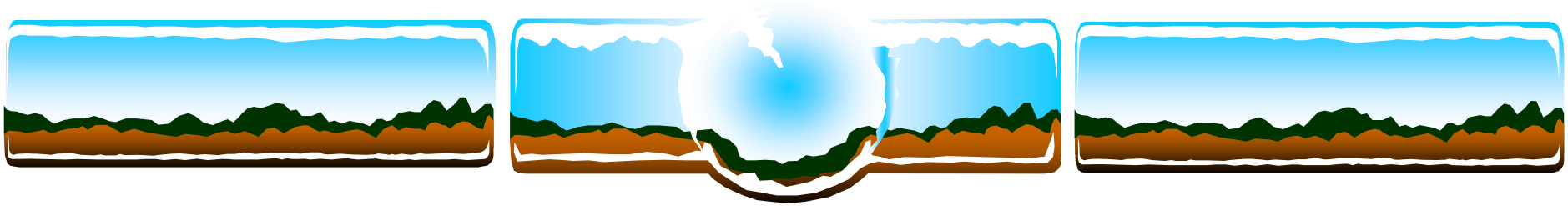


Sex Determination

Sexual Reproduction

For most diploid eukaryotes, sexual reproduction is the only mechanism resulting in new members of a species.

Meiosis in the sexual organs of parents produces haploid gametes, which unite during fertilization to restore the diploid phenotype in the offspring.

Sexual Reproduction

For most organisms, sexual reproduction requires some form of sexual differentiation.

In higher forms of life, this is manifested as phenotypic dimorphism between males and females of a species.

Traditionally, the symbol ♂ designates male

and the symbol ♀ designates female

Sex characteristics

Primary Sex Characteristics: Refer to the gonads (ovaries and testes) and associated structures.

Secondary Sex Characteristics: Refer to the overall appearance of the organism, external genitalia and mammary glands

Definitions

Unisexual=dioecious=gonochoric: Refer to an individual who possesses *only* male *or* female sexual organs, not both.

Bisexual=monoecious=hermaphroditic: Refer to individuals who possess *both* male *and* female reproductive organs.

Both states are common in the plant and animal kingdoms, and under normal conditions, are fertile.

Definitions

Intersex: Usually reserved for individuals of intermediate or indeterminate sexual differentiation. This state is not normal and the affected individuals are often sterile.

Caenorhabditis elegans

Referred to as *C. elegans*, this roundworm is a popular model species for developmental biologists.

Among other characteristics, the cell lineage of all 959 cells is precisely characterized, with each cell tracing back to the embryonic stage according to a specific plan.

C. elegans

Hermaphrodite →

Male →

Sex in *C. elegans*

Two sexual phenotypes:

1) Male—have only testes
2) Hermaphrodite—have both testes and ovaries.

During larval development, testes form and produce sperm, which is then stored.

Also during larval development, ovaries form in the hermaphrodite, but oogenesis does not occur until the worm reaches the adult stage.

Sex in *C. elegans*

When the adult stage is reached, oocytes form and are fertilized by the stored sperm.

The vast majority of the offspring will be hermaphrodites; only about 1% are males.

As adults, the males can mate with hermaphrodites, in which case the offspring will be approximately 50:50 male:hermaphrodite.

Sex in *C. elegans*

C. elegans does not have a Y chromosome.

The female phenotype is determined by presence of two X chromosomes and two copies of each autosome.

(ratio of X chromosomes:autosomes=1.0)

The male phenotype is determined by presence of a single X chromosome and two copies of each autosome.

(ratio of X chromosome:autosomes=0.5)

Heterogametic vs Homogametic

Homogametic: gender of an organism due to presence of two of the same sex chromosome. (e.g. XX)

Heterogametic: gender of an organism due to presence of two different sex chromosomes (e.g. XY)

In mammals, females are the homogametic sex, and males are the heterogametic sex.

Heterogametic vs Homogametic

In most birds, reptiles, and amphibians, the *female* is the heterogametic sex.

This is also the case in some plants and insects.

Sex Determination

In *mammal*s, the default pathway of sexual development is *female*.

What this means is that an embryo will develop as a female unless chemical signals are present that indicate it should develop as a male.

Sex Determination

Remember Klinefelter and Turner syndromes?

It is the presence of the Y chromosome that determines maleness.

So, no matter how many extra X chromosomes are present in Klinefelter syndrome, the individual is always male. And in Turner syndrome, a single X chromosome is sufficient to determine femaleness.

The Y Chromosome

The Y chromosome doesn't have a lot of genes on it, but it encodes the important gene that determines the male phenotype:

Testis determining factor (*SRY* gene): SRY stands for sex region Y. It encodes testis determining factor, which directs the embryonic gonads to develop into testes and begin secreting the male hormones **testosterone and Mullerian Inhibiting Substance**.

Male development in mammals

Mullerian Inhibiting Substance: Suppresses the formation of female ductal structures (uterus, Fallopian tubes, etc.)

Testosterone: Promotes the formation of male ductal structures (vas deferens, etc.) and associated sex glands (e.g. prostate) as well as the external genitalia.

Male development in mammals

So, you can see that development of the male phenotype requires first and foremost *the presence of an active SRY gene* to direct formation of the testes, which will then drive formation of the appropriate ductal structures and external genitalia.

Development of the male phenotype in mammals is all about suppressing the female phenotype.

Male development in mammals

If the organism does not have an active SRY gene, which encodes testis determining factor, it will develop into a female, even though it is genetically male.

If the organism does not have an active MIS gene, Mullerian (female) ductal structures will form, but the external genitalia will be normal. An affected individual is usually sterile because the testes do not develop normally and the presence of female ducts interferes with sperm transport.

Male development in mammals

If an individual has a mutation such that the testes do not secrete testosterone or the testosterone receptor is non-functional, the internal structures and gonads will develop into male structures, but the external genitalia will be female. These individuals are sterile and will not go through puberty.

The Conclusion

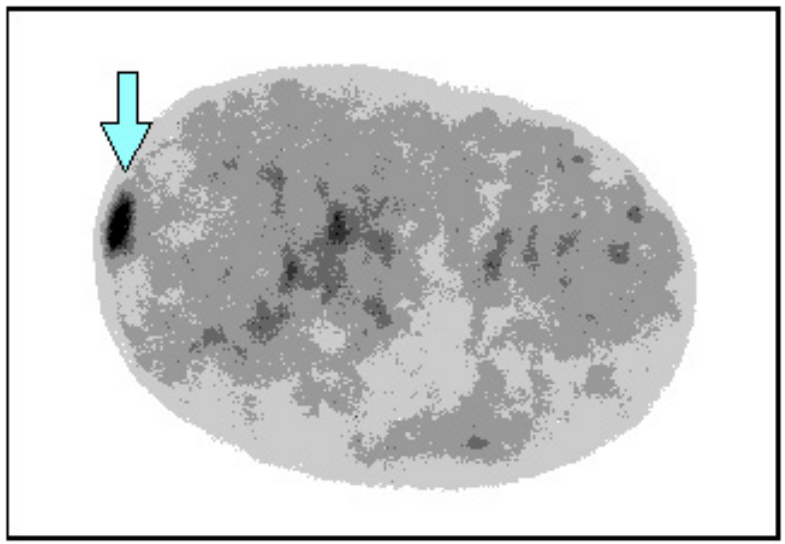
Male development in mammals is *directed* at every step. If there is a loss of direction, the subsequent development will follow the female pathway.

Dosage Compensation

Dosage compensation is the mechanism that keeps females (XX) from expressing twice as much of X-chromosome genes as males (XY), who have only one X chromosome.

Both sexes are rendered roughly equal by inactivation of one X chromosome in females.

Barr Bodies



A Barr body is, simply, the extra, inactivated X chromosome.

Barr Bodies

No Barr bodies are observed in Turner (XO) females.

One Barr body is observed in Klinefelter (XXY) males and normal (XX) females.

All but one X chromosome is inactivated and are visible as Barr bodies in extra-X (XXX, XXXX, XXXY, etc.) individuals.

Dosage compensation is incomplete

Individuals with Klinefelter, Turner and extra-X syndromes are not perfectly normal, though.

There are two probable explanations:

First, the extra X chromosomes may not be inactivated right away and therefore may influence development prior to inactivation.

Dosage compensation is incomplete

Second, Barr bodies may not be completely inactivated such that the extra X chromosomes may produce over-expression of some X-linked genes at different times.

X-Inactivation

It is thought that early in embryonic development, X-inactivation occurs **randomly** (maternal or paternal chromosome is not targeted) in somatic cells of females.

Once inactivation has occurred, though, the same X chromosome will be inactivated in progeny cells after mitotic cell division (i.e., if the maternal X chromosome was inactivated in the progenitor, the maternal X chromosome will be inactivated in the daughter cells).

Calico cats: X-inactivation in action

In cats, base coat color is encoded on the X chromosomes.

Male cats have only one X chromosome, so can only express one base color.

Females have two X chromosomes, so can express two base colors. For example, say the sire of a kitty contributed the black gene and the dam contributed the red gene.

Calico cats: X-inactivation in action

- Hair follicles derived from embryonic cells in which the maternal chromosome was inactivated will grow black hairs (express the paternal gene).
- Hair follicles derived from embryonic cells in which the paternal chromosome was inactivated will grow red hairs (express the maternal gene).
- Tortoiseshell cats do not have white patches, which is controlled by a separate gene.

Tortoiseshell—no white

Calico Cat—with white

The Mechanism of Inactivation

Remember DNA methylation? That plays an important role in X-inactivation.

Now, I introduce you to another, more important player.

The Mechanism of Inactivation

There is a large gene on the end of the p-arm of the X chromosome thought to be a primary driver of inactivation.

It is called the **X-inactive specific transcript (*Xist*)**, and expression of this transcript from an X chromosome results in inactivation of that chromosome.

Xist is a strange gene

The *Xist* gene is big, over a million bases long.

The RNA is not translated, and is thought to be a structural component of the inactivation process by physically associating with the inactive chromosome.