SEX DETERMINATION IN HUMANS

A lesson plan based on

Lecture 4: Sexual Evolution: From X to Y

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Learning Outcomes

Students should be able to:

1. Distinguish between autosomes and sex chromosomes.
2. Describe sex determination in humans.
3. List some similarities and differences between the X and Y chromosomes.
4. Understand the concept of genetic linkage.
5. Explain how crossing over creates recombinant chromosomes.
6. Describe a possible scenario for the evolution of the sex chromosomes from ancestral autosomes.
7. Describe how deletions in the Y chromosome could lead to male infertility.
8. Explain the reproductive technology known as ICSI (intracytoplasmic sperm injection) that allows infertile males to become biological fathers.
9. Discuss the ethical concerns of using laboratory techniques to allow infertile males to reproduce.

Concepts

Gene
Allele
Heterozygous
Autosome
Homologous chromosomes
Nonhomologous chromosomes
Sex determination
Genetic linkage
Crossing Over
Recombinant DNA
Deletion
Infertility

DISCUSSION of the lecture concepts (This could be done as a class discussion or group assignment)

1. What's the evolutionary value of mixing genetic information (recombination)?
2. Why don't brothers and sisters look more alike?
   Why don't children look more like their parents?
3. What sex chromosomes do YOU have?

Discuss the normal sex chromosome pairing and mention some unusual genetic conditions that result from extra sex chromosomes or the absence of a sex chromosome. Why doesn't nature favor the abnormal sex complements?

4. A man who carries a defective (mutated) Y chromosome will pass the defective chromosome on to which of his children?

-all his children
-half of his children
-only his sons **
-only his daughters

5. Historically, women have been held responsible (blamed!) for not producing the male heir. Are women responsible for the sex of the child? Which parent actually determines the gender of the child?

6. Why are more men colorblind than women? (The man need only inherit one X with the sex-linked gene that causes colorblindness and he will have the condition (remember he has one X and one Y); females would have to inherit two X's with the disorder to have full blown colorblindness since it is a recessive disorder (takes two recessive alleles for expression).

7. What is the expected phenotypic ratio (physical manifestation) of children from a normal female and a colorblind male?

8. If you were infertile due to a mutation of a sex chromosome would you want to use artificial methods to create an offspring? How would you feel about passing infertility on to your child?

Answer Keys and Discussion Points

Concepts Defined

Gene – a unit of hereditary information consisting of a particular nucleotide sequence found on a chromosome.

Allele – an alternative form of a gene.

Homozygous – describes a genetic condition characterized by the presence of two identical alleles for a given gene.

Heterozygous – describes a genetic condition characterized by the presence of two different alleles for a given gene; the individual contains one dominant and one recessive allele in a gene pair.

Autosomes – the name for all the chromosomes that are not sex chromosomes; chromosomes that occur in homologous pairs in both males and females and do not bear the genes determining sex.

Homologous chromosomes – a pair of chromosomes that are matched because they have the same physical appearance and possess genes for the same characteristics; one homologous chromosome is inherited from the father and the other homologous chromosome is inherited from the mother.

Nonhomologous chromosomes – chromosomes that are not alike; when compared, these chromosomes are different physically and bear genes for different characteristics.

Sex chromosomes – the pair of chromosomes that determine sex in an organism; the X and Y chromosomes in humans.

Sex determination – the combination of sex chromosomes that determine the sex of an offspring; in humans the sex chromosomes of a normal female are XX and the sex chromosomes of a normal male are XY.

Genetic linkage – the inheritance of certain genes as a group because they are found close together on the same chromosome; linked genes on sex chromosomes or autosomes do not show independent assortment.

Crossing Over – homologous chromosomes exchange segments.

Recombinant DNA – DNA that has been altered as a result of the recombination of genes; the formation of new combinations of different alleles of each gene on a chromosome; the result of crossing over.

Deletion – a mutation in which segments of the gene are removed.

Infertility – the inability to conceive; can be due to problems in either the male or the female or both partners.

DISCUSSION of the lecture concepts (This could be done as a class discussion or group assignment)

1. What's the evolutionary value of mixing genetic information (recombination)?

   Answer: The process of crossing-over to "unlink" genes and create recombinant chromosomes leads to genetic variation in offspring. This variation is essential to evolution. Because organisms vary from one another within a population, one individual may have characteristics that give that individual an advantage over another individual. This ensures the survival of populations as they deal with a changing environment and with time may lead to changes in species.

2. Why don't brothers and sisters look more alike? Why don't children look more like their parents?

   Answer: Sexual reproduction results in offspring that are highly varied which means there are genetic differences between siblings and between children and their parents. Each chromosome from a homologous pair comes from a different parent and thus for many genes there will be many versions when those genes are compared. The way chromosomes pair during meiosis and orient themselves prior to separation is a matter of chance and leads to many different combinations of chromosomes in eggs and sperm. Chromosome pairing is an opportunity for crossing-over between homologous chromosomes that results in recombinant chromosomes. Finally, there is another opportunity for variation as random fertilization of eggs by sperm occurs (Which egg with its unique combination of chromosomes is fertilized by which sperm cell with its unique combination of chromosomes?). And we can't forget that sometimes changes in the genetic composition of a chromosome occur that are called mutations. A mutation results in instant genetic variation and sometimes will be expressed in a physical way within the organism. Thus we may look alike within families and as a species because we share many genes in common but the many differences in our genetic composition, accounts for our differences in appearance. Only identical twins that share identical genetic information look alike.

3. What sex chromosomes do YOU have? Or think you have? Discuss the normal sex chromosome pairing and mention some unusual genetic conditions that result from extra sex chromosomes or the absence of a sex chromosome. Why doesn't nature favor the abnormal sex complements?

   Answer: The normal combination of sex chromosomes in a male is XY and XX in a female. But often, unless you undergo special testing, you may not know exactly what your sex chromosomes are. Some people have abnormal numbers of sex chromosomes. For example, Turner syndrome (X0) females have only one X chromosome, Trisomy X (XXX) females have three X chromosomes, Klinefelter syndrome (XXY) males have an extra X chromosome, and some males have extra Y chromosomes (XYY). Nature doesn't favor the abnormal sex complements because so often these conditions result in infertility and unusual physical appearances. For example, Turner syndrome females do not develop secondary sex characteristics and have a short stature with skin folds around the neck and other physical abnormalities. Klinefelter syndrome males show partial breast development, broad hips, and small testes and are sterile.

4. A man who carries a defective (mutated) Y chromosome will pass the defective chromosome on to which of his children?

   Answer: Only his sons. The Y chromosome, whether defective or not, is passed from father to son; female children will not receive a Y chromosome but will receive two X's

(one from father and one from mother). Thus sons that receive a defective Y will experience the same problems that their father experienced with the defective Y.

5. Historically, women have been held responsible (blamed!) for not producing the male heir. Are women responsible for the sex of the child? Which sex actually determines the gender of the child?

Answer: King Henry VIII blamed his wife and subsequently had her beheaded for not producing a male heir. Now we know that women are not responsible for the sex of a child. Rather, the father should be "blamed" since the father determines the sex of the child with the contribution of either a sperm cell containing the X chromosome (child will be female) or a sperm cell containing the Y chromosome (child will be male). The egg made by the mother only contains the X chromosome.

6. Why are more men colorblind than women?

Answer: The man need only inherit one X with the sex-linked gene that causes colorblindness and he will have the condition (remember he has one X and one Y); females would have to inherit two X's with the disorder to have full blown colorblindness since it is a recessive disorder (takes two recessive alleles for expression).

7. What is the expected phenotypic ratio (physical manifestation) of children from a normal female and a colorblind male?

Answer: All children will not have colorblindness (rarely, females that are carriers will show some degree of colorblindness).

Colorblindness is a sex-linked disorder with the abnormal gene found on the X chromosome. The disorder appears more frequently in males; an affected male passes the abnormal allele to a daughter that does not express colorblindness (because she has another X without the abnormal allele and she would have to have both X's with abnormal alleles to express the disorder); the daughter is then able to bear colorblind sons because she is able to contribute the X with the gene for colorblindness. In this specific question, we will need to assume the normal mother has both X's without the gene for colorblindness and will pass a normal X to all her children. Father, who is colorblind, will pass the X with the colorblindness gene to all of his female children.

XX (normal mother) x $X^{C}Y$ (colorblind father)

The female children from this union will be carriers of colorblindness and will have normal vision, since only one of their X's contains the colorblindness gene. However, these females will be able to pass colorblindness to some of their male children (some sons will inherit X and some will inherit X^{C}).

8. If you were infertile due to a mutation of a sex chromosome would you want to use artificial methods to create an offspring? How would you feel about passing infertility on to your child?

Answers will obviously vary. Discuss the meaning of the word "ethical" and how ethical concerns may influence some people in their opinions.

Outline of Lecture Notes

1. All chromosomes besides X and Y are autosomes.
2. Sex chromosomes of the normal male are X and Y; the normal female has two X's.
3. The X and Y chromosomes share similarities and differences:
   -They share genes in common. Half of the genes found on the Y are also found on the X and these genes have nothing to do with a particular sex. Their gene commonality suggests the sex chromosomes probably evolved from a pair of identical autosomes.
   -The Y chromosome is 1/3 the size of the X and contains approximately 30 genes compared to the 1000 genes of the X.
   -The Y chromosome has genes that are male specific in that their expression determines maleness (sex determination), external organs and internal accessory organs, and sperm production (fertility).
4. All genes on a given chromosome (autosome or sex chromosome) belong to the same linkage group (and are often called linked genes). Genes of the linkage group do not obey Mendel's Laws (review).
5. Crossing over between chromosomes (homologous chromosomes) creates recombinant chromosomes by rearranging genes that were previously linked.
6. Data suggests that the X and Y chromosome evolved from ancestral autosomes approximately 300 million years ago. The shared genes that remain today on both X and Y are considered living fossils. Possibly the Y chromosome acquired a specific gene that played a role in sex determination and genes related to maleness began to migrate to the Y chromosome from various autosomes. The resulting composition differences over time between the Y and the X prevented recombination; these differences may have been beneficial to male and female members of a species. Two X chromosomes are still able to exchange segments (recombine).
7. Sometimes a mutation known as a deletion occurs in a chromosome. A deletion on a Y chromosome can cause male infertility. Three percent of the male population has this form of infertility. It appears the Y chromosome sometimes will fold over on itself, lining up patches of similar genetic sequences in a recombination effort. When it does this it sometimes accidentally deletes the genes important for sperm development that are found between the similar patches. These changes in the Y chromosome can occur early in male embryonic development or in a single sperm donating it's Y during fertilization.
8. ICSI = Intracytoplasmic sperm injection is a laboratory technique that injects a sperm cell from an infertile man into an egg. Sons conceived with this method will inherit a defective Y chromosome and thus like their fathers will also be infertile.
9. The ICSI method raises ethical questions about the use of artificial conception to produce offspring of successive generations.