Sex determination in *C. elegans*

Introduction:

C. elegans is a highly used model organism in the research. It has been so extensively used that we sometimes call it *Arabidopsis thaliana* of the animal kingdom.

Reasons for using it as model organism are as under:

- Small size, 1mm long.
- Small life cycle, 3 days.
- Transparent animal, it allows researchers to observe each cell.
- Small genome size 5 pairs of autosomes and 1 pair of XX sex chromosomes.
- Hermaphrodite, it allows self-fertilization and relatively easy expression of recessive mutations via homozygosity.
- Sexual dimorphism, it allows crosses for recombination mapping and other standard genetic testing.

Sex determination in *C. elegans* (Chromosomal basis):

C. elegans has two different sexual forms: 1. Hermaphrodite 2. Male. Thus, they show sexual dimorphism.

Hermaphrodites are most common and have a pair of X chromosomes (XX) and 5 pairs of autosomes. Occasionally, there is formation of males from hermaphrodites due to meiotic non-disjunction. These males have only single X chromosome (XO) and 5 pairs of autosomes.

Frequency of male formation is 1/500 when meiotic non-disjunction occurs in hermaphrodites while if there is cross fertilization or mating between XX and XO then brood is 1:1 for XX:XO genotypes.

The hermaphrodites produce sperm during larval development and oocytes during adulthood. Thus, they are capable of self-fertilization as well as cross fertilization. Males produce only sperms.

This process is dependent on the X:A ratio.

- X:A = 1.0 Hermaphrodite.
- X:A = 0.5 Male.

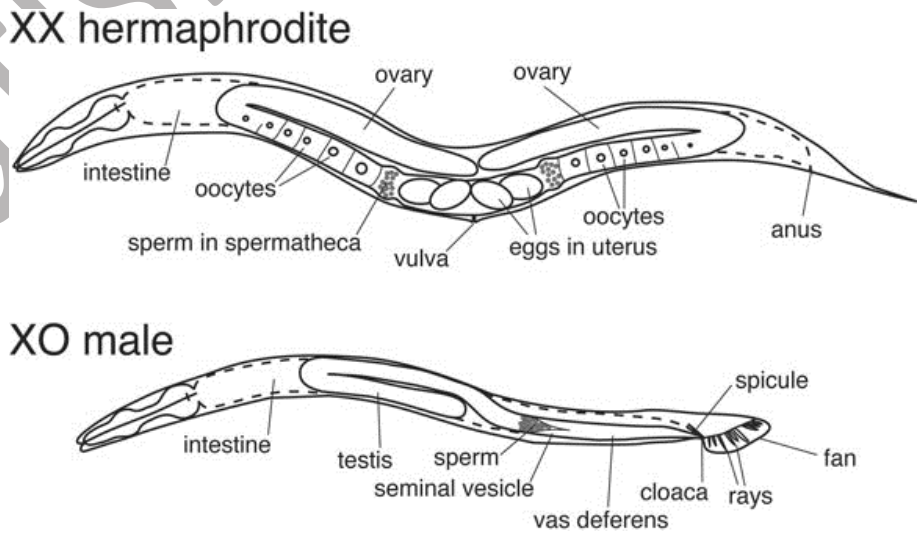

Figure: Sexual dimorphism in *C. elegans*

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Sex determination in *C. elegans* (Molecular basis):

The molecular basis of sex determination in C. elegans is a complex interplay of molecules which is regulated by the primary sex determination signal i.e. X:A ratio. It is this ratio that initiates the sex determination cascade in the early embryo.

The X:A ratio affects the sexual development pathway by targeting a gene called as xol-1. Its activity is needed in development of males but not for the hermaphrodites. In males the genotype is XO while it is XX in case of hermaphrodites due to which products and elements of X gene are present at twofold concentration in the cell when compared to males. This product concentration can be called as dosage and hermaphrodites have double the dose when compared to the males. It is this difference in dosage which is used as an ON/OFF signal for control of xol-1 gene. Thus, gene is inactive in hermaphrodites and its activation is must for the development of males.

This ON/OFF for xol-1 can be described as net outcome of contest between activity of genes located in the X chromosome and autosomes.

X-chromosomes have X signal elements (XSEs) and their products communicate the X-chromosome dosage and cause repression of xol-1 in a dosage dependent manner. Autosomes have dosage sensitive genes called as autosomal signal elements. (ASEs) that communicate ploidy and activate xol-1.

In XX worms i.e. hermaphrodites, double dose of XSEs opposes the double dose of ASEs and leads to suppression of xol-1 and activation of the pathway for hermaphrodite development while in XO worms i.e. males, single dose of XSEs can`t oppose the double dose of ASEs due to which xol-1 is activated and we find development of males.

Global pathway of sex determination in *C. elegans*:

It is a regulatory pathway that controls the sexual fate of somatic cells whose activity differs between sexes. This pathway is called as global because it is applicable on all the cells and is different from the specialized regulatory pathways involved in controlling the sexual differentiation of specific tissues and lineages.

The global pathway has two parts:

1. X:A signal to sdc genes is involved in control of sex determination and dosage compensation.
2. her-1 onwards the pathway is specific for sex determination.

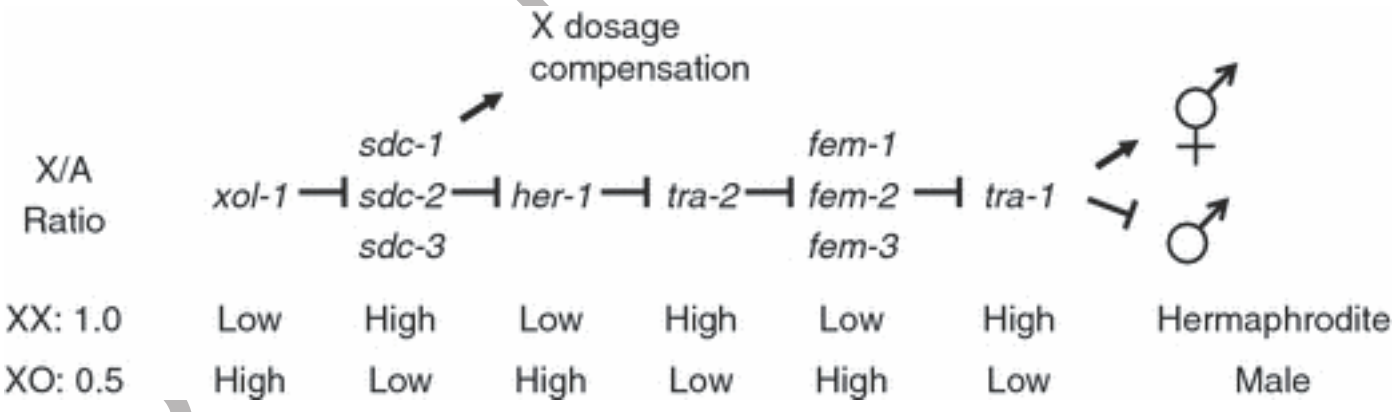

Figure: Global sex determination pathway in *C. elegans*

This pathway involves negative regulators of gene expression in a series as is described below.

In XO animals, xol-1 is high and it inhibits the sdc gene activity. This inhibition of sdc leads to upregulation of her-1 gene activity and its product binds to the product of tra-2 gene to cause inactivation. Thus, her-1 activity leads to inactivity in tra-2.

Pratap Singh

This inactivation of tra-2 leads to upregulation in fem genes and their products together cause inactivation of tra-1. tra-1 is a positive regulator of female differentiation and if its activity is absent then hermaphrodite formation can`t take place and we get XO male worms.

In XX animals, xol-1 is low and it leads to activation of sdc genes. They inhibit her-1 activity and thus tra-2 remains active. The activity of tra-2 leads to absence of fem gene activity and thus tra-1 is also active. Since tra-1 promotes female differentiation we get to see hermaphrodite worms.

The proteins encoded by the tra-1 genes contain zinc finger domains and represent transcription factors. These domains are highly similar to the *Drosophila* Ci protein and vertebrate GLI protein which are both regulated by Hedgehog signaling via Patched and Smoothened co-receptors.

Dosage compensation: It is an example of epigenetic gene regulation. In XX animals, sdc genes are also involved in dosage compensation so that products of genes on the X-chromosome are not present in double amount. This is achieved by reducing the gene activity to half on both the X-chromosomes. In *C. elegans*, we don`t see random inactivation of one of the X-chromosomes. Thus, we don`t see Barr body formation in the worms.

In different organisms we see different strategies for dosage compensation and it is compared in the figure below.

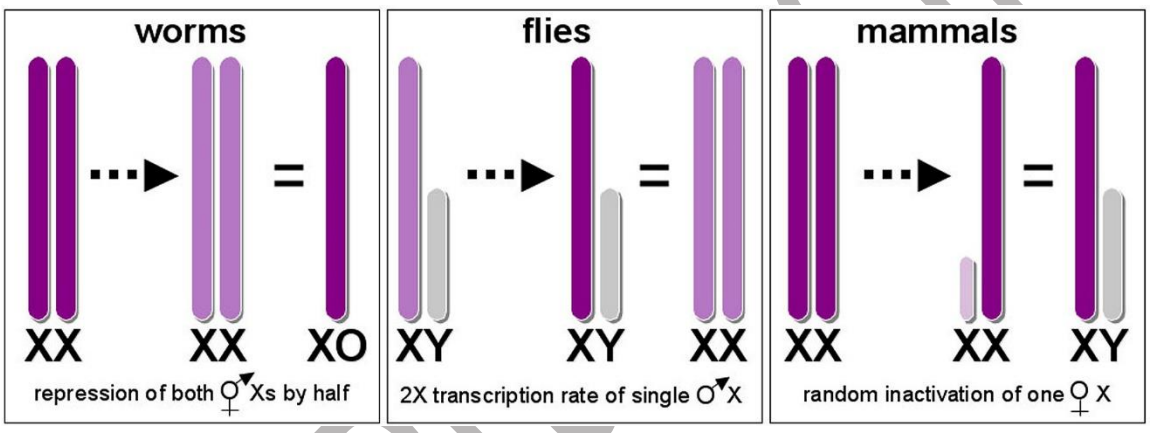

Figure: Strategies for dosage compensation in *C. elegans, Drosophila* and mammals.

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