# DEV3011 Lecture Notes

## Lecture 1

What is Developmental Biology?

- Development – progressive change in form (from simple to complex) that involves growth and differentiation
- Developmental biology – the study of development
    - Applies throughout life
    - Most often focuses on embryogenesis
- Modern developmental biology is a synthesis of three key areas
    - Embryology (embryos)
    - Cytology (cells) and histology (tissues)
    - Genetics
- How does the embryo construct itself?
    - Differential gene expression – genes turning on and off at certain time points
    - Cell to cell communication
- The over-arching aim of developmental biology is to understand the genetic and cellular mechanisms that produce a complex multi-cellular organism from a single cell

Why Study Developmental Biology?

- Understanding, diagnosing and treating developmental disorders (congenital birth defects) – e.g. cleft palate
- Knowledge derived from developmental biology informs our understanding and treatment of cancers and other adult diseases
- Understanding cell differentiation leads to cell-based therapies for human diseases
    - Embryonic stem (ES) cells
    - Induced pluripotent stem (iPS) cells

Preformist View of Development:

- Adopted during the middle ages
- Belief was that a preformed individual (homunculus) lived within the head of the sperm
- In 1677, Dutch microscopist Antonie van Leeuwenhoek was one of the first to observe spermatozoa
    - He described the spermatozoa of about 30 species and believed he saw in semen "all manner of great and small vessels, so various and so numerous that I do not doubt they be nerves, arteries and veins… And when I saw them, I felt convinced that, in no full-grown body, are there any vessels which maybe not be found likewise in semen."

Epigenesis:

- The concept that all the organs are formed 'de novo' ('from new') as an embryo develops
- The sole way that animals transition from egg to adult is by developing an embryo
    - Cleavage
    - Patterning (establishing the body plan)
    - Morphogenesis (emergence of and changes in form)
    - Cell differentiation
    - Growth

Questions to Ask About Embryo Development:

- Are all of these cells the same?
- When and how do these cells become different?
- Do these cells communicate with each other? How?
- What is the influence of the environment on these cells?
- What tissues do each of these cells contribute to?

Concepts in Developmental Biology – Pattern Formation:

- Developmental biology describes pattern formation in the developing embryo
    - One cell → many cells → organised cells → tissues → organs
- Pattern formation requires
    - Differential gene expression
    - Signalling between cells
- Pattern formation arises through
    - Cell proliferation
    - Cell migration

    - Changes in cell shape and size
    - Cell differentiation
    - Cell-cell interactions (as well as with the extra-cellular matrix)
    - Programmed cell death (apoptosis)

Two Major Approaches to the Study of Developmental Biology:

- Descriptive approaches ('see it')
    - What parts of the embryo form different organs?
    - What comparisons can we see in the development of different organisms?
    - What are the changes in tissues in birth defects?
- Manipulative approaches ('move it', 'lose it')
    - How do molecules or processes cause visible changes in embryos?
    - How do embryonic cells respond to perturbations?
    - How do cells order themselves into tissues and organs?
    - How do genes control development? (gene editing)

Cell Potency and Development:

- Cells of early embryo (shortly after fertilisation) are pluripotent
    - Can form almost any cell type in the body
- Cell fate – the developmental destination of a cell if left undisturbed in the embryo
    - Cell fate is progressively restricted as pluripotency is lost
- Developmental options of a cell are progressively narrowed
- Cell fate restriction is governed by
    - The cell's genome (gene expression)
    - The cell's history (factors it has been exposed to, where it has been moved from)
    - The cell's interactions with its neighbours

Fate Mapping – Following Lineages of Cells:

- A descriptive approach ('see it')
- Fate map – a diagram that 'maps' adult tissues or structures to regions of the embryo that gives rise to that structure
- Based on lineage tracing – labelling a group of cells and seeing where they end up
    - E.g. labelling groups of cells with fluorescent dyes, e.g. green fluorescent protein (GFP), in the frog embryo

Cell Fate Manipulative Experiments:

- Defect experiment
    - A portion of the embryo is destroyed and the impact on subsequent development is observed
- Isolation experiment
    - A portion of the embryo is removed and cultured to observe the fate of the tissue
- Recombination/transplantation experiments
    - One part of the embryo is removed and replaced with another part from the same embryo
    - One part of the embryo is removed and replaced with another part from a different embryo

Cell Fate Commitment:

- Once the fate has become restricted, the cell can undergo both specification and determination
    - Specification – cell is capable of differentiating autonomously (in a dish) and cell fate in embryo is biased in vivo but still can be reversed
    - Determination – cell differentiates autonomously if placed in another region of the embryo and cannot be reversed
- The cell then becomes differentiated
    - The cells will adopt their final phenotype in a progressive process of fate commitment
    - Cells often exit the cell cycle
    - Usually irreversible (unless forced)
- E.g. blood cell formation

Types of Specification:

- Autonomous specification – cell fate is specified by factors deposited in egg and that become asymmetrically distributed at cell division
    - Occurs early in development
    - Not influenced by external factors
    - Occurs in invertebrates

- Conditional specification – not due to intrinsic factors but fate determined through interactions with other cells and is conditional upon this
    - Usually occurs later in development
    - Occurs in vertebrates

Autonomous Specification:

- The fate of each cell is predetermined by the factors it carries
    - Cells have unique identities
    - Cells can differentiate to their fate in vitro
    - Results in loss of body parts when cells are removed
- E.g. autonomous specification in the early tunicate (sea squirt) embryo
    - When blastomeres are separated, each forms the structures that it would have formed in the embryo

Conditional Specification:

- What a cell becomes depends upon its position in the embryo
- Fate is determined by interactions with neighbouring cells
- If cells are removed, neighbouring cells can compensate (or 'regulate')
    - E.g. tadpole development
- Twinning in humans demonstrates the highly regulative nature of early embryos
    - A great example of conditional specification – if cells are separated early in development, each can compensate and form an embryo
    - The cells are not autonomously specified as they could change fate if placed elsewhere

Conservation of Development Among Organisms:

- Vertebrate embryos develop in the same way, involving similar patterns of cell movement and differentiation, organisation and tissue morphogenesis
- Implies the conservation of underlying genetic mechanisms

Model Organisms:

- Researchers cannot study human embryos due to ethical reasons
- Other organisms are used to 'model' normal and abnormal human development
- Commonly used invertebrate models include
    - D. melanogaster – fly
    - C. elegans – round worm
- Advantages to using model organisms include
    - Easy to keep
    - Rapid life cycles (10 days in fly, 3 days in worm)
    - Easy to genetically modify over multiple generations
    - Key genes known
    - Fate of most (or all) cells are known (959 cells in C. elegans)
- Model organisms provide an opportunity to study conserved developmental processes
    - Pattern-forming genes
    - Master genes that specify cell lineages
    - Genes that regulate cell phenotype
    - Genes that code for tissue-specific functional products

## Lecture 2

Advantages of Studying Development in Zebrafish:

- Optically clear – in vivo imaging
- Fast external development
- High numbers of offspring
- Vertebrate
    - Useful as a biomedical research model
- Easy and inexpensive to keep
- Excellent for screening
    - Forward genetics ('gene discovery')
    - Drug screening (gain/loss of function)
- Easy to manipulate – reverse genetics
    - Gain of functions – transgenics