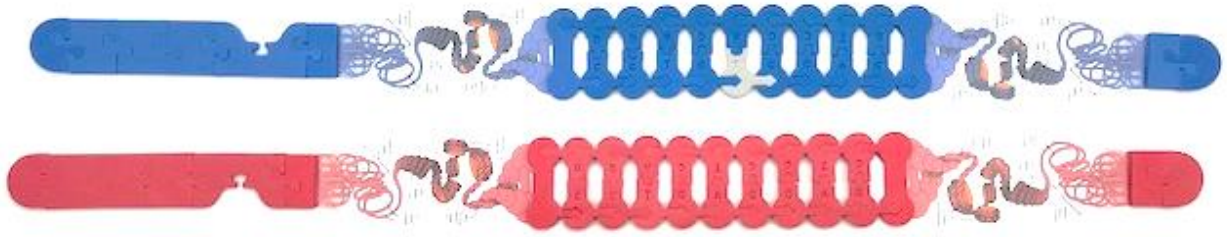
You have identified that a change in a single nucleotide results in a change in the amino acid sequence in the protein. Why is this significant?

Examine the genetic codon chart above to determine the properties for the two identified amino acids.

Answer Part 3 questions 5 - 6.

Each person has two copies of every gene in their genome. Sometimes the alleles are the same on each chromosome. Sometimes the gene sequences differ resulting in different **alleles** on each of the homologous chromosomes.



Answer Part 3 question 7.

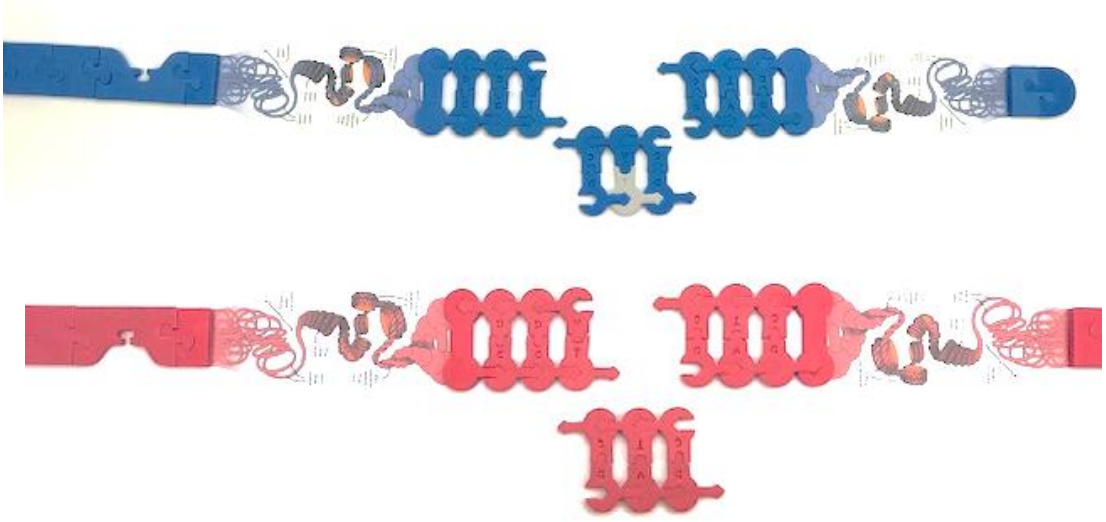
Constructing Punnett Squares

In traditional Punnett squares a capital letter represents the dominant allele while a small letter represents the recessive allele for a trait.

Answer Part 3 question 8.

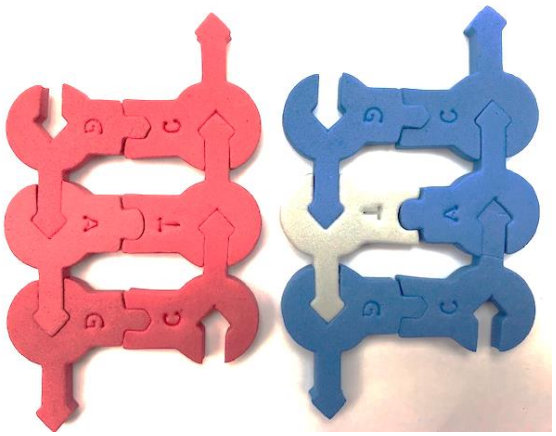
Step 7: Now we will do the same cross using the DNA sequences for the amino acids that are affected by the mutation. The focus of our cross will be on the triplet DNA code that contains the **point mutation**.

Insert improved photo of homologous chromosomes with the sequences highlighted.

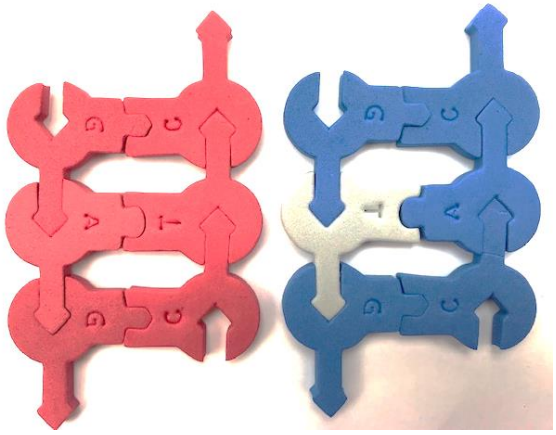


Step 8: Construct the DNA sequences for each of the heterozygous parents as follows:

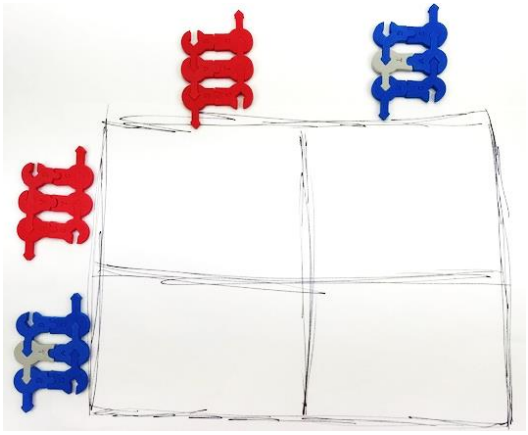
Maternal Parent Sequence



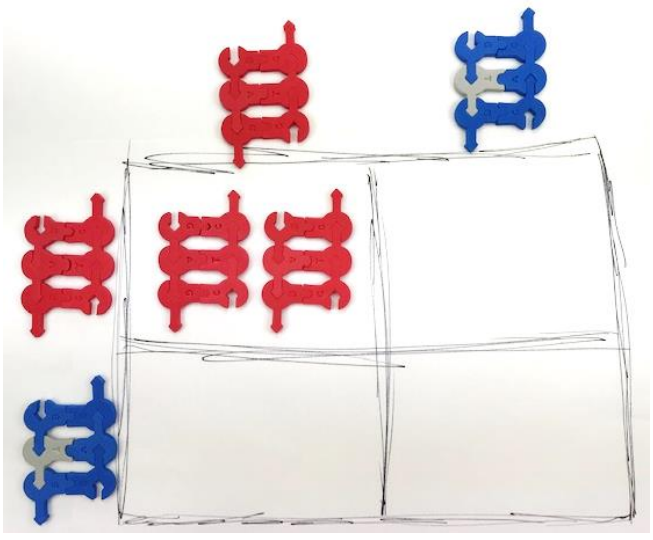
Paternal Parent Sequence



Step 9: Model the Punnett square using the parental sequences you have constructed. See photo below.



Step 10: Complete the Punnett square using DNA sequences to fill in each of the squares. The first box has been done for you. See photo below.



Answer Part 3 questions 9 - 12.

Step 10: Model a cross between an unaffected "carrier" parent (heterozygous) with an affected parent (homozygous for sickle cell disease) using the DNA sequences.

Answer Part 3 questions 13-15.

Step 11: Model a cross between a normal beta-globin parent (homozygous) with an affected parent (homozygous for sickle cell disease) using the DNA sequences.

Answer Part 3 questions 16 – 18.

Modes of Inheritance: Huntington Disease - An Example of Dominant Inheritance

Introduction: **Huntington disease** is a progressive brain disorder that causes uncontrolled movements, emotional problems, and loss of cognition. The most common form of this disorder usually appears in a person's thirties or forties. Mutations in the HTT gene, found on chromosome 4, cause Huntington disease. The HTT gene provides instructions for synthesizing a protein called **huntingtin** whose role appears to affect nerve cell function. The mutation involves a DNA segment known as a **CAG** trinucleotide repeat. Normally, the **CAG** segment is repeated 10 to 35 times within the gene. In people affected with Huntington disease the **CAG** segment is repeated 36 to more than 120 times. In the example below, one segment **CAG** would represent a repeat of 25 times. Two segments of **CAG** would represent a trinucleotide repeat of 50 times.

It is important to note that not all dominantly inherited conditions are due to repeat sequences.

Answer Part 3 questions 19 - 20.

Step 12: Using the sequence examples shown below. Construct the DNA sequence for a parent that is normal for the huntingtin protein.

Normal Huntington sequence (25 repeats)			**Huntington sequence (50 repeats)**		
3'	**G T C**	5'	3'	**G T C G T C**	5'
5'	**C A G**	3'	5'	**C A G C A G**	3'

Step 13: Construct a model DNA sequence for a parent that is heterozygous for Huntington disease where the affected chromosome shows a **CAG** repeat of 75 times.

Answer Part 3 questions 21 - 23.

Modes of Inheritance: Hemophilia - An Example of Sex-linked Inheritance

Introduction: **Hemophilia** is a **sex-linked recessive** blood clotting disorder where affected individuals experience protracted bleeding following an injury or surgery. In the most severe cases, incessant bleeding occurs after only minor trauma or even spontaneously without any damage at all! Complications can result from bleeding into the brain, muscles, joints, or other internal organs.

The major types of hemophilia are hemophilia A and hemophilia B caused by mutations in the F8 and F9 genes, respectively, located on the X chromosome. The F8 gene provides instructions for making a protein called coagulation factor VIII. Coagulation factor IX is a related protein produced from the F9 gene. Changes in these genes result in altered or missing proteins that cannot function effectively in the blood clotting process.

The X chromosome is the largest submetacentric (centromere slightly off center) chromosome in the human genome. The Y chromosome is one of the smallest acrocentric human chromosomes. Biologically speaking, a typical human female has two X chromosomes while a typical human male has one X and one Y chromosome.

Please use a capital **H** to represent the dominant normal clotting allele and a lower-case **h** to represent the recessive hemophilia allele. A female that carries hemophilia would be written as $\mathbf{X^HX^h}$. Remember that the Y chromosome <u>does not</u> carry the clotting factor genes!

Answer Part 3 question 24-25.

Step 13: We will model hemophilia inheritance between a carrier female and a non-hemophiliac male. Construct the following maternal X chromosomes. Note that the X chromosome on the left has the normal F8 gene DNA sequence of:

3’	**G C T**	5’
5’	**C G A**	3’

The DNA sequence for the X chromosome on the right is one of several alleles for F8 gene resulting in hemophilia.

3’	**A C T**	5’
5’	**T G A**	3’

This is only one example of several mutations in the F8 gene that cause hemophilia.

Answer Part 3 question 26.

Step 14: Model the following paternal X and Y chromosomes. Note that the X chromosome on the left has the normal F8 gene DNA sequence of:

3’	**G C T**	5’
5’	**C G A**	3’

The paternal set of chromosomes only has one X chromosome. The second chromosome is a Y chromosome that contains no gene for the F8 gene.

Step 15: Remove the DNA sequences from the maternal chromosomes.

Step 16: Remove the DNA sequence from the X chromosome of the paternal chromosome set and the Y chromosome.

Step 17: Place the maternal and paternal parts in the Punnett square as shown right:

Step 18: Construct the pieces and complete the Punnett square.

Answer Part 3 questions 27-30.