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Unit-II

TOPIC: Model Organisms In Stem Cell Research

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MODEL ORGANISMS

- E-Coli
- Arabidopsis thaliana
- Yeast
- Coenorhabditis elegans

What is Model organisms?

- ✓ A model organism is a non-human species that is suitable for studying a specific trait, disease, or phenomenon, due to its short generation time, characterized genome, or **similarity to humans**.
- ✓ Model organisms are **in vivo models** and are **widely used to research human disease** when human experimentation would be unfeasible or unethical.

Examples; **Fly, fish, rodent or pig, whose biology is well known and accessible for laboratory studies.**

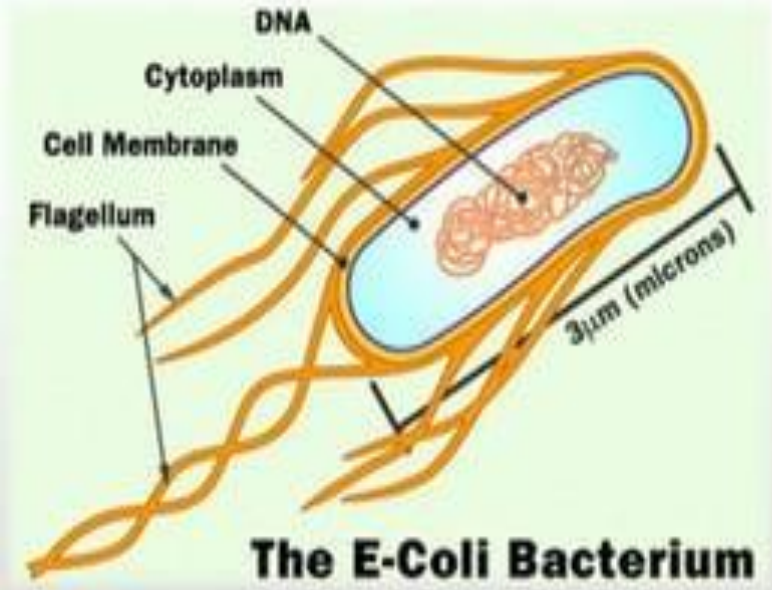
While selecting model organism the following features such as...

- Small size.
- They must develop rapidly with short generation time.
- Must be amenable to observation and experimentation.
- Availability of genome sequence.
- Easy for transformation.
- A comprehensive online database.
- A growing array of tools and techniques for molecular genetic studies.
- E.g., Genetic manipulation, identification and selection of genes.

Escherichia coli

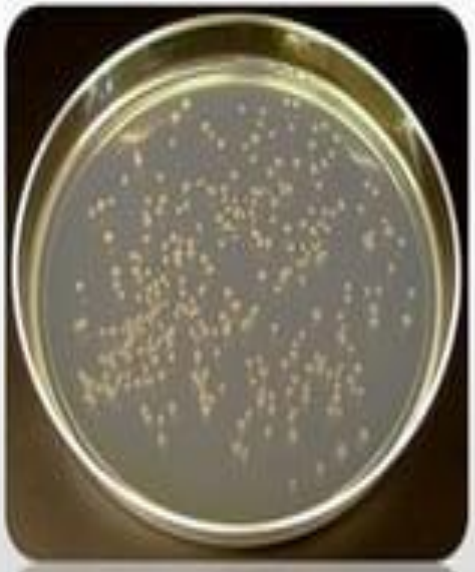
- Escherichia coli or E. coli is a Gram-negative, rod-shaped bacteria that is a normal inhabitant of the lower **gastrointestinal tract of warm blooded animals**.
- *E. coli* is **expelled** into the environment within **fecal matter**. The bacterium grows massively in fresh fecal matter under aerobic conditions for 3 days, but its numbers decline slowly afterwards.
- The E. coli **genome is relatively small, 4.5 to 5.5 Mbp** and simple when compared to our own.

E. coli is a model organism because…



- It is an unicellular organism. There are no ethical concerns about growing, manipulating, and killing bacterial cells, unlike multicellular model organisms like mice or chimps.
- They are able to reproduce and grow very rapidly, **doubling its population about every 20 minutes**. This is helpful in research to get subsequent generations within a short time.
- They can survive and adaptive to variable growth conditions.

- Culture media containing simple and inexpensive ingredients and nutrients can successfully spur E. coli to grow and divide.
- It is easy to culture in laboratory in liquid medium or solid medium within petriplates.
- In liquid culture, E.coli cells will grow to a concentration of a billion cells per milliliter, and trillion of bacterial cells can be easily grown on a single test tube.
- When E. coli cells are diluted and spread onto the solid medium of a petridish, individual bacteria reproduce asexually, giving rise to a concentrated clump of 10 million -100million genetically identical cells , called a colony.



- This colony formation makes it **easy to isolate** genetically pure strains of the bacteria.
- Most strains are **harmless**.
- They can be **manipulated and engineered easily**.
- Mutants are easily obtained using well established methods and **screening techniques**, which has enabled many biochemical processes to be linked to the molecular genetic level.
- E Coli Genome is found to be a **circular DNA molecule** 4.6 million base pairs in length, containing **4288 annotated protein-coding genes** (organized into 2584 operons), seven ribosomal RNA (rRNA) operons, and 86 transfer RNA (tRNA) genes.
- Current research areas for E. coli include acting as a vector, a host for genetic elements and synthesis of proteins of interest

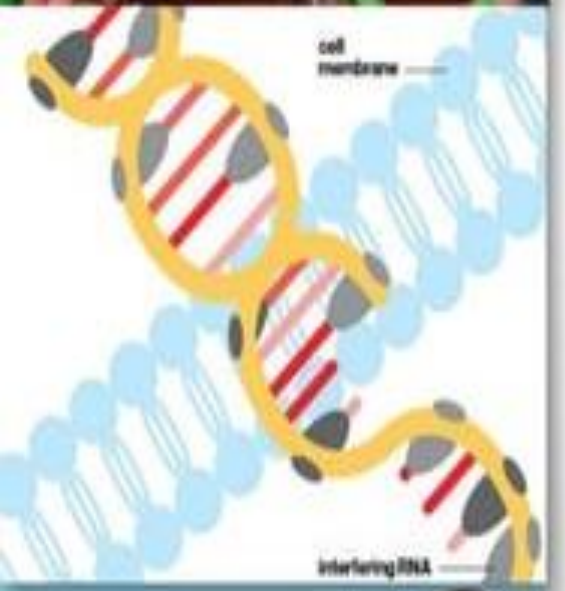
Arabidopsis thaliana

- Arabidopsis is a popular model organism **used in plant biology and genetics.**
- It is a member of **Brassicaceae** family.
- It is a small flowering weed.
- It grows luxuriantly in temperate regions of the world.
- They are vary in size, shape, physiological characters and DNA sequence.
- It has a **small genome** and It has only 5 chromosomes.

- The immune system of plants are widely diversified and can recognize viruses, microbes, worms, insects, etc.
- These are biotic stress caused to plants.
- Now a days, A. thaliana mostly used in the study of genome structure, gene regulation, development and evolution of plants.
- Also it provides the important basic information about plant genetics, that is applied to other economically important plants.
- Efficient transformation by Agrobacterium tumefaciens. Forward genetics identified many mutants over 1500 freely available from stock centre; Reverse genetic resources excellent and over 100,000 insertions at precise sequenced locations.

Why do we need Arabidopsis as a model....?

- Plants constitute over 90% of the world's biomass; 250,000 species of flowering plant.
- Each plant can produce the 10,000 to 40,000 seeds.
- It has ability to grow in the laboratory.
- Many variants are available.
- Ability to **self fertilization** and out cross.
- It found 125 million base pairs of DNA and 18 % genes were common with human genome.
- Average gene size is about 200 bp.
- It is the first plant has done Complete genome were sequenced in year of 2000.



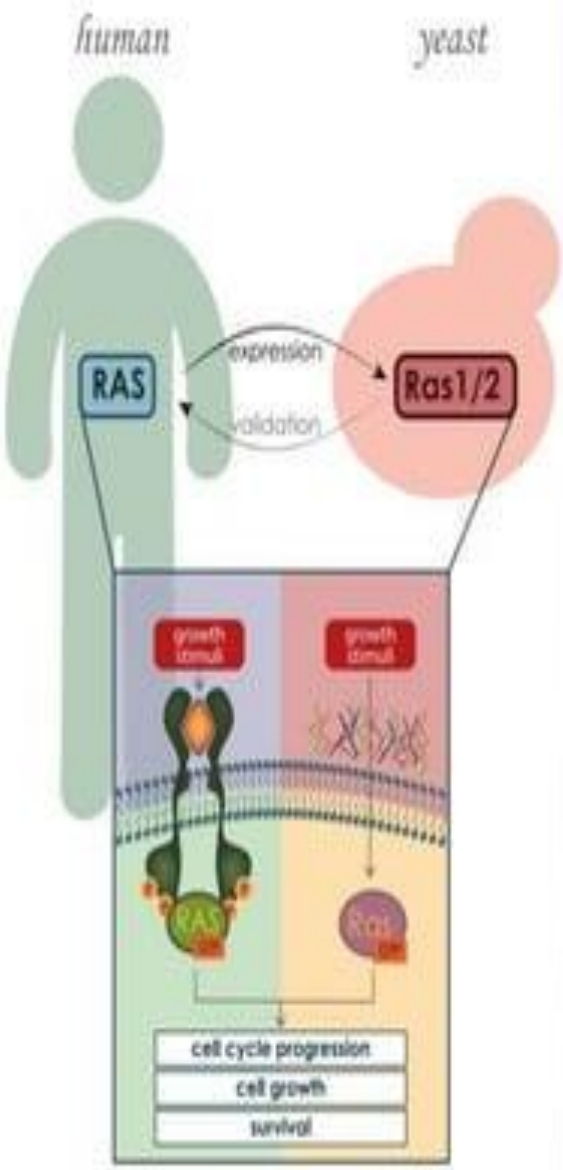
- Important biological processes are plant specific; photosynthesis that fixes carbon and produces oxygen.
- Plants are economically important; in agriculture or in secondary metabolites as medicines and in nutrition.
- Plants evolved multicellularity independently, and use **different mechanisms of cell to cell communication**.
- Plants represent important **genetic model systems**; transposons and gene silencing were first identified in plants.

Arabidopsis is a useful model plant,

- Simple genome.
- Easy maintenance and space-efficient.
- Applicable similarities with other plants.
- It has a potential to help increase food production quantity and quality to feed a growing world population.
- Due to these overall applications makes Arabidopsis as a model plant organism

yeast

- Yeasts are eukaryotic, single-celled microorganisms classified as members of the **fungus kingdom**.
- Most yeasts reproduce **asexually by mitosis**, and many do so by the asymmetric division process known as budding.
- With their **single-celled growth habit**, yeasts can be contrasted with molds, which grow hyphae.
- Yeast sizes vary greatly, depending on species and environment, typically measuring **3–4 µm in diameter**, although some yeasts can grow to **40 µm in size**.



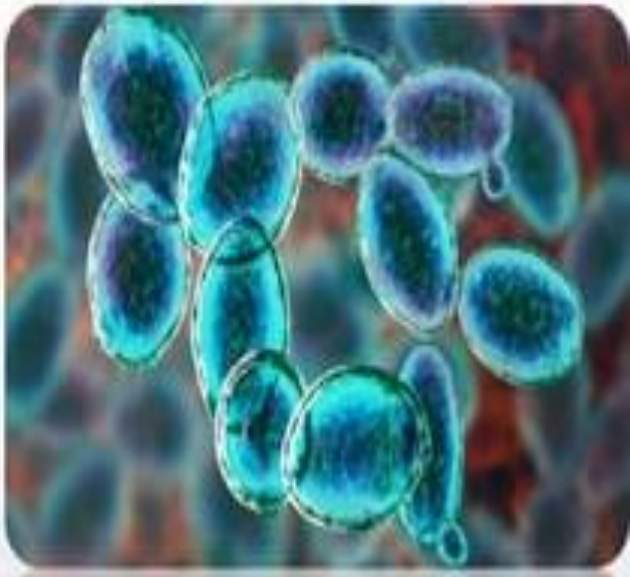
- Yeast is one of the simplest eukaryotic organisms but many essential cellular processes are the same in yeast and humans.
- It is therefore an important organism to study to understand basic molecular processes in humans.

- Yeast was the **first eukaryotic organism to have its genome sequenced**.
- Yeast chromosomes share a number of important features with human chromosomes.
- **Fission yeast** (*Schizosaccharomyces pombe*) has become a popular system for **studying cell growth and division**.
- It is useful partly because it is easy and inexpensive to grow in the lab, but also because its cells have a regular size and grow only in length, making it **very simple to record cell growth**.

Yeast has many High-throughput genomics data

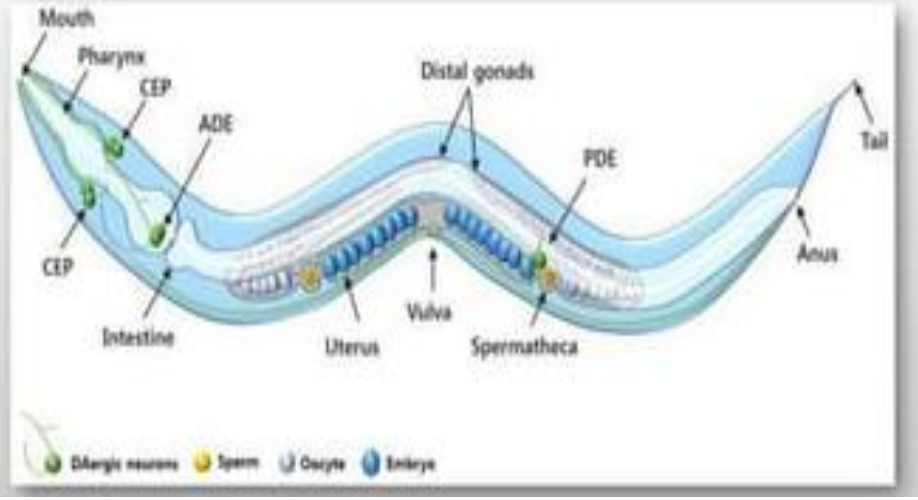
- **Gene expression** (by microarray or RNA-seq)
  – Cell cycle, deletion strain, chemical perturbations
- **Transcription regulation** (binding by transcription factors)
  – ChIP-chip, ChIP-seq
- **Protein-protein interactions and complex data**
  – Yeast Two-Hybrid (Y2H), TAP-tagging, literature curation
- **Genetic interactions and pathways**
  – Synthetic Genetic Array (SGA)
- **Chemical genomics**
  – Small molecule – gene interactions
- **High content morphological screening**

- Yeast is a powerful model organism that has enabled a **better understanding of human biology and disease**.
- Between 2001 and 2013, four Nobel Prizes were awarded for discoveries involving yeast research, an impressive number for a single organism.
- The genome of ***S. cerevisiae* yeast** was published in 1996 and the ***S. pombe*** sequence in 2002.
- As a result, projects have been initiated to determine the **functions of all the genes in these genomes**. One such project, the **Saccharomyces Genome Deletion Project**, aimed to **produce mutant strains of yeast** in which each one of the **6,000 genes in yeast is mutated**.



Caenorhabditis elegans

- *Caenorhabditis elegans* is a free-living, **transparent nematode** (roundworm), about 1 mm in length, which lives in temperate soil environments.
- *C.elegans* is unsegmented, vermiform, and bilaterally symmetrical, with a cuticle integument, four main epidermal cords and a fluid-filled pseudocoelomate cavity.
- *C. elegans* has two sexes: **hermaphrodites** and **males.**
- Individuals are almost all hermaphrodite, with males comprising just 0.05% of the total population on average.



C.elegans is studied as a model organism for a variety of reasons…

- The organism is **transparent** and **easy for manipulation and observation** , feeds on bacteria ,cheaply housed and **cultivated in large number** (1000 worms / petridish) in the laboratory.
- Most investigators grow C.elegans on agar-filled petridishes that are covered with a lawn of bacteria.
- It is a multicellular eukaryotic organism that is **simple enough to be studied in great detail.**
- Strains are cheap to breed and can be frozen. When subsequently thawed they **remain viable**, allowing long-term storage.
- In addition, *C. elegans* is transparent, facilitating the **study of cellular differentiation** and other **developmental processes in the intact organism**.

- Researchers who **study apoptosis** (programmed cell death) use *C. elegans* as an experimental organism in the hope of finding treatments for **certain types of human cancers, such as leukemia**.
- By studying apoptosis in *C. elegans*, researchers hope to **identify genes that switch-on cell death in cancer cells**.
- Researchers have explored the neural mechanisms responsible for several interesting behaviors shown by *C. elegans*, including **chemotaxis, thermotaxis, mechanotransduction, and male mating behavior**.
- It can be stored for a **long term in the laboratory**.
- *C. elegans* was the first multicellular organism to have its genome completely sequenced.

- A useful feature of *C. elegans* is that the function of **specific genes can be disrupted by by RNA interference.**
- Silencing the function of a gene in this way can sometimes allow a researcher to infer what the function of that gene may be.
- The nematode can either be soaked in or injected with a solution of double stranded RNA , **the sequence of which is complementary to the sequence of the gene that the researcher wishes to disable**.
- RNA interference in *C. elegans* can also be done by **simply feeding the worms transgenic bacteria expressing RNA complementary to the gene of interest.**
- This strategy for gene loss of function experiments is the easiest of all animal models, and thus, **scientists were able to knock down 86% of the ~20,000 genes in the worm, establishing a functional role for 9% of the genome**

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THANK YOU