Embryonic development in *C. elegans*

Most of the *C. elegans* individuals are hermaphrodite. The gonads are present as two U-shaped arms and are connected by a common uterus.

The distal end of each gonad arm has a cap made of somatic distal tip cell (DTC). DTC covers the distal end of the germline where proliferative zone is present. Cells in this zone divide by mitosis and when they enter transition zone and move beyond they undergo meiosis.

Early meiosis events form sperm and they become stored in spermathecal. Late meiosis events form eggs which get fertilized as they roll and pass through the spermatheca. The embryos pass through the vulva to move outside where further development takes place.

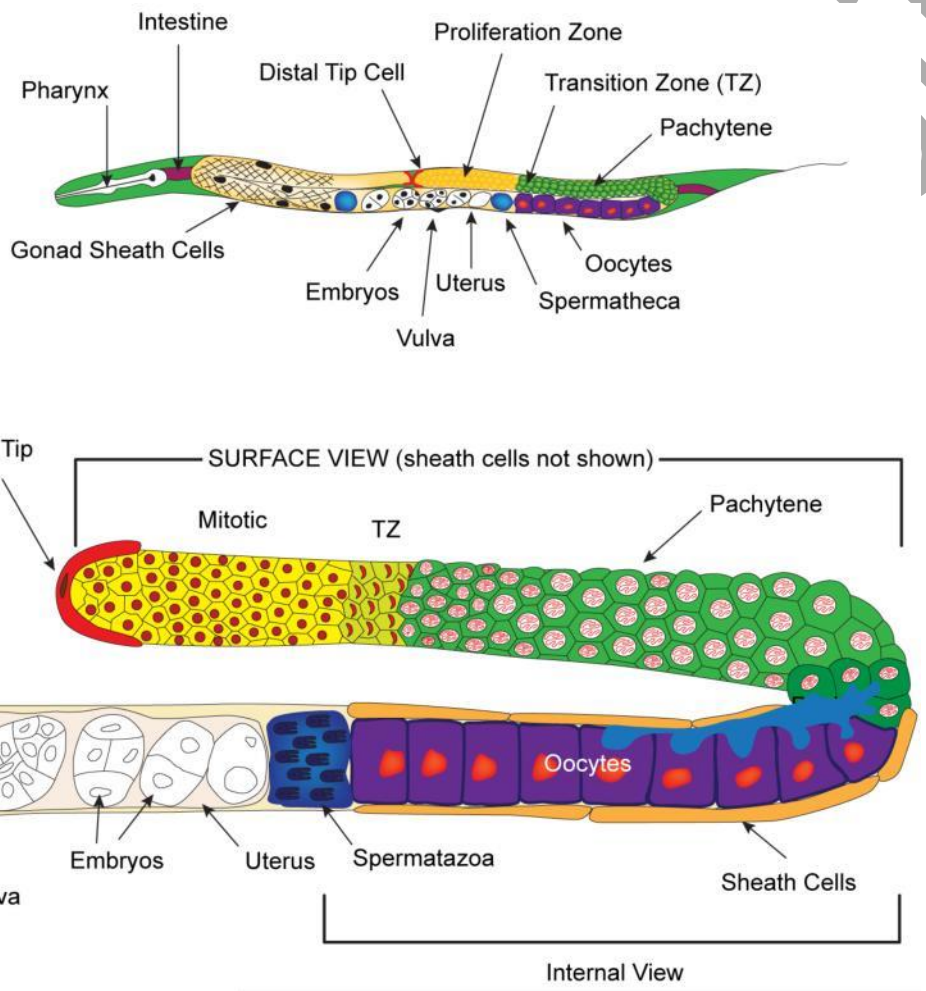

Fig: Gonads in *C. elegans*.

Top one shows complete arrangement of gonads as discussed in the content.

Bottom one shows close up view and distinctive cell populations as is discussed in the content.

Pachytene represents the developing oocytes.

Sheath cells surround the gonad but are not shown in the surface view.

Cleavage and axis formation in *C. elegans*:

The zygote undergoes rotational holoblastic cleavage. The early cleavage with each asymmetric division produces one founder cell and they go on to give rise to structures in the developed worm.

Founder cells called AB, E, MS, C and D give rise to somatic cell based structures and the founder cell from P1-P4 lineage gives rise to sperms and eggs.

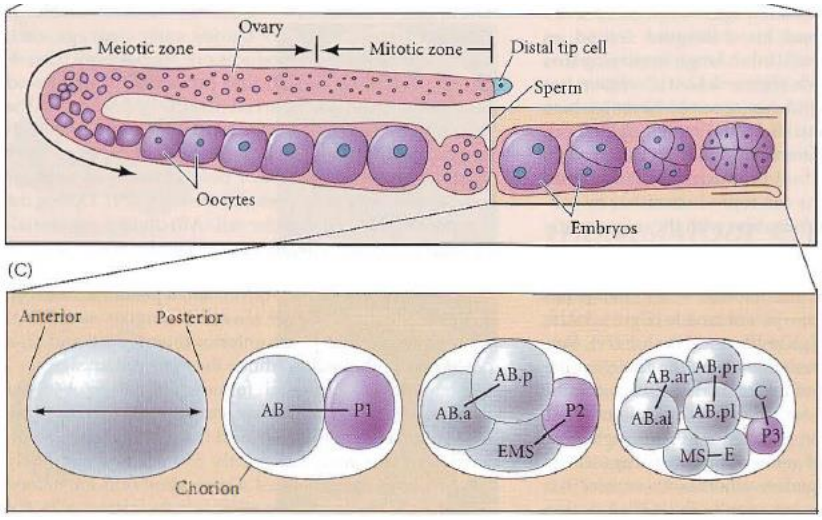

Figure: Early rotational holoblastic cleavage in *C. elegans* embryo.

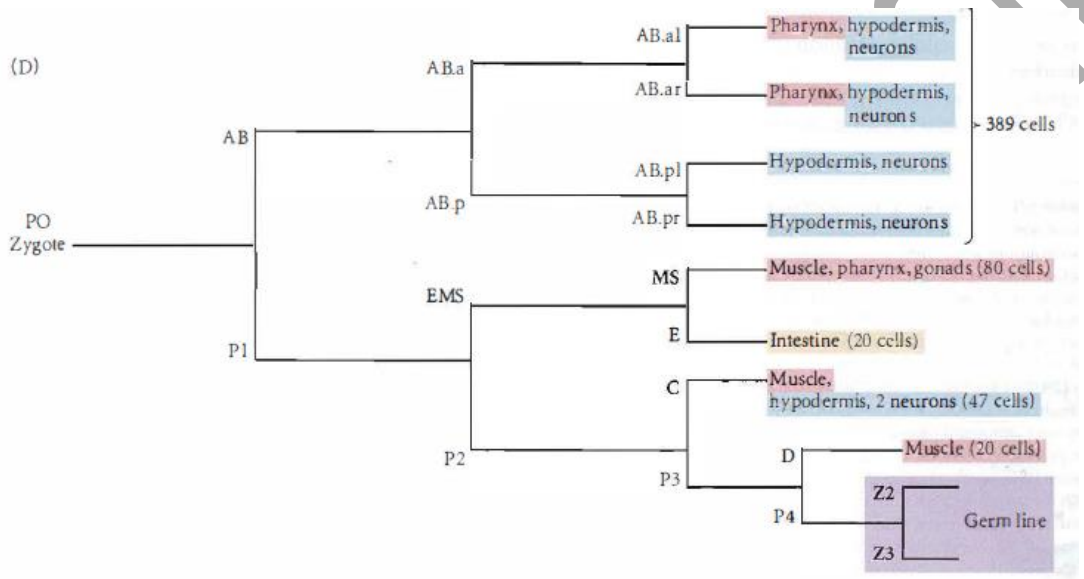

Figure: Formation of Founder cells and their final fates in *C. elegans*.

In this way, newly hatched larva produces its 558 cells and as it becomes adult each hermaphrodite worm contains 959 somatic nuclei (some cells are also multinucleated).

Organogenesis

Vulva formation in *C. elegans*:

Vulva is formed from six vulval precursor cells (VPCs) during the larval stage. VPCs are present below the gonad and are connected to the gonads by anchor cell.

The anchor cells secrete a paracrine factor called as LIN-3 that initiates formation of vulva. This collection of six VPCs is called an equivalence group as member of the group is competent to receive induction signal from the anchor cell and assume any of the three possible fates. The fate depends on the proximity of the VPCs to the anchor cell.

- The cells directly below the anchor cell divide to form central vulval cells.
- Two cells present on either side of the central cells divide to form lateral vulval cells.
- The remaining three cells that are farthest from the anchor cell divide to become hypodermal cells.

If anchor cell is destroyed or or lin-3 gene is silenced, then all the VPCs divide once and become hypodermal tissue and there is no formation of vulva.

If three central VPCs are destroyed, then outer three VPCs will generate vulval cells than differentiating into hypodermal cells.

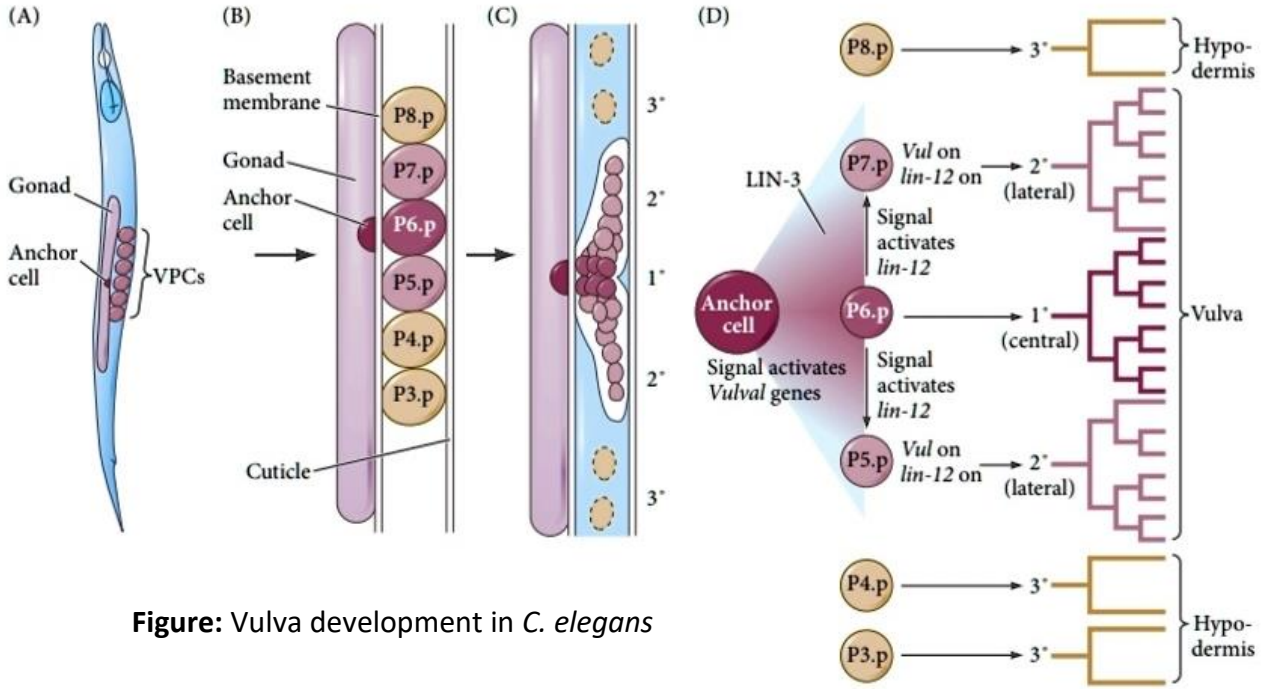

Figure: Vulva development in *C. elegans*

LIN-3 mechanism of action:

LIN-3 is released by the anchor cells and binds to its receptor called LET-23 which is present on the VPCs.

LET-23 is a receptor tyrosine kinase (RTK) and on activation the cascade leads the signal to nucleus.

In nucleus, it leads to phosphorylation of LIN-31 protein and release of its inhibition by losing the inhibition partner protein.

Now, LIN-31 works as a transcription factor which promotes vulval cell fates.

LIN-3 and LIN-12:

1. LIN-3 forms a concentration gradient and the cell which receives maximum signal becomes central vulval cell, the cells which receive moderate signal become lateral vulval cell and those of the six VPCs which receive so less of the signal that it is not enough to generate any effect will become hypodermal cells.
2. The cell which is closest to the anchor cell and is designated to form central vulval cell also signals the two adjacent cells. This instructs the adjacent cells to not generate central vulval fate.
3. This signal from central VPC leads to activation of LIN-12 receptor protein which is an example of Notch protein.
4. This signal due to activation of LIN-12 activates a microRNA called mir-61.

5. This leads to repression of genes for central vulval fate and promotion of genes involved in forming lateral vulval cells.

The lateral cells do not give any signal to the peripheral VPCs which plays a role in their differentiation as hypodermal cells.

Formation of anchor cell and LIN-12:

Formation of anchor cells is mediated by the products of lin-12 gene. In wild type, hermaphrodite, worms there are two adjacent cells i.e. Z1.ppp and Z4.aaa have the potential to differentiate into anchor cell.

Their mutual interactions lead to a chance outcome which ensures that one of them differentiates into anchor cell while the other one differentiates into precursor of the uterine tissue. This decision regarding fate is taken during second larval stage and involves LAG-2 protein as signal and LIN-12 protein as receptor.

LAG-2 is an example of delta protein and LIN-12 is an example of Notch protein and this signaling is an example of Delta-Notch signaling and also juxtacrine signaling. The model for this process is discussed below:

- The cells are equivalent and both produce some amount of ligand and receptor both.
- LAG-2 is signal and LIN-12 is receptor.
- The cell producing more of LAG-2 signal instructs the other cell to stop the production of LAG-2, the ligand and increase the production of LIN-12 the receptor.
- The cell producing LAG-2 or the signal becomes the anchor cell.
- The cell producing LIN-12 or the receptor becomes the ventral uterine precursor.

- In **loss of function lin-12** mutants both the cells become anchor cells.

- In **gain of function lin-12** mutants both the cells become uterine precursors.

- Thus, we can say that lin-12 gene function is needed in the cell whose fate is to become uterine precursor and presumptive anchor cells do not require functional lin-12 gene.