What is a Model Organism?

When researchers look for an organism to use in their studies, they look for several traits. Among these are size, generation time, accessibility, manipulation, genetics, conservation of mechanisms, and potential economic benefit. Selected bacteria, fungi, plants or animals that can be bred and studied with simple methods and are therefore of great importance for biological and biomedical research. Model organisms are, as being used as a model, usually the first organisms of a kingdom whose entire genome was decoded. This further pushes their research capabilities.

History of Model Organisms

The history of model organisms began with the idea that certain organisms can be studied and used to gain knowledge of other organisms or as a control (ideal) for other organisms of the same species. Model organisms offer standards that serve as the authorized basis for comparison of other organisms which crucial for the development of phylogenetic trees. Today, phylogenetic analyses have become central to understanding biodiversity, evolution, ecology, and genomes.
In the middle of the 19th century men like Charles Darwin and Gregor Mendel and their respective work on natural selection and the genetics of heredity were a corner stone for genetic research in general. Darwin's notebooks from 1837 shows one of the first evolutionary tree sketches. In the 20th century this elemental work on plants and free-living animals continued in laboratories where Drosophila, *E.coli* and lab mice where introduced as new model organism. These organisms have led to many advances in the past century.

Model organisms. Why?

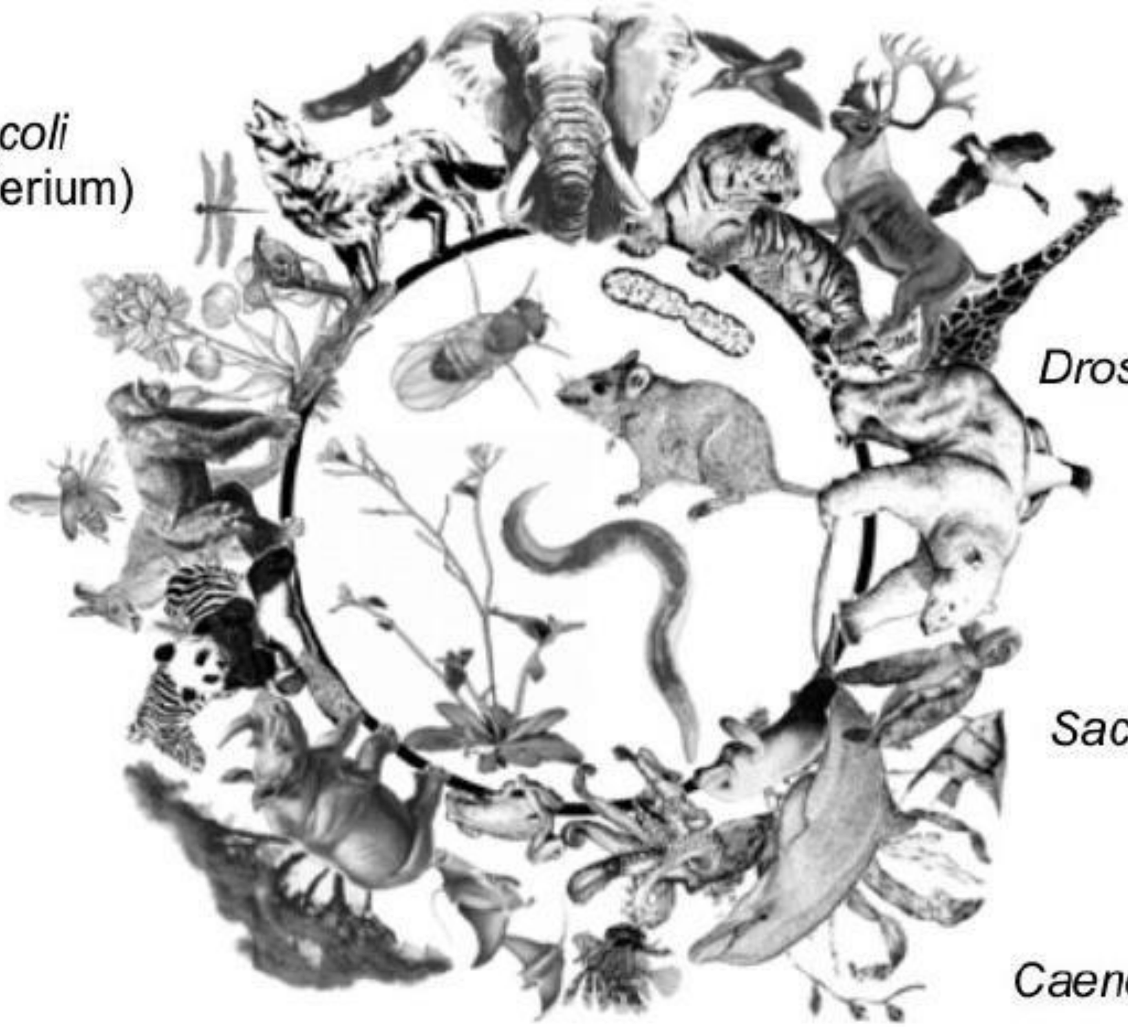
- Genome can be manipulated experimentally.
- Short life-cycle.
- Minimal living requirements.
- Small genome (some of them)!
- Easy to grow in lab.
- Small in size.
- Accumulated knowledge about the organism.
- Organism does NOT need to be BEAUTIFUL!!

Expectations

- You know the importance of models in science.
- You know the most important model organisms.
- You know general characteristics of the model organisms.
- You know the taxonomic representation of each model organism.

Model organisms

How do we learn about all these molecules and mechanisms involved?



Escherichia coli (intestines' bacterium)

Arabidopsis thaliana (plant)

Neurospora crassa (bread mold)

Drosophila melanogaster (fruit fly)

Saccharomyces cerevisiae (budding yeast)

Caenorhabditis elegans (worm)

Model Organisms in Genetics & Molecular Biology

(List of model organism from Prokaryotes, Protista, Plants, Invertebrate Animals and Vertebrate Animals with their uses in the biological research)

Class of Organism	Name	Specific uses
Bacteria	*Escherichia coli*	Most widely used model organism in molecular genetics
	Bacillus substilis	Molecular genetics
Fungus	*Cunninghamella elegans*	Fungal metabolism, Animal drug metabolism
	Neurospora crassa	Meiosis, crossing over, linkage, metabolic regulation, circadian rhythm
	Saccharomyces cervisiae	Molecular biology, cytology
	Arabidopsis thaliana	Plant molecular biology, Plant physiology, Plant Genetics, Developmental biology, Population genetics, cytology etc.
Invertebrate Animals	*Caenorhabditis elegans*	A nematode, genetic development, physiology, molecular biology
	Drosophila melanogaster	Classical genetics, molecular genetics, population genetics, developmental biology

Model Organisms in different Kingdoms

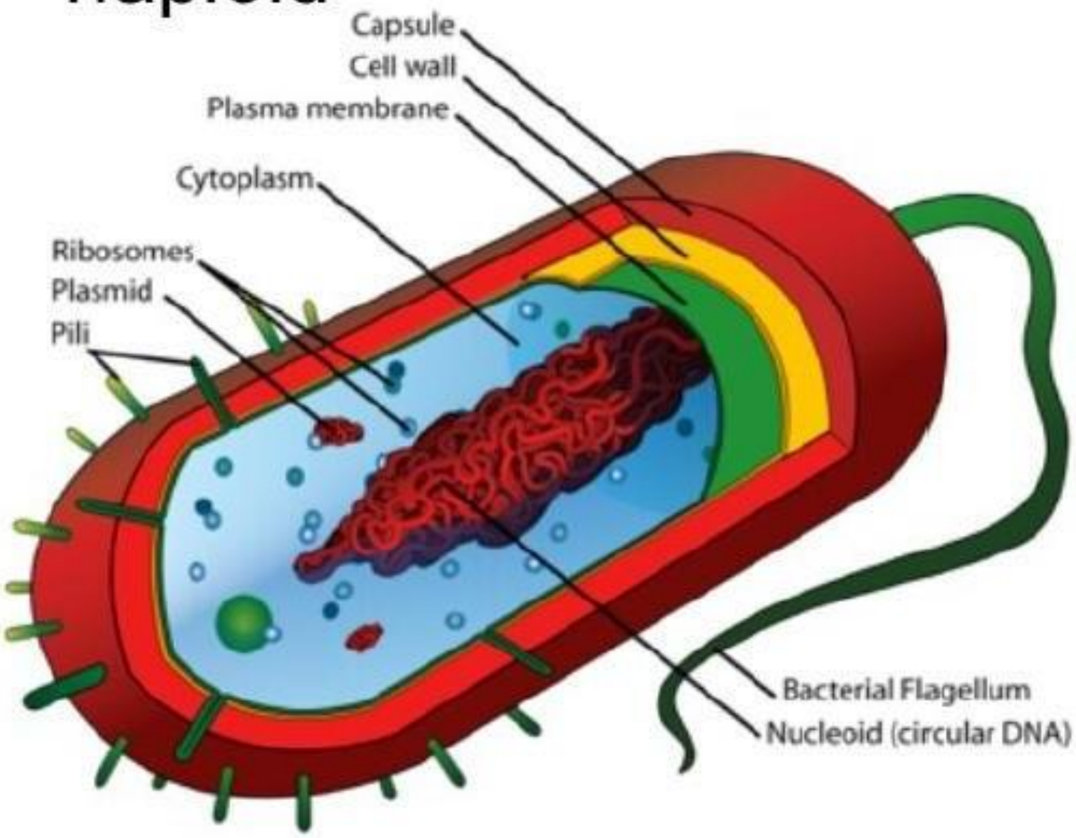
Outline

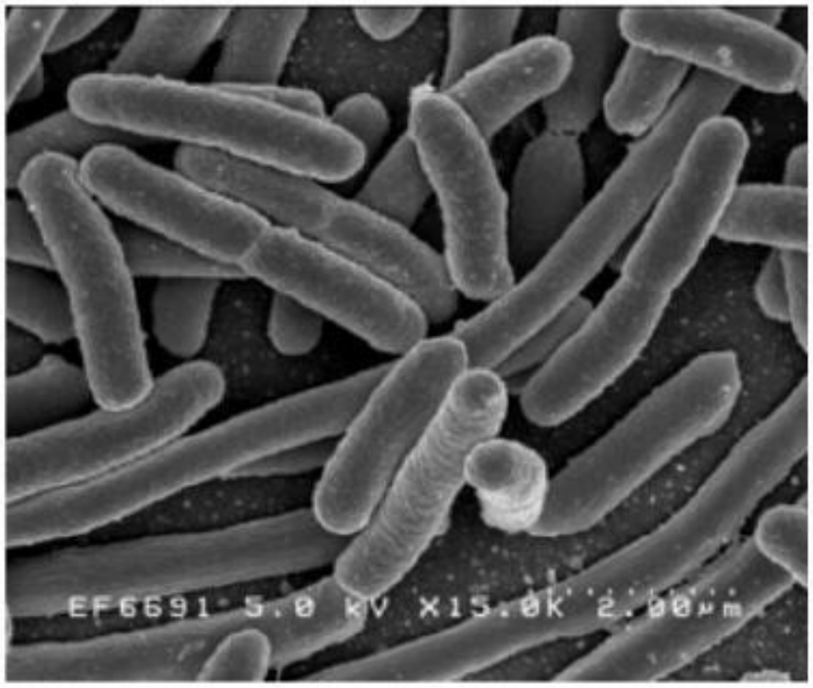
Prokaryote	Escherichia coli	*E. coli* can be grown and cultured easily and inexpensively. Cultivated strains (e.g. E. coli K12) are well-adapted to the laboratory environment where they have been intensively investigated for the past 60 years making it the most widely studied prokaryotic model organism. In 1946 the first bacterial conjugation was described using *E. coli* as a model bacterium, similar to the first experiments to understand phage genetics.
Fungi	Neurospora crassa	*N. crassa* is a type of red bread mold. Because of its haploid lifecycle which eases analysis of recessive traits and uncomplicated cultivation the fungi is frequently used for meiosis, metabolic regulation, and circadian rhythm research. X-rays experiments and analysis of malfunction in specific enzymes led to the "one gene, one enzyme" hypothesis. It is important in the elucidation of molecular events involved in circadian rhythms, epigenetics and gene silencing, cell polarity, cell fusion, development, as well as many aspects of cell biology and biochemistry. Knock out variants of wild type *N. crassa* are widely studied to determine the function of genes.
	Saccharomyces cerevisiae	A variety of human proteins like cell cycle and signaling proteins as well as enzymes were first discovered by studying their homologs in yeast, especially in *S. cerevisiae*. As a eukaryote, it shares the complex internal cell structure of plants and animals without the high percentage of non-coding DNA. The single-cell organism, has a short generation and can be easily cultured. It was the first eukaryotic genome to be fully sequenced and deletion mutants are covering more than 90 % of the genome. *S. cerevisiae* divides with meiosis, allowing it to be a candidate for sexual genetics research. td>

Animals	Caenorhabditis elegans	*C. elegans* is a free-living, transparent nematode. It is a multicellular eukaryotic organism, yet is simple enough to be studied in great detail - an excellent model for understanding the genetic control of development and physiology. *C. elegans* was the first multicellular organism whose genome was completely sequenced and a fixed number of 1031 cells. It is one of the simplest organisms with a nervous system and as of 2012, the only organism to have its connectome completed. The organism is used to study chemotaxis, thermotaxis, mechanotransduction, learning, memory, and mating behaviour.
	Drosophila melanogaster	The fruit fly *D. melanogaster* was one of the very first model organisms, jumping from nature to laboratory animal in the beginning of the 20th century. The fly is widely used for biological research in genetics, physiology, microbial pathogenesis, and life history evolution. Thomas Hunt Morgan was the first to realize the potential of mapping the chromosomes of *D. melanogaster* and all known mutants, today it is the genetically best-known eukaryotic organism. The principal of processes such as transcription and replication can be transferred to other eukaryotes, including humans - about 60% of genes are conserved between the two species. Recently, Drosophila has been used for neuropharmacological research.
Plants	Arabidopsis thaliana	*A. thaliana* is the most researched model organism in fundamental research in plant molecular genetics. Its small stature and genome and short generation time facilitates rapid genetic studies predestining the plant as a tool for understanding the molecular biology of many traits, including flower development and light sensing. Arabidopsis was the first plant to have its genome sequenced. *A. thaliana* can be genetically transformed using >*A. tumefaciens* via the 'floral dip' method. With the method plants and in specific *A. thaliana* are the most easily transformed multicellular organism, essential to many subsequent investigations. Many phenotypic and biochemical mutants have been mapped which helps to understand RNA-directed RNA methylation (transcriptional silencing).

Escherichia coli (intestines' bacterium)

- Prokaryote.
- Single celled organism.
- haploid





- Small in size
- ~ 2um in length
- ~ 0.5 um in width

Yes *E. coli* is a model organism because…

- *E. coli* 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.

- 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. Current research areas for *E. coli* include acting as a vector, a host for genetic elements and synthesis of proteins of interest.

E. coli and its use as a model organism in metabolic engineering

There is a growing demand for a sustainable source of fuels and chemicals. This can potentially be achieved by using renewable sources such as biomass and wastewater as a starting source.

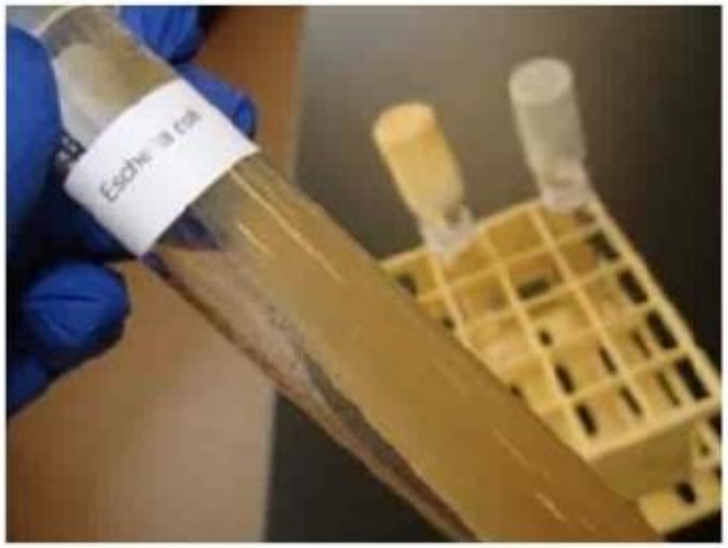
Because there are tools available to manipulate the genome of *E. coli*, it is a good candidate as a model organism for metabolic engineering; this is where *E. coli* is genetically manipulated so that it becomes able to produce desired chemicals from various sources during growth.

Modern techniques can be applied to optimize the production of engineered chemicals; this includes the integration of systems biology with metabolic engineering. For example, analysis of the proteins produced by an *E. coli* strain, or its proteome, can be used as a guide.

In a study, a proteomics approach was used to assess which *E. coli* membrane proteins were linked to phenylpropanoid tolerance and transport, and thus enabled the identification of potential target proteins which can be utilized in metabolic engineering.

Escherichia coli (intestines' bacterium)

- Easy to grow in lab
- Can be grown into millions of copies
- Fast growth
- Easy to culture, store, and manipulate genetically



Advantages of *E.coli* as a model organism

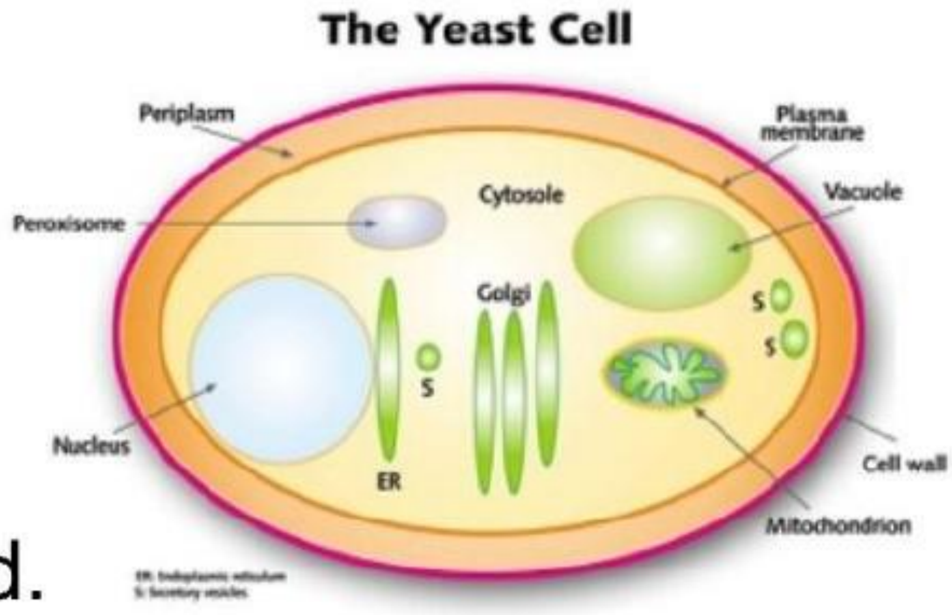
- Rapid reproduction and small size.
- Under optimal conditions , they can reproduce every 20 mts. , in a mere 7 hrs., a single bacterial cell can give rise to more than 2 millions descendants.
- Thus enormous numbers of cells can be grown quickly , so that even very rare mutations will appear in a short period of time .
- Consequently , numerous mutations in E. coli everything from colony appearance to drug resistance , have been isolated and characterized.
- E.coli is easy to culture in the laboratory in liquid medium or on solid medium within petriplates.
- In liquid culture , E.coli cells will grow to aconcentration of a billion cells per milliliter, and trillion of bacterial cells can be easily grown on a single test tube.
- When E. coli ells are diluted and spread onto the solid medium of a petri dish , 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.

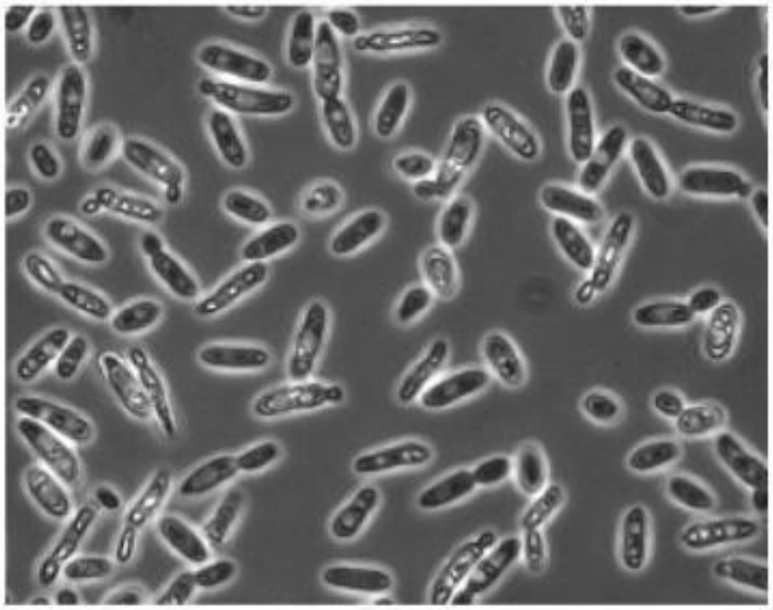
Role of E.coli in biotechnology

- E. coli plays an important role in modern biological engineering and industrial microbiology.
- The work of Stanley Norman Cohen and Herbert Boyer in E. coli, using plasmids and restriction enzymes to create recombinant DNA, became a foundation of biotechnology.
- Considered a very versatile host for the production of heterologous proteins, researchers can introduce genes into the microbes using plasmids, allowing for the mass production of proteins in industrial fermentation processes.
- Genetic systems have also been developed which allow the production of recombinant proteins using E. coli. One of the first useful applications of recombinant DNA technology was the manipulation of E. coli to produce human insulin.
- Modified E. coli cells have been used in vaccine development, bioremediation, and production of immobilised enzymes.
- E. coli cannot, however, be used to produce some of the larger, more complex proteins which contain multiple disulfide bonds or proteins that also require post-translational modification for activity.

Saccharomyces cerevisiae (budding yeast)

- Eukaryote.
- Fungi.
- Single celled organism.
- Grows haploid or diploid.
- Sexual and asexual life cycles.
- Small in size (~ 5-10 um in diameter).





- ***S. cerevisiae*** is the main organism in wine production besides other yeasts; because of its :
  - enormous fermentation capacity
  - low pH and high ethanol tolerance.
- It is the beer yeast as it ferments sugar to alcohol even in the presence of oxygen.
- Used in baking because it produces CO_2 from sugar very rapidly.
- Used to produce commercially important proteins.
- Also used for drug screening and functional analysis because it is a eukaryote but can be handled as easily as bacteria.
- One of the most important eukaryotic cellular model system.

WHY

Other important yeasts

Are not used as models ?

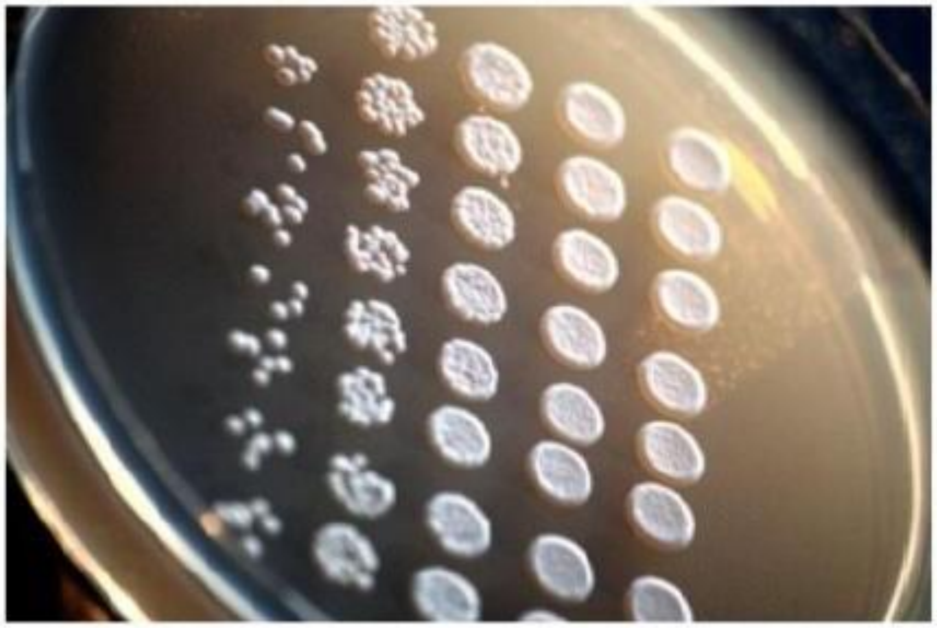
- ***Schizosaccharomyces pombe*** the fission yeast; important model organisms in molecular and cellular biology; used for certain fermentations only

- ***Candida albicans*** not a good model since it lacks a sexual cycle; but studied intensively because it is human pathogen.

- ***Pichia stipidis***, ***Hansenula polymorpha, Yarrovia lipolytica*** have smaller importance for genetic studies , protein production hosts.

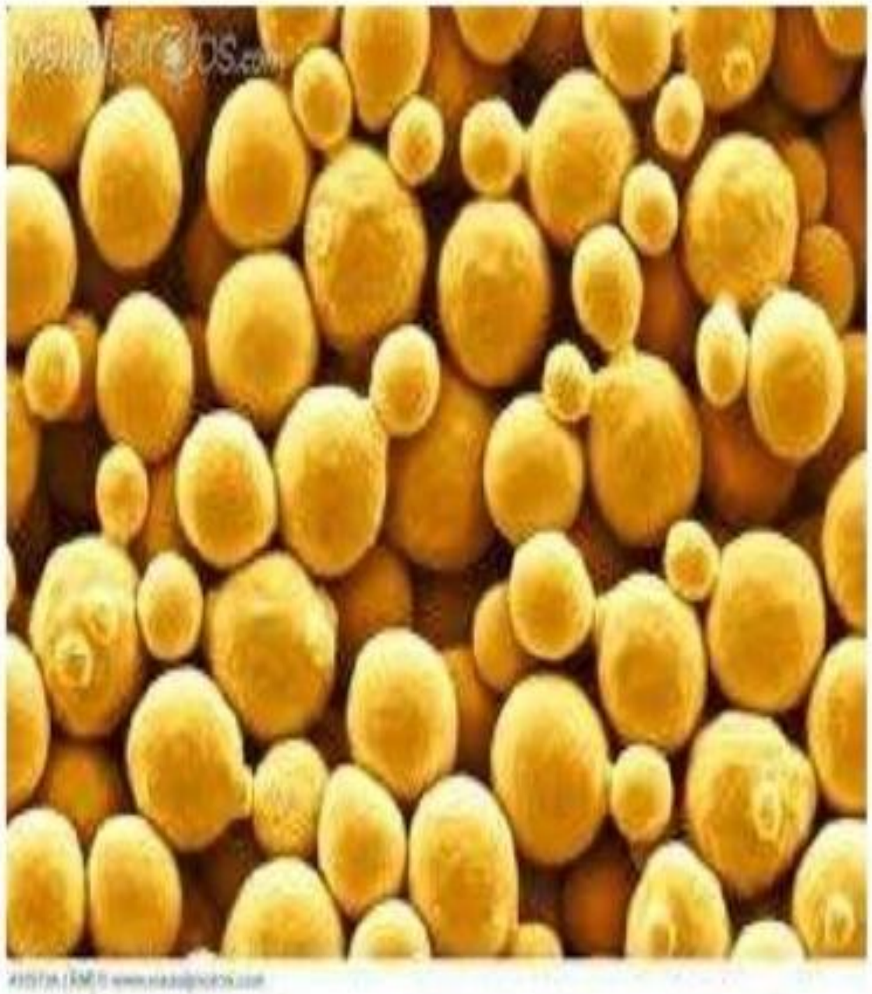
Saccharomyces cerevisiae (budding yeast)

- Easy to grow in lab
- Fast growth
- Easy to culture, store, and manipulate genetically



YEAST

- **Transformation methods i.e spheroplast method was first proved in *Saccharomyces cerevisiae.***
- **Entire genome library on yeast is available.**
- **In research like tetrad dissection, spore analysis.**

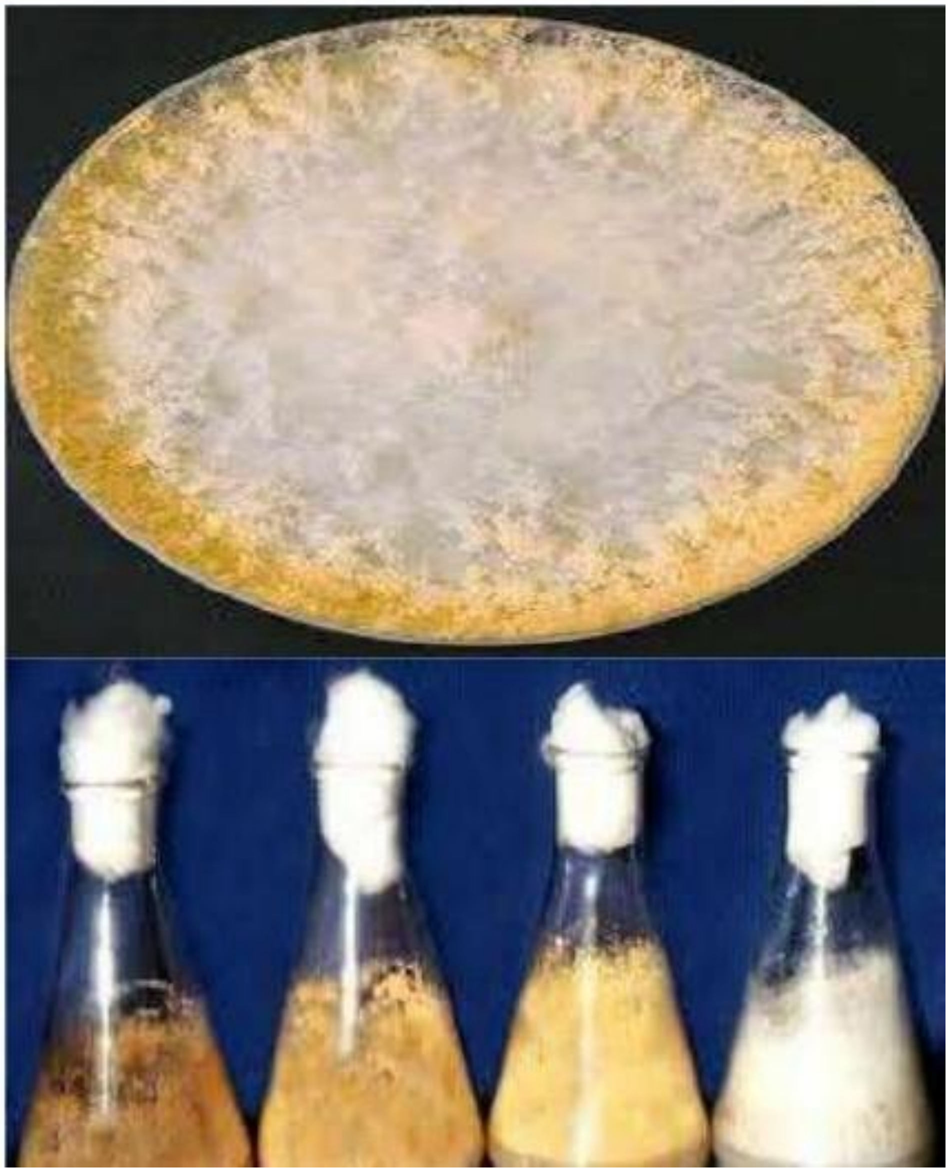


Neurospora as an Model Organism

- Neurospora crassa has been used in the laboratories since 1941.
- A Vast store of information has been acquired from Neurospora crassa during 75 years of research.
- Around 1000 loci has been mapped on the chromosomes.
- Gene sequencing is in progress.

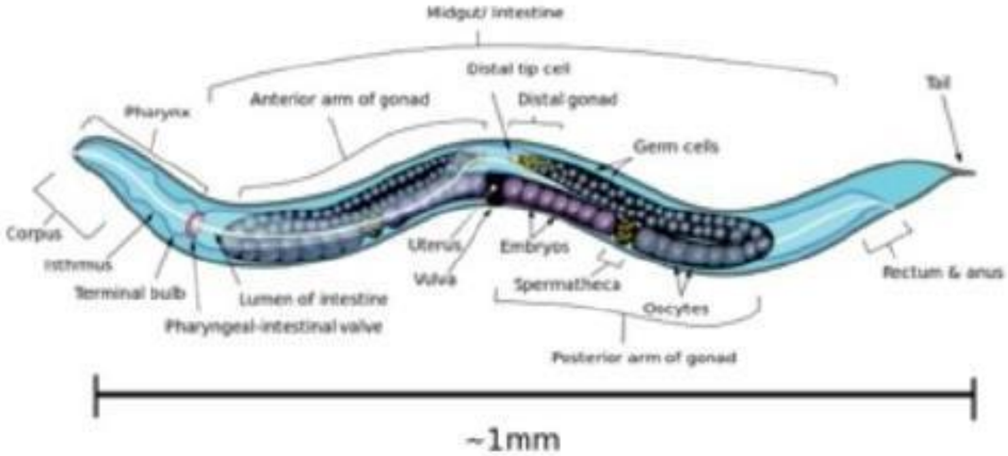
Unique Characters of Neurospora crassa

- They are easy to culture, as the nutritional requirement is simple.
- They form orange coloured colonies and they reproduce fast.
- Growth of Neurospora is rapid and generation time is less than 3 weeks.



Caenorhabditis elegans (worm)

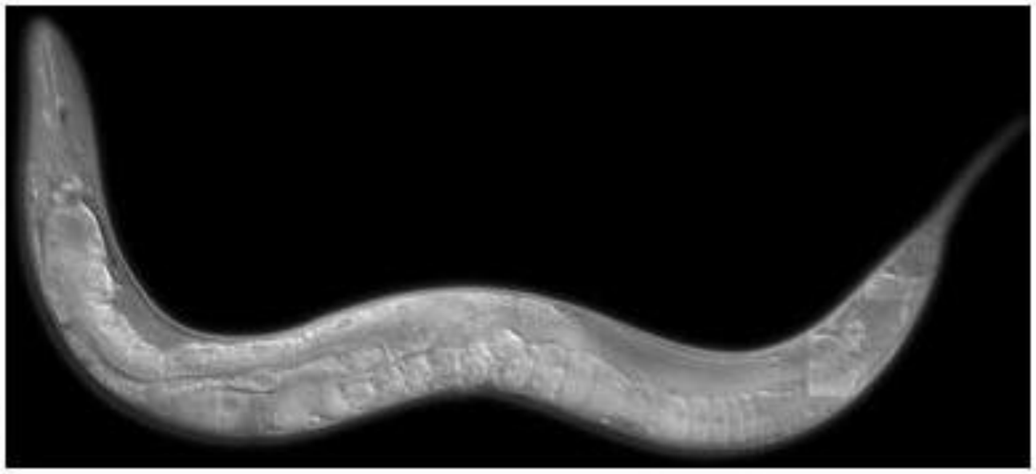
- Eukaryote.
- Animal - Nematode.
- Multicellular.
- Hermaphrodite.
- Sexual and asexual life cycles.
- Small in size (~ 1 mm in length).
- Diploid.



Caenorhabditis elegans

introduced in 1963 by Sydney Brenner

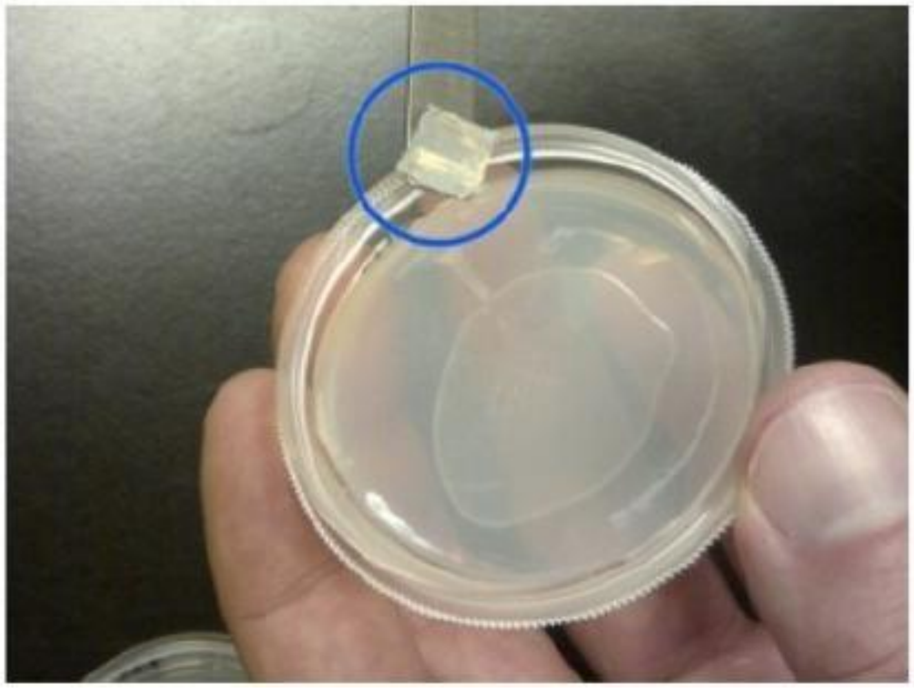
- A new model system specifically chosen for its simplicity
- Goal: the genetic dissection of development and behavior
- Success: Today's "Worm Community" ~15,000 scientists
- 3 Nobel Prizes ('02, '06, '09)



- Features:
  - Size: 1 mm in length
  - Generation time: 3 days
  - Life Span: 2-3 weeks
  - ~300 progeny per generation
  - Cultivate in lab on petri dishes
  - Transparent
  - Only 959 cells!

Caenorhabditis elegans (worm)

- Easy to grow in lab
- Fast growth
- Short life cycle
- Known number of cells



- Easy to culture, store, and manipulate genetically.
- Eggs can be stored.

C.elegans as a model organism

- ***C. elegans* is studied as a model organism for a variety of reasons.**
- 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.
- Nematodes have a fixed, genetically determined number of cells, a phenomenon known as eutely. The developmental fate of every single somatic cell (959 in the adult hermaphrodite; 1031 in the adult male) has been mapped out.
- These patterns of cell lineage are invariant between individuals, in contrast to mammals where cell development from the embryo is more largely dependent on cellular cues.

C.elegans as a model organism

- In both sexes, a large number of additional cells (131 in the hermaphrodite, most of which would otherwise become neurons), are eliminated by programmed cell death (apoptosis).
- 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.
- *C. elegans* is one of the simplest organisms with a nervous system.
- In the hermaphrodite, this comprises 302 neurons whose pattern of connectivity has been completely mapped out.
- Researchers have explored the neural mechanisms responsible for several interesting behaviors shown by *C. elegans*, including chemotaxis, thermotaxis,mechanotransduction, and male mating behavior.

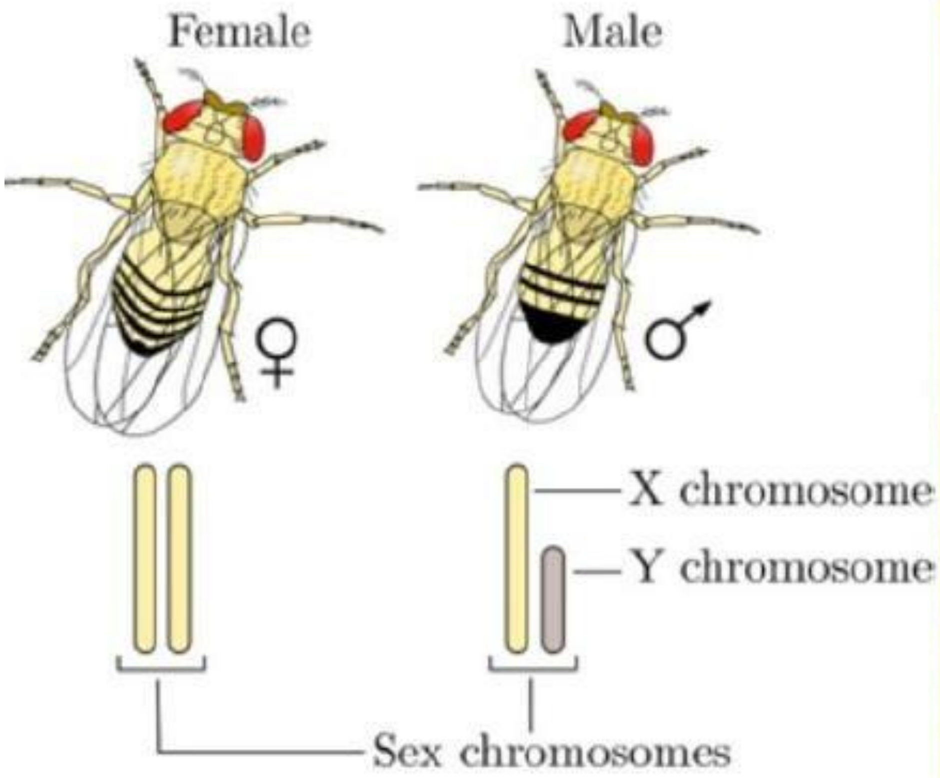
C.elegans as a model organism

- A useful feature of *C. elegans* is that the function of specific genes can be disrupted by by RNA interference (RNAi).
- 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 (RNAi) 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

- C.elegans can be stored for a long term in the laboratory.
- A 15% glycerol solution is used for the freezing of *C. elegans*.
- Samples are cooled at 1°C per minute. Freshly starved young larvae survive freezing best.
- About 35 to 45% of the worms stored in liquid nitrogen survive.
- The worms can also be stored at −80°C for over ten years, but survival is not as great as for worms stored in liquid nitrogen at −196°C.

- The roundworm, *Caenorhabditis elegans,* has a simple but nonetheless sophisticated nervous system, and displays simple behaviors, such as movement, feeding, and mating. These properties make it well suited for neurobiology and behavioral genetics.

Drosophila melanogaster (fruit fly)



- Eukaryote.
- Animal - Insect.
- Multicellular.
- Diploid
- Sexual life cycle.
- Sexual dimorphism
- ~ 2.5 mm in length

Drosophila melanogaster (fruit fly)

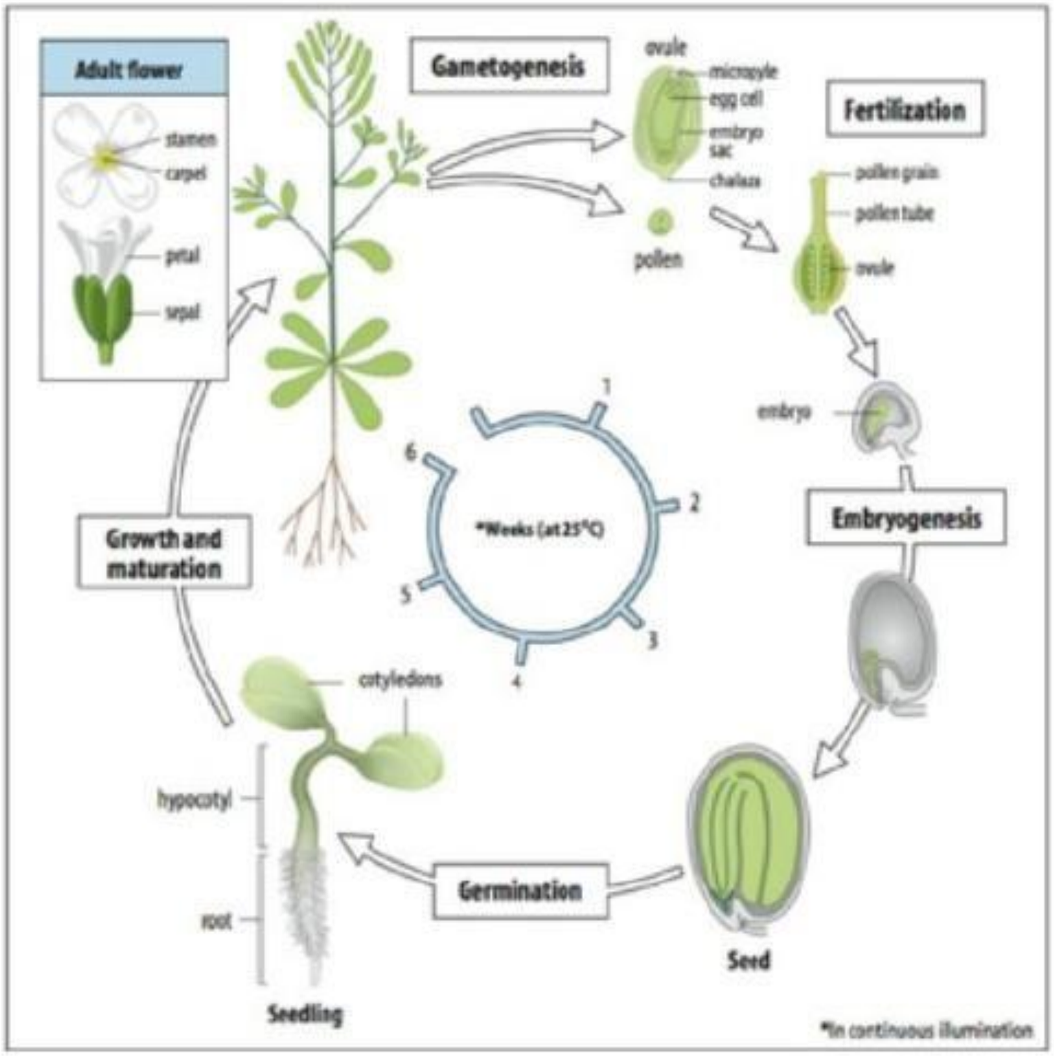
- Easy to grow in lab
- Occupies relatively a small space
- Short life cycle
- Easy and manipulate genetically.
- A living stock has to be maintained.

Drosophila as a model organism:

- **In terms of base pairs,** the fly genome is only around 5% of the size of the human genome -- that is, 132 million base pairs for the fly, compared with 3.2 billion base pairs for the human.
- **In terms of the number of genes,**, however, the comparison isn't nearly so lopsided: The fly has approximately 15,500 genes on its four chromosomes, whereas humans have about 22,000 genes among their 23 chromosomes. Thus **the density of genes per chromosome in *Drosophila*** is higher than for the human genome.
- Humans and flies have **retained the same genes from their common ancestor** (known as homologs) over about 60% of their genome.
- Based on an initial comparison, approximately **60% of genes associated with human cancers and**

Arabidopsis thaliana (plant)

- Eukaryote.
- Plant - Dicot.
- Diploid.
- 20-25 cm in height

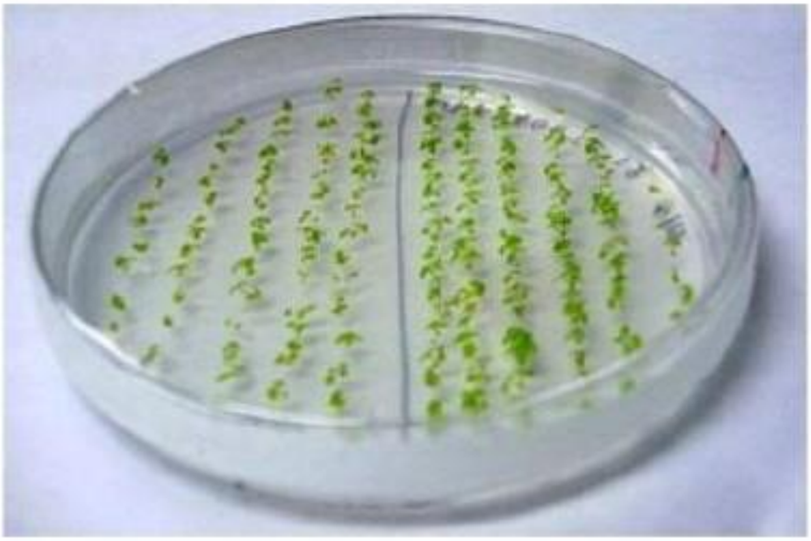


- *Arabidopsis thaliana* also known as thale-cress or mouse-ear cress or arabidopsis
- It is a member of *Brassicaceae* family
- Grows as weed in many parts of world
- For a complex multicellular eukaryote
- Except in role of model genetic organism it has no economic use
- Number of variants were found called as ecotypes
- That are vary in size, shape, physiological characters and DNA sequence

Arabidopsis thaliana (plant)

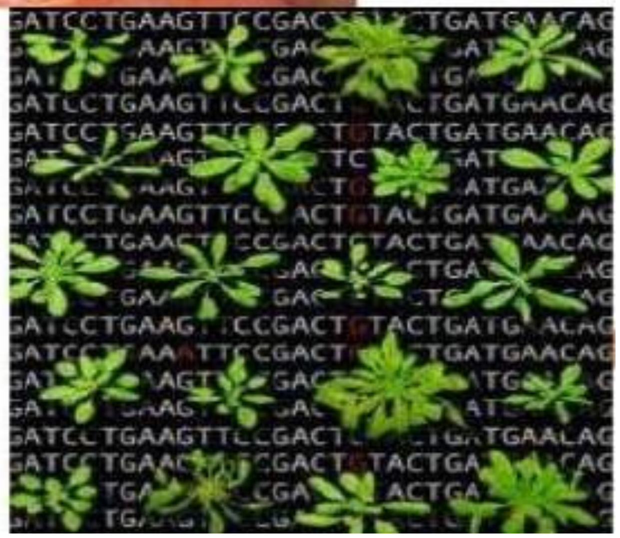
- Easy to grow in lab
- Occupies a small space
- Short life cycle
- Easy to cross
- Seeds can be stored.






Advantages

- Small genome
- Small plant size
- Short generation time i.e. 6 weeks
- 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



CONTRIBUTION IN THE GENETICS

- *A. thaliana* majorly involved in the study of-
  - Plant Genome Organization
  - Gene Regulation
  - Genetics of plant development
  - Genetic of flowering

Making Knockout Plants

- It is easily susceptible to *Agrobacterium* which contain Ti plasmids, the vehicles for T-DNA insertion
- Easy to establish many knockout lines within short amount of time
- Basic life processes similar to those of more complex crop plants such as corn, soybean, and wheat
- It can be assumed that the basic set of genes that control these processes are the same, making findings applicable to other species

SUMMARY

- 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