Developmental Biology BY1101

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Lecture 2

Model organisms

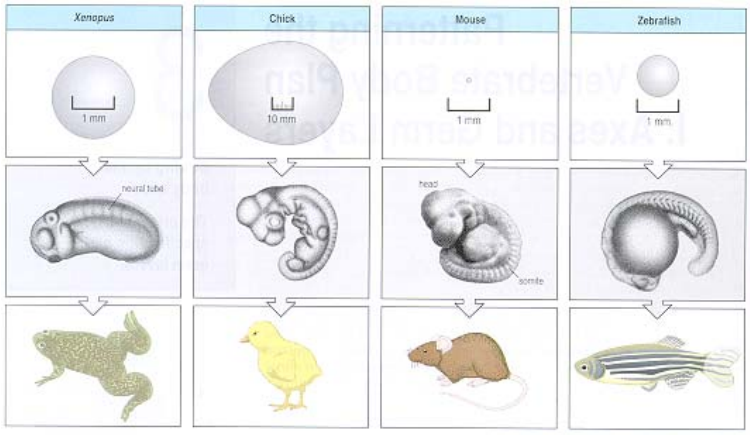
An introduction to the organisms that are most commonly used to study development and a discussion of their relative advantages and disadvantages for different types of experimental approach.

We generally do not study development in humans.
Why?

- Observation is difficult inside the uterus.
- Morally and ethically we would not want to perform experiments on human embryos.
- We wouldn't want to (nor could we) breed humans to look at effects of gene mutations on embryos.

Researchers study development in model organisms to identify general principles

Developmental processes are so fundamental that there are striking similarities in the development of very varied organisms.



Despite different adult forms, these organisms share similar developmental mechanisms. This is shown by the similarity of the basic embryo plan for vertebrate embryos as shown in the middle row above. The adult forms of these vertebrate animals look quite different and the eggs from which they arise are also different in size and design, but during development of the embryo the overall design and body plan is very similar.
When the primary research goal is to understand broad biological principles - of development in this case - the organism chosen for study is called a model organism.

- Researchers select model organisms that lend themselves to the study of a particular question.
  For example, frogs were early models for observing development of an

animal embryo because their large eggs are easy to observe and manipulate, and fertilization and development occurs outside the mother's body.

When choosing a model organism for research, there are a number of different aspects to be considered:

1. Biological considerations: Is this organism biologically suited to the type of study? Obviously a frog cannot be used to study the particular features of mammalian development. An important biological consideration for the study of development is accessibility of the egg and embryo for observation and manipulation.
2. Practical considerations. e.g. cost, space requirements and the ease of handling and breeding the organism.
3. Historical considerations: If a model has been used in the past then its biology will be well understood and specific tools will have been developed.

In general terms the researcher chooses the model organism that best allows them to take a particular kind of approach to ask particular questions:

For **observing development and morphological analysis:**

Advantages in this case would be large eggs, accessible embryos, short development time, and easy to keep in the lab.

So the organisms of choice for this kind of work would be the amphibian (frog) and the chicken.

For **manipulating the embryo; "experimental embryology"**:

Advantages would be large accessible embryos, robust embryos that can tolerate manipulation or embryos that can be grown in a dish, in culture.

So again good organisms of choice here would be the frog or the chick.

For **Developmental genetics**:

Advantages would be ease of breeding in the laboratory, short generation interval (time from fertilization to sexual maturity), simple or small genome and ease of observing embryos to see mutant effects.

Organisms that have been widely used for this are the fruit fly (*Drosophila*), the zebrafish (*Danio*), the nematode worm (*Caenorhabditis elegans*), The plant *Arabidopsis thaliana*, the mouse (despite major disadvantages, see below).

Some examples of model organisms that have been widely used for developmental studies and their particular advantages:

❖ Invertebrate Animals:

The fruit fly *Drosophila melanogaster* was first chosen as a model organism by geneticist T.H. Morgan and intensively studied by generations of geneticists after him.

- The fruit fly is small and easily grown in the laboratory.
- It has a generation time of only two weeks and produces many offspring.
- Embryos develop outside the mother's body.
- Amenable to large scale mutational screens to identify genes involved in particular functions e.g. forming the right body parts in the right place. So flies with mutated versions of all genes in the genome have been isolated.
- In addition, there are vast amounts of information on its genes and other aspects of its biology. The genome has been sequenced and is contains 13,600 genes.

The nematode worm *Caenorhabditis elegans* normally lives in the soil but is easily grown in petri dishes.

- Only a millimeter long, it has a simple, transparent body with only a few cell types and grows from zygote to mature adult in only three and a half days.
- Its genome has been sequenced.
- It is easy to identify mutant animals: Because individuals are hermaphrodites, it is easy to detect recessive mutations: Self-fertilization of heterozygotes will produce some homozygous recessive offspring with mutant phenotypes.
- The huge advantage is its simplicity: every adult *C. elegans* has exactly (only) 959 somatic cells. These arise from the zygote in virtually the same way for every individual.
- By following all cell divisions with a microscope, biologists have constructed the organism's complete **cell lineage**, a type of *fate map*.

A fate map traces the development of an embryo.

See Campbell and Reece figure 47.18. We will look at an example of the value of this model in lecture 10.

❖ Vertebrate animals

The frog *Xenopus laevis*

Advantages

- Ease of access and manipulation of the egg and embryo

  allowing experimental manipulation, assay inductive interactions

- Robust embryos, can tolerate manipulation in relatively simple lab facilities.
- Parts of the embryo can easily be cultured.
- Rapid development, 4 days to a free swimming tadpole.

- A well-established system

Disadvantages

- No genetics. Complex, uncharacterised genome.
- Animals cannot be bred for multiple generations in the lab.

The chicken (*Gallus*) as a model system

Advantages

- Large easily obtainable eggs
- Development can be observed by cutting a hole in the shell
- The embryos can be removed and cultured allowing manipulation.
- Methods developed for cell lineage analysis

  allows experimental manipulation and cell lineage studies
- Complex development similar to mammals

Disadvantages

- Not good for classical genetics. It has a complex genome with many small chromosomes. But the genome is now being sequenced.

The mouse *Mus musculus* has a long history as a mammalian model of development.

- Much is known about its biology, including its genes.
- The genome is well characterized and almost completely sequenced
- Sophisticated and elaborate techniques exist to manipulate mouse genes:
  - transgenic mice and
  - mice in which particular genes are "knocked out" by mutation.

Disadvantages:

Mice are complex animals with a genome as large as ours, and their embryos develop in the mother's uterus, hidden from view.

- The embryo develops *in utero* and is inaccessible.
  we are restricted to snap shots of development
- Embryo culture is difficult and limited.
- The generation interval is long (3 months)
- Difficult to find genes by mutational screens, because of the above.

But the mouse is still an important model system because we want to be able to study

development in a mammal. It serves as a good model for human development.

Another vertebrate model, **the zebrafish *Danio rerio***, was more recently chosen and developed because it has a unique combination of advantages: It combines the advantages of large, accessible, easily observable eggs and embryos with advantages for carrying out genetic studies i.e. ease of breeding in the laboratory and small simple genome.

- These small fish (2 - 4 cm long) are easy to breed in the laboratory in large numbers.
- The transparent embryos develop outside the mother's body so are very easy to observe.
- Although generation time is two to four months, the early stages of development proceed quickly.
  - -By 24 hours after fertilization, most tissues and early versions of the organs have formed.
  - -After two days, the fish hatches out of the egg case.
- Molecular techniques have been developed to manipulate genes.
  The genome was rapidly mapped and sequenced.

❖ Plant development

For studying the molecular genetics of **plant development**, an important model is a small weed ***Arabidopsis thaliana*** (a member of the mustard family).

- One plant can grow and produce thousands of progeny after eight to ten weeks.
- A hermaphrodite, each flower makes ova and sperm.
- For gene manipulation research, scientists can induce cultured cells to take up foreign DNA (genetic transformation).
- Its relatively small genome, about 100 million nucleotide pairs, has already been sequenced.

Plant development is a very important field of study. However we will not be dealing with it further in this course. Below are listed the major differences between plant and animal development:

Major differences between plant and animal development:

The overall schemes of morphogenesis in animals and plants are very different.
There are two major differences:

1. In animals, but not in plants, *movements* of cells and tissues are involved in transforming the embryo.
2. In plants, morphogenesis and growth in overall size are not limited to embryonic and juvenile periods.

-Apical meristems are responsible for the plant's continual growth and formation of new organs, such as leaves and roots.

-In animals, ongoing development in adults is restricted to the differentiation of cells, such as blood cells, that must be continually replenished.

Key concepts in lecture 2:

1. Researchers study development in model organisms to identify general principles. Researchers select model organisms that lend themselves to the study of a particular question.

2. Developmental processes are so fundamental that there are striking similarities in the development of very varied organisms.

3. When choosing a model organism for research, there are a number of different aspects to be considered: biological considerations, practical considerations and history.

4. We reviewed the advantages and disadvantages of each of the following models:

- The fuitfly *Drosophila* - very valuable for studying the genetics of development
- The big advantage of the worm *C. elegans* is its simplicity-with only 959 cells- the lineage of all cells has been traced through development
- The frog and the chick are both very valuable for their large and easily obtained eggs- important to observe and manipulate the embryo. Historically very important
- The mouse, like all mammals, is very difficult to use in the study of development because the embryo develops inside the mother- but because we want to learn more about ourselves it is a very important model
- The zebrafish model was only recently developed and is good for both genetics and observation/manipulation of the embryo.

5. Plants and animals have very fundamental differences in the way they develop. Two major differences:-
    - Plants can grow and produce new organs throughout their lives.
    - Movements of cells are important during animal but not plant development.

Lecture 2: Learning outcomes: you should be able to ….

A) Present the concept of using a model to study general principles and why certain species are more suitable than others for developmental research.

B) Describe the models most commonly used in the study of development and the advantages that each offers.

C) Discuss how different models offer different advantages that make them suitable for different types of research.

Key terms to be familiar with: model organism, descriptive embryology, experimental embryology, cell lineage analysis, apical meristem.