SEX DETERMINATION

Sex determination

Primary sex determination relates to the formation of ovaries or testes. This can be regulated by genes and/or environmental factors. In alligators sex is determined by the temperature rt which eggs are incubated. Many species are hermaphrodite. Secondary sexual characteristics are also under genetic regulation.

Single genetic sex determining systems:

Unicellular eukaryotes can have sex determining systems in which two alleles of a single gene determine sex. In hymenoptera, heterozygosity at one gene determines femaleness.

Sex chromosome systems

Three different sex chromosome systems have been described, XX-XO, XX-XY anil ZZ-ZW. The sex which has two identical sex chromosomes is called homogametic and the sex with different sex chromosomes heterogametic.

Sex determination in Drosophila

In this species sex is determined by the ratio of X chromosomes to sets of autosomes. If the ratio is equal or greater than 1.0 the fly is female; if lower than 0.5 the fly is male. Gynandromorphs are flies with male and female sex phenotypes in different parts of their body. This is due to changes in the number of X chromosomes in somatic cells due to nondisjunction.

Sex determination in humans

In humans the study of sex chromosome aneuploids has shown (hat the presence *of a* Y chromosome determines maleness irrespective of the presence of different numbers of X chromosomes. A gene, *SRY,* responsible for inducing maleness has been mapped to the Y chromosome.

Sex determination in plants

Most plants are hermaphrodite, but some examples of XX-XY sex chromosome systems are known in dioecious plants. In *Melandritim* sex is determined by the ratio of X chromosomes to Y chromosomes.

Secondary sexual characteristics

Mutations in genes such the testosterone receptor gene can lead XY individuals to develop female secondary sexual characteristics. Transfer of bkxid cells between male and female twins in cattle can produce freemartins which have defective testes composed of cells containing two X chromosomes.

Evolution of sex chromosomes

Sex chromosomes have evolved on several different occasions. The sex chromosomes evolve from a pair of homologous autosomes. In some species the two sex chromosomes are identical, homomorphic. A small region of homology between the two remains. It is known as the pseudoautosomal region.

Sex determination

The sex of an individual can be determined at several levels. This topic is principally concerned with primary sex determination, which relates to whether an individual develops testes or ovaries. Secondary sexual characteristics - forms of development associated with one sex or the other - such as feather-coloring, presence of horns or manes, are also under genetic control.

Unicellular organisms can have simple systems for sex determination, but multicellular species differ greatly in the strategies they employ to generate the male and female gametes that are necessary for sexual reproduction. In many instances a single individual may have male and female reproductive organs. Such individuals are known as hermaphrodites. This is common in many invertebrates and in plant species. Hermaphrodites can be of both sexes simultaneously or may change from one sex to ;lie other. The importance of genes in determining sex in such species is clearly less than in most higher organisms, however there is evidence that genes can regulate the timing and extent of different sexual phases in some hermaphrodite invertebrate species.

Hermaphroditism, in animals, is not entirely limited to invertebrates. Several fish species such as bass undergo sex-reversal, often under environmental or hormonal influence. Domestic fowl can also occasionally undergo spontaneous sex-reversal. The most clear-cut example of environmentally determined sex is found in alligators where the temperature at which eggs are incubated determines the sex of the individual.

Simple genetic sex-determining system

Probably the simplest sex determining mechanism is found in yeast. Two alleles of a single gene determine mating type. In S. *cerevisiae* a gene on chromosome 3 known as MAT has two alleles a and a. For most of its life cycle S. *cereoisiae* is haploid (has only one set of chromosomes), and the yeast cell will carry either the a or a allele. This determines mating type. Only yeast cells of opposite mating types can fuse to form diploids which undergo meiosis and release new haploid spores. Thus the MAT gene can be regarded as an early type of sex-determining system. A similar single gene system is responsible for sex determination in unicellular algae species such as *Chlamydomonas.*

The hymenoptera (ants, bees and wasps) havr an unusual method of sex determination. Male bees (drones) develop from eggs that were not fertilized and are haploid. Female bees (workers and queens) develop from fertilized eggs and are diploid. It was thought that the difference in ploidy was the sex determining factor. However, the mechanism depends on a gene with multiple alleles. If this gene is heterozygous the fly will be female. Haploid drones cannot be heterozygous at any gene since they have only one copy of each chromosome. Intensive inbreeding results in high levels of homozygosity and in highly inbred bee stocks diploid males have been detected.

Sex chromosome systems

In many species, sex determining genes are associated with specific chromosomes known as sex chromosomes. Several different sex chromosome systems are known:

- **XX-XO system.** This is found in many insect species. Females contain a pair of chromosomes known as X chromosomes. Males have only one X chromosome. This is the case in grasshoppers, and the bug *Protenor* and is sometimes known as the **Protenor** system.

- XX-XY. This is found in mammals and also in certain insects including *Drosophila* (the fruit fly). Here females have two copies **of the X** chromosome and males have an X and a Y chromosome.

- *Z Z -ZW.* This is essentially the reverse of the XX-XY system, where the female is ZW and the male ZZ. It is found in birds, lepidoptcra (butterflies) and snakes.

The terms homogametic and heterogametic are used to describe these systems. Homogametic means that with respect to sex chromosomes gametes are all identical. For instance, in the XX-XY system females are the homogametic sex as all gametes will carry one X chromosome. In the ZZ-ZW system the female is the heterogametic sex as two classes of gametes containing either Z or W as the sole sex chromosome are found in equal numbers.
Although two species may share the same sex chromosome system, this does not mean the genes which determine sex operate in similar ways. To illustrate this point three different examples of the XX-XY sex chromosome system are compared below.

Sex determination in *Drosophila*

Sex is determined in *Drosophila by* the ratio of X chromosomes to sets of autosomes (sets of autosorries simply refers to the ploidy of the fly). When the ratio is 1.0 or greater flies are female. When it is 0.5 or less flies are male. Intermediate values give rise to intersex flies. Some typical examples are given in *Table 1*.
Extreme ratios such as 0.33 and 1.5 give rise to flies that are called metamales or metafemales. Although clearly of their respective sex these flies are poorly developed and have a shortened life-span.

The fact that sex determination is a result of a balance of X chromosomes and autosomes suggests that genes that cause female development are clustered on the X chromosome and genes for maleness on the autosomes. One important point to note concerns (he Y chromosome. The data above indicate that it has no role in sex determination in *Drosophila*. This is correct, but although flies that l.ick a Y chromosome may be male, they are infertile because a gene on the Y chromosome is essential for the development of functional sperm.

A similar genetic balance mechanism regulates sex determination in other species such as the nematode *Caenarhabditis elegans* (round worm). However this is slightly more complex as male and hermaphrodite individuals exist in this species.

One significant feature of sex determination in *Drosophila is* the presence of abnormal flies known as **gynandromorphs.** These are the result of non-disjunction (see Topic Bl) in the somatic cells of the flies. If this results in a change in the number of X chromosomes in a cell the X: autosome ratio will

Table 1. Ratio of X chromosomes to sets of autosomes, and ***sex*** *determination in* Drosophila

Number of X	Number of sets of autosomes (A)	X : A ratio	Sex chromosomes (X)
3	2	1.5	Female
3	3	1.0	Female
2	2	1.0	Female
2	3	0.67	Intersex
1	2	0.5	Male
1	3	0.33	Male

Sex determination in humans

be changed and may affect the sex of the cell. This can occur because in flies sex is determined autonomously in every cell. As the cell continues to divide, its descendants will form a patch of cells (clone) which, depending on their position in the organism, may differentiate to form structures of the opposite sex to that of the rest of the fly. In the most extreme case, loss of an X chromosome in the first division after fertilization can result in a fly which develops bilaterally into two halves, one male and the other female. This type of event is not found in mammals where the production of secondary sexual characters is determined hormonally.

Sex determination in humans

Sex determination in humans is typical of the process in other mammalian species, and although the sex chromosomes are XX and XY, the genetic basis of sex determination differs markedly from that described for *Drosophila.* Our understanding of this subject comes from the study of sex chromosome aneuploids. Aneuploidy of sex chromosomes arises more frequently than for autosomes because very few genes are present on the Y chromosome, and due to the phenomenon of X chromosome inactivation, only one X chromosome is expressed in any cell. Hence alterations to the numbers of sex chromosomes have less effect on viability than do changes to the autosomes. The sex of several sex chromosome aneuploids is given in *Table 2.* Not all of these sex chromosome configurations result in fertile individuals and individuals with the more extreme deviations from normal suffer severe mental retardation.

From these examples it is dear that at the chromosomal level the presence of a Y chromosome is the factor which determines maleness in humans. During early embryonic development the presence of a Y chromosome causes the un-dirferentiated gonad to grow more rapidly and subsequently to develop into testes. In birds, where the ZZ-ZW sex determining system is essentially the reverse of the XX-XY, the presence of a W chromosome induces the development of ovaries from undifferentiated gonads. A specific gene, SKY, mapping to the Y chromosome in both humans and mice has been isolated that is responsible for the switch from female to male development in embryos.

Table 2. Relationship between sex chromosome numbers and Sex determination in humans

Sex chromosomes	Chromosome number	Sex
X	45	Female
XXX	47	Female
XXXX	48	Female
XXXXX	49	Female
XYY	47	Male
XXY	47	Male
XXXY	48	Male

Sex determination In plants

Most angiospenns are hermaphrodite, flowers contain both male and female organs. However, in some species male and female flowers are borne on separate plants (dioecious). One plant genus in which the chromosomal basis of sex determination has been worked out is *Melandrium* (Campion). Here the ratio of X: Y chromosomes is the important factor in determining whether plants produce male or female flowers. This implies that genes on both of the sex chromosomes interact to produce the sex phenotype. Studies of plants that had radiation-induced deletions in X or Y chromosomes showed that the Y chromosome contains regions that repress female development and induce male development, whereas the X chromosome has regions that stimulate development of female flowers.

Secondary sexual characteristics

As noted at the start of this topic the production of secondary sexual characteristics is also under genetic control. This is well illustrated by the gene *Tfin* in mammals. This codes for a protein that acts as the receptor for the male-specific steroid hormone, testosterone, and is expressed in both males and females. Testosterone is produced only in the testes and is responsible for secondary sexual characteristics in males. Mutant alleles of this gene are responsible for a syndrome known as testicular feminization (androgen insensitivity). Here, the presence of a Y chromosome causes testes to form and these produce testosterone. However, the hormone has no effect on target cells because they lack functional testosterone receptors. Individuals with this syndrome develop as infertile females. Their gonads are testes but these remain internal, and their sex chromosomes are XY.

A different misalignment of primary and secondary sexual differentiation occurs in **freemartins.** These are sheep, goats or cattle that develop as infertile females, but have defective internal testes. Cells of the testes and other organs have two X chromosomes, but the blood contains some cells that have X and Y sex chromosomes. This abnormal development is only found in females that have been a member of a pair of mixed sex twins. The embryonic blood supplies of twins in these species are fused *in utero* and hence XY blood cells and hormones can enter the circulation of the female twin. This is sufficient to force the gonads to develop into testes, and to block partially normal female development even though the animal is genetically XX- The male twin is not affected by the presence of XX cells in its blood system.

These two examples should indicate the complex interactions that can occur between the genetic and hormonal determinants of developmental processes.

Evolution of sex chromosomes

It is generally considered that sex chromosomes evolved from a pair of homo-logous autosomes. This process must have taken place a number of different times during evolution. One of the best examples is found in snakes. Sex chromosomes have been studied in primitive and highly evolved snake species. In primitive species the two sex chromosomes appear identical **(homomorphic).** The two chromosomes are only differentiated by the fact that the W chromosome replicates late in S phase. In more advanced species the W chromosome becomes reduced in size, heterochromatic and clearly different from the Z. The pair of sex chromosomes retain only a small region of homology. This is known as the **pseudoautosomal region** and **is** required to allow the two chromosomes to pair and segregate accurately at meiosis. In vertebrates the sex chromosome which is limited to the heterogametic sex, (Y or W) is generally found to carry few genes and to accumulate large amounts of satellite DNA sequences and constitutive hetero-chromatin.