Genetics Lecture 9 Sex Determination

reproductive modes

- In the biological world, a wide range of reproductive modes and life cycles are observed.
- Some organisms are entirely asexual, displaying no evidence of sexual reproduction.
- Some organisms alternate between short periods of sexual reproduction and prolonged periods of asexual reproduction.
- Orderly transmission of genetic material from parents to offspring, and the resultant phenotypic variability, relies on the processes of segregation and independent assortment that occur during meiosis.
- Meiosis produces haploid gametes so that, following fertilization, the resulting offspring maintain the diploid number of chromosomes characteristic of their kind.
- Thus, meiosis ensures genetic constancy within members of the same species.

- These events, seen in the perpetuation of all sexually reproducing organisms, depend ultimately on an efficient union of gametes during fertilization.
- In turn, successful fertilization depends on some form of sexual differentiation in the reproductive organisms.
- In many animal species, including humans, the differentiation of the sexes is more evident as phenotypic dimorphism of males and females.
• Dissimilar, or heteromorphic chromosomes, such as the XY pair in mammals, characterize one sex or the other in a wide range of species, resulting in their label as sex chromosomes.

• Nevertheless, in many species, genes rather than chromosomes ultimately serve as the underlying basis of sex determination.

• As we will see, some of these genes are present on sex chromosomes, but others are autosomal.

• Extensive investigation has revealed variation in sex-chromosome systems—even in closely related organisms—suggesting that mechanisms controlling sex determination have undergone rapid evolution many times in the history of life.

Life Cycles Depend on Sexual Differentiation

• In describing sexual dimorphism (differences between males and females) in multicellular animals, biologists distinguish between primary sexual differentiation, which involves only the gonads, where gametes are produced, and secondary sexual differentiation, which involves the overall appearance of the organism, including clear differences in such organs as mammary glands and external genitalia as well as in nonreproductive organs.

• In plants and animals, the terms unisexual, dioecious, and gynodioecious are equivalent; they all refer to an individual containing only male or only female reproductive organs.

• Conversely the terms bisexual, monoecious, and hermaphroditic refer to individuals containing both male and female reproductive organs, a common occurrence in both the plant and animal kingdoms.

• These organisms can produce both eggs and sperm.

Zea mays

• The life cycles of many plants alternate between the haploid gametophyte stage and the diploid sporophyte stage.

• The processes of meiosis and fertilization link the two phases during the life cycle.

• The relative amount of time spent in the two phases varies between the major plant groups.

• In some nonseed plants, such as mosses, the haploid gametophyte phase and the morphological structures representing this stage predominate.

• The reverse is true in seed plants.
• Maize (Zea mays) or corn, exemplifies a monoecious seed plant, meaning a plant in which the sporophyte phase and the morphological structures representing that phase predominate during the life cycle.
• Both male and female structures are present on the adult plant.
• Thus, sex determination occurs differently in different tissues of the same organism, as shown in the life cycle of this plant.
• The stamens, which collectively constitute the tassel, produce diploid microspore mother cells, each of which undergoes meiosis and gives rise to four haploid microspores.
• Following meiosis, only one of the four haploid megaspores survives.
• It usually divides mitotically three times, producing a total of eight haploid nuclei enclosed in the embryo sac.
• Two of these nuclei unite near the center of the embryo sac, becoming the endosperm nuclei.
• At the micropyle end of the sac, where the sperm enters, sit three other nuclei: the oocyte nucleus and two synergids. The remaining three, antipodal nuclei, cluster at the opposite end of the embryo sac.
When contact is made at the micropyle, the two sperm nuclei enter the embryo sac.

One sperm nucleus unites with the haploid oocyte nucleus, and the other sperm nucleus unites with two endosperm nuclei.

This process, known as double fertilization, creates the diploid zygote nucleus and the triploid endosperm nucleus, respectively.

Each ear of corn can contain as many as 1000 of these structures, each of which develops into a single kernel.

Each kernel, if allowed to germinate, gives rise to a new plant, the sporophyte.

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**Caenorhabditis elegans**

The nematodes' usefulness is based on the fact that adults consist of 959 somatic cells, the precise lineage of which can be traced back to specific embryonic origins.

There are two sexual phenotypes in these worms: males, which have only testes, and hermaphrodites, which during larval development form two gonads, which subsequently produce both sperm and eggs.

The eggs that are produced are fertilized by the stored sperm in a process of self-fertilization.
• The vast majority of organisms that result genes located on both the X chromosome and autosomes.
• C. elegans lacks a Y chromosome altogether — hermaphrodites have two X chromosomes, while males have only one X chromosome.
• It is believed that the ratio of X chromosomes to the number of sets of autosomes ultimately determines the sex of these worms.
• A ratio of 1.0 (two X chromosomes and two copies of each autosome) results in hermaphrodites, and a ratio of 0.5 results in males.
• The absence of a heteromorphic Y chromosome is not uncommon in organisms.

X and Y Chromosomes Were First Linked to Sex Determination Early in the Twentieth Century
• In 1906, Edmund B. Wilson demonstrated that female somatic cells in the butterfly Protenor contain 14 chromosomes, including two X chromosomes.
• During oogenesis, an even reduction occurs, producing gametes with seven chromosomes, including one X chromosome.
• Male somatic cells, on the other hand, contain only 13 chromosomes, including one X chromosome.
• During spermatogenesis, gametes are produced containing either six chromosomes, without an X, or seven chromosomes, one of which is an X.

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<table>
<thead>
<tr>
<th>Gender</th>
<th>Chromosome Number</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>14 (2X + 12A)</td>
<td>Gametes</td>
</tr>
<tr>
<td>Male</td>
<td>13 (2X + 11A)</td>
<td>Gametes</td>
</tr>
</tbody>
</table>
\]

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The presence or absence of the X chromosome in male gametes provides an efficient mechanism for sex determination in this species and also produces a 1:1 sex ratio in the resulting offspring.

This mechanism, now called the XX/XO, or Protenor, mode of sex determination, depends on the random distribution of the X chromosome into one-half of the male gametes during segregation.

The Y Chromosome Determines Maleness in Humans

The first attempt to understand sex determination in our own species occurred almost 100 years ago and involved the visual examination of chromosomes in dividing cells.

Efforts were made to accurately determine the diploid chromosome number of humans, but because of the relatively large number of chromosomes, this proved to be quite difficult.

It was believed that the sex-determining mechanism in humans was based on the presence of an extra chromosome in females, who were thought to have 48 chromosomes.

However, in the 1920s, Theophilus Painter counted between 45 and 48 chromosomes in cells of testicular tissue and also discovered the small Y chromosome, which is now known to occur only in males.

In his original paper, Painter favored 46 as the diploid number in humans, but he later concluded incorrectly that 48 was the chromosome number in both males and females.

For 30 years, this number was accepted.

Then, in 1956, a better way was discovered to prepare chromosomes for viewing.

This improved technique led to a strikingly clear demonstration of metaphase stages showing that 46 was indeed the human diploid number.

Of the normal 23 pairs of human chromosomes, one pair was shown to vary in configuration in males and females.

These two chromosomes were designated the X and Y sex chromosomes.
• We might believe that this observation is sufficient to conclude that the Y chromosome determines maleness.
• However, several other interpretations are possible.
• The Y could play no role in sex determination; the presence of two X chromosomes could cause femaleness; or maleness could result from the lack of a second X chromosome.
• The evidence that clarified which explanation was correct came from study of the effects of human sex-chromosome variations.
• As such investigations revealed, the Y chromosome does indeed determine maleness in humans.

Klinefelter and Turner Syndromes
• In about 1940, scientists identified two human abnormalities characterized by aberrant sexual development, Klinefelter syndrome (47,XXY) and Turner syndrome (45,X).
• Individuals with Klinefelter syndrome are generally tall and have long arms and legs and large hands and feet.
• They usually have genitalia and internal ducts that are male, but their testes are rudimentary and fail to produce sperm.
• At the same time, feminine sexual development is not entirely suppressed.
• Slight enlargement of the breasts (gynecomastia) is common, and the hips are often rounded.
• This ambiguous sexual development, referred to as intersexuality can lead to abnormal social development.
• Intelligence is often below the normal range as well.
• In Turner syndrome, the affected individual has female external genitalia and internal ducts, but the ovaries are rudimentary.
• Other characteristic abnormalities include short stature (usually under 5 feet), cognitive impairment, skin folds on the back of the neck, and underdeveloped breasts.
• In 1959, the karyotypes of individuals with these syndromes were determined to be abnormal with respect to the sex chromosomes.
• Individuals with Klinefelter syndrome have more than one X chromosome.
• Most often they have an XXY complement in addition to 44 autosomes, which is why people with this karyotype are designated 47,XXY.
• Note the convention used in designating these chromosome compositions: the number states the total number of chromosomes present, and the symbols after the comma indicate the deviation from the normal diploid content.

![Karyotype Diagram]

- These Klinefelter and Turner karyotypes and their corresponding sexual phenotypes led scientists to conclude that the Y chromosome determines maleness and thus is the basis for phenotypic sex determination in humans.
- In its absence, the person's sex is female, even if only a single X chromosome is present.
- The presence of the Y chromosome in the presence of two X chromosomes characteristic of Klinefelter syndrome is sufficient to determine maleness, even though male development is not complete.
- Similarly, in the absence of a Y chromosome, as in the case of individuals with Turner syndrome, no masculinization occurs.
- Note that we cannot conclude anything regarding sex determination under circumstances where a Y chromosome is present without an X because Y-containing human embryos lacking an X chromosome (designated 45,Y) do not survive.
47,XXX Syndrome

- The abnormal presence of three X chromosomes along with a normal set of autosomes (47,XXX) results in female differentiation.
- The highly variable syndrome that accompanies this genotype, often called triplo-X, occurs in about 1 of 1000 female births.
- Frequently, 47,XXX women are perfectly normal and may remain unaware of their abnormality in chromosome number unless a karyotype is done.
- In other cases, underdeveloped secondary sex characteristics, sterility, delayed development of language and motor skills, and mental retardation may occur.
- In rare instances, 48,XXXX (tetra-X) and 49,XXXXX (penta-X) karyotypes have been reported.
- The syndromes associated with these karyotypes are similar to but more pronounced than the 47,XXX syndrome.

47,XYY Condition

- Another human condition involving the sex chromosomes is 47,XXY.
- Patricia Jacobs discovered that 9 of 315 males in a Scottish maximum security prison had the 47,XXY karyotype.
- These males were significantly above average in height and had been incarcerated as a result of antisocial (nonviolent) criminal acts.
- Of the nine males studied, seven were of subnormal intelligence, and all suffered personality disorders.

The possible correlation between this chromosome composition and criminal behavior piqued considerable interest, and extensive investigation of the phenotype and frequency of the 47,XXY condition in both criminal and noncriminal populations ensued.
- Above-average height (usually over 6 feet) and subnormal intelligence have been generally substantiated, and the frequency of males displaying this karyotype is indeed higher among people in penal and mental institutions than among un-incarcerated populations.
- A particularly relevant question involves the characteristics displayed by XYY males who are not incarcerated.
- The only nearly constant association is that such individuals are over 6 feet tall.
- Since Walzer and Gerald’s work, it has become clear that many XYY males are present in the population who do not exhibit antisocial behavior and who lead normal lives.
Sexual Differentiation in Humans

• Once researchers had established that, in humans, it is the Y chromosome that houses genetic information necessary for maleness, they attempted to pinpoint a specific gene or genes capable of providing the "signal" responsible for sex determination.

• During early development, every human embryo undergoes a period when it is potentially hermaphroditic.

• By the fifth week of gestation, gonadal primordia (the tissues that will form the gonad) arise as a pair of gonadal (genital) ridges associated with each embryonic kidney.

• The embryo is potentially hermaphroditic because at this stage its gonadal phenotype is sexually indifferent-male or female reproductive structures cannot be distinguished, and the gonadal ridge tissue can develop to form male or female gonads.

• As development progresses, primordial germ cells migrate to these ridges, where an outer cortex and inner medulla form (cortex and medulla are the outer and inner tissues of an organ, respectively).

• The cortex is capable of developing into an ovary, while the medulla may develop into a testis.
Because gonadal ridges can form either ovaries or testes, they are commonly referred to as bipotential gonads.

What is the switch that triggers gonadal ridge development into testes or ovaries?

The presence or absence of a Y chromosome is the key.

If cells of the ridge have an XY constitution, development of the medulla into a testis is initiated around the seventh week.

However, in the absence of the Y chromosome, no male development occurs, the cortex of the ridge subsequently forms ovarian tissue, and the Mullerian duct forms oviducts (Fallopian tubes), uterus, cervix, and portions of the vagina.

Depending on which pathway is initiated, parallel development of the appropriate male or female duct system then occurs, and the other duct system degenerates.

If testes differentiation is initiated, the embryonic testicular tissue secretes hormones that are essential for continued male sexual differentiation.

The presence of a Y chromosome and development of the testes also inhibit formation of female reproductive organs.

In females, as the 12th week of fetal development approaches, oogonia within the ovaries begin meiosis, and primary oocytes can be detected.

By the 25th week of gestation, all oocytes become arrested in meiosis and remain dormant until puberty is reached some 10 to 15 years later.

The Y Chromosome and Male Development

The human Y chromosome, unlike the X, was long thought to be mostly blank genetically

It is now known that this is not true, even though the Y chromosome contains far fewer genes than does the X

Data from the Human Genome Project indicate that the Y chromosome has at least 75 genes, compared to 900-1400 genes on the X.

Current analysis of these genes and regions with potential genetic function reveals that some have homologous counterparts on the X chromosome and others do not.
• For example, present on both ends of the Y chromosome are so-called pseudoautosomal regions that share homology with regions on the X chromosome and synapse and recombine with it during meiosis.
• The presence of such a pairing region is critical to segregation of the X and Y chromosomes during male gametogenesis.
• The remainder of the chromosome, about 95 percent of it, does not synapse or recombine with the X chromosome. As a result, it was originally referred to as the nonrecombinating region of the Y (NRY).
• More recently researchers have designated this region as the male-specific region of the Y (MSY).
• As you will see, some portions of the MSY share homology with genes on the X chromosome, and others do not.

• The MSY is divided about equally between euchromatic regions, containing functional genes, and heterochromatic regions, lacking genes.
• Within euchromatin, adjacent to the PAR of the short arm of the Y chromosome, is a critical gene that controls male sexual development, called the sex-determining region Y (SRY).
• In humans, the absence of a Y chromosome almost always leads to female development; thus, this gene is absent from the X chromosome.
• At 6 to 8 weeks of development, the SRY gene becomes active in XY embryos.
• SRY encodes a protein that causes the undifferentiated gonadal tissue of the embryo to form testes.

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