Classical Genetics: Section 1-Observe the pedigree chart below (see figure 1). Circles are female and squares are male. Shaded circles or squares means the individual has a particular trait and an open circle or square means that the individual does not have that trait. The individuals are numbered to facilitate referencing them in your response to the questions below.
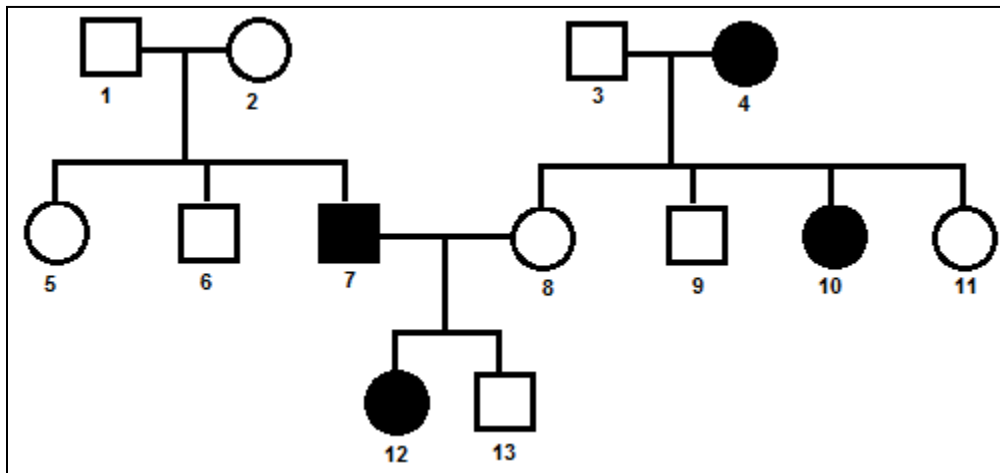

Figure 1

Q1. Based on this pedigree chart, is it possible that the trait is caused by a sex-linked recessive allele? Explain.

The fact that 7 has the trait and 1and 2 do not have the trait suggests that the trait is recessive.

The fact that 10 has the trait and 3 does not means that it cannot be sex-linked, and thus must

be autosomal.

Q2. Give as much of the genotype as possible for the 13 individuals listed. D=dominant allele. d=recessive allele.

1	2	3	4	5	6	7	8	9	10	11	12	13
Dd	Dd	Dd	dd	D_	D_	Dd	Dd	Dd	Dd	Dd	Dd	Dd

Classical Genetics: Section 2-In Drosophila (fruit flies), Gray body (G) is dominant over black body (g); Normal wings (V) is dominant over vestigial wings (v) and large bristles (B) is dominant over small bristles (b). This information is summarized in table 1 below:

Trait	Dominant Allele	Symbol	Recessive Allele	Symbol
Body Color (BC)	Gray	G	Black	g
Wing Size (WS)	Normal	V	Vestigial	v
Bristle Size (BS)	Large	B	Small	b

Table 1

Here are results from two crosses:

GgVv X GgVv	GgBb X GgBb .
597 Gray (BC) Normal (WS)	903 Gray (BC) Large (BS)
204 Black (BC) Vestigial (WS)	308 Gray (BC) Small (BS)
43 Gray (BC) Vestigial (WS)	294 Black (BC) Large (BS)
39 Black (BC) Normal (WS)	98 Black (BC) Small (BS)

Q1. Based on the data above, what can you conclude about the position of the 3 alleles on the Drosophila Flies' chromosomes? Explain.

The cross involving Body Color and Bristle Size (G and B) resulted in a 9:3:3:1 ratio indicating the genes segregated independently. In other words, those two genes are on separate chromosomes. On the other hand, the cross involving Body Color and Wing Size (G and V) suggests that the genes are linked, but crossed over in 82 of 883 offspring.

The ratio of the offspring with both dominant trait to offspring with both recessive traits is 3:1.

Q2. Which of Mendel's laws is exemplified by the data obtained in the 2nd cross? Explain.

The Law of Independent Assortment. The segregation of the Body Color alleles occurred independently of the separation of the Bristle Size alleles.

Q3. What chromosomal phenomena resulted in the 43 Gray (BC) Vestigial (WS) and 39 Black (BC) Normal (WS) offspring? Explain.

Crossing over. We know from the 3:1 ratio of the Gray/Normal:Black/Vestigial that the genes are linked. So the only way to have Gray/Vestigial or Black/Normal is if a crossover occurred between the two genes.

Q4) What is the map distance between the genes (in map units) controlling body color and wing size? Show your work.

The distance between the two genes is (82/883) x 100 or 9.3 map units.

Classical Genetics: Section 3- In a plant called "blue eyed Mary (*C. parviflora*) there is a two step process used to make a blue colored pigment in the flower. Each step is dependent on an enzyme. Gene A codes for the enzyme needed in the first step and Gene B codes for the enzyme needed in the second step. The genes are not linked. The reaction is summarized in Figure 1.
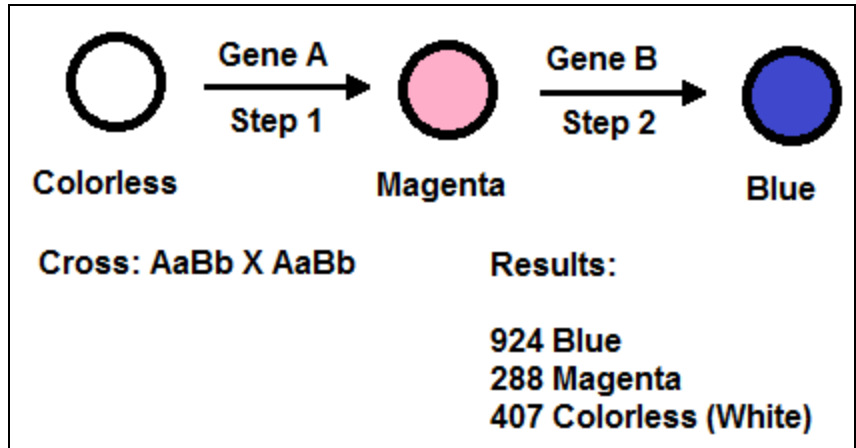

Figure 1

Q1. What is the phenotypic ratio expected in the cross: AaBb X AaBb?

Show Work Here

_____9 Blue: 3 Magenta: 4 Colorless_____

9 A_B_   Blue

_____

3 A_bb   Magenta

_____

3 aaB_   Colorless

_____

1 aabb   Colorless

Q2. Do the actual results shown in figure 1 support the null hypothesis? Explain. Use the Chi Square table provided by your teacher. Show all work below.

Offspring	Expected (e)	Observed (o)	(o-e)	$(o-e)^2$	$(o-e)^2/e$
Blue	910	924	14	196	0.215
Magenta	304	288	-16	256	0.842
Colorless	405	407	2	4	0.00899
				X^2=sum	1.07

There are two Degrees of Freedom: The Chi Square value is lower than 5.99 meaning that that the data does support the null hypothesis…these results can be explained by chance alone; so we need not look for other factors to explain the very small deviation. We are over 95% sure that the inheritance mechanism that we considered is consistent with the data collected…that is…any deviation could be explained by chance alone.

Q3. If the offspring are colorless (white), can you tell whether the plant makes the enzyme necessary for step two of the chemical reaction? Explain. (Bonus: What type of inheritance is involved in this cross?)

If the offspring are white (colorless), one knows that they do not make enzyme A, but one does not know if enzyme B is produced. This is an example of epistatic inheritance.

Classical Genetics: Section 4-In a slightly different twist from the last problem involving corn, the production of the purple pigment anthocyanin requires a two step process dependent on enzymes coded by unlinked genes A and B respectively (see Figure 1).
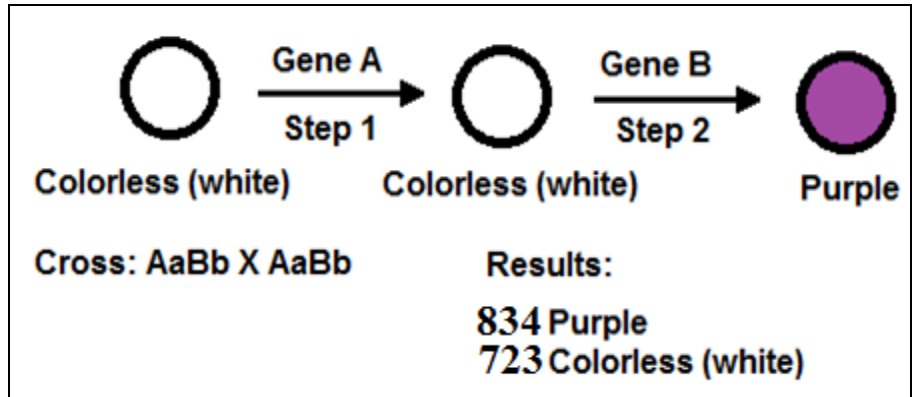

Cross: AaBb X AaBb

Results:

834 Purple
723 Colorless (white)

Figure 1

Q1. What is the phenotypic ratio expected in this cross?

_____9 Purple: 7 White_____

Show Work Here

9 A_ B_	Purple
3 A_ bb	White
3 aa B_	White
1 aa bb	White

Q2. Do the actual results (see figure 1) support the null hypotheis? Explain. Use the Chi Square table provided by your teacher. Show all work below.

Offspring	Expected (e)	Observed (o)	(o-e)	$(o-e)^2$	$(o-e)^2/e$
Purple	876	834	-42	1764	2.01
White	681	723	42	1764	2.59
				X^2=sum	4.60

There is one degree of freedom: The Chi Square value is higher than 3.84 meaning that the data does not support the null hypothesis…these results cannot be explained by chance alone; so we need not look for other factors to explain the deviation. One factor might be based on experimental error.

Q3. (Bonus: What type of inheritance is involved in this cross?). Explain.

This cross exemplifies complementary genes. Both enzymes are needed to make the purple pigment, hence at least one dominant allele is needed in both genes in order to make the purple pigment.

Classical Genetics: Section 5-The following questions relate to diseases which are caused by a sex-linked recessive allele.

Q1. A woman who is normal has a brother who dies from Duchenne's Muscular Dystrophy. Her parents are both normal. What are the chances that she is a carrier of the disease?

Show Work Here

_____50%_____ D = normal. d = Duchenne's Muscular Dystrophy

The Woman's Parents are: $X^D X^d$ and $X^D Y^o$

She definitely received an X^D from her father

and there is a 50% chance she received an X^d

from her mother and that would make her a

carrier.

Q2. Hemophelia is also caused by a sex-linked recessive allele. A girl's mother is normal, but she has a brother and father with the disease, but she is normal. What are the chances that she is a carrier of the disease? What are the chances that her mother is a carrier?

Show Work Here

____100 % and100%_____ H = normal and h = hemophelia

The Woman's Parents are: $X^H X^h$ and $X^h Y^o$

Since she is normal, she must have received the

X^H from her mother, but the father had to have

contributed an $X^{h,}$ therefore is a 100% chance

that she is a carrier. Her normal mother had to

have passed an X^H to her. Since her brother had

the disease, he must be $X^h Y^o$. Since the mother

contributed an X^H to her and an X^h to her

brother, the mother must be a carrier.

Q3. The girl's mother and father are expecting another child. What are the chances that the child will have the disease?

Show Work Here

_____50%_____ The 4 possible genotypes (phenotypes) of the

offspring are $X^h X^h$ (female, hemophelia), $X^H X^h$

(female, normal), $X^h Y^o$(male, hemophelia),

$X^H Y^o$ (male, normal) in equal (25%) frequency.

Classical Genetics: Section 6-Tay-Sachs disease is caused by an autosomal recessive allele. The disease is due to a mutation in the HEXA gene on chromosome 15 such that the individuals with the disease are unable to make hexaminidase A. This results in the buildup of fatty substances called gangliosides which eventually causes the premature death of brain cells. Most children with the disease die by the time they are 4 years old.

Q1. A couple is expecting a baby. Both members of the couple each lost a sibling to this disease. What are the chances that the baby will have the disease? Explain.

If someone who is normal loses a sibling to Tay-Sachs, then both of their parents must be carriers, so there is a 2/3 chance that each member of this couple are carriers or a

$$2/3 \text{ x } 2/3 = 4/9$$

chance that they are BOTH carriers. If they are BOTH carriers there is a 1/4 chance that they will have a child with the disease. So,

$$4/9 \text{ x } 1/4 = 4/36 \text{ or } 1/9$$

chance that this couple will have a Tay-Sachs child.

Q2. A test has been developed to identify carriers of Tay-Sachs by measuring the activity of hexaminidase. Carriers of the Tay-Sachs allele make lower amounts of the enzyme than noncarriers, but that is sufficient to break down the gangliosides and so carriers show no symptoms of the disease. Based on that description, should Tay-Sachs inheritance be considered to exemplify intermediate inheritance or normal dominance? Justify your response.

At the organismic level this is a straight forward case of "dominance", but at the biochemical level this is a case of intermediate inheritance since about half of the normal amount of enzyme is made. The concept of "dominance" has become more nuanced as we learn more about genetics at the cellular and molecular level.

 Classical Genetics: Section 7-The gene for normal hemoglobin (Hb^A) is codominant with the gene for sickle cell hemoglobin (Hb^S). Table 1 to the right summarizes the effects of the three possible genotypes.

Genotype	Phenotype
$Hb^A\ Hb^A$	Normal Erythrocytes
$Hb^A\ Hb^S$	No Anemia, Erthrocytes Sickle when Oxygen Concentrations are Low
$Hb^S\ Hb^S$	Severe Anemia Sickling of the Erythrocytes

Q1. How is the heterozygous condition of Tay-Sachs disease (see previous section) different from the heterozygous condition involving sickle cell hemoglobin?

Table 1

Both the Hb^A or Hb^S code for proteins that are made, albeit, the Hb^S codes for abnormal hemoglobin molecules which do not transport oxygen effectively and which stick together in chains that cause RBCs to become misshapen. Since both proteins are made, this is a case of codominance. Carriers of Tay-Sachs make an intermediate amount of the Hexaminidase A.

Q2. What advantage do heterozygotes for sickle cell hemoglobin have in certain parts of the world?

Heterozygotes have resistance to malaria, but hardly show symptoms of sickle cell anemia. So the heterozygote has an advantage over both types of homozygotes in areas where malaria is prevalent.

Q3. What are the chances of having a child with sickle cell anemia if both parents are heterozygous for the trait?

25% or 1/4 chance of having a child with sickle cell anemia.

See Punnet square to the right.

	Hb^A	Hb^S
Hb^A	$Hb^A\ Hb^A$	$Hb^A\ Hb^S$
Hb^S	$Hb^A\ Hb^S$	$Hb^S\ Hb^S$
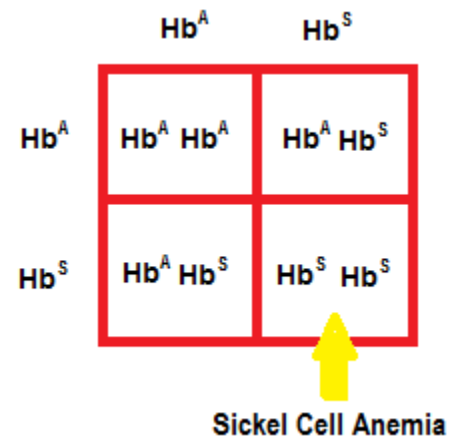
Sickel Cell Anemia

Q4. Justify the following statement: The use of the terms dominance, codominance and intermediate inheritance are *arbitrary*. Use the examples of Tay-Sachs and Sickle Cell Anemia to support the claim.

Codominance is when proteins are coded for by each allele. Intermediate or incomplete dominance is when one allele is expressed and so half of the amount of coded protein is made.

Classical Genetics: Section 8- ABO Blood type exemplifies an inheritance pattern in which there are three alleles in the population; I^A, I^B and i. I^A and I^B are codominant and i is recessive. This genetic pattern known as multiple alleles increases the number of phenotypes that are possible. In this case, there are four possible phenotypes (specifically blood types); A, B, AB and O.

Q1. What are the possible phenotypes (blood type) from each of the following crosses?

Cross	Mother	Father	Possibe Blood Type s) of Child
1	A	A	A, O
2	A	B	A, B, AB, O
3	A	AB	A, B, AB
4	A	O	A, O
5	AB	AB	A, B, AB
6	AB	O	A, B
7	O	O	O

Work Space

Cross 1: If either parent is homozygous ($I^A I^A$), then the children must be type A. But if <u>both</u> are heterozygous (I^A i), then they could have children with type O blood as well.

Cross 2: Since we do not know the geneotypes, if we assume that both parents are heterozygous (I^A i and I^B i) they could have children with any of the four blood types; A, B, AB and O.

Cross 3: The mother could be $I^A I^A$ or I^A i but the father must be $I^A I^B$. If the mother is homozygous they could have either have children with type A or type AB blood. But if the mother is heterozygous they could also have children with type B blood as well.

Cross 4: The mother could be $I^A I^A$ or I^A i but the father must be ii. If the mother is homozygous they could only have children with type A blood, but if she is heterozygous, they could also have children with type O blood.

Cross 5: Both parents must be $I^A I^B$. Therefore they could have children with blood types A, B, and AB, but not blood type O.

Cross 6: The parents must be $I^A I^B$ and ii. So their children are either I^Ai or I^Bi which means they their children have either types A or B blood.

Cross 7: The parents must both be ii which means they can only have children who are ii. So their children must all have type O blood.

Classical Genetics: Section 9-Imaginary genes R, B and D are linked on the same "arm" of the same chromosome.

R=round head is dominant over r=square head
B=brown belly is dominant over b=white belly
D=dark eyes is dominant over d=light eyes

The following cross is made: RrBbDd X rrbbdd. For the triple heterozygote parent the three dominant alleles are on the same chromosome. However, the order of the three alleles is not known.

The cross, repeated many times results in the following offspring:

373	round head, brown belly, dark eyes
361	square head, white belly light eyes
89	square head, brown belly, light eyes
94	round head, white belly, dark eyes
28	square head, brown belly, dark eyes
35	round head, white belly, light eyes
9	round head, brown belly, light eyes
11	square head, white belly, dark eyes

Q1. What is the order of the genes on the chromosome, RBD or RDB or BRD. What are the map distances between the alleles?

Note that the cross is between a triple heterozygote (whose phenotype shows all three dominant traits) and a triple homozygous recessive (whose phenotype shows all three recessive traits).

Now examine the 8 classes of offspring. The first two categories (373 and 361) are called parental because their phenotypes are the same as the parents. That is what we expect if there is no crossing over. Consider the punnet square shown to the right. If there is no crossing over, then the offspring will be the same as the parents….hence they are called parental. Since crossing over usually does not occur, they would be in the highest frequency.
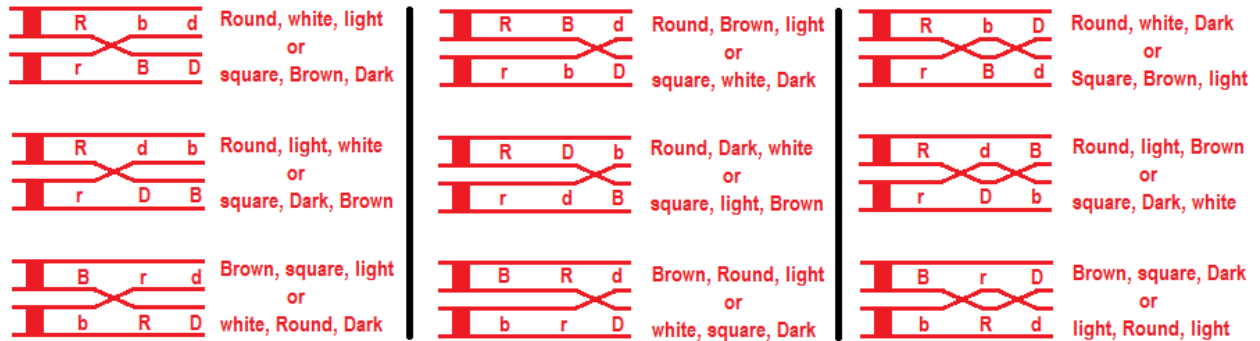
The next four "classes" of offspring (89, 94, 28 and 35) are single crossovers…that is crossovers between the first two alleles and then crossovers between the second two alleles. But the question is….what is the order of the alleles.

	R B D	r b d
r b d	RrBbDd	rrbbdd
r b d	RrBbDd	rrbbdd

Also note the last two categories (9 and 11) are most rare…they are double crossovers.
Since you are asked to choose from three possible gene orders (RBD, RDB and BRD), let's consider which one would match our results. Note that the triple homozygote recessive parent will only produce rbd or rdb or brd gametes. What type of games might the heterozygous parent produce?

You were given 3 possible gene orders RBD (first row), RDB (second row) and BRD (third row). We are just considering the product of the chromatids involved in the crossover event. Also, we can assume that the heterozygote parent could only produce rbd, rdb or brd gametes. That being the case, to the right of each chromosome are the possible phenotypes of the offspring resulting from the single or double crossovers.

| R b d | Round, white, light or | R B d | Round, Brown, light or | R b D | Round, white, Dark or |
| r B D | square, Brown, Dark | r b D | square, white, Dark | r B d | Square, Brown, light |

| R d b | Round, light, white or | R D b | Round, Dark, white or | R d B | Round, light, Brown or |
| r D B | square, Dark, Brown | r d B | square, light, Brown | r D b | square, Dark, white |

| B r d | Brown, square, light or | B R d | Brown, Round, light or | B r D | Brown, square, Dark or |
| b R D | white, Round, Dark | b r D | white, square, Dark | b R d | light, Round, light |

Note that only the middle row is consistent with the 2 single crossover categories and the 1 double crossover categories. Hence, the order of the genes is RDB (or rdb)

*Note: See middle row, NOT middle column.

Order of Alleles ___RDB_____

Map distance: Between B and D $[(89+94+9+11)/1000]\times100=(203/1000)\times100$ or 20.3 MU
               Between R and D $[(35+28+9+11)/1000]\times100=(83/1000) \times 100=8.3$ MU
               Between R and B   20.3+8.3=28.6 MU (MU=map units)

Q2. Which of the following offspring were NOT the product of a crossover event? 373, 361
                                        Single crossover event? 89,94. 28. 35
                                        Double crossover event? 9. 11

Q3. In the space below, draw the crossover event(s) that leads to offspring that WERE the product of at least one chromosomal crossover.
Shown in the middle row (not column) of crossover diagrams above.

Classical Genetics: Section 10-If one wants to study patrilineal (male) descent, then Y-chromosome sequencing is the most informative approach. On the other hand, if one wants to study matrilineal (female) descent, then mitochondrial DNA sequencing is most informative.

Q1. Explain why sequencing mitochondrial DNA is most useful when looking for the most recent woman from whom all humans evolved.

Mitochondria are passed only from mother to child (male or female). Males do not pass on mitochondria that are in their sperm to their children. So, in theory, mitochondrial DNA can be traced back in time to the first earliest women who existed…and the same would be true even going back to pre-human hominids. Hominidae is the family of primates that includes humans and their ancestors.

Q2. Till recently, there was a disparity in the calculation of when our last common maternal and paternal ancestor existed. In fact the date of our last common maternal ancestor was believed to be up to three times older than our last common paternal ancestor. A study of the Y-chromosome[1] seems to have eliminated that disparity. Explain why sequencing the Y-chromosome is most useful when looking for the most recent man from whom all humans evolved.

Y-chromosomes are passed on from males to their sons. So, just as mitochondria can be traced by matrilineal descent, the Y chromosomes can be used to show patrilineal descent…including to the earliest men and even going back to pre-human hominids.

Endnotes

1. Cann, R. "Y Weigh In Again on Modern Humans". Science. 2013; 341:465-467. August 2, 2013.