Chapter 15

The Chromosomal Basis of Inheritance

Key Concepts

15.1 Mendelian inheritance has its physical basis in the behavior of chromosomes

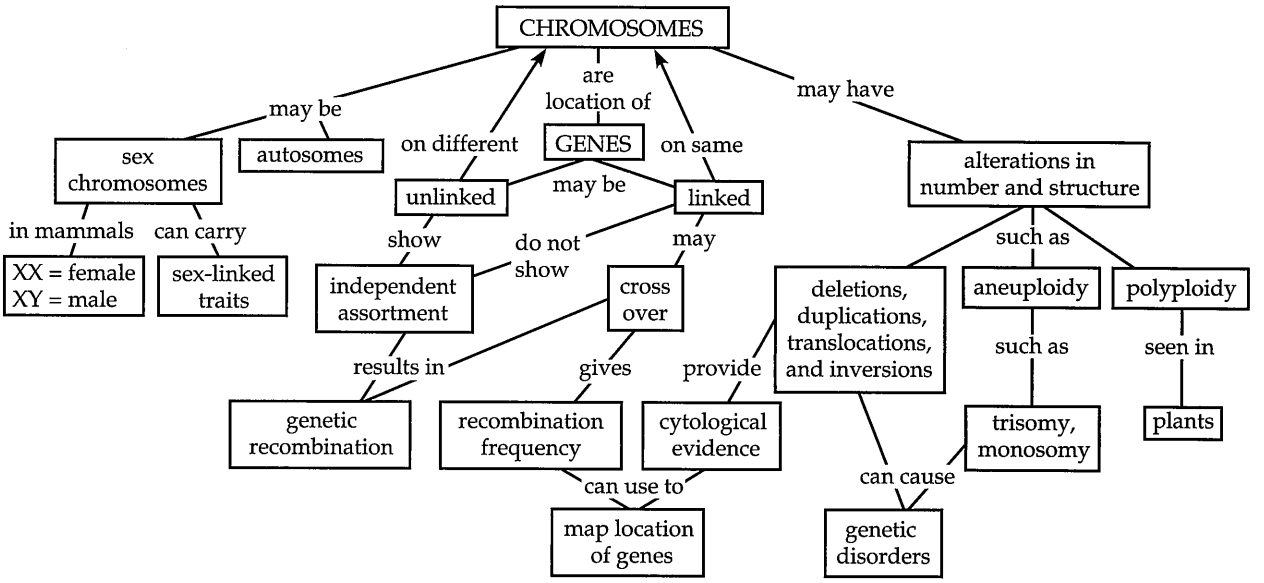
15.2 Linked genes tend to be inherited together because they are located near each other on the same chromosome

15.3 Sex-linked genes exhibit unique patterns of inheritance

15.4 Alterations of chromosome number or structure cause some genetic disorders

15.5 Some inheritance patterns are exceptions to the standard chromosome theory

Framework



Chapter Review

15.1 Mendelian inheritance has its physical basis in the behavior of chromosomes

Mendel's laws, combined with cytological evidence of the process of meiosis, led to the **chromosome theory of inheritance:** Genes occupy specific positions (loci) on chromosomes, and chromosomes undergo segregation and independent assortment in the process of meiosis in gamete formation.

Morgan's Experimental Evidence: **Scientific Inquiry**
T. H. Morgan, working with the fruit fly, *Drosophila melanogaster,* was the first to identify a specific gene with a specific chromosome. Fruit flies are prolific breeders and have only four pairs of chromosomes, which are easily distinguishable with a microscope. The sex chromosomes occur as XX in females and XY in male flies.

The normal phenotype found most commonly in nature for a character is called the **wild type,** whereas alternative traits, assumed to have arisen as mutations, are called *mutant phenotypes.*

Morgan discovered a mutant white-eyed male fly that he mated with a wild-type red-eyed female. The F_1 were all red-eyed. In the F_2, however, all female flies were red-eyed, whereas half of the males were red-eyed and half were white-eyed. Morgan deduced that the gene for eye color was located only on the X chromosome. Males have only one X, so their phenotype is determined by the eye-color allele they inherit from their mother. This association of a specific gene with a chromosome provided evidence for the chromosome theory of inheritance.

■ INTERACTIVE QUESTION 15.1

Complete this summary of Morgan's crosses with the mutant white-eyed fly by filling in the Punnett square and showing the phenotypes and genotypes of the F_2 generation. (*w* stands for the mutant recessive white allele; w^+ for the wild-type red allele.) The Y indicates that male flies, with only one X chromosome, carry only a single allele for this eye color gene.

P Generation			
Phenotype	red-eyed (wild-type) female	x	white-eyed male
Genotype	w^+w^+		wY

F_1 Generation			
Phenotype	red-eyed female	x	red-eyed male
Genotype	w^+w		w^+Y

F_2 Generation

ova \ sperm		

Phenotype

_____ _____ _____ _____

Genotype

_____ _____ _____ _____

15.2 Linked genes tend to be inherited together because they are located near each other on the same chromosome

Genes that are located on the same chromosome and tend to be inherited together are called **linked genes.**

***How Linkage Affects Inheritance:* Scientific Inquiry** Morgan performed a testcross of F_1 dihybrid wild-type flies with flies that were homozygous recessive for black bodies and vestigial wings and found that the offspring were not in the predicted 1:1:1:1 phenotypic classes. Rather, most of the offspring were the same phenotypes as the P generation parents—either wild type (gray, normal wings) or double mutant (black, vestigial). Morgan deduced that these traits were inherited together because their genes were located on the same chromosome.

Genetic recombination results in offspring with combinations of traits that differ from those found in either parent.

Genetic Recombination and Linkage In a cross between a dihybrid heterozygote and a recessive homozygote, one-half of the offspring will be **parental types** and have phenotypes like one or the other of the P generation parents, and one-half of the offspring, called **recombinant types (recombinants),** will have combinations of the two traits that are unlike the parents. This 50% frequency of recombination is observed when two genes are located on different chromosomes, and it results from the random alignment of homologous chromosomes at metaphase I and the resulting independent assortment of alleles.

■ INTERACTIVE QUESTION 15.2

In a testcross between a heterozygote tall, purple-flowered pea plant and a dwarf, white-flowered plant,

a. what are the phenotypes of offspring that are parental types?

b. what are the phenotypes of offspring that are recombinants?

Linked genes do not assort independently, and one would not expect to see recombination of parental traits in the offspring. Recombination of linked genes does occur, however, due to **crossing over,** the reciprocal trade between nonsister (a maternal and a paternal) chromatids of synapsed homologous chromosomes during prophase of meiosis I. The percentage of recombinant offspring is called the *recombination frequency.*

■ INTERACTIVE QUESTION 15.3

With unlinked genes, an equal number of parental and recombinant offspring are produced. With linked genes, (more/fewer) parentals than recombinants are produced. (Circle and then explain your answer.)

Linkage Mapping Using Recombination Data: **Scientific Inquiry** A **genetic map** is an ordered list of genes on a chromosome. A. H. Sturtevant suggested that recombination frequencies reflect the relative distance between genes; genes located farther apart have a greater probability that a crossover event will occur between them. Sturtevant used recombination data to create a **linkage map,** defining one **map unit** (or centimorgan) as equal to a 1% recombination frequency.

The sequence of genes on a chromosome can be determined by finding the recombination frequency between different pairs of genes. Linkage cannot be determined if genes are so far apart that crossovers between them are almost certain. They would then have the 50% recombination frequency typical of unlinked genes. Such genes are *physically linked* but *genetically unlinked.* Distant genes on the same chromosome may be mapped by adding the recombination frequencies determined between them and intermediate genes.

Sturtevant and his colleagues found that the genes for the various known mutations of *Drosophila* clustered into four groups of linked genes, providing additional evidence that genes are located on chromosomes, in this case, on the four *Drosophila* chromosomes.

The frequency of crossing over may vary along the length of a chromosome, and a linkage map provides the sequence but not the exact location of genes on chromosomes. **Cytogenetic maps** locate gene loci in reference to visible chromosomal features.

■ INTERACTIVE QUESTION 15.4

Recombination frequency is given below for several gene pairs. Create a linkage map for these genes, showing the map unit distance between loci.

j, k 12% *k, l* 6%

j, m 9% *l, m* 15%

15.3 Sex-linked genes exhibit unique patterns of inheritance

The Chromosomal Basis of Sex Sex is a phenotypic character usually determined by sex chromosomes. In humans and mammals, females, who are XX, produce ova that each contain an X chromosome. Males, who are XY, produce two kinds of sperm, each with either an X or a Y chromosome. Whether the gonads of an embryo develop into testes or ovaries depends on the presence or absence of the gene *SRY,* found on the Y chromosome, whose protein product regulates many other genes. A few other genes on the Y chromosome are necessary for normal functioning of the testes.

Other sex-determination systems include X-0 (in grasshoppers and some other insects), Z-W (in birds and some fishes and insects), and haplo-diploid (in bees and ants).

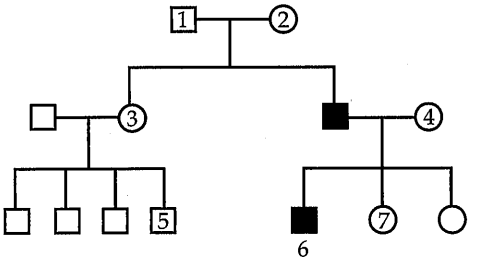
Inheritance of Sex-Linked Genes Sex chromosomes may carry genes, called **sex-linked genes,** for traits that are not related to sex. In humans, *sex-linked* typically refers to a gene on the X chromosome. Males inherit their sex-linked alleles from only their mothers; daughters inherit sex-linked alleles from both parents. Recessive sex-linked traits are seen more often in males, since they are *hemizygous* for sex-linked genes.

Duchenne muscular dystrophy is a sex-linked disorder resulting from the lack of a key muscle protein. **Hemophilia** is a sex-linked recessive trait characterized by excessive bleeding due to the absence of one or more blood-clotting proteins.

X Inactivation in Female Mammals Only one of the X chromosomes is fully active in most mammalian female somatic cells. The other X chromosome is contracted into a **Barr body** located inside the nuclear membrane. M. Lyon demonstrated that the selection of which X chromosome is inactivated is a random event occurring independently in embryonic cells. As a result of X-inactivation, both males and females have an equal dosage of genes on the X chromosome. A gene called *XIST* is active on the X chromosome that forms the Barr body. Its RNA product may trigger DNA methylation and X-inactivation.

■ INTERACTIVE QUESTION 15.5

Two normal color-sighted individuals produce the following children and grandchildren. Fill in the probable genotype of the indicated individuals in this pedigree. *Squares are males, circles are females, and solid symbols represent color blindness. Choose an appropriate notation for the genotypes.*



Genotypes:

1. _____ 4. _____ 7. _____

2. _____ 5. _____

3. _____ 6. _____

15.4 Alterations of chromosome number or structure cause some genetic disorders

Abnormal Chromosome Number **Nondisjunction** occurs when a pair of homologous chromosomes does not separate properly in meiosis I or sister chromatids do not separate in meiosis II. As a result, a gamete receives either two or no copies of that chromosome. A zygote formed with one of these aberrant gametes has a chromosomal alteration known as **aneuploidy,** a nontypical number of a particular chromosome. The zygote will be either **trisomic** for that chromosome (chromosome number is $2n + 1$) or **monosomic** ($2n - 1$). Aneuploid organisms usually have a set of symptoms caused by the abnormal dosage of genes. A mitotic nondisjunction early in embryonic development is likely to be harmful.

Polyploidy is a chromosomal alteration in which an organism has more than two complete chromosomal sets, as in *triploidy* ($3n$) or *tetraploidy* ($4n$). Polyploidy is common in the plant kingdom and has played an important role in the evolution of plants.

■ INTERACTIVE QUESTION 15.6

a. What is the difference between a trisomic and a triploid organism?

b. Which of these is likely to show the most deleterious effects of its chromosomal imbalance?

Alterations of Chromosome Structure Chromosome breakage can result in chromosome fragments that are lost, called **deletion;** that join to a sister chromatid (during meiosis) or the homologous chromosome, called **duplication;** that rejoin the original chromosome in the reverse orientation, called **inversion;** or that join a nonhomologous chromosome, called **translocation.** A *nonreciprocal* crossover can result in a deletion and duplication in nonsister chromatids, caused by nonequal exchange between chromatids.

A homozygous deletion is usually lethal. Duplications and translocations also are typically harmful. Even though all the genes are present in proper quantities in inversions and translocations, the phenotype may be altered due to the influence of neighboring genes on the expression between the relocated genes.

■ INTERACTIVE QUESTION 15.7

Two nonhomologous chromosomes have gene orders, respectively, of *A-B-C-D-E-F-G-H-I-J* and *M-N-O-P-Q-R-S-T.* What types of chromosome alterations would have occurred if daughter cells were found to have a gene sequence on the first chromosome of *A-B-C-O-P-Q-G-J-I-H*?

Human Disorders Due to Chromosomal Alterations The frequency of aneuploid zygotes may be fairly high in humans, but development is usually so disrupted that the embryos spontaneously abort. Some genetic disorders, expressed as syndromes of characteristic traits, are the result of aneuploidy. Fetal testing can detect such disorders before birth.

Down syndrome, caused by trisomy of chromosome 21, results in characteristic facial features, short stature, heart defects, and mental retardation. The incidence of Down syndrome increases for older mothers.

XXY males exhibit *Klinefelter syndrome,* a condition in which the individual has abnormally small testes, is sterile, and is usually of normal intelligence.

Males with an extra Y chromosome do not exhibit any well-defined syndrome. Trisomy X results in females who are healthy and distinguishable only by karyotype. Monosomy X individuals (X0) exhibit *Turner syndrome* and are phenotypically female, sterile individuals with short stature and usually normal intelligence.

Structural alterations of chromosomes, such as deletions or translocations, may be associated with specific human disorders. The *cri du chat* syndrome is caused by a deletion in chromosome 5; chronic myelogenous leukemia is a cancer that is associated with a reciprocal chromosomal translocation.

■ INTERACTIVE QUESTION 15.8

What is an explanation for the observation that most sex chromosome aneuploidies have less deleterious effects than do autosomal aneuploidies?

15.5 Some inheritance patterns are exceptions to the standard chromosome theory

Genomic Imprinting A few dozen traits in mammals have been identified that seem to depend on which parent supplied the alleles for the trait. In this **genomic imprinting,** which occurs during gamete formation, certain genes are imprinted or not, depending on whether ova or sperm are being produced. Imprinted alleles are not expressed in the offspring. When this generation makes gametes, old maternal and paternal imprints are removed, and alleles are imprinted according to the sex of the parent. Most of the mammalian genes subject to imprinting identified so far are involved in embryonic development. The addition of methyl groups may inactivate the imprinted gene, assuring that the developing embryo has only one active copy.

Inheritance of Organelle Genes Exceptions to Mendelian inheritance are found in the case of *extranuclear genes* located on small circles of DNA in mitochondria and plant plastids, which are transmitted to offspring in the cytoplasm of the ovum. Some rare human disorders are caused by mitochondrial mutations, and maternally inherited mitochondrial defects may contribute to diabetes, heart disease, and Alzheimer's disease.

Word Roots

aneu- = without (*aneuploidy:* a chromosomal aberration in which certain chromosomes are present in extra copies or are deficient in number)

cyto- = cell (*cytogenetic maps:* charts of chromosomes that locate genes with respect to chromosomal features)

hemo- = blood (*hemophilia:* a human genetic disease caused by a sex-linked recessive allele, characterized by excessive bleeding following injury)

mono- = one (*monosomic:* a chromosomal condition in which a particular cell has only one copy of a chromosome, instead of the normal two; the cell is said to be monosomic for that chromosome)

non- = not; **dis-** = separate (*nondisjunction:* an accident of meiosis or mitosis in which both members of a pair of homologous chromosomes or both sister chromatids fail to move apart properly)

poly- = many (*polyploidy:* a chromosomal alteration in which the organism possesses more than two complete chromosome sets)

re- = again; **com-** = together; **bin-** = two at a time (*recombinant:* an offspring whose phenotype differs from that of the parents)

trans- = across (*translocation:* attachment of a chromosomal fragment to a nonhomologous chromosome)

tri- = three; **soma-** = body (*trisomic:* a chromosomal condition in which a particular cell has an extra copy of one chromosome, instead of the normal two; the cell is said to be trisomic for that chromosome)

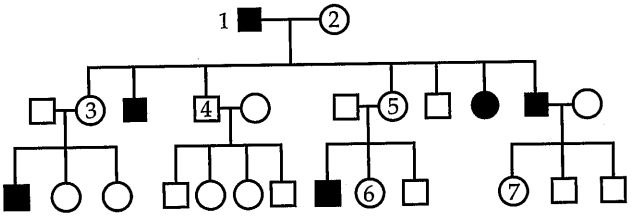
Structure Your Knowledge

1. Mendel's law of independent assortment applies to genes that are on different chromosomes. However, two of the genes Mendel studied were actually located on the same chromosome. Explain why genes located more than 50 map units apart behave as though they are not linked. How can one determine whether these genes are linked and what the relative distance is between them?
2. You have found a new mutant phenotype in fruit flies that you suspect is recessive and sex-linked. What is the single, best cross you could make to confirm your predictions?
3. Various human disorders or syndromes are related to chromosomal abnormalities. What explanation can you give for the adverse phenotypic effects associated with these chromosomal alterations?

Genetics Problems

Again, one of the best ways to learn genetics is to do problems.

1. The following pedigree traces the inheritance of a genetic trait.



   a. What type of inheritance does this trait show?
   b. Give the predicted genotype for the following individuals:
      1. _____ 5. _____
      2. _____ 6. _____
      3. _____ 7. _____
      4. _____
   c. What is the probability that a child of individual #6 and a phenotypically normal male will have this trait?

2. The following recombination frequencies were found. Determine the order of these genes on the chromosome.
   a, c 10% b, c 24%
   a, d 30% b, d 16%

3. In guinea pigs, black (*B*) is dominant to brown (*b*), and solid color (*S*) is dominant to spotted (*s*). A heterozygous black, solid-colored pig is mated with a brown, spotted pig. The total offspring for several litters are black solid = 16, black spotted = 5, brown solid = 5, and brown spotted = 14. Are these genes linked or unlinked? If they are linked, how many map units are they apart?

4. A woman is a carrier for a sex-linked lethal gene that causes an embryo with the gene to spontaneously abort. She has nine children. How many of these children do you expect to be boys?

5. A dominant sex-linked gene *B* produces white bars on black chickens, as seen in the Barred Plymouth Rock breed. A clutch of chicks has equal numbers of black and barred chicks. (Remember that sex is determined by the Z-W system in birds: ZZ are males, ZW are females.)
   a. If only the females are found to be black, what were the genotypes of the parents?
   b. If males and females are evenly represented in the black and barred chicks, what were the genotypes of the parents?

Test Your Knowledge

MULTIPLE CHOICE: *Choose the one best answer.*

1. The chromosomal theory of inheritance states that
   a. genes are located on chromosomes.
   b. chromosomes and their associated genes undergo segregation during meiosis.
   c. chromosomes and their associated genes undergo independent assortment in gamete formation.
   d. Mendel's laws of inheritance relate to the behavior of chromosomes in meiosis.
   e. all of the above are correct.

2. A wild type is
   a. the phenotype found most commonly in nature.
   b. the dominant allele.
   c. designated by a small letter if it is recessive or a capital letter if it is dominant.
   d. a trait found on the X chromosome.
   e. your basic party animal.

3. Sex-linked traits
   a. are carried on an autosome but expressed only in males.
   b. are coded for by genes located on a sex chromosome.
   c. are found in only one or the other sex, depending on the sex-determination system of the species.
   d. are always inherited from the mother in mammals and fruit flies.
   e. depend on whether the gene was inherited from the mother or the father.

4. Linkage and cytogenetic maps for the same chromosome
   a. are both based on mutant phenotypes and recombination data.
   b. may have different orders of genes.
   c. have both the same order of genes and intergenic distances.
   d. have the same order of genes but different intergenic distances.
   e. are created using chromosomal abnormalities.

5. The genetic event that results in Turner syndrome (X0) is probably
   a. nondisjunction.
   b. deletion.
   c. parental imprinting.
   d. monoploidy.
   e. independent assortment.

6. A 1:1:1:1 ratio of offspring from a dihybrid testcross indicates that
   a. the genes are linked.
   b. the dominant organism was homozygous.
   c. crossing over has occurred.
   d. the genes are 25 map units apart.
   e. the genes are not linked or are more than 50 map units apart.

7. Genes *A* and *B* are linked and 12 map units apart. A heterozygous individual, whose parents were *AAbb* and *aaBB*, would be expected to produce gametes in the following frequencies:

a.	44% *AB*	6% *Ab*	6% *aB*	44% *ab*
b.	6% *AB*	44% *Ab*	44% *aB*	6% *ab*
c.	12% *AB*	38% *Ab*	38% *aB*	12% *ab*
d.	6% *AB*	6% *Ab*	44% *aB*	44% *ab*
e.	38% *AB*	12% *Ab*	12% *aB*	38% *ab*

8. A female tortoiseshell cat is heterozygous for the gene that determines black or orange coat color, which is located on the X chromosome. A male tortoiseshell cat
   a. is hemizygous at this locus.
   b. must have had a tortoiseshell mother.
   c. must have resulted from a nondisjunction and has a Barr body in each of his cells.
   d. must have three alleles for coat color, one from his father and two from his mother.
   e. would be hermaphroditic.

9. A color-blind son inherited this trait from his
   a. mother.
   b. father.
   c. mother only if she is color-blind.
   d. father only if he is color-blind.
   e. mother only if she is not color-blind.

10. Genomic imprinting
    a. explains cases in which the phenotypic effect of an allele depends on the gender of the parent from whom that allele is inherited.
    b. may involve the silencing of an allele by methylation so that offspring inherit only one active copy of a gene.
    c. is greatest in females because of the larger maternal contribution of cytoplasm.
    d. is more likely to occur in offspring of older mothers.
    e. involves both a and b.

11. A cross of a wild-type red-eyed female *Drosophila* with a violet-eyed male produces all red-eyed offspring. If the gene is sex-linked, what should the reciprocal cross (violet-eyed female × red-eyed male) produce? (Assume that the red allele is dominant to the violet allele.)
    a. all violet-eyed flies
    b. 3 red-eyed flies to 1 violet-eyed
    c. a 1:1 ratio of red and violet eyes in both males and females
    d. red-eyed females and violet-eyed males
    e. all red-eyed flies

12. Which of the following chromosomal alterations does not alter genic balance but may alter phenotype because of differences in gene expression?
    a. deletion
    b. inversion
    c. duplication
    d. nondisjunction
    e. genomic imprinting

13. Two true-breeding *Drosophila* are crossed: a normal-winged, red-eyed female and a miniature-winged, vermilion-eyed male. The F_1 all have normal wings and red eyes. F_1 offspring are crossed with miniature-winged, vermilion-eyed flies. The following offspring of that cross were counted:
    233 normal wing, red eye
    247 miniature wing, vermilion eye
    7 normal wing, vermilion eye
    13 miniature wing, red eye
    From these results you could conclude that the alleles for miniature wings and vermilion eyes are
    a. both X-linked and dominant.
    b. located on autosomes and dominant.
    c. recessive, and these genes are located 4 map units apart.
    d. recessive, and these genes are located 20 map units apart.
    e. recessive, and the deviation from the expected 9:3:3:1 ratio is due to epistasis.

14. Tests of social behavior given to Turner's syndrome volunteers (who are X0) found a correlation between scores on "behavioral inhibition" tasks and the source of the lone X chromosome. These test results appear to be an example of
    a. parental imprinting of a gene on the X chromosome.
    b. Y-linked inheritance.
    c. meiotic nondisjunction.
    d. chromosomal reciprocal translocation.
    e. nonreciprocal crossover.

15. Suppose that alleles for a sex-linked character for wing shape in *Drosophila* show incomplete dominance. The X^+ allele codes for pointed wings, the X^r for round wings, and X^+ X^r individuals have oval wings. In a cross between an oval-winged female and a round-winged male, the following offspring were observed: oval-winged females, round-winged females, pointed-winged males, and round-winged males. A rare pointed-winged female was noted. What could account for this unusual offspring?
    a. a crossover between the two X chromosomes
    b. a crossover between the X and Y chromosomes
    c. a nondisjunction in meiosis II between two X^+ chromatids
    d. a nondisjunction in meiosis I between the X^+ and X^r chromosomes
    e. an X^+0 female formed when an X^+ ovum was fertilized by a sperm in which there was no sex chromosome due to a nondisjunction

16. What is the function of the gene *SRY*?
    a. codes for an RNA molecule that coats the X chromosome and initiates X-inactivation
    b. codes for RNA that activates the Y chromosome
    c. codes for a protein that regulates genes that control the development of ovaries
    d. located on the Y chromosome and codes for a protein that regulates genes that control development of testes
    e. located on the Y chromosome and required for production of normal sperm

17. A mutation in a mitochondrial gene has been linked to a rare muscle-wasting disease. This disease is
    a. found more often in males than females.
    b. found more often in females than males.
    c. inherited in a simple Mendelian fashion.
    d. caused by a translocation of a nuclear gene.
    e. inherited from the mother.

18. In which of the following would you expect to find a Barr body?
    a. an ovum
    b. a sperm
    c. a liver cell of a man
    d. a liver cell of a woman
    e. a mitochondrion

19. A cross between a wild-type mouse and a dwarf mouse homozygous for a recessive mutation in the *Igf2* gene produces heterozygotes offspring that are normal if the dwarf parent was the mother, but dwarf if the dwarf parent was the father. Which of the following explains these results?
    a. sex-linked inheritance
    b. monosomy
    c. genomic imprinting by the mother
    d. inheritance of mitochondrial genes
    e. a mutant *XIST* allele

20. Which of the following statements is *not* true about genetic recombination:
    a. Recombination of linked genes occurs by crossing over.
    b. Recombination of unlinked genes occurs by independent assortment of chromosomes.
    c. Genetic recombination results in offspring with combinations of traits that differ from the phenotypes of both parents.
    d. Recombinant offspring outnumber parental-type offspring when two genes are 50 map units apart on a chromosome.
    e. The number of recombinant offspring is proportional to the distance between two gene loci on a chromosome.