Biology 234
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Chapter 17
Changes in Chromosome Structure and Chromosome Number

Practice Questions:

Answer the following questions with one or two sentences.

1. What do you call a chromosome that has the centromere placed more or less in the middle?
2. What do you call a chromosome that has the centromere placed closer to one end than the other?
3. What do you call a chromosome that has the centromere placed virtually at one end of the chromosome, so that the chromosome essentially has only one arm.
4. What is a metacentric chromosome?
5. What is a telocentric chromosome?
6. What is an acrocentric chromosome?
7. What do you call or label the short arm of a chromosome?
8. What do you call or label the long arm of a chromosome?
9. What is the name of the accidental event that sometimes happens during meiosis, and which gives rise to trisomy or monosomy?
10. What is the n number for humans?
11. What do you call the phenomenon whereby unfertilized eggs can develop into adult organisms?
12. List the names of two organisms that are capable of Parthenogenesis?
13. What is Giemsa Stain used for?
14. Name a type of stain that you can use to stain 'bands' on metaphase chromosomes?
15. Name one example of a human chromosome reciprocal translocation that you've learned about in class.
16. Name one example of a *Drosophila* paracentric inversion that you've learned about in class.

Be able to answer the following questions in one or two paragraphs:

1. What is the purpose of deletion mapping?
2. What is "pseudodominance?" What genetic assay makes use of pseudodominance?
3. What is the "n" number for an organism? What does this mean?
4. What is parthenogenesis?
5. What is a karyotype?
6. What is the difference between autopolyploidy and allopoloploidy?
7. (In transplant immunology, what is the difference between an autograft, an allograft, and a xenograft?)

8. What is a chromosomal ideogram?
9. What is a paracentric inversion?
10. What is a pericentric inversion?
11. What is polyploidy?
12. What is autopolyploidy?
13. What is allopolyploidy?
14. What is trisomy?
15. What is monosomy?
16. What is aneuploidy?
17. What is a metacentric chromosome?
18. What is an acrocentric chromosome?
19. What is a telocentric chromosome?
20. What is the q arm of a chromosome?
21. What is the p arm of a chromosome?
22. What is an inversion loop?
23. What is a deletion loop?
24. What is cruciform pairing, and what type of chromosome re-arrangement is it associated with?

Be able to explain the following in one hand-written page or less:

1. What are the causes and symptoms of Down Syndrome?
2. What are the causes and symptoms of Chronic Myeloid Leukemia?
3. What are the causes and symptoms of Burkitt's Lymphoma?
4. What are the causes and symptoms of Klinefelter Syndrome?
5. What are the causes and symptoms of Triple-X syndrome?
6. What are the causes and symptoms of Turner Syndrome?
7. What is the difference between a homozygote, a heterozygote, and a hemizygote?
8. Using cytology (ie-how chromosomes appear under a microscope) how can you tell that a person (or a model organism like a fruit fly) is heteroozygous for a chromosome deletion?
9. Same question as above, but for a chromosome duplication?
10. Same question as above, but for a pericentric inversion?
11. Same question as above, but for a paracentric inversion?
12. Explain what causes an inversion loop to form.
13. Explain what causes a deletion loop to form.
14. Explain what deletion mapping is used for, and how it works.
15. What is pseudodominance, and which type of genetic analysis makes use of it?

DELETION MAPPING PROBLEMS:

Deletion Mapping (also known as Deficiency Mapping) is a method of finding out where genes are located on chromosomes. The method only works with **model organisms**, can only be used to locate **RECESSIVE mutations**, and relies on the experimenter having access to a library of stocks that have chromosomal deletions with known breakpoints. The method uses the genetic phenomenon of **pseudodominance** to locate a mutation (and therefore a gene) relative to bands on the chromosome.

A good example is the ***Drosophila* Genome Project**, which has a library containing thousands of individual stocks of fruit flies, each of which has a small deficiency in a chromosome. It was a tremendous amount of work to create this library! Researchers had to expose adult flies to X-rays, causing different types of chromosome rearrangements (including deletions), and then carefully stain and look at the chromosomes of the mutant progeny. By comparing the banding patterns of the mutant chromosomes to atlases containing the ideograms of normal *Drosophila* chromosomes, they were able to determine which parts of the chromosomes were missing, and assemble the various stocks into a library. Because the generation of chromosomal deletions is a random process, they were never able to generate exact deletions to exact bands. So, when you use this technique, you have to test a series of overlapping deletions, each of which removes several bands, and then compare the results in order to assign the position of a gene to a specific band.

This method of locating genes can only be used to map the locations of recessive mutations, because it relies on pseudodominance, where you are able to see the recessive phenotype of a mutation only when it is paired with a deficiency, rather than the Wild-Type allele. Only a few of the model organism genome projects were able to generate a deficiency library, mainly because many model organisms (like mice and rats for example) don't produce enough progeny per mating; and are too difficult to maintain to make it practical. (ie-it's difficult to maintain a chromosome deficiency library that contains 5000 different mutant strains of fruit flies, but it would be impossible to maintain a library that contained 5000 different mutant strains of mice!)

Example 1: The *Drosophila* ***vg*** ('vestigial') mutation is a mutation that causes fruit flies to be born with crumpled, non-functional, 'vestigial' wings. You have reason to believe it is located on Chromosome 2, somewhere between bands **2q1 and 2q7**. You look in the *Drosophila* Genome database, and see that the **Drosophila** deficiency library and see that the library has six deficiency strains that carry deficiencies to this region of **Chromosome 2**. You order these stocks from the Stock Center in Bloomington Indiana, and do a deletion mapping experiment. You get the following results. Where is the gene that is associated with the ***vg*** mutation? Give the location as a single band.

Deficiency Strain	Extent of deletion	Wing Phenotype
A	2q1-2q2	Normal
B	2q2-2q3	VESTIGIAL
C	2q2-2q4	VESTIGIAL
D	2q3-2q5	VESTIGIAL
E	2q4-2q6	Normal
F	2q5-2q7	Normal

Answer: 2q3

Example 2: There is a recessive mutation called ***eye*** that causes the model organism Zebrafish (*Danio rerio*) to be born without eyes. You have reason to believe that it is located on the short arm of Chromosome 3, between **3p5** and **3p10**. You get the following results. Where is the the gene that is affected by the ***eye*** mutation located? Give an exact band.

Deficiency Strain	Extent of deletion	Eyes? Y/N
A	3p5-3p6	Eyes
B	3p5-3p8	NO EYES
C	3p6-3p8	NO EYES
D	3p7-3p9	NO EYES
E	3p8-3p10	Eyes

Example 3: Normally, deletion mapping can only be used to map the locations of recessive mutations, which means that this method is only of limited use for doing genetic dissection. Mainly because doing genetic dissection involves first doing a random mutagenesis screen, and you've already learned that a random mutagenesis screen is biased in favor of generating DOMINANT mutations. (Think about how you do a random mutagenesis screen in fruit flies, for example. You feed an adult female EMS, in order to cause random point mutations, and then look for mutant offspring. The only way you could see mutant offspring that carry a RECESSIVE mutation is if you'd mutated BOTH COPIES of the gene at once, which is very unlikely.) If you've generated a series of dominant negative mutations (like E(var) mutations), it would therefore be impossible to find out where they are using deletion mapping.

There are a few exceptions, however. One notable exception is that you can do a random mutagenesis screen, generate recessive mutations, and see the recessive phenotypes in an organisms that reproduce parthenogenically. Many insects (bees, wasps), some lepidopterans (ie-moths) and some reptiles are capable of parthenogenesis. For example, you could feed EMS to a Queen Bee, and then look for recessive phenotypes in the haploid Drone bees. Another exception is if you feed EMS to a female fruit fly, and then only look at the phenotypes of her MALE progeny. Recessive mutant phenotypes will be seen in MALE offspring if they were mutations to genes located on the X chromosome, because males are hemizygous for the X chromosome.

Here is such an example from the Honeybee (*Apis melliferia*): You wish to find out which genes are involved in antennae development in honeybees. You do a random mutagenesis screen by feeding a Queen Bee EMS, and then looking for DRONES (haploid males) that don't have antennae. You generate and isolate 10 mutant strains of bee, where the male drones do not have antennae. You then do a complementation analysis, and find that these 10 strains fall into 3 complementation groups, and therefore there are actually only three genes involved in antennae development in bees. You have reason to believe that one of them is located on the long arm Chromosome 30 (bees have 31 chromosomes) between bands 3q5 and 3q9. You check the Honeybee Genome Project database and see that there are five deficiency stocks in the stock library. You order them, do a deletion mapping analysis, and get the following results. Which band is the gene located at?

Stock Number	Deficiency region	Phenotype
Df101	3q5-3q6	Antennae
Df102	3q5-3q7	NO antennae
Df103	3q6-3q9	NO antennae
Df104	3q7-3q9	NO antennae
Df105	3q8-3q9	Antennae

Ans.: 3q7

Human Genetic Disorders Involving Chromosome Rearrangements:

Be able to explain a few things about how the following genetic disorders work:

1. **Chronic Myeloid Leukemia:** Autosomal dominant, single gene (oncogene), gain of function mutation caused by a translocation. A dominant, gain of function mutation that causes leukemia by placing a cell division gene (***ABL1***) that is normally turned off, under the control of an antibody promoter that is normally turned on in leukocytes (the ***BCR*** gene). This is caused by a **t(9;22)** reciprocal translocation that is called the Philadelphia Chromosome**. The *ABL1* gene is a proto-oncogene, and the translocation causes a dominant, gain of function mutation, converting it to an oncogene.**

2. **Burkitt's Lymphoma: t(8;14)** Autosomal dominant, single gene, gain of function mutation caused by a translocation. A dominant, gain of function mutation that causes lymphoma by placing a cell division gene (***Myc***), which is normally turned off, under the control of an antibody gene promoter that is often turned on in lymphocytes. **The *Myc* gene is a proto-oncogene, and the translocation causes a dominant, gain of function mutation, converting it to an oncogene.**

Human Genetic Disorders Involving Changes in Chromosome Numbers (aneuploidy):

Be able to explain a few things about how these genetic disorders work:

1. Down Syndrome: (Trisomy 21). Autosomal. Three copies of chromosome 21. Symptoms: mental retardation, reduced fertility, short stature, thick neck, enlarged tongue, digestive problems, minor heart problems. Symptoms caused by a change in gene dosage (three copies of every gene on chromosome 21 instead of two). Mother's age is a risk factor, with odds of having a Down Syndrome baby increasing dramatically for mothers in their 40s.

2. Klinefelter Syndrome: Sex linked. XXY due to nondisjunction event in father. Phenotypically male. Symptoms: Tall stature, testicular atrophy, gynecomastia.

3. Triple-X Syndrome: Sex linked. XXX due to nondisjunction event in mother. Phenotypically female. No major difference in appearance etc. from a regular XX woman. Therefore, rarely diagnosed.

4. Turner Syndrome: Sex linked. X0. Phenotypically female. Symptoms: short stature, 'shield' shaped chest, heart shaped face, webbed neck, minor heart problems. Webbed neck is sometimes fixed with cosmetic surgery. Hormone treatment to increase female appearance.

Suggested problems from Chapter 17.
46, 48, 60.