“IT IS NOT BIRTH, MARRIAGE OR DEATH, BUT GASTRULATION WHICH IS TRULY THE MOST IMPORTANT TIME IN YOUR LIFE.”

Lewis Wolpert, 1986

Overview of next three lectures
1. 1st Class: Introduction to gastrulation
   1. Basic concept
   2. Germ layer formation

2. 2nd Class: Interaction of signals
   1. Nodal and its relatives
   2. FGF and its relatives
   3. Other minor players

3. 3rd Class: Formation of body axis
   1. Body axis formation
   2. Breaking the asymmetry

Overview of today’s lecture
1. Basic concepts and cell movement
2. Gastrulation in different species
3. Mesoderm induction

Basic concepts of gastrulation

What is gastrulation?

Gastrulation is the event to create different cell types.

What is the goal of gastrulation?

Gastrulation is the event to create different cell types.
1. Morphological features first described by Rusconi and Dutrochet, and again by Ernst von Baer.

2. The actual name of gastrulation was first used by Ernst Haeckel in 1872.

3. The germ layer concept and the names of ectoderm, mesoderm, and endoderm were named by Sir Ray Lankester.

1. Invagination: Inward movement of a sheet of cells
2. Ingression: Individual cells migrate from the epithelial sheet as mesenchymal cells
3. Involution: A sheet of cells roll over to generate additional layer of cells inside
4. Epiboly: A sheet of cells spread and become thinner
5. Intercalation: Two adjacent sheets of cells become one sheet
6. Convergent extension: Specialized intercalation that occurs in certain direction
Overview of today’s lecture

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Specification of germ layers: Evolutionary perspectives

Deuterostome

Protostome

Blastopore

Specification of germ layers in Drosophila, a protostome

Specification of germ layers in Sea urchin

Specification of germ layers in fish and amphibians

Formation of blastopore in amphibians

Specification of germ layers in birds and mammals

Specification of germ layers: Ingression at the node

Coordinated movement of ectoderm and mesendoderm
Overview of today’s lecture

1. Basic concepts and cell movement
2. Gastrulation in different species
3. Mesoderm induction

How mesoderm is specified?

Peter Nieuwkoop’s experiments and mesodermal induction

Induction and Competency

1. Induction is a process by which one group of cells signals to a second group of cells altering their ultimate developmental state.
2. Competency is an ability of a group of cells to respond to an inducing signal. Competence is directly related to the age of a tissue during development.

Two components of inductive system

1. A signal generated by the inducing cell.
2. A receptive system that directly or indirectly controls gene expression in the responding cell, i.e., competence.

Nieuwkoop’s induction experiments I

Mesoderm

C. elegans  zebrafish
Conclusions from the Experiment

1. Mesoderm is induced when endoderm and ectoderm are juxtaposed.
2. Signals arise from endoderm and received by ectoderm, i.e., the ectoderm is induced to form mesoderm.

Nieukoop’s Induction Experiments II

Conclusions from the Experiment

1. Mesoderm is induced when endoderm and ectoderm are juxtaposed.
2. Signals arise from endoderm and received by ectoderm, i.e., the ectoderm is induced to form mesoderm.
3. The signal from the endoderm is secreted.
4. Signal only acts over a short distance.
5. Ectoderm is only competent for this signal for a short period during development.

Methods to Identify the Mesoderm Inducing Signal

1. Cut and Dump: Place animal cap tissue in the presence of potential mesodermal inducer and score for expression of mesodermal markers and cellular movements.
2. Functional Screen: Inject embryos with potential gene or cDNA library, cut animal caps, score as above.
3. Expression Screen: Differential screen between ectoderm and endoderm. Alternatively, pick cDNA from tissue specific library and perform in situ.

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Remaining Questions

1. How is the “Signal” propagated?
2. How far is the signal propagated?
What is Brachyury?

1. It is expressed throughout the mesoderm from its formation.
2. Immediate early response factor to mesoderm inducing signals in a dose dependent manner.
3. It is required for the proper mesoderm formation.
4. Overexpression of Brachyury is sufficient to convert ectoderm to mesoderm.
5. Evolutionarily conserved.

Brachyury Expression in Development

1. Mouse
2. Xenopus

Brachyury is a T-Box Protein

1. Family of transcription factors that has T-box domain.
2. Function as 'Classical Transcription Factors'
   - Localize to the nucleus
   - Bind DNA in a sequence specific fashion
   - Regulate transcription of neighboring genes
3. Multiple family members are expressed in space and domain.
4. Mutated in development and disease.

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Identify Endoderm Specific Signal

Subtractive Hybridization

Criteria for Mesodermal Inducer Based on Nieuwkoop's Studies

1. Gene or protein must be expressed and active in the correct time and place.
2. Protein must be secreted and act at a distance.
3. Protein must be necessary and sufficient to induce mesoderm in ectoderm in a protein synthesis independent fashion.