Development

Differential cell behaviours
(division, differentiation, growth, patterning, movement)

the emergence of organised structures
(tissues, organs)
## Basic Principles of Development

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<tr>
<th>Event</th>
<th>Principle</th>
<th>Outcome</th>
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<tr>
<td>Cleavage</td>
<td>1- Cell Division</td>
<td>• multicellular organism</td>
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<td></td>
<td>2- Pattern Formation</td>
<td>• Defining the Axes: Body Plan</td>
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<td>3- Morphogenesis</td>
<td>• initiating Germ Layer Formation</td>
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<tr>
<td>Gastrulation</td>
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<td>4- Cell Differentiation</td>
<td>• Formation of 3 Germ layers</td>
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<td>5- Growth</td>
<td>• Blood, Muscle, Nerves …</td>
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<td>Organogenesis</td>
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<td>• maturity</td>
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</table>
Developmental cycles for various species

Differences:
- shape & look of embryo
- length of dev. cycle

Common aspects:
- cleavage/gastrulation/organogenesis

Mouse

Fruit Fly (Drosophila)

Chicken
Cleavage
Cell division

- Cleavage: NO INCREASE in size of the embryo - process of just generating many cells
- Extraordinarily QUICK cell division (much more than in tumours)
- The decrease in cytoplasmic/nuclear ratio is crucial

- Cleavage parcels up the newly divided nuclei with increasingly smaller sub-divisions of pre-existing cytoplasm and nuclear material (although DNA content remains the same!).
  - Differential distribution of cellular molecules (mRNA and proteins)
  - New cells will “inherit” cytoplasm and nuclei with differing amounts of these molecules.
Examples of specific cellular distribution patterns of cellular components in fertilized oocytes

Frog oocyte

Drosophila oocyte

Bicoid mRNA on anterior pole (in situ hybridisation)

Vg-1 mRNA in vegetal cortex (in situ hybridisation)
As cleavage proceeds:

Oocyte  ➔  Morula  ➔  Blastula

(1 cell)  (clump of cells)  (bigger but hollow ball of cells)

- Cell heterogeneity ➔

- Cell division ➔

- Maternal determinants ➔

- Embryonic gene expression ➔
Localisation of cytoplasmic factors (specific mRNAs and proteins) is used as **morphogenetic information** to lay the blueprint for the body plan (body axis formation).

- **maternal vs zygotic factors**
- **A-P & V-D axis**

- **Cleavage**
- **Pattern formation**

[Fruit fly diagram]

[Frog diagram]

[Zebrafish diagram]
Body Plan Organisation of a fruit fly
Gastrulation
Morphogenesis - formation of 3 germ layers

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<th>Xenopus</th>
<th>Chick</th>
<th>Mouse</th>
<th>Zebrafish</th>
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<tr>
<td>Embryos at the beginning of gastrulation</td>
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<tr>
<td>Embryos at around the phylotypic stage</td>
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GASTRULATION is the re-arrangement of the blastula to form:

- **Outer ectoderm**: skin and (central) nervous system
- **Inner mesoderm**: most of the organs
- **endoderm**: linings of digestive and respiratory system

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**Frog**

**Chicken**
Morphogenesis or *Developmental Mechanics*:

- Cell adhesion
- Cell shape
- Cell movement
- Cell proliferation/death
- Extracellular materials

- Changes in these qualities at the single cell level alter the form of the cell groups, the tissues, organs and the entire embryo.

- New shapes are moulded and sculpted, cells alter their behaviours.

This is moulding and sculpting, but there is no sculptor; the clay forms itself.
Gastrulation is dependent on
Organizers or signalling centres

Spemann organizer

Hensen’s node
In the fertilized oocyte (zygote):

- **Sperm entry** defines location of the organizer!
  - Cortex rotates with respect to internal cytoplasm (microtubule-driven)
  - Differentially distributed cytoplasmic molecules of cortex will be shifted with respect to differentially distributed molecules of internal cytoplasm ➢ **cortical rotation** ➢ V-D axis ➢ Nieuwkoop center (as part of Spemann organizer)
The **Nieuwkoop center** cells can **induce** changes in neighbouring cells…….
**Intracellular induction** causes cell shaping & re-arrangement through

‘Autonomous’ signals: zygotic transcription factors
or

**cell conditioning signals:** zygotic secretion factors
Cleavage ends:

- cytoplasm: nucleus ratio while cells divide
- maternally derived molecules
  (transcriptional repressors in the oocyte cytoplasm?)
- increase zygotic gene expression of autonomous & cellular signalling molecules

Gastrulation starts:
induction of the Organizer by zygotic signalling molecules
----------this signals to neighbouring cells
----------controls organization of the Blastula
----------instigates & orchestrates cell re-arrangements
----------to give a 3 layered, patterned embryo
Gastrulation process in frog
Chicken

Cleavage

Gastrulation
The end result of gastrulation in vertebrates generating:

A tube with 3 basic layers

**Ectoderm** = outer layer
- epidermis (skin)
- neural (CNS & PNS)

**Endoderm** = inner layer
- absorptive cells
- secretory cells

**Mesoderm** = middle layer
- notochord
- muscle
- skeleton
- connective
- kidney
- blood

Cell Differentiation / Tissue & Organ development
Organogenesis

Cell differentiation

Further induction processes mediate cell differentiation-tissue and organ development:

Example 1
Example 2
Limb formation: **Apical Ectodermal Ridge**

Example 3
Brain compartmentalization: **Isthmus**  
(defines boundary between mid- and hindbrain)
Developmental events are controlled by differential gene expression,

which drives cascades of gene-regulatory events,

which define differential cell behaviours,

which underlie major developmental processes

crucial to study gene expression & protein function

Next week:
Molecular mechanisms underlying development