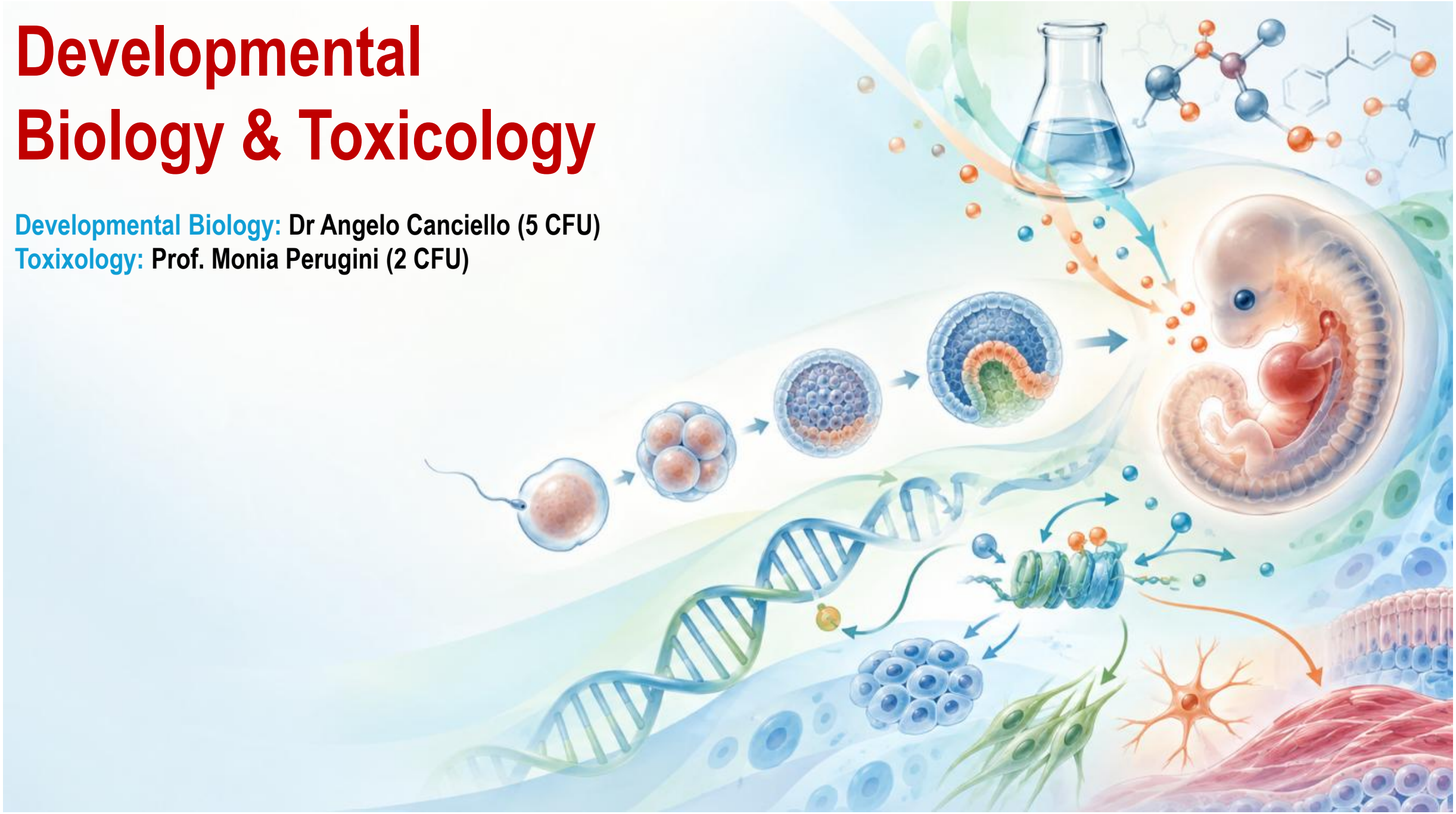
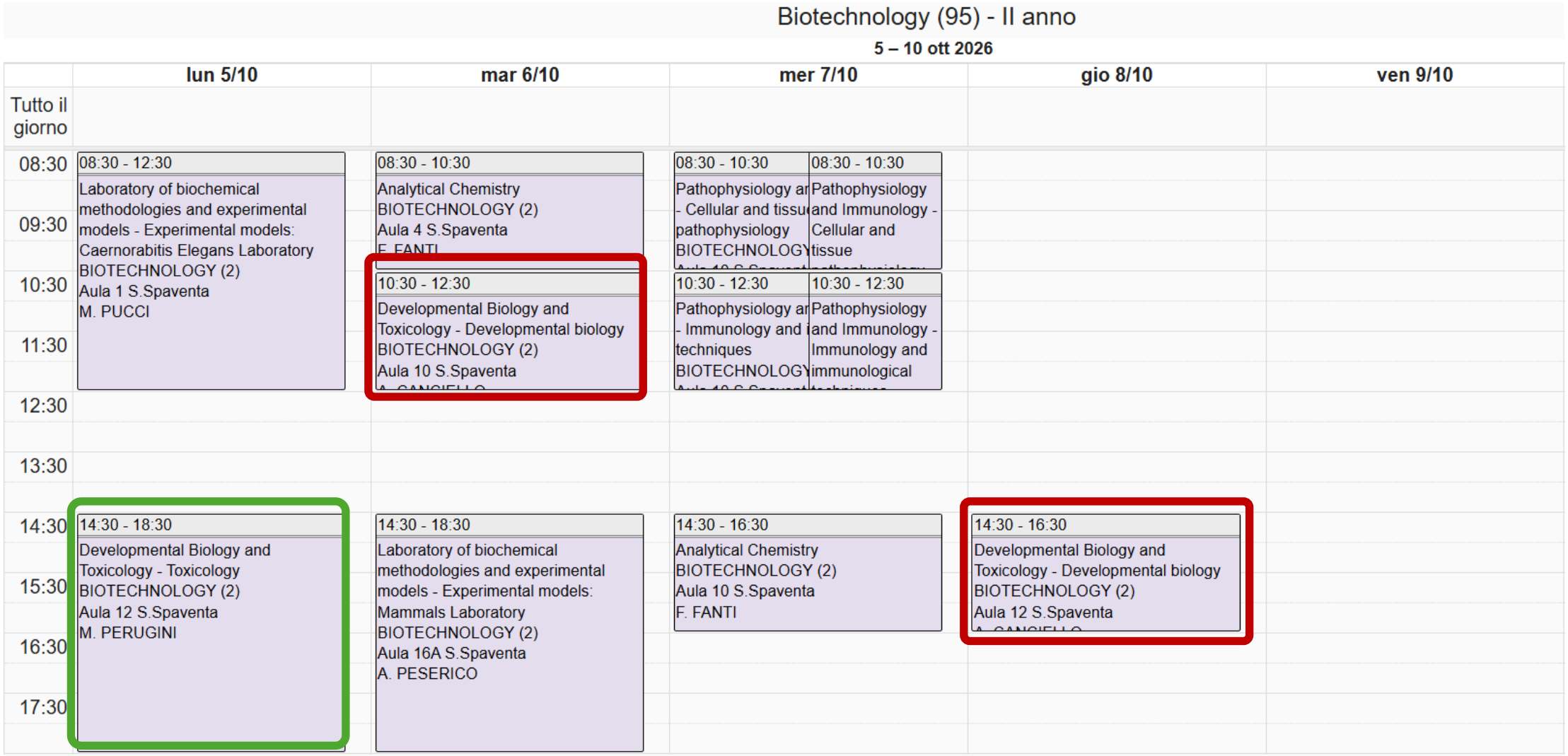
Developmental Biology & Toxicology

Developmental Biology: Dr Angelo Canciello (5 CFU)
Toxixology: Prof. Monia Perugini (2 CFU)





Developmental Biology: Dr Angelo Canciello (5 CFU)

Toxixology: Prof. Monia Perugini (2 CFU)

Examination Phases

1. *Peer-assessment activities*

2. *Written Test (multiple chioice questions)*

3. *Oral Test confirmation*

Developmental Biology: Dr Angelo Canciello (5 CFU)
Toxixology: Prof. Monia Perugini (2 CFU)

Peer-learning and peer-assessment activity

6 hours | 3 lessons

Lesson 18 - Guided group work and presentation preparation

Duration: 2 hours | **Textbook:** Course content plus recent reviews and primary research articles | **Depth:** Guided collaborative work

Students will be organised primarily into groups of four. Groups of three will be used only to manage remaining students. With a cohort of 80-100 students, approximately 20-26 groups are expected. Topics should be assigned at least two weeks before the presentation.

Each group must integrate:

- Content covered during the course.
- At least one recent review article.
- At least one recent original research article.
- Older landmark studies when scientifically necessary.

Definition of recent literature: As a general rule, students should prioritise publications from the previous five years, while retaining older landmark studies when they are necessary to explain the origin of a concept or mechanism.

Introduction to Developmental Biology

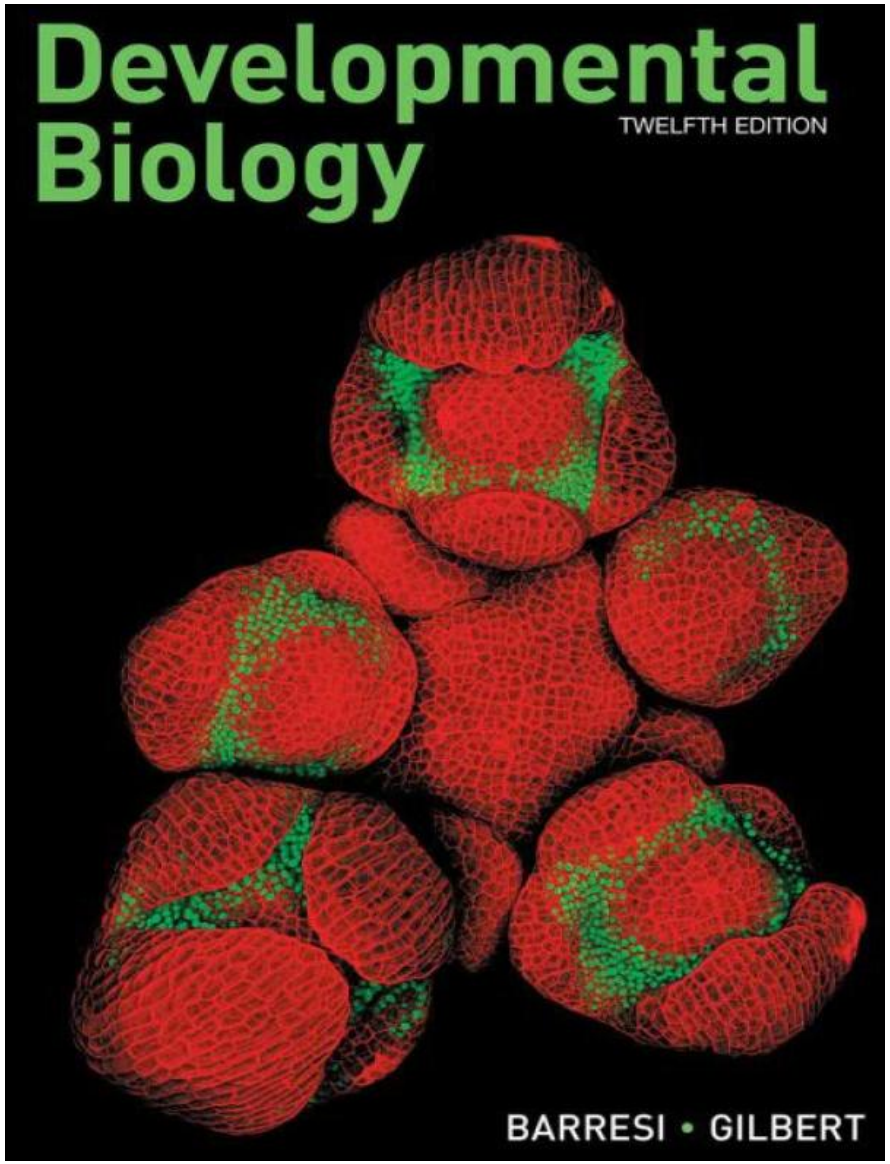


Questions, life cycles and model organisms

Developmental Biology

Second-year BSc in Biotechnology

Learning outcomes and lesson roadmap

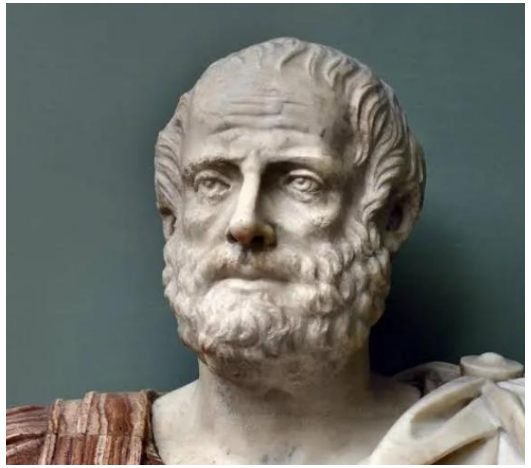


By the end of this lesson, students should be able to:

- Define **developmental biology** and distinguish it from embryology.
- Identify the major questions addressed by developmental biologists.
- Describe the general animal life cycle and the principal stages of embryogenesis.
- Explain how gastrulation establishes the three embryonic germ layers.
- Distinguish **morphogenesis** from **cell differentiation**.
- Explain why different experimental questions require different model organisms.
- Describe the general logic of **find-it, lose-it and move-it** experiments.

Gilbert and Barresi, 12th ed.

Questions of Developmental Biology



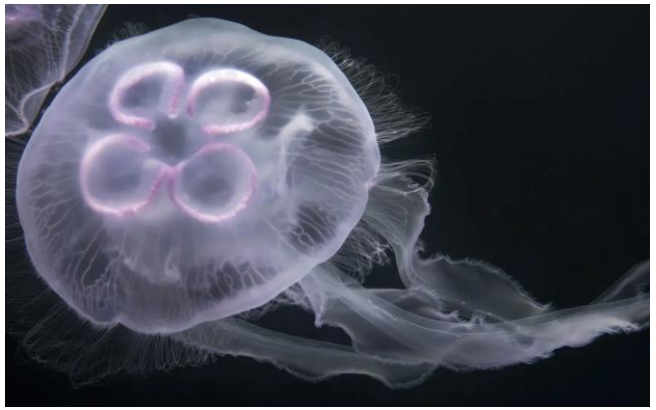
Aristoteles, Greek Philosopher

"*Wonder is the source of knowledge and, the animal development, is certainly a remarkable source of amazement*"

- How is the body plan established so reproducibly?
- Why are organs positioned where they are?
- How does a simple embryonic tissue generate complex structures?
- Why can some organisms regenerate body parts whereas others cannot?
- How do male and female anatomies arise?

Developmental biology is the study of the **process by which animals and plants grow and develop.** It **explores how a single cell**, like a fertilized egg, **changes into a complex, organized living thing**





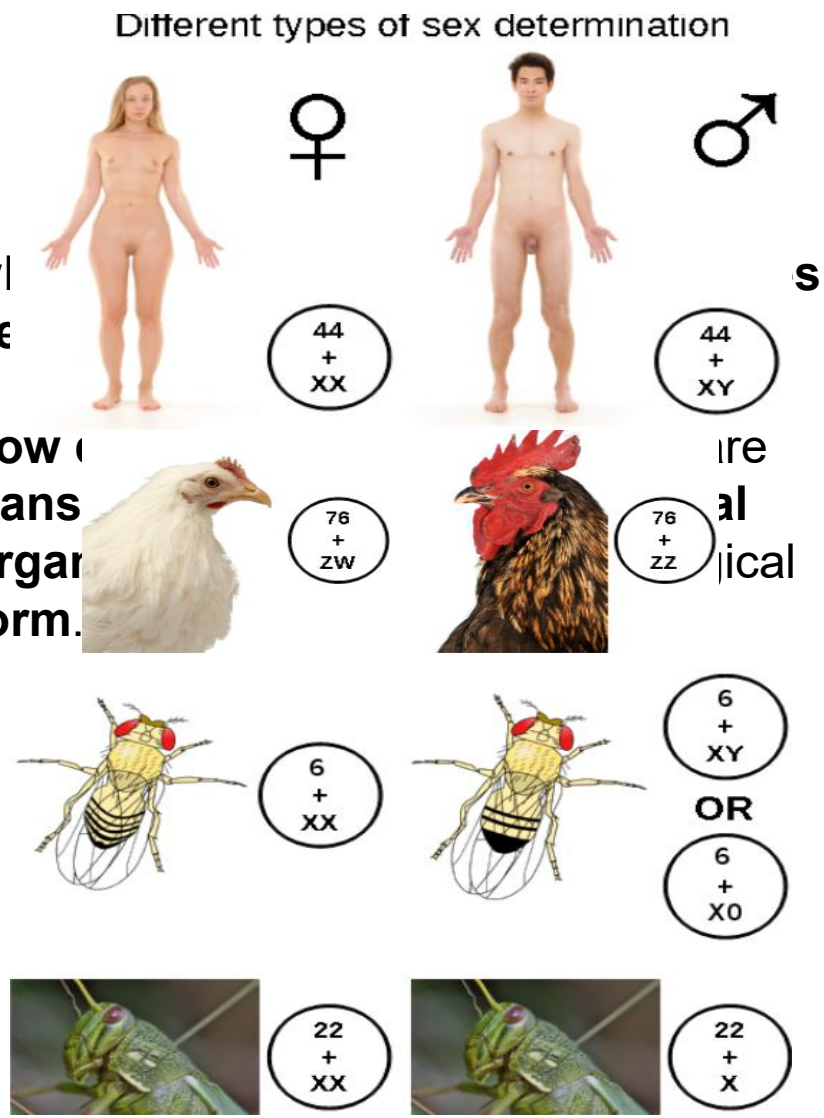


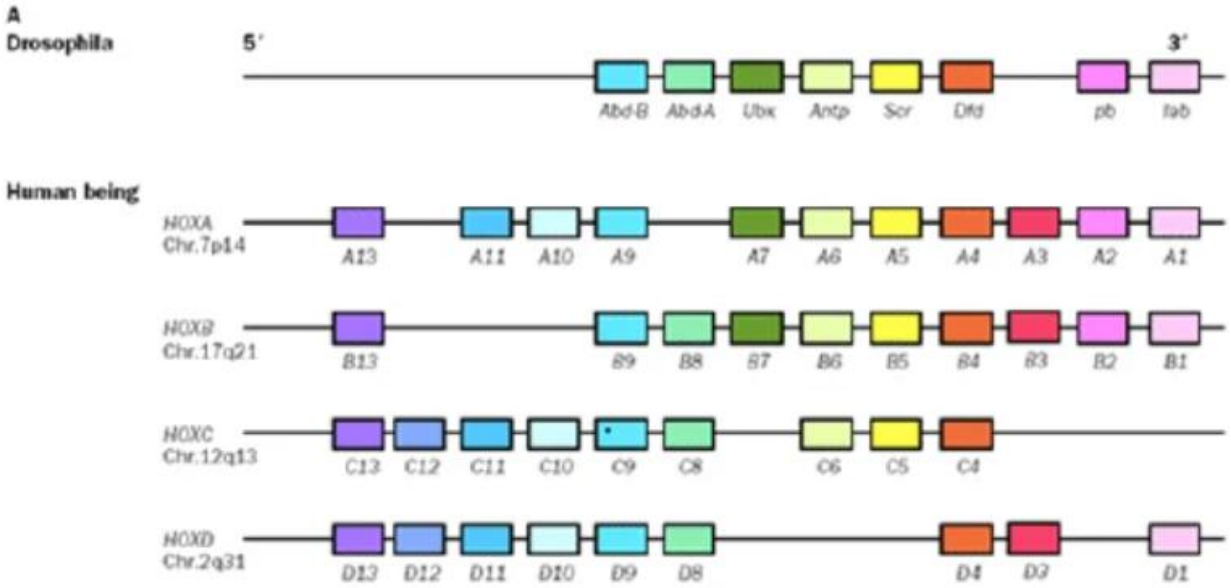


genes → proteins → cell behaviours → tissues → organs → organism

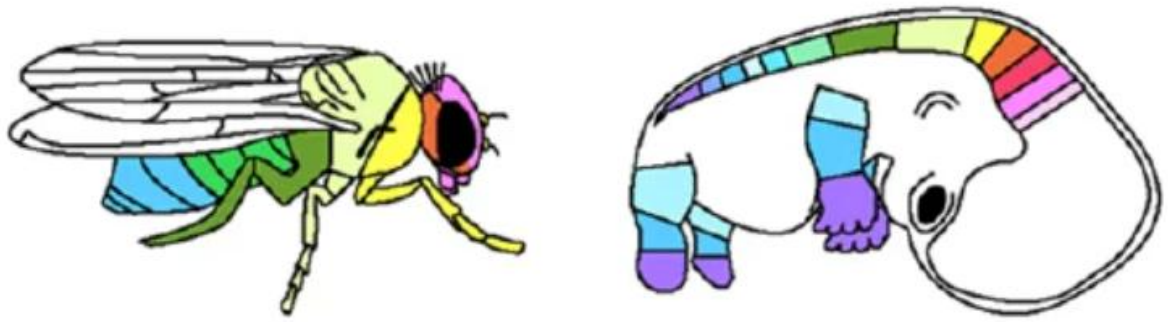
Questions of Developmental Biology

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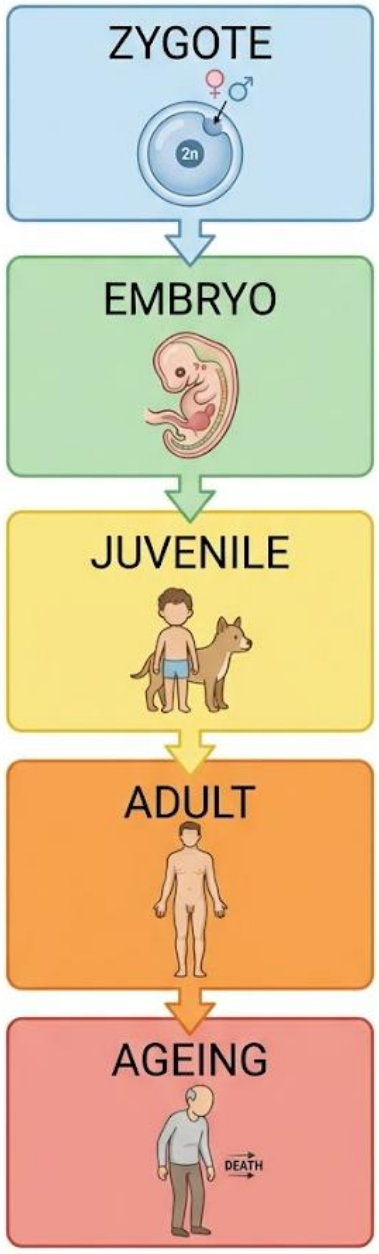




B



What is developmental biology?



- **Developmental biology** investigats how organisms change over time at molecular, cellular, tissue and anatomical levels.
- It asks how **a single fertilized cell produces an organised multicellular organism** containing many specialised cell types.
- Development involves coordinated changes in **gene expression, cell behaviour, tissue organisation and organ function**.
- The discipline includes embryonic development but also **postembryonic growth, metamorphosis, tissue maintenance, regeneration and ageing**.
- Development is therefore not simply an increase in size: it is the **progressive production** of biological **diversity, order and function**.

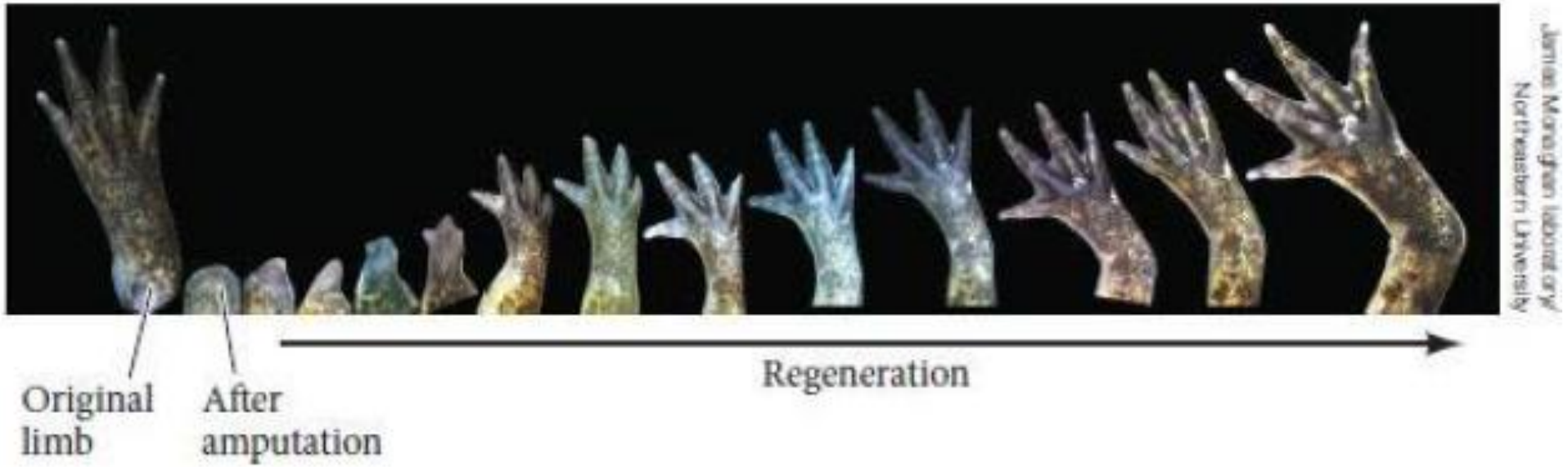
The embryo as a self-constructing system

- ***Unlike a machine, an organism must remain functional while it is constructing itself***.
- Development usually begins with a single cell, the **zygote**, produced by fertilization.
- The zygote **generates all somatic cell lineages** through repeated **mitotic divisions** and progressive **cell-fate decisions**.
- Developing **cells must obtain energy**, **communicate** and **respond to their environment** before mature organs exist.
- Cells also construct the tissues and signals that will guide their own subsequent behaviour.
- Embryonic development is therefore a dynamic process of **self-organisation under genetic and environmental control**.



Development continues throughout life

- **Embryology** traditionally studies the period *between fertilization and birth or hatching*.
- **Developmental biology** extends *beyond embryogenesis* and *includes* all *organised biological change throughout life*.
- **Postembryonic development** includes growth, **sexual maturation**, **metamorphosis** and the **maturation of organ systems**.
- Adult tissues continue to develop through **cell renewal**, **stem-cell activity**, **wound repair** and **physiological adaptation**.
- **Some animals** retain extensive **regenerative ability**, whereas others regenerate only selected cells or tissues.
- **Ageing** can also be studied as **a progressive alteration of developmental** and tissue-maintenance programmes.



Two overarching objectives of development

Development accomplishes two fundamental objectives:

It generates **cellular diversity and spatial order** within an individual organism.

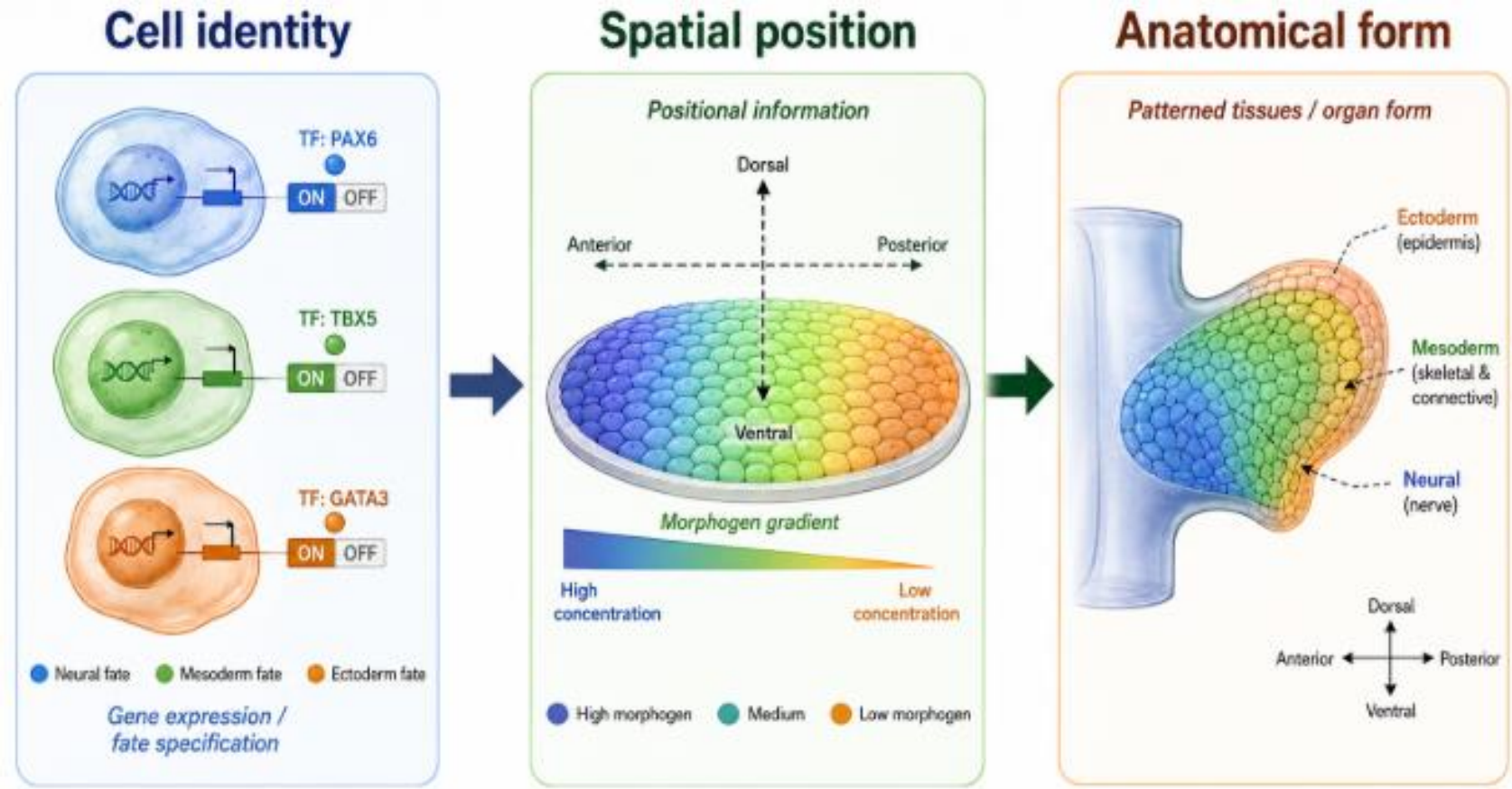
*The first objective asks **how a zygote produces an organised adult body***

It ensures the **continuity of life** from one generation to the next.

*The second asks **how the adult produces** specialised **germ cells capable of beginning another generation***

- **Somatic development and reproduction** are therefore connected components of the **same life cycle**.
- **Developmental biology integrates both objectives** by **studying how** biological **information is transmitted, interpreted and expressed** over time.

First aim's major questions: diversity, pattern and form



- These questions are interdependent: **differentiated cells** must **appear at the correct time**, in the **correct position** and in the correct number.
- A developmental explanation must therefore **connect molecular regulation with cellular behaviour** and **anatomical outcome.**

- **Differentiation:** How does one zygote generate hundreds of structurally and functionally distinct cell types?
- **Growth:** How are cell proliferation, cell size and tissue dimensions regulated?

- **Morphogenesis:** How do cells construct ordered tissues, organs and body structures?
- **Pattern formation:** How are different cells and tissues positioned in reproducible spatial arrangements?

Second aim's major questions: continuity, plasticity and context



- **Reproduction:** How are germ cells specified, matured and used to transmit biological information?
- **Regeneration:** Why can some organisms reconstruct lost structures, whereas others have limited regenerative capacity?
- **Environmental integration:** How do temperature, nutrition, microorganisms and chemicals influence development?
- **Evolution:** How can inherited modifications of developmental mechanisms generate new biological forms?

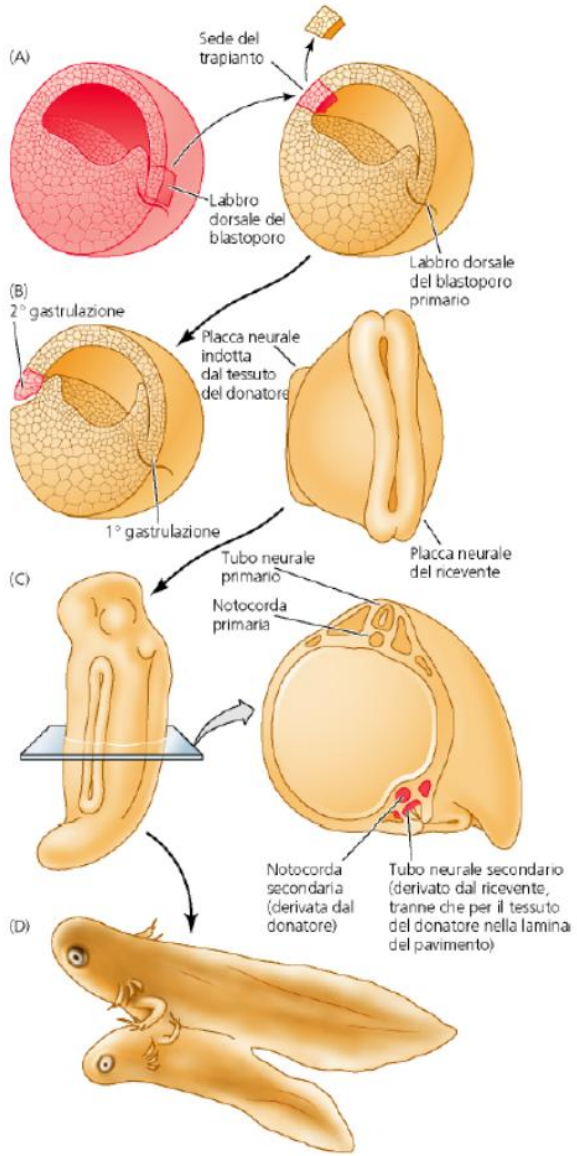
- **Development** must be **robust enough** to produce a functional organism **but flexible enough** to respond to environmental conditions.
- **Abnormal development** can result when genetic information, cellular processes or environmental signals disrupt this coordination.

“We are faced with riddles, but we have not lost hope of solving them… riddles waiting for a solution, what else could a scientist wish for?”



Hans Spemann (Stoccarda, 27giugno 1869 – Friburgo in Brisgovia, 9settembre 1941)

Hilde Mangold, PhD student died in 1924

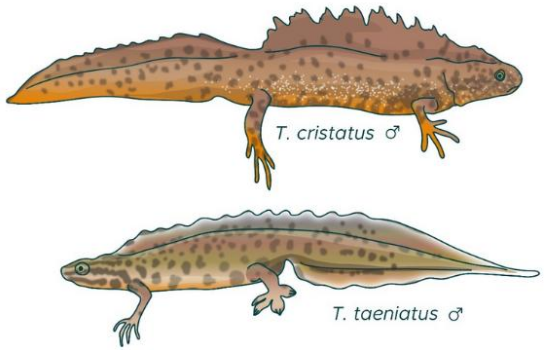


Spemann hypothesized that, during **gastrulation**, the embryo contains a **control center** capable of directing the formation of the **body axis**. He had already observed that manipulating the **dorsal lip of the blastopore** in newt embryos could lead to **duplication of the embryonic axis**, suggesting the presence of an **organizing region** that governs early development.

- Transplantation of the **dorsal lip of the blastopore** from *Triturus cristatus* (unpigmented donor) into the **ventral side** of *Triturus taeniatus* (pigmented host).

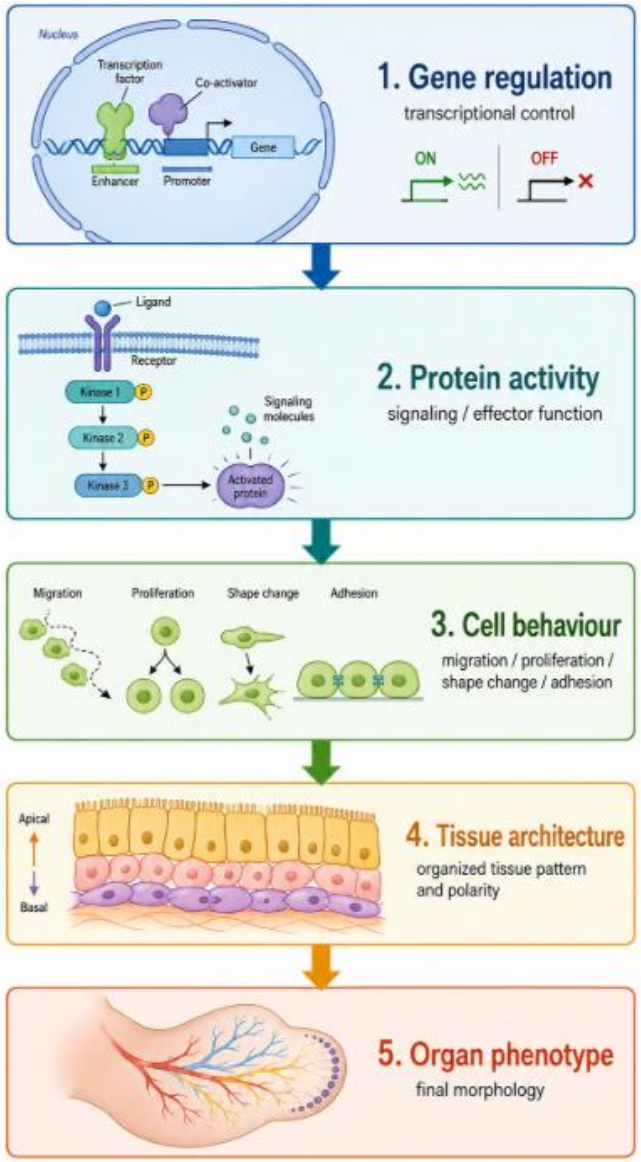
- Formation of a **secondary embryonic axis**: neural tube, notochord, somites, and organized tissues.
- Donor tissue acted as a **developmental organizer**, inducing host cells.

- First demonstration of **embryonic induction**
- Identification of the **Spemann–Mangold Organizer**





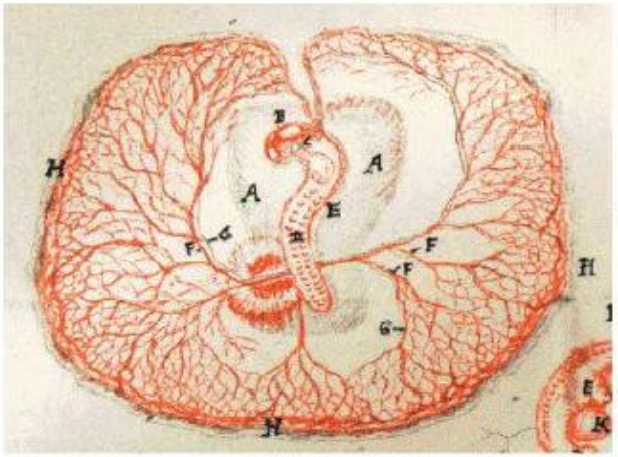
Developmental explanations operate across scales

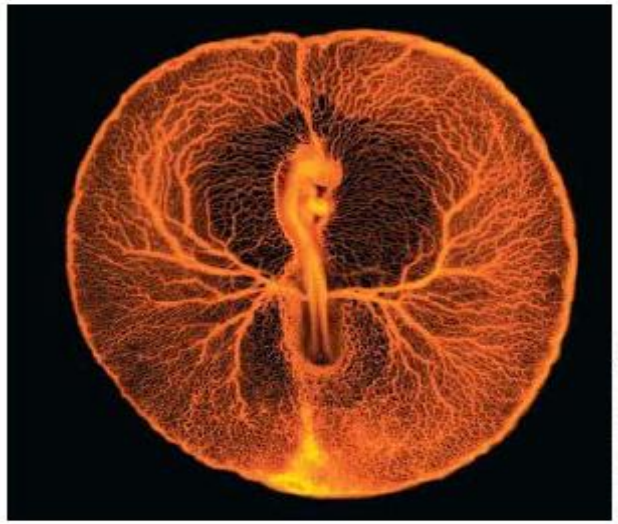


A complete developmental explanation links multiple levels:

- **Genes and regulatory DNA** determine where and when developmental programmes can be activated.
- **RNA and proteins** execute regulatory, structural and signalling functions.
- **Cells** change identity, shape, adhesion, position, proliferation and survival.
- **Tissues** fold, extend, fuse, separate and interact with neighbouring tissues.
- **Organs** acquire a reproducible structure and physiological function.
- The final phenotype emerges from causal connections across these scales, not from the action of a single gene in isolation.

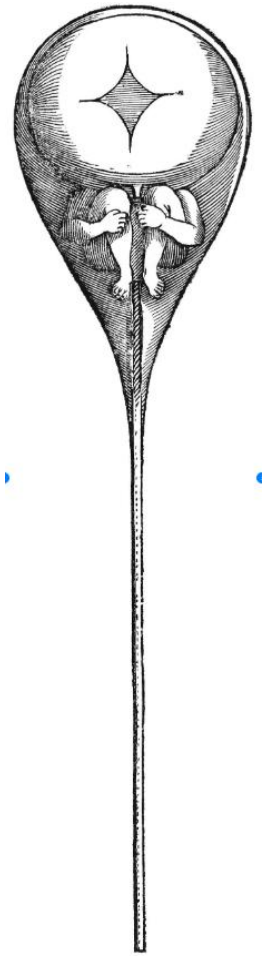
Comparative embryology: from observation to hypothesis





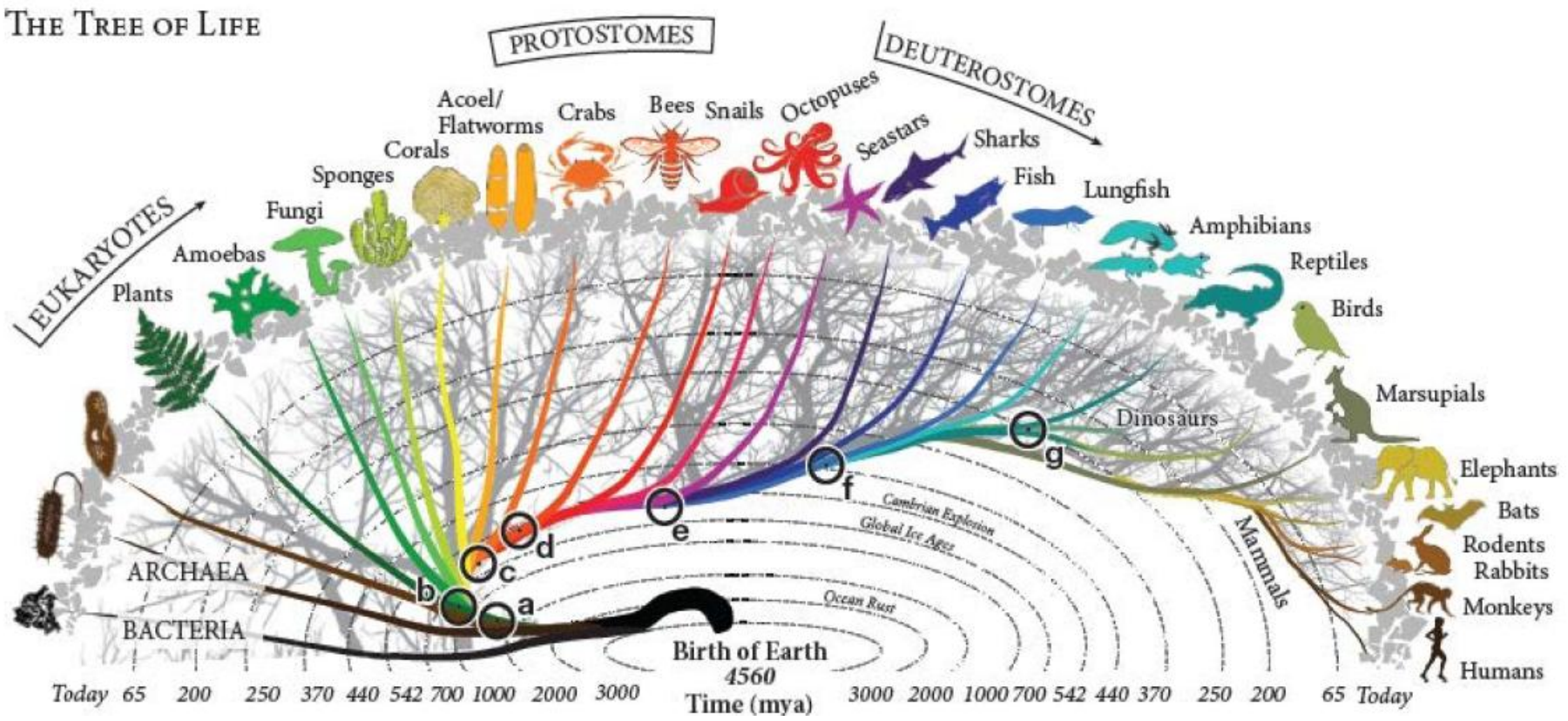
- Developmental biology originated from the **systematic observation and comparison** of embryos. **Comparative** observations reveal both **shared developmental principles** and species-specific solutions.
- Historical embryologists used **morphology to identify recurring structures** such as the neural tube, somites, heart and blood vessels.
- Modern developmental biology **extends these observations by identifying the genes, signals and cell behaviours** that generate each structure.
- Description establishes **what happens**; experimental analysis asks **how and why it happens**.
- **Comparative embryology remains valuable** when comparisons are used to formulate mechanistic hypotheses rather than merely catalogue similarities.

Epigenesis vs Preformationism



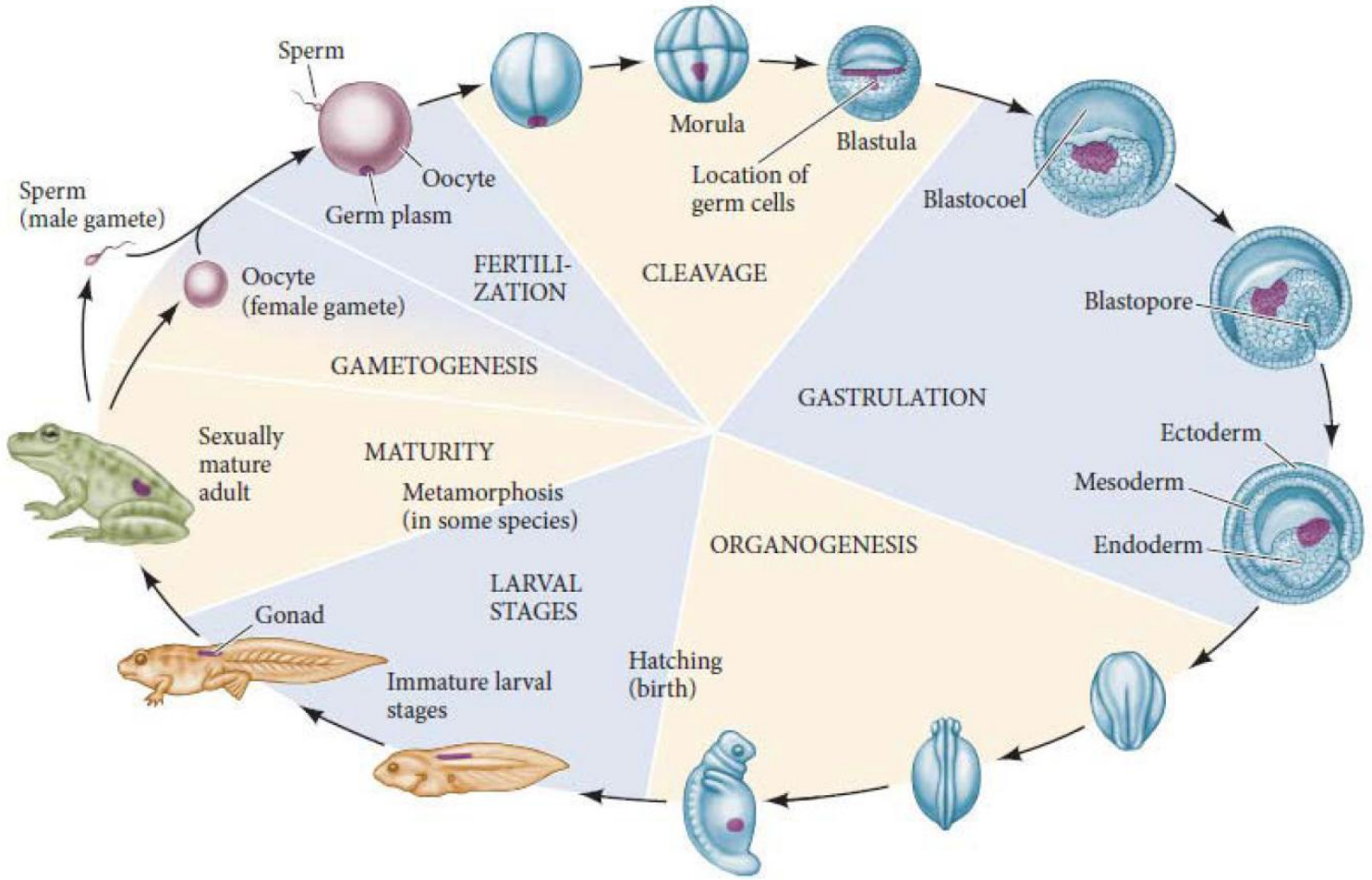
Malpighi's drawing of a two-day chick embryo compared with a modern image of a similar stage.

LUCA: Last Universal Common Ancestor



The theory of evolution is fundamentally based on all life on Earth originating from a common ancient ancestor, so named **LUCA**, the **last universal common ancestor**. This means all forms of life are related to one another. The letters a–g denote the locations of common ancestors, including those of plants (b) and of multicellular organisms (a).

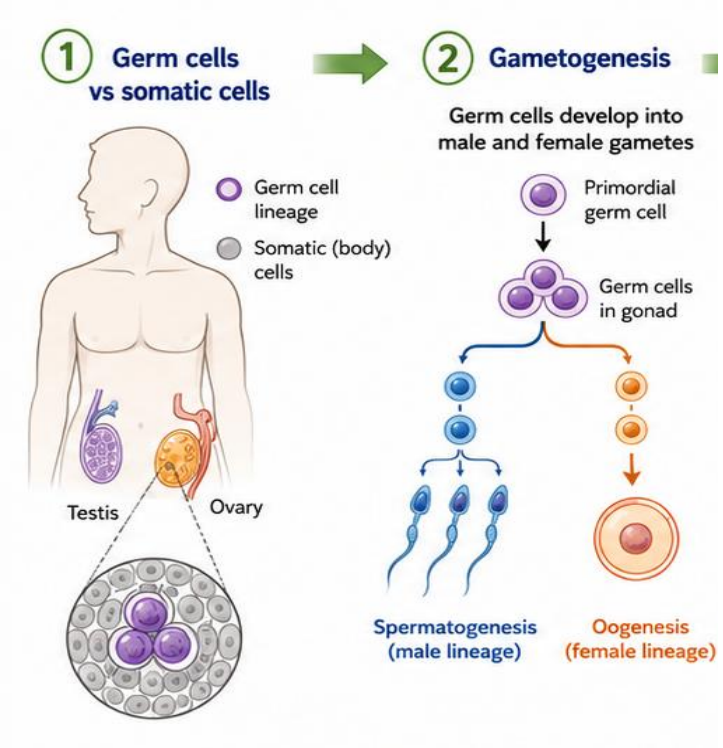
The animal life cycle and embryonic development



Animal life cycles are circular rather than strictly linear.

1. **Gametogenesis** produces specialised haploid sperm and egg cells.
2. **Fertilization** combines the gametes and initiates the development of a new individual.
3. **Embryogenesis** includes cleavage, gastrulation, neurulation and early organogenesis.
4. **Birth or hatching** is followed by postembryonic growth, maturation and, in many species, metamorphosis.
5. **The sexually mature** adult generates the gametes that begin the next cycle.
6. **Senescence and death** end the individual life history but not the biological continuity of the lineage.

Gametogenesis prepares the next generation



- **Gametogenesis** is the developmental process that produces mature sperm and egg cells.
- **Germ cells** are functionally distinct from the somatic cells that form the body of the individual.
- **Meiosis** reduces chromosome number and generates genetically diverse haploid cells.
- **Gametes** subsequently acquire specialised structures that enable recognition, fusion and early development.
- **The egg** usually contributes most of the cytoplasm, organelles and regulatory molecules required during the earliest stages.
- **Sperm and egg nuclei** each contribute one haploid genome to the new embryo.
- Gametogenesis thus connects development of the adult with development of its offspring.

Fertilization initiates a new organism

- **Fertilization** begins when mature sperm and egg cells recognise and interact with one another.
- **Fusion of the gamete membranes activates the egg** and initiates the transition from egg to embryo.
- The **haploid male and female** pronuclei contribute to the formation of a **diploid zygotic genome.**
- Fertilization combines reproduction with genetic recombination and biological continuity.
- It also **establishes or influences early cellular asymmetries** in many species.
- **Mechanisms that prevent entry of additional sperm** protect the embryo from abnormal chromosome numbers.
- The molecular details differ among species, but gamete recognition, fusion and egg activation are conserved functional requirements.

(A)



(B)

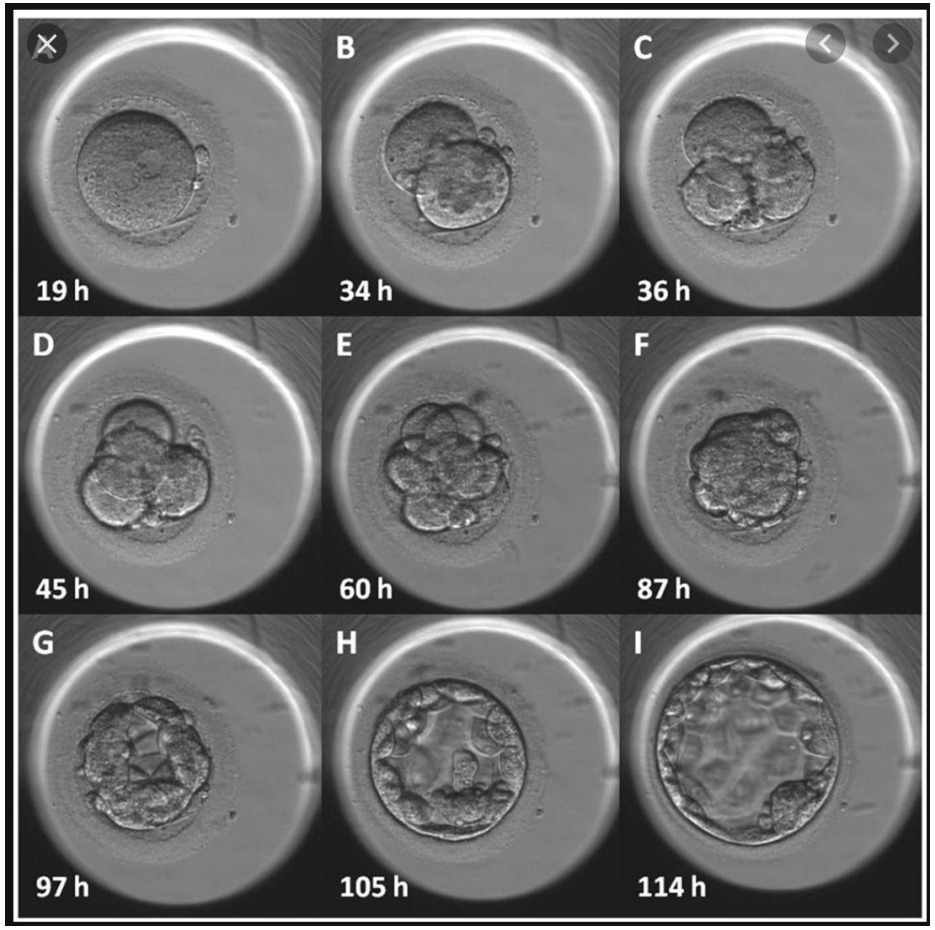


Cleavage partitions the zygote

- **Cleavage** increases cell number and partitions the cytoplasm into blastomeres.
- **Cleavage** consists of a rapid series of mitotic divisions immediately following fertilization.
- Early cleavage ***usually increases cell number without substantially increasing total embryonic volume***.
- The large zygotic cytoplasm is progressively divided among smaller cells called **blastomeres**
- Repeated divisions commonly produce a multicellular structure called a **blastula**.
- A fluid-filled internal cavity, the **blastocoel**, forms in many animal embryos.

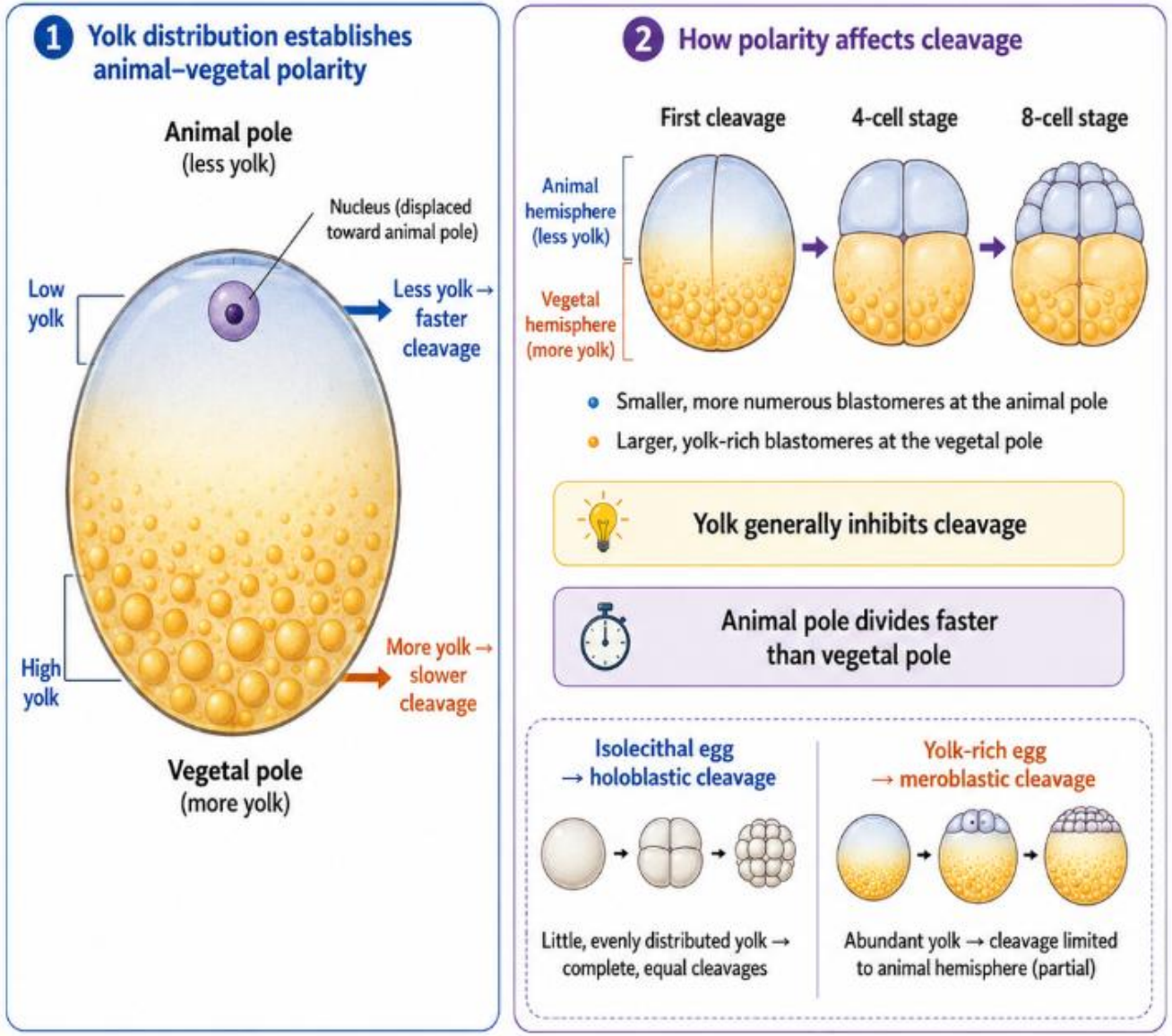
- Cleavage **establishes the cellular substrate** on which later cell interactions and fate decisions act.
- The **geometry and timing** of cleavage **vary according to species**, **yolk distribution** and inherited cellular mechanisms.

Zygote → ***Morula***



Morula → ***Blastocyst***

Cleavage General Features



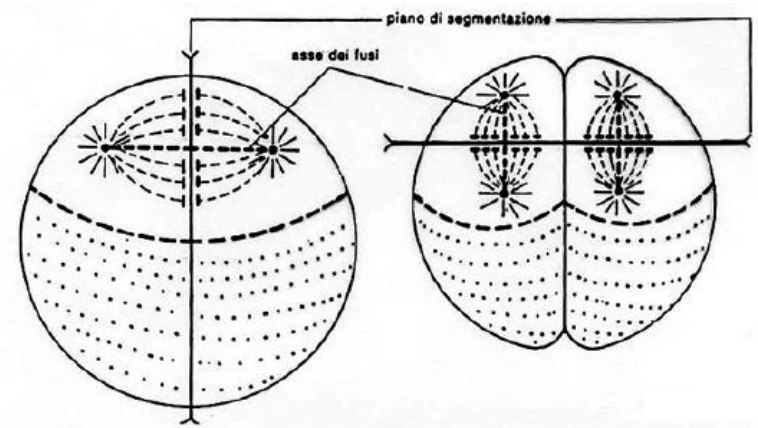
PARAMETERS INFLUENCING THE CLEAVAGE PATTERN

- ***Amount of yolk***
- ***Yolk distribution***
- ***Mitotic spindle orientation factors***

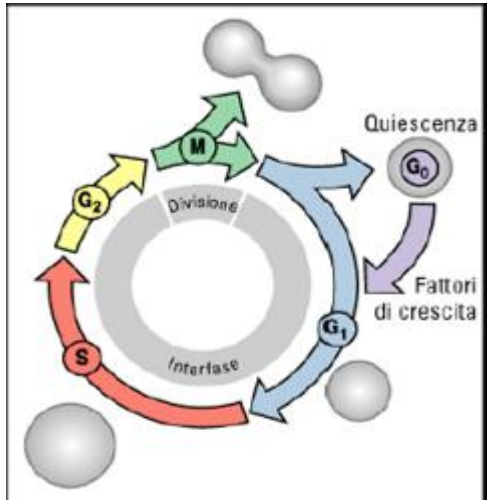
N.B. Yolk is inert, therefore it constitutes an obstacle to cell division

Hertwig's Law states that **a cell divides perpendicular to its longest axis**. Specifically:

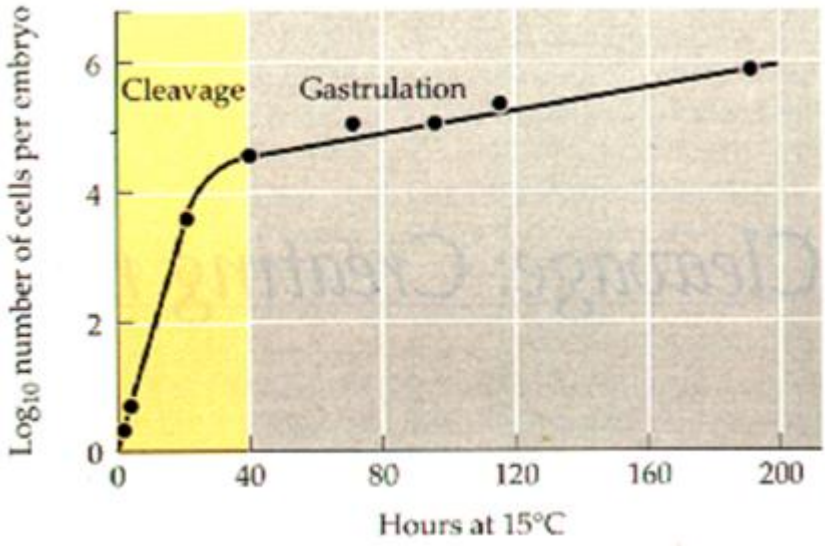
- The **mitotic spindle** aligns parallel to the longest dimension of the cell's active cytoplasmic mass.
- The **cleavage plane** (division furrow) forms perpendicular to the spindle axis, resulting in two daughter cells cut across the cell's shortest dimension.



Cleavage and cell division

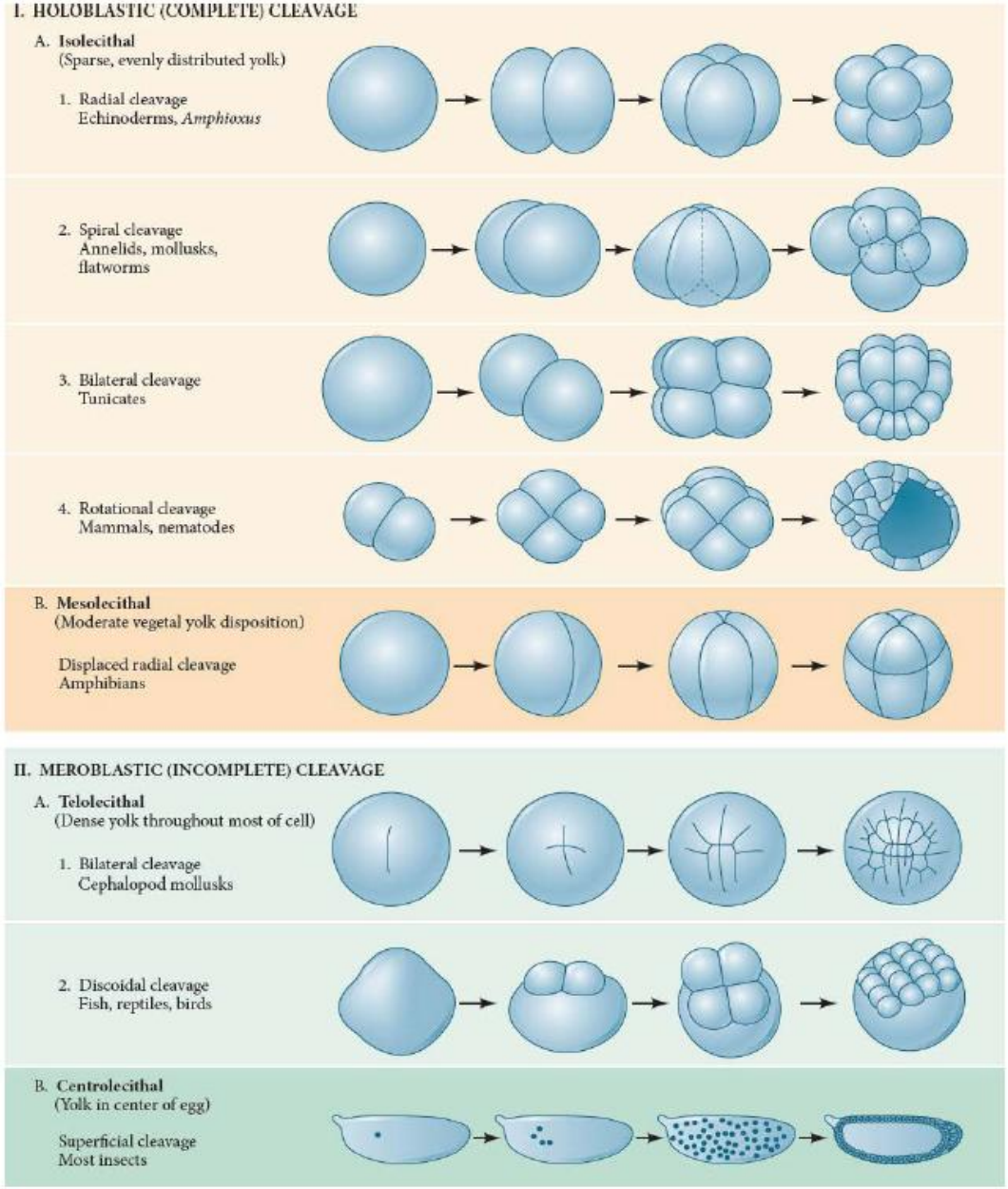


- Early cleavage is often extremely rapid because the embryo frequently **skips the G1 and G2 phases** of the cell cycle, alternating mainly between **DNA synthesis (S phase)** and **mitosis (M phase)**.
- This rapid schedule allows the embryo to generate large numbers of cells quickly and to restore a more appropriate **nuclear-to-cytoplasmic ratio**.



- **Absence or low levels of transcriptional activity** (silent embryonic genes)
- **Initial maternal cell cycle control** → activation of embryonic genes
- **Late zygotic control**

Major cleavage patterns



- **Holoblastic cleavage** divides the **entire egg** and is typical of eggs containing **little or moderate yolk**.
- Holoblastic cleavage **may be radial, spiral, bilateral** or **rotational**, depending on spindle orientation and inherited cellular organisation.
- **Meroblastic cleavage** divides **only part of the egg** because **abundant yolk prevents** the cleavage furrow from crossing the complete cell.
- Discoidal meroblastic cleavage is characteristic of fish, reptiles and birds.
- **Yolk amount and distribution strongly influence cleavage** but do not explain every species-specific pattern.
- Cleavage patterns differ, yet each must generate an organised population of cells capable of undergoing gastrulation.

Embryological Anatomical Directional Terms

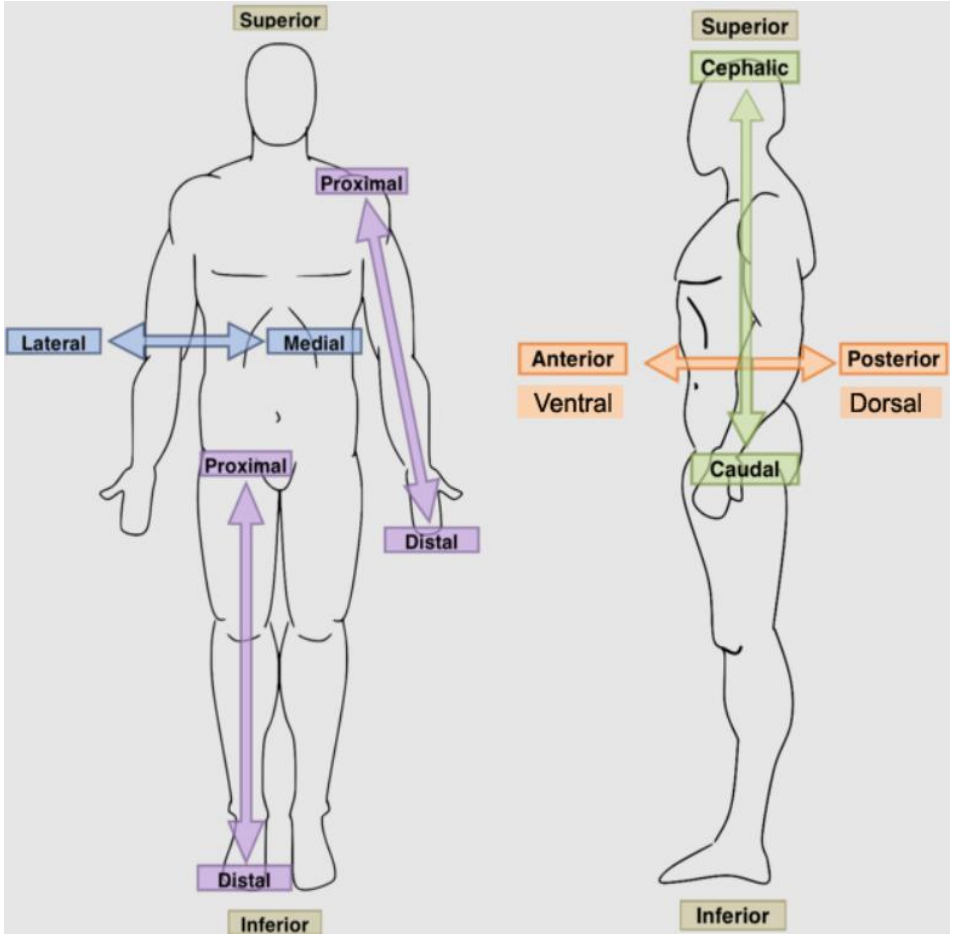
In embryology, directional terms relate to the long axis of the neural tube and the early curved shape of the embryo, differing from standard adult anatomical terminology

1. Longitudinal Axis (Head-to-Tail)

- **Cranial / Rostral:** Toward the head or the anterior end of the neural tube (Rostral specifically refers to structures within the brain).
- **Caudal:** Toward the tail or the inferior end of the embryonic body

2. Dorso-Ventral Axis (Back-to-Belly)

- **Dorsal:** Toward the back surface of the embryo.
- **Ventral:** Toward the belly or the anterior surface of the embryo.



3. Medial-Lateral Axis (Center-to-Side)

- **Medial:** Toward the midline or the central longitudinal axis of the embryo.
- **Lateral:** Away from the midline, toward the outer sides of the body.

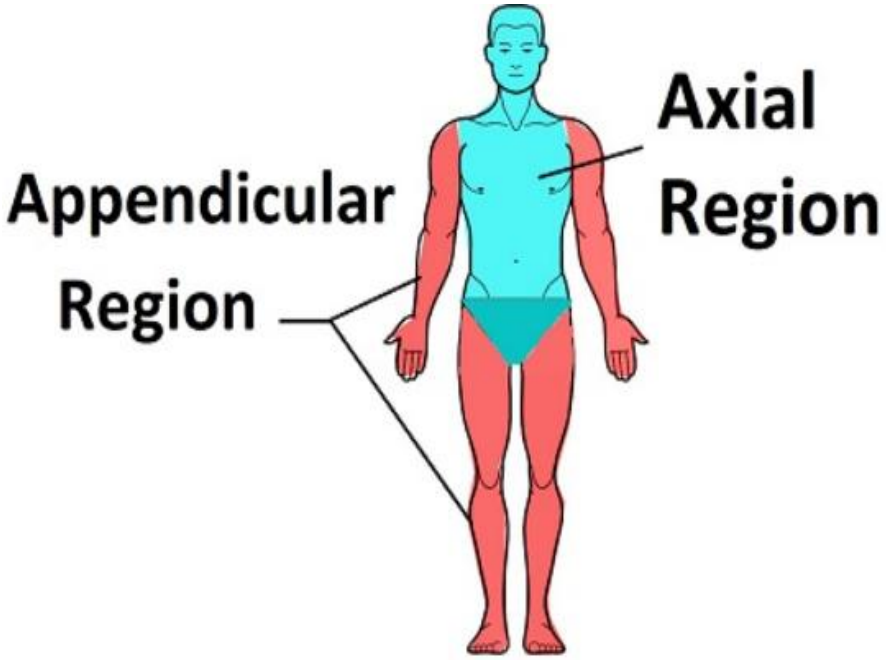
4. Limb & Organ Development

- **Proximal:** Closer to the point of attachment or the main body trunk.
- **Distal:** Farther away from the point of attachment (e.g., developing digits).

Embryological Anatomical Directional Terms

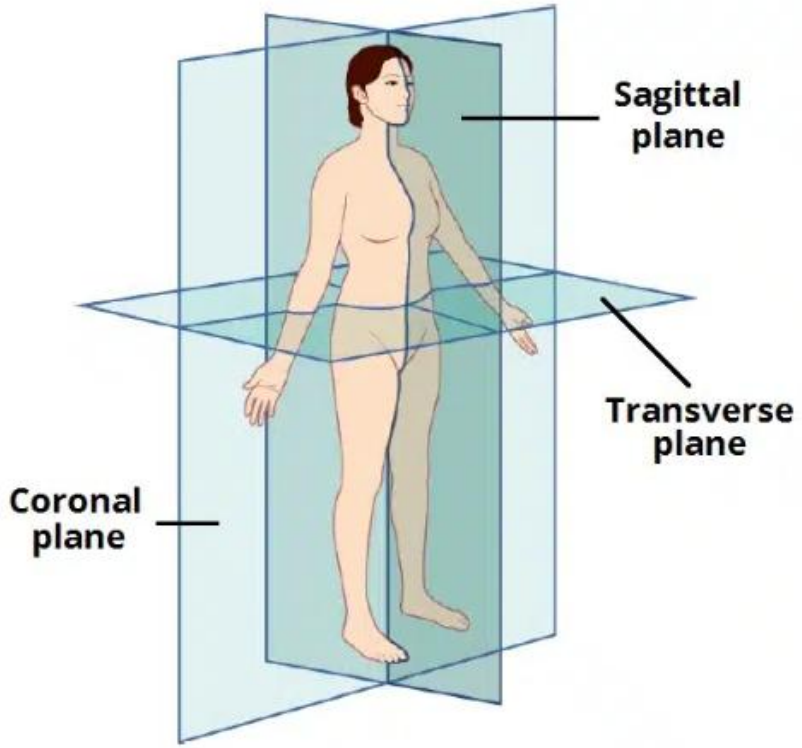
Regional Terms

- **Axial:** Located directly on or along the central longitudinal axis of the embryo (e.g., notochord, head, neck and trunk, the core of the body);
- **Paraxial:** Located immediately adjacent to or alongside the central axis (e.g., paraxial mesoderm)
- **Appendicular:** Specific of the upper and the lower limbs

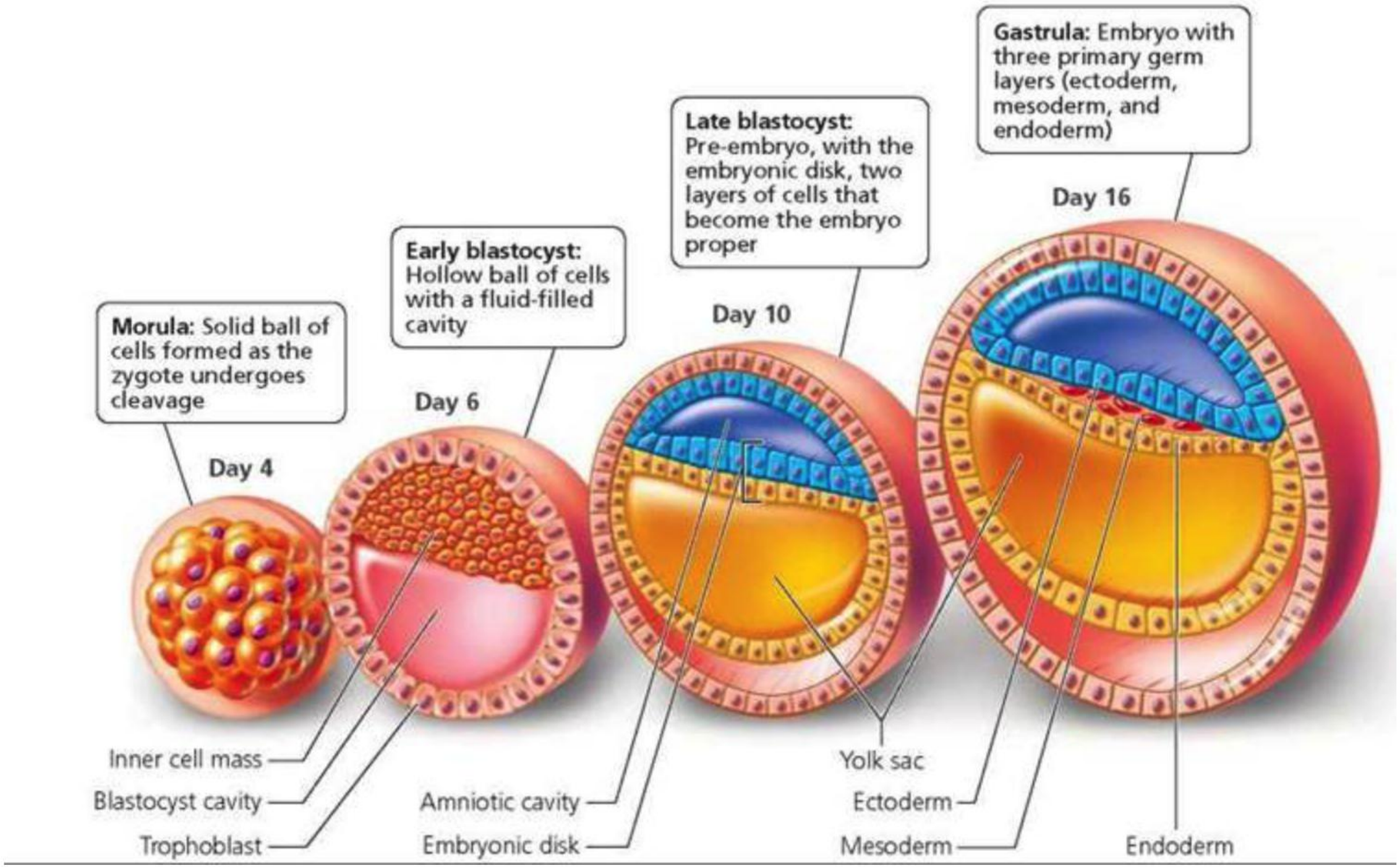


Anatomical Planes

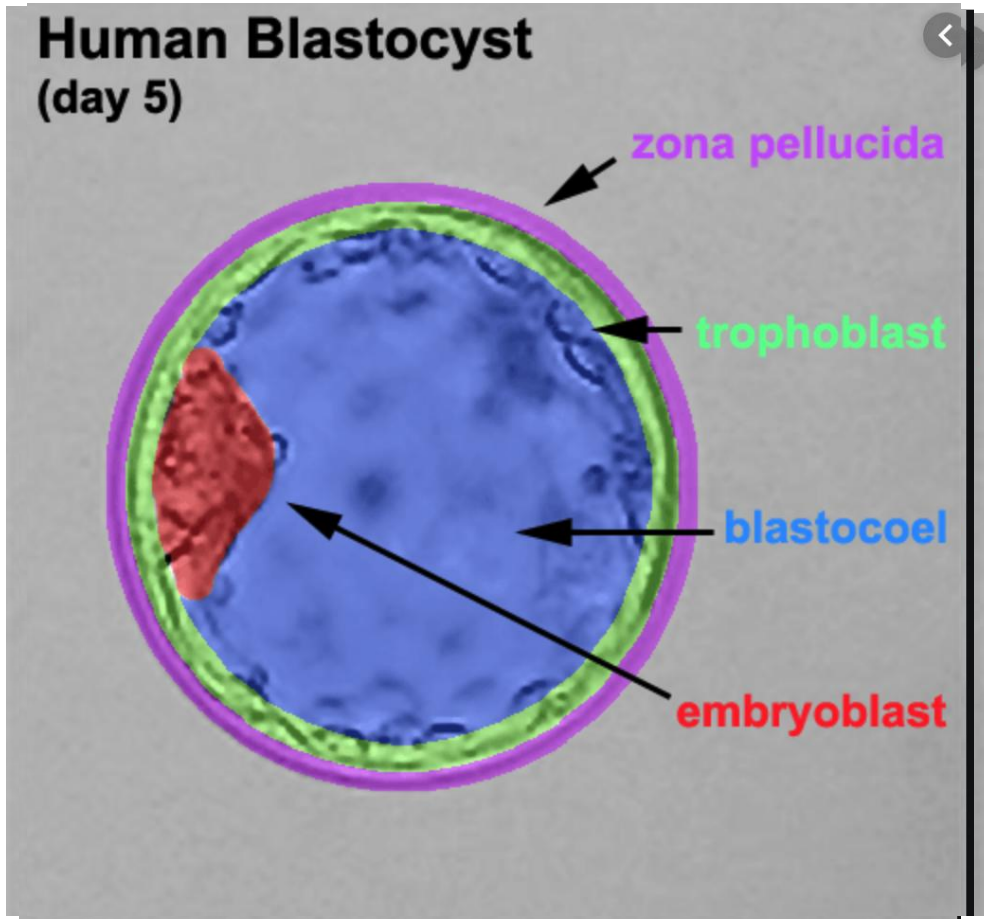
- **Sagittal (vertical) plane**: a cut dividing the body into left and right portions.
- **Coronal (Frontal) plane**: a vertical cut dividing the body into anterior (front) and posterior (back) portions.
- **Transverse (horizontal) plane**: a horizontal cut dividing the body into superior (upper) and inferior (lower) portions.



Cleavage: From Morula to Blastocyst

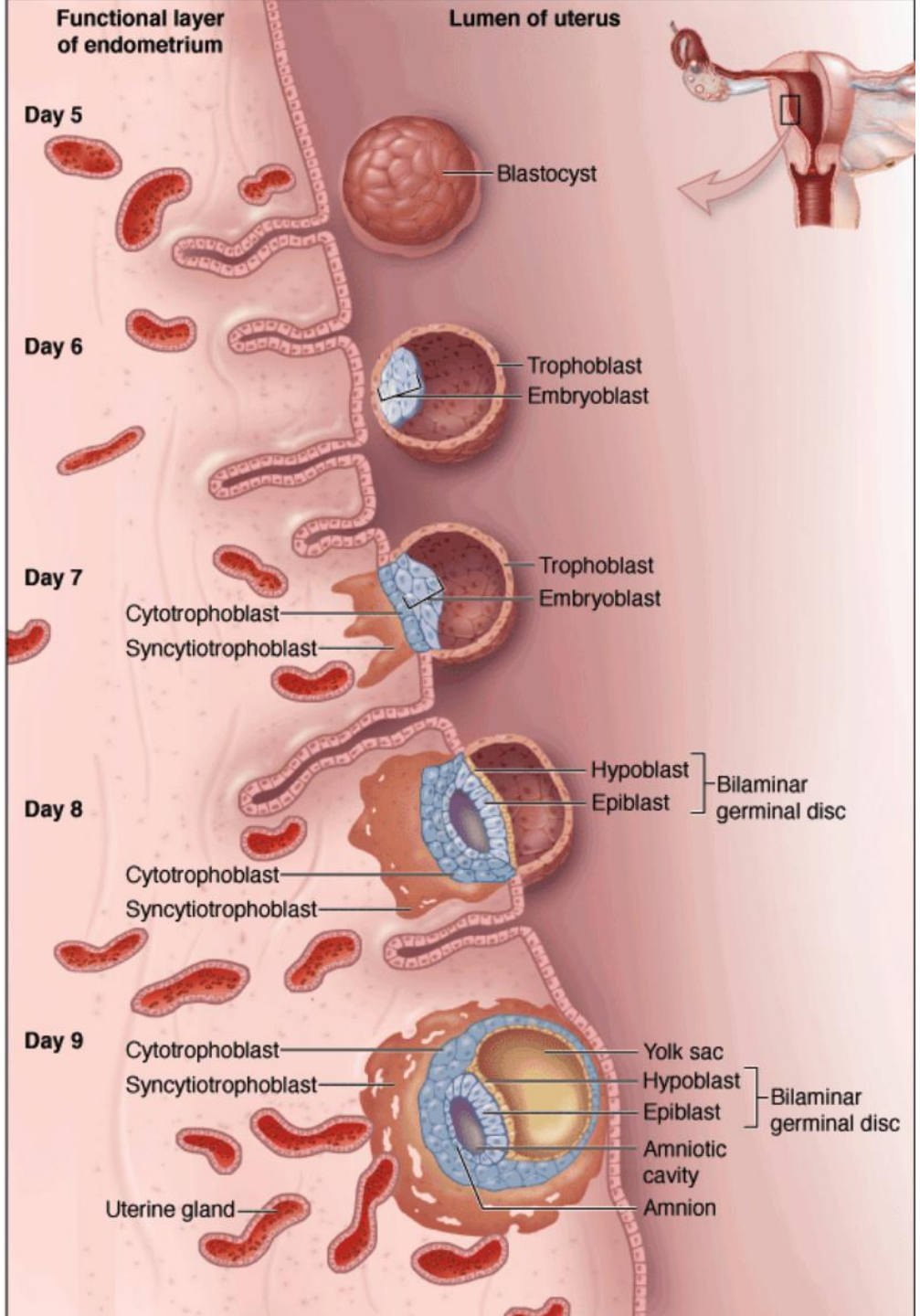


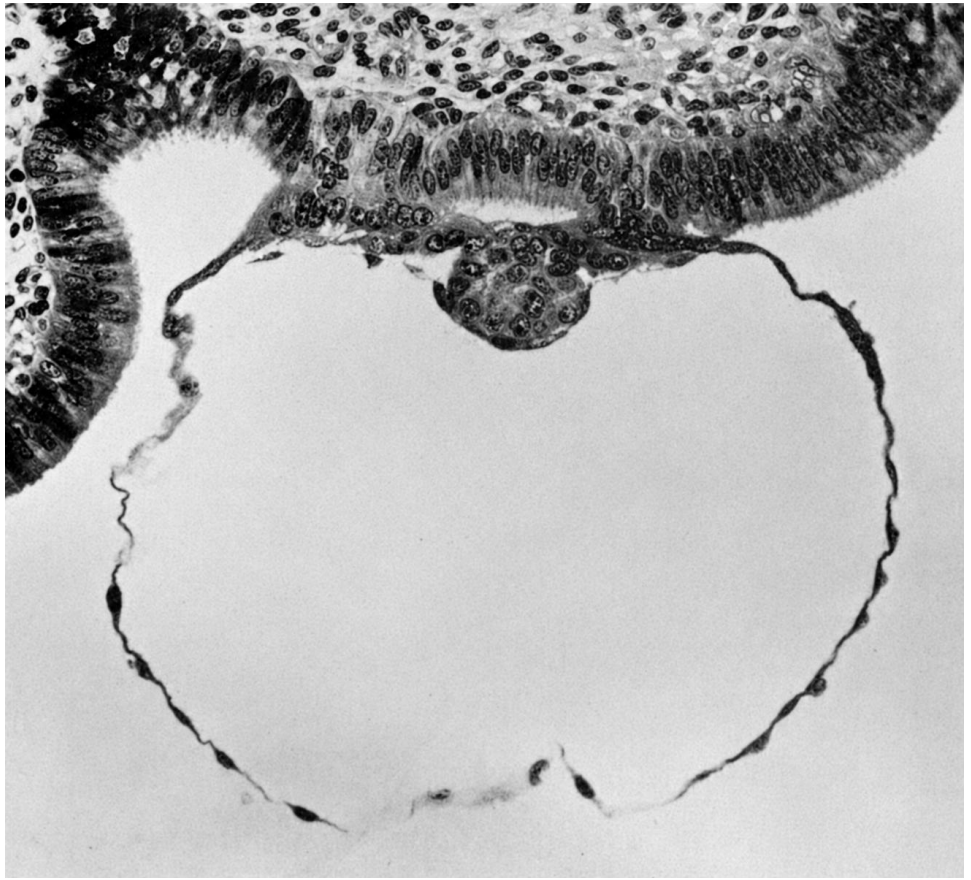
Anatomy of the Blastocyst



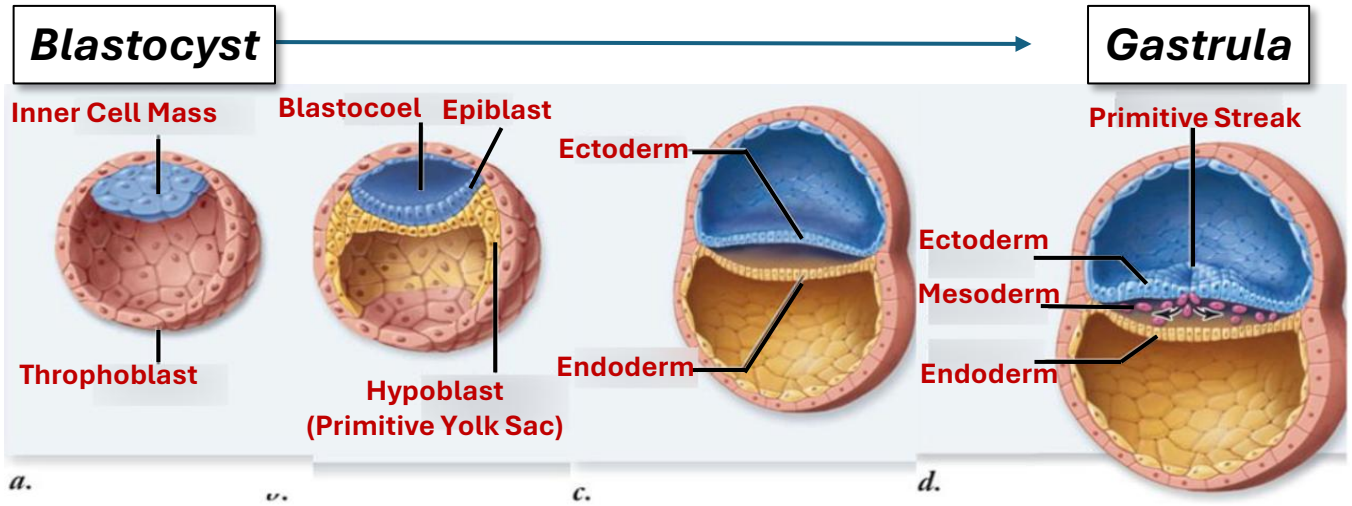
- **Zona pellucida** is a clear, thick outer layer of glycoproteins that surrounds a mammalian egg cell. It protects the egg, helps sperm bind to it during fertilization, and stops extra sperm from entering the egg after one gets inside.
- **Trophoblast:** The outer epithelial cell layer of the mammalian blastocyst. It mediates attachment to and invasion of the uterine endometrium and contributes extensively to the **fetal component of the placenta**.
- **Cytotrophoblast:** The inner, **mononuclear and mitotically active** trophoblast layer. Cytotrophoblast cells proliferate and differentiate to generate other trophoblast populations, including the syncytiotrophoblast.
- **Syncytiotrophoblast:** The outer, **multinucleated trophoblast layer** formed by fusion of cytotrophoblast cells. It directly contacts maternal tissues, promotes implantation by invading the endometrium, contributes to maternal–fetal exchange, and secretes hormones such as **human chorionic gonadotropin (hCG)**.
- **Embryoblast / Inner cell mass (ICM):** A cluster of cells located inside the mammalian blastocyst that gives rise primarily to the **embryo proper** and to some extraembryonic tissues. It later differentiates into the **epiblast** and **primitive endoderm (hypoblast)**.
- **Blastocoel:** The **fluid-filled cavity** that forms within the blastula or blastocyst. In mammals, it separates the inner cell mass from much of the surrounding trophoblast and helps establish the characteristic architecture of the blastocyst.

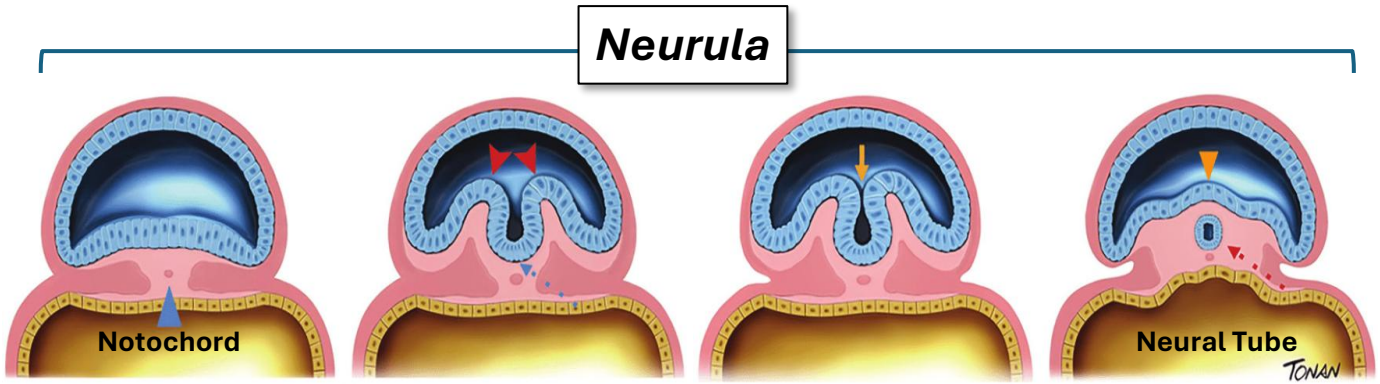
IMPLANTATION: primate emrbyogenesis





Gastrulation reorganises the embryo

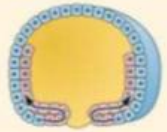
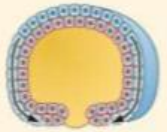




- **Gastrulation** is a **coordinated series of cell** and **tissue movements** that reorganises the blastula.
- These rearrangements establish the **three primary germ layers**: **ectoderm, mesoderm and endoderm**.
- Cells entering the embryo generally contribute to mesodermal and endodermal structures, whereas **other cells remain externally positioned**.
- Gastrulation also **contributes to the formation** of the **primitive digestive cavity** and the organisation of the **body axes**.
- **Cell fate** becomes **closely linked to spatial position and communication** with surrounding cells.
- **Neurulation and organogenesis** transform germ layers into tissues and organ primordia.

Types of Cell Movement during Gastrulation

TABLE 1.1 • Types of Cell Movements during Gastrulation[a]

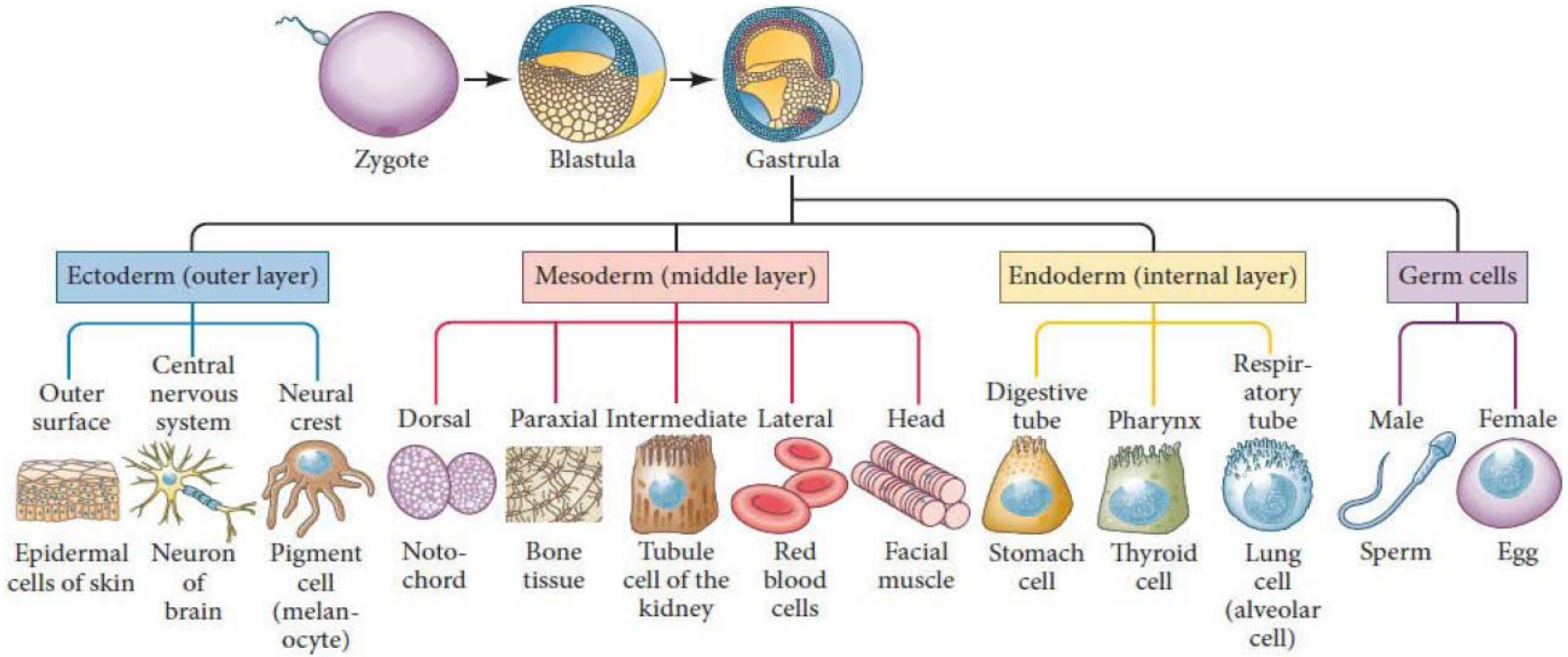
Type of movement	Description	Illustration	Example
Invagination	Folding inward of a region of cells in a cell layer (epithelium), quite similar to the inward budding that produces a soft rubber ball that is compressed at one point.		Endoderm of the sea urchin
Involution	Introduction of an outer cell layer into the interior as an expanding sheet that then spreads along the internal surface of the remaining cells.		Mesoderm of amphibians
Ingression	Migration of individual cells from the outer cell layer into the interior of the embryo. The cells become distinct mesenchymal cells (they separate from one another) and migrate in an independent manner.		Mesoderm of the sea urchin, *Drosophila* neuroblasts
Delamination	Division of a cell layer into two or more parallel layers. Despite their shared cellular base at the point of entry, the result is the formation of an entirely new cell layer.		Formation of the hipoblast in mammals and birds
Epiboly	Movement of sheets of epithelial cells (usually ectodermal cells) that spread as a unified group, sometimes individually, to envelop internal layers of the embryo. Epiboly may occur by cell division, changes in cell shape, or intercalation of a small number of intermediate layers; often all three mechanisms are involved.		Formation of the ectoderm in amphibians, sea urchin and tunicates

Gastrulation reorganises the embryo

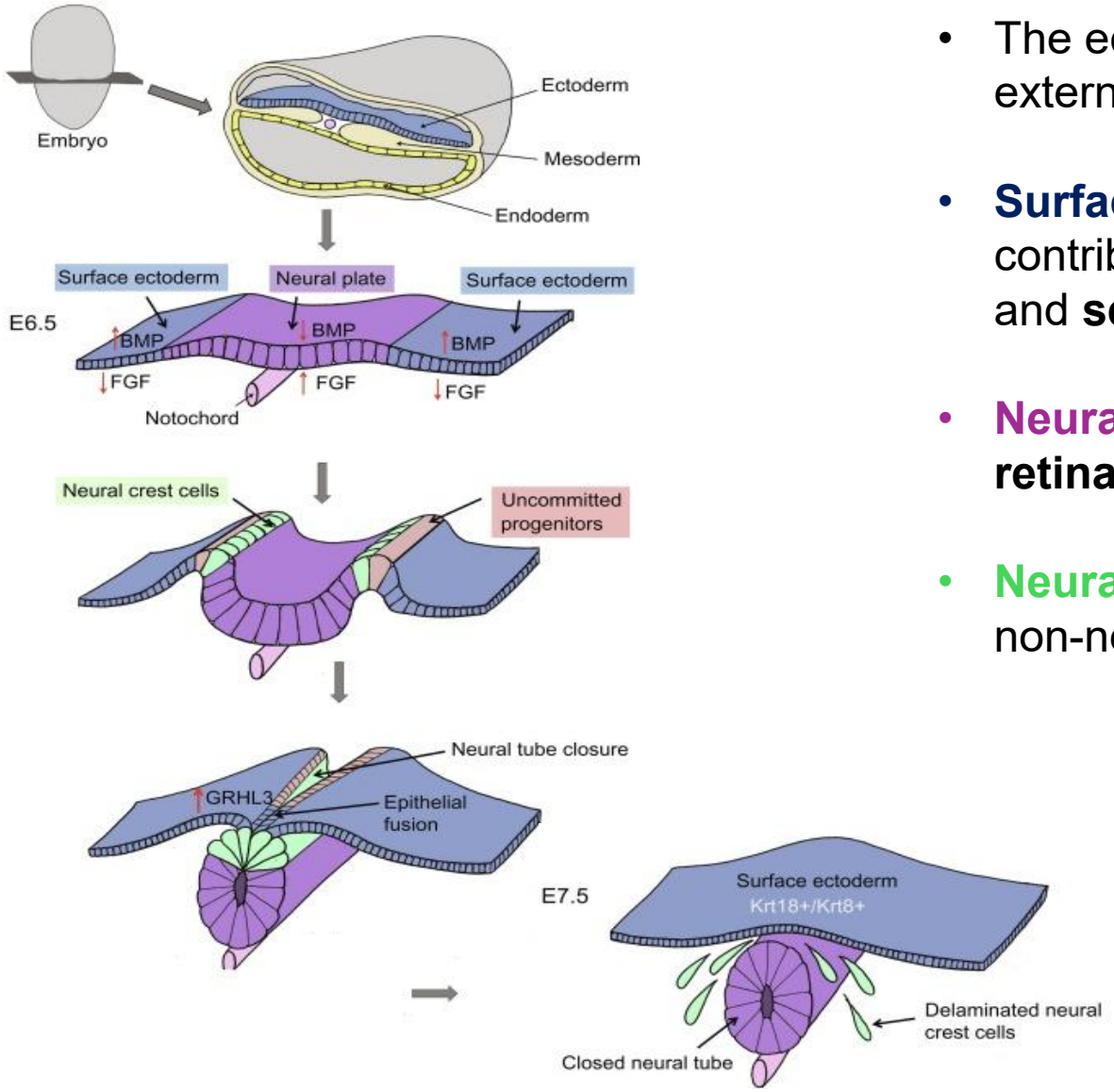
- **Ectoderm** occupies the external region of the gastrulated embryo.
- **Mesoderm** forms between ectoderm and endoderm.
- **Endoderm** occupies the internal region and contributes to the primitive digestive tube.

- Each germ layer generates **multiple differentiated cell types and organ** systems.
- **Germ-layer** identity **describes developmental origin, not the final position** of every descendant cell.

- **Germ cells** are generally treated as a distinct lineage rather than as derivatives of one specific germ layer.

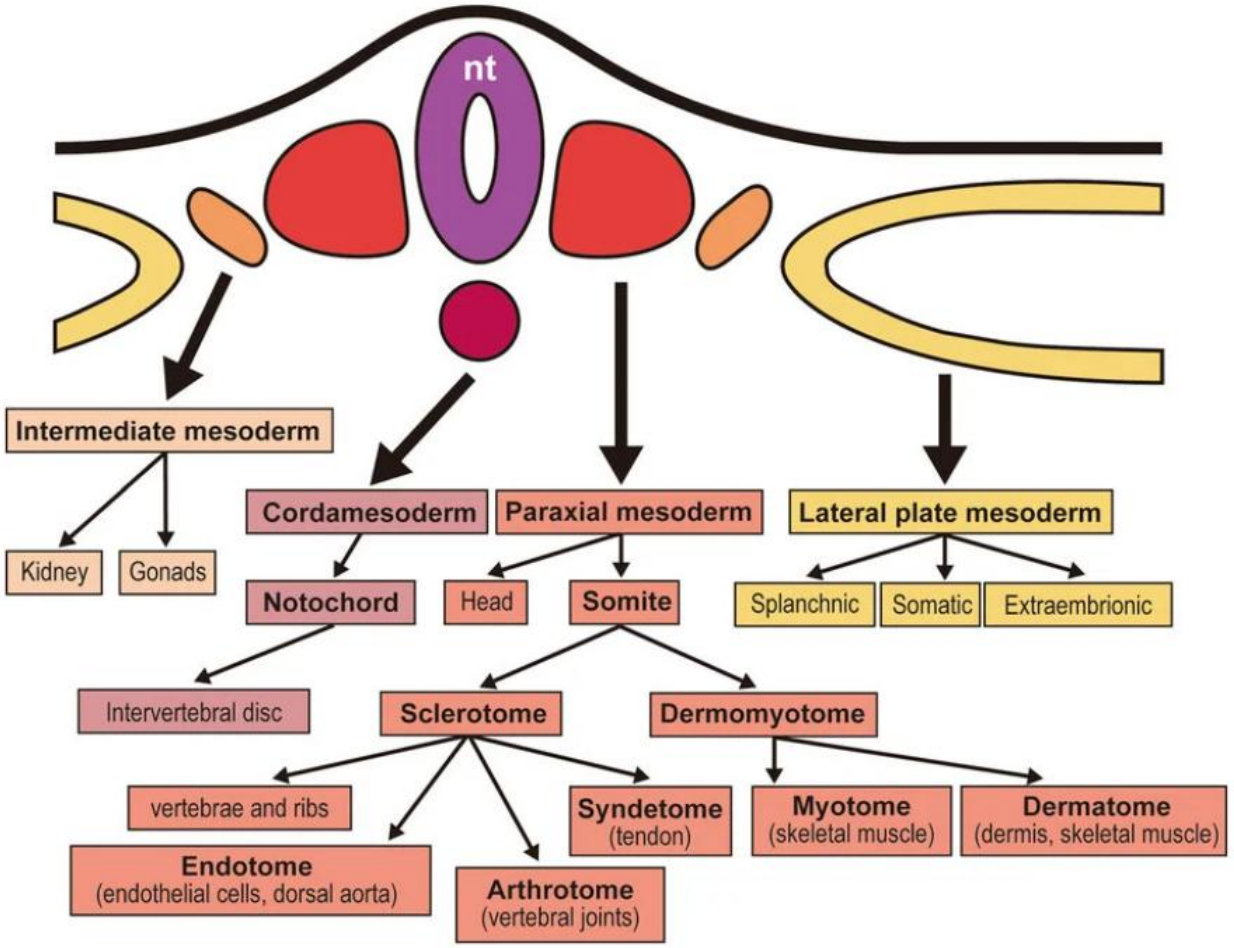


Principal derivatives of the ectoderm



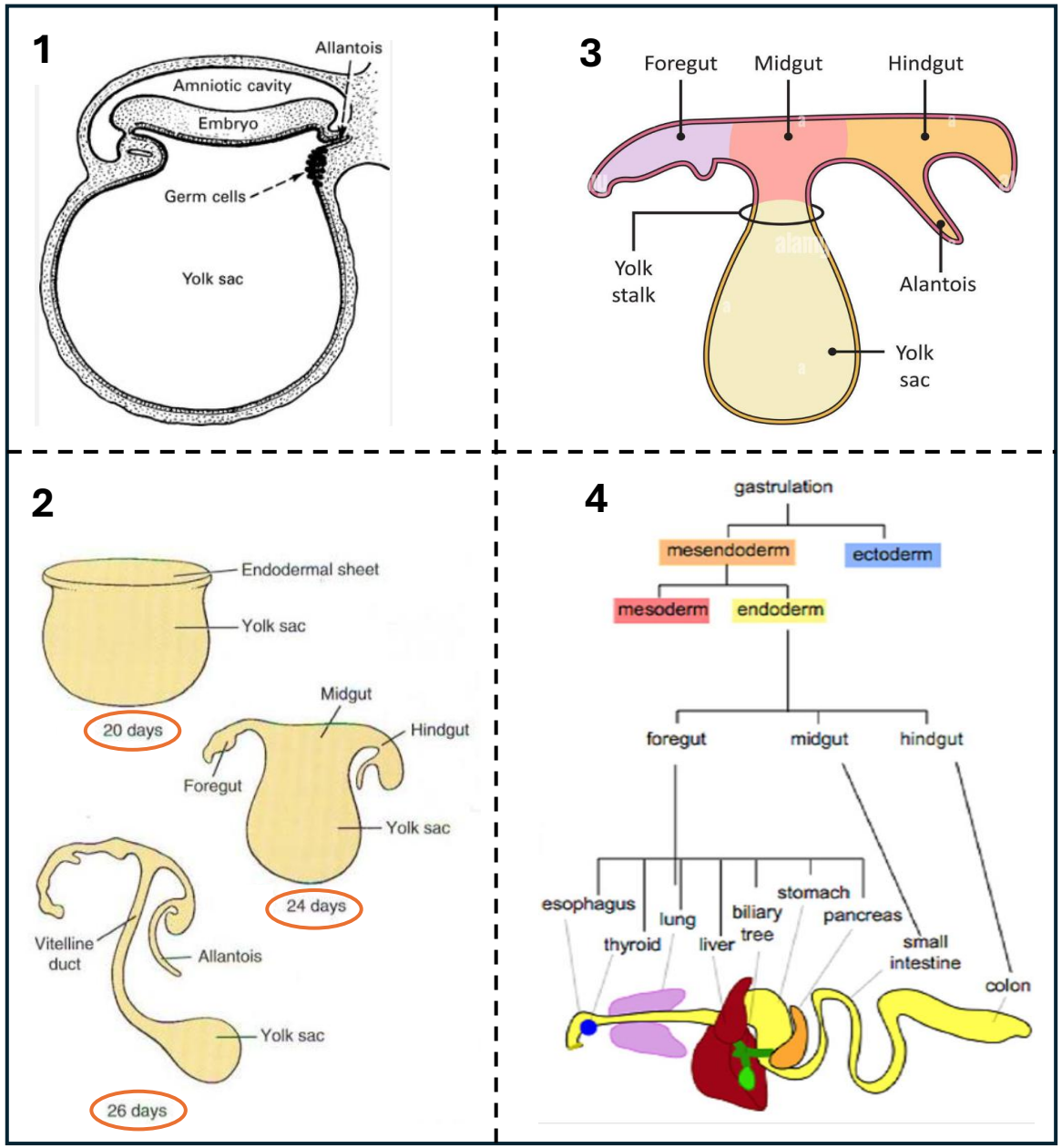
- The ectoderm generates structures that interact with the external environment and process sensory information.
- **Surface ectoderm** forms the **epidermis** and contributes to structures such as **hair, nails, glands** and **sensory epithelia**.
- **Neural ectoderm** forms the **brain, spinal cord** and **retina**.
- **Neural crest cells** originate at the border of neural and non-neural ectoderm and then migrate extensively.
- **Neural crest derivatives** include much of the **peripheral nervous system, pigment cells** and selected **craniofacial tissues**.
- **Ectodermal derivatives** are diversified through inductive signals and differences in spatial position.

Principal derivatives of the mesoderm



- Mesoderm generates many **tissues** responsible for **support, movement, circulation** and **internal transport**.
- Major derivatives include **skeletal, cardiac and smooth muscle**.
- Mesoderm contributes to **connective tissues, cartilage, bone** and **much of the dermis**.
- **Blood cells**, the **heart** and the **vascular system** are predominantly mesodermal.
- The **kidneys**, **gonads** and associated **reproductive ducts** also arise mainly from mesoderm.
- **Different mesodermal regions acquire distinct identities** along the body axes.
- Mesoderm formation and patterning **require signals exchanged with both ectoderm and endoderm**.

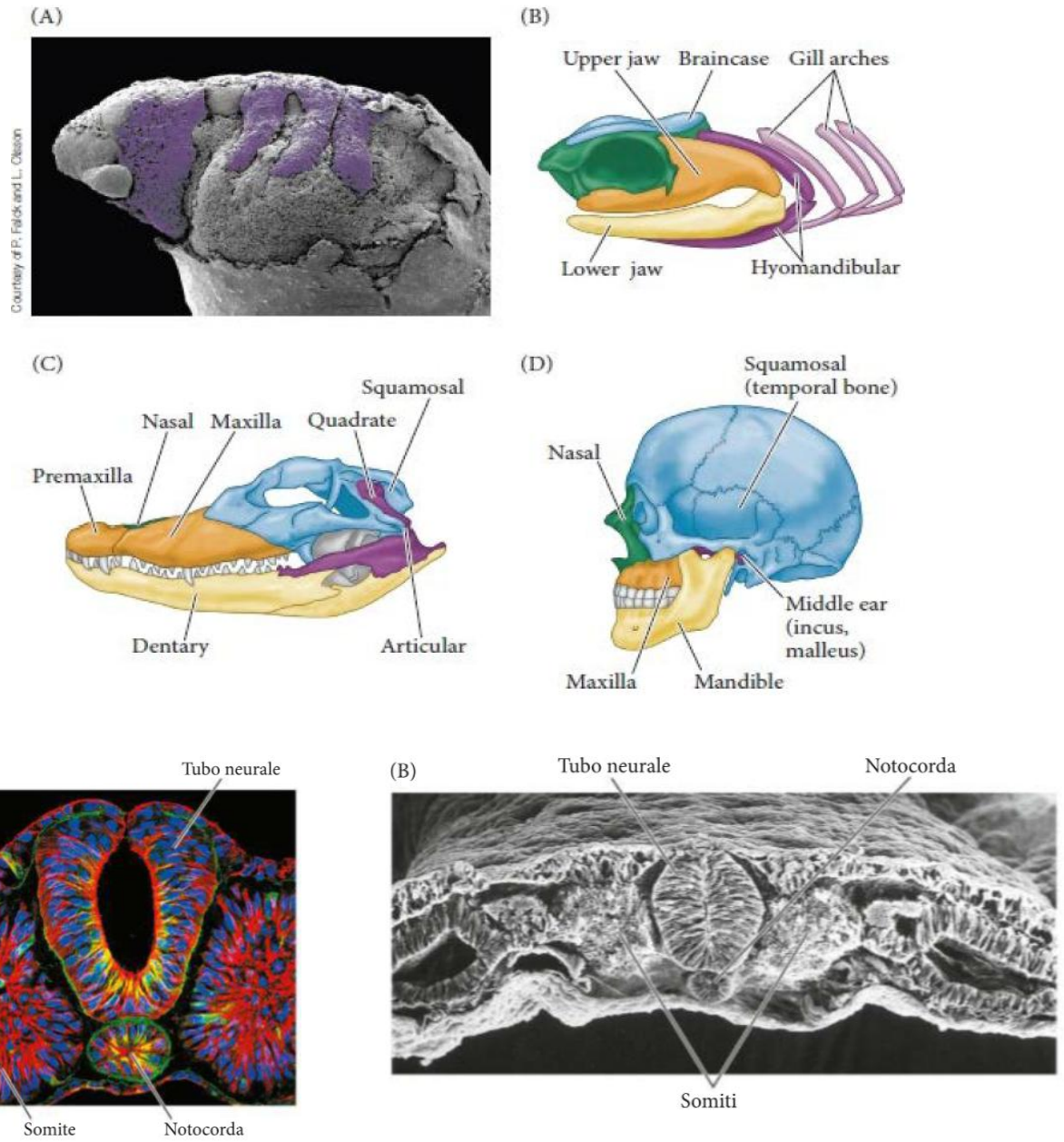
Principal derivatives of the endoderm



- Endoderm forms **much of the epithelial lining** of the **primitive gut** and its associated organs.
- It contributes to the epithelial **lining of the digestive and respiratory systems**.
- Endodermal outgrowths **participate in the formation** of organs such as the **liver and pancreas**.
- Endoderm also **contributes to epithelial components of** the **thyroid, parathyroid** and **thymus**.
- Surrounding mesoderm supplies connective tissue, muscle and blood vessels to many endoderm-derived organs.
- **Mature organs** therefore **commonly contain cells originating from more than one germ layer**.

Karl Ernst von Baer and the common vertebrate developmental plan

- **Karl Ernst von Baer** expanded Pander's work on the chick embryo and became one of the founders of **comparative embryology**.
- He recognised that **vertebrate embryos share** a **common developmental organisation**, even though the adult forms of fish, amphibians, birds and mammals are very different.
- Von Baer showed that the **germ layers give rise**, in broad terms, to **comparable categories of tissues and organs in all vertebrates**.
- He also described the **notochord**, a dorsal mesodermal rod that divides the embryo into right and left halves and helps induce the overlying **ectoderm to form** the **nervous system**.



The four principles of von Baer and the phylotypic stage

- **Principle 1: The general features** of a large animal group **appear earlier** in development **than** the **specialised features** of smaller groups.

*Thus, vertebrate embryos first share traits such as **pharyngeal arches, notochord, neural tube and primitive kidneys**.*

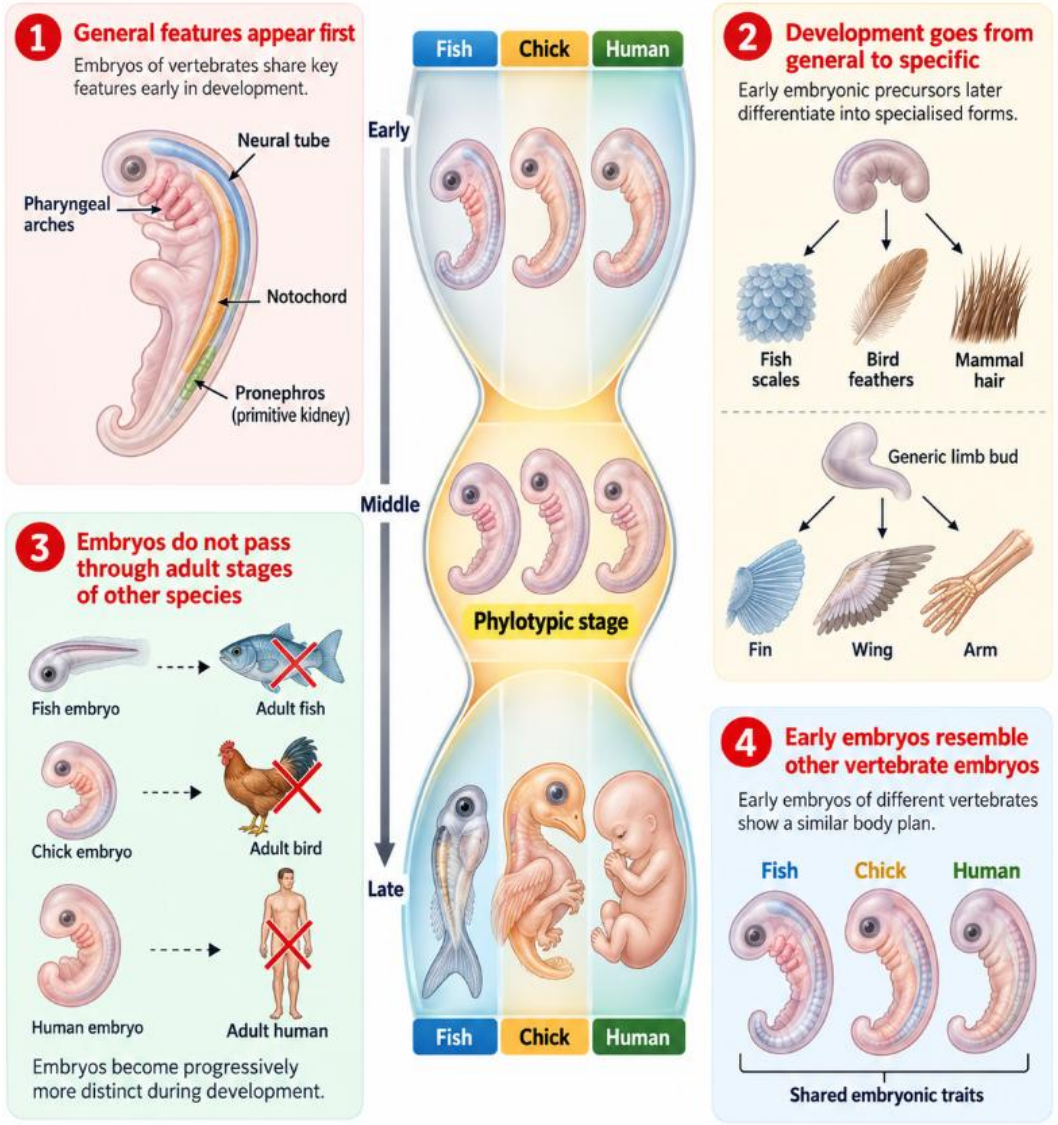
- **Principle 2: Development proceeds** from the **more general to** the **more specific**.

*For example, vertebrate skin begins from a common embryonic plan and only later differentiates into **fish scales, reptile scales, feathers, hair, claws or nails**. The same is true for limbs, which initially develop similarly before diverging into **legs, wings or arms**.*

- **Principle 3: The embryo of one species** does **not** pass through the **adult stages of other species**. Instead, it becomes progressively **more distinct** from them during development.

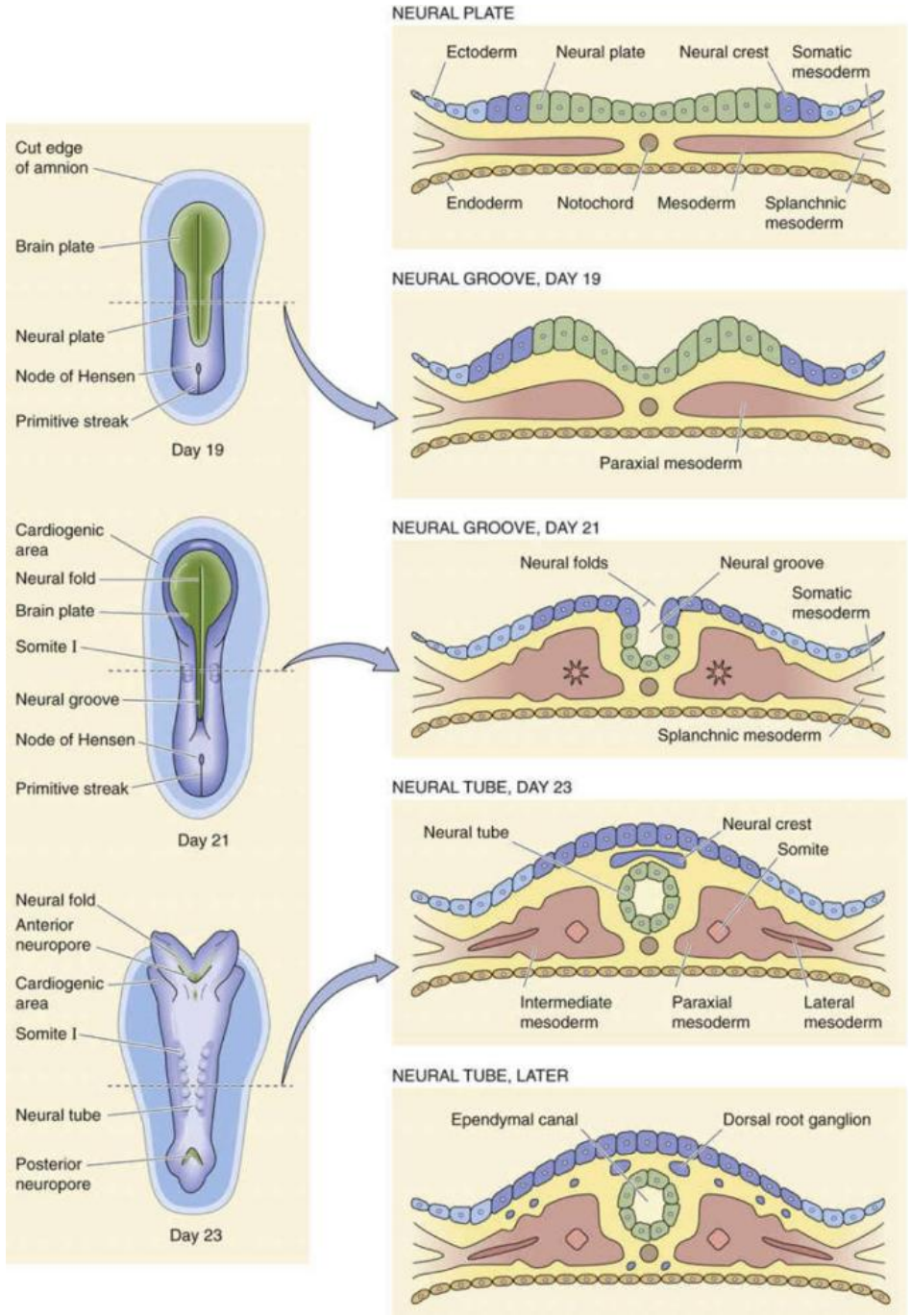
Human embryos, for example, do not pass through a "fish stage" or a "bird stage."

- **Principle 4: Therefore, the early embryo** of a more derived vertebrate **resembles the early embryos of other vertebrates**, not the adult forms of those vertebrates.



Vertebrate embryos converge on a similar body plan during the phylotypic stage, then diverge into species-specific forms.

Neurulation establishes the neural tube



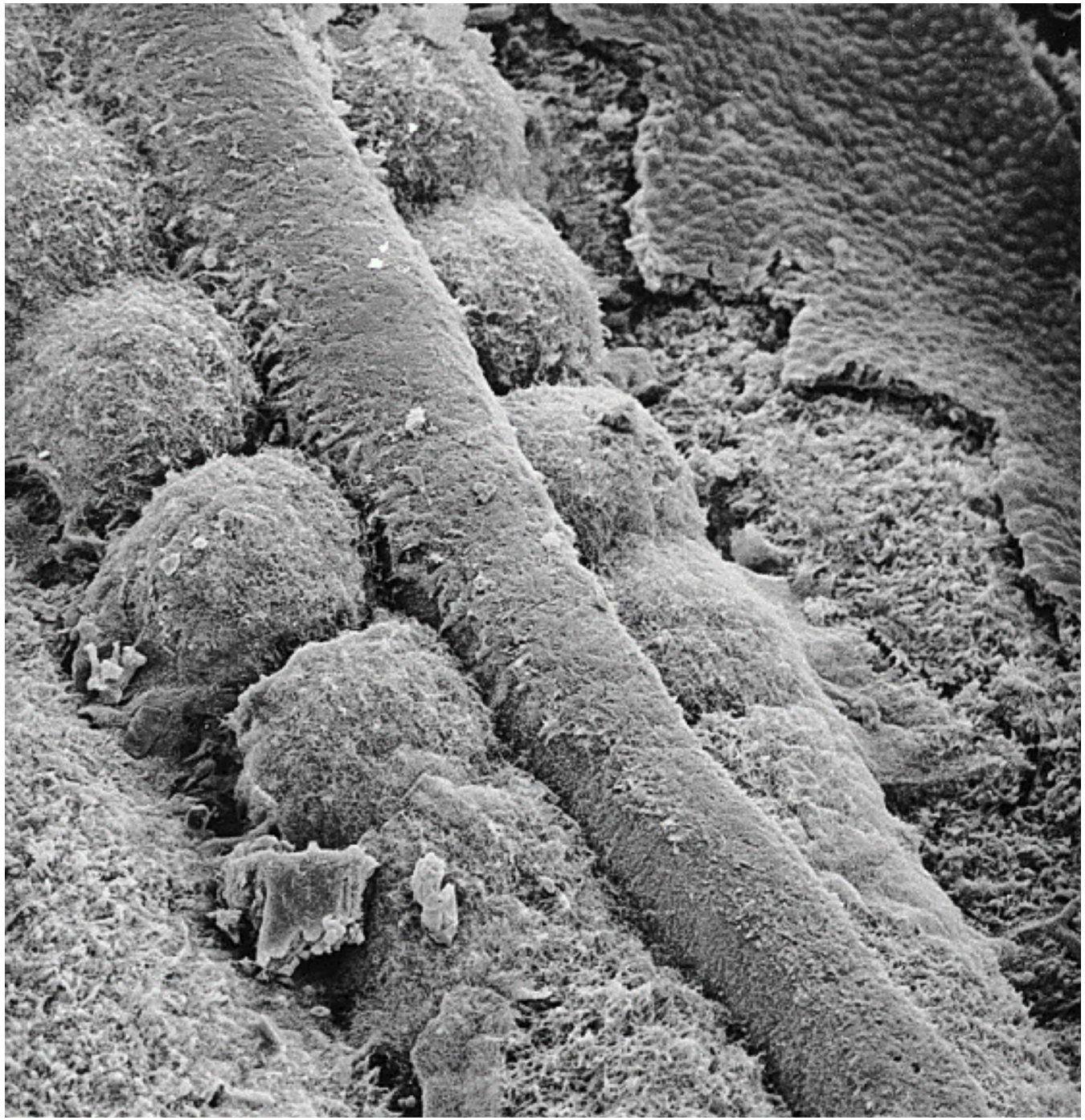
- **Neurulation** is the developmental process through which the early nervous system is established.
- Signals from underlying axial mesoderm induce overlying ectoderm to acquire a neural identity.
- The neural ectoderm thickens to form the **neural plate**.
- Changes in cell shape and tissue architecture elevate and move the neural folds toward the dorsal midline.
- Fusion of the folds produces the **neural tube**, the precursor of the brain and spinal cord.
- Surface ectoderm closes above the neural tube and contributes to the future epidermis.
- Neurulation illustrates the integration of induction, differentiation and morphogenesis.

What are somites?

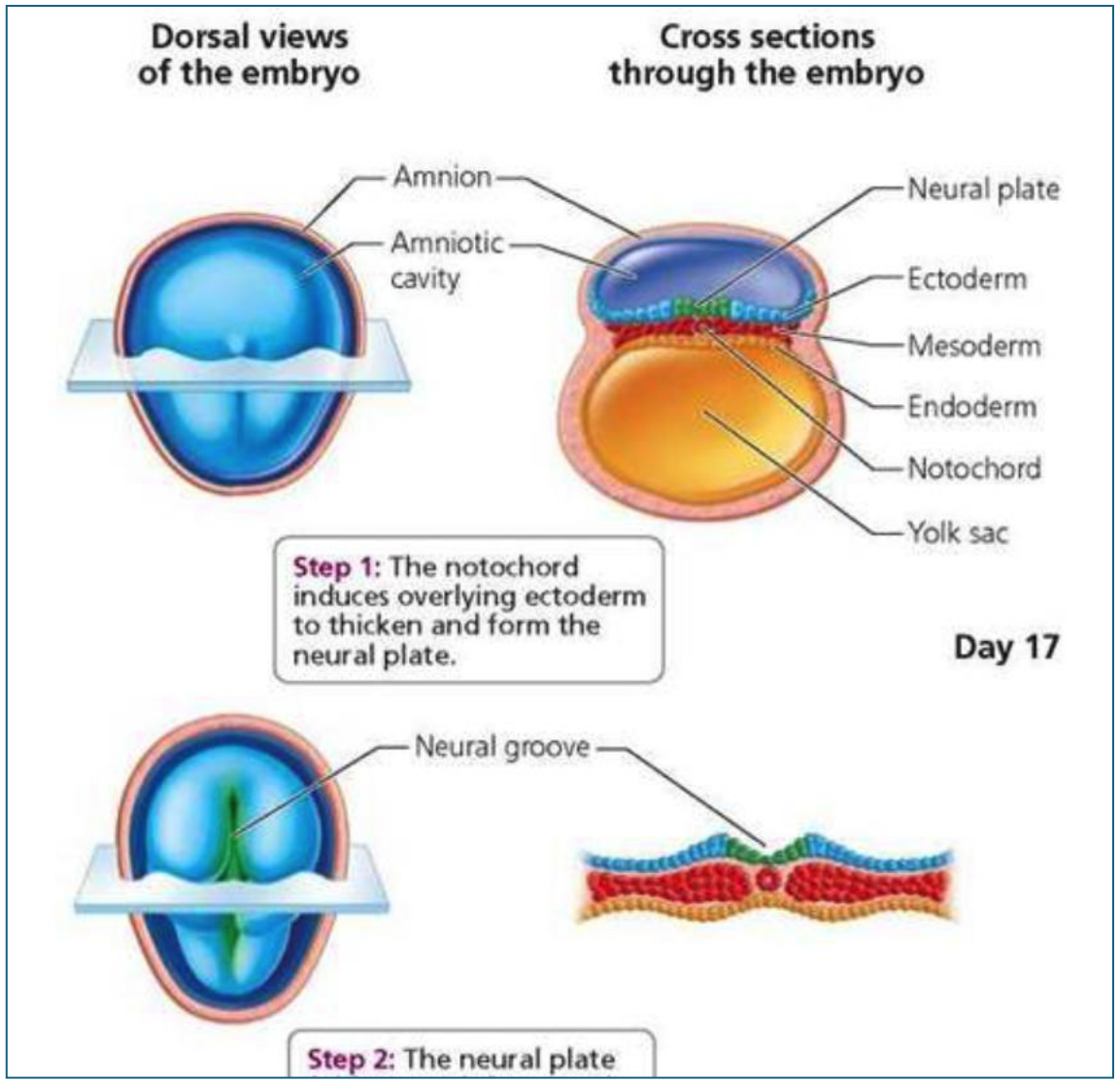
- Bilateral pairs of mesoderm along A/P axis

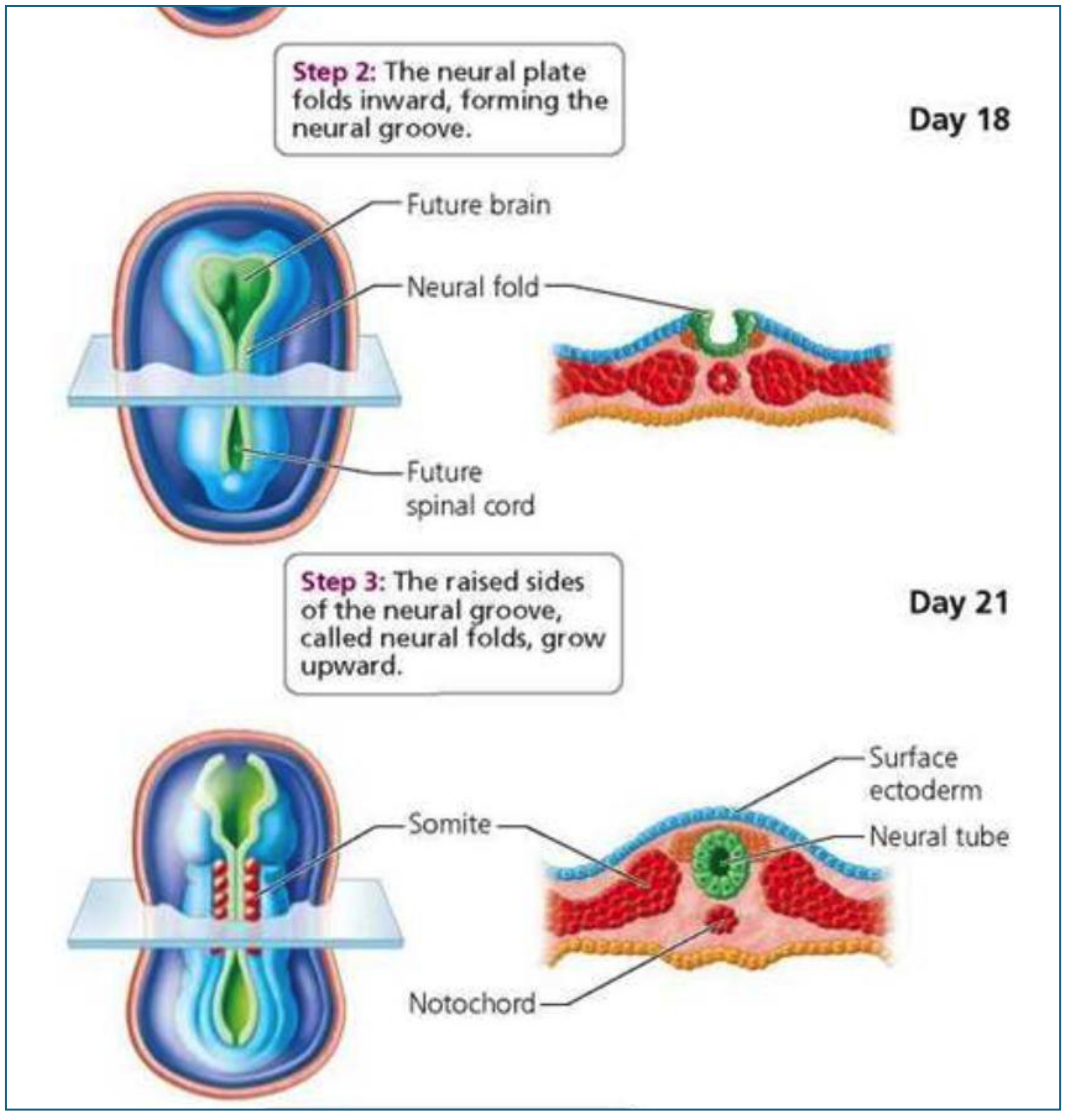
- Sclerotome → vertebrae, rib cage
- Myotome → skeletal muscle
- Dermatome → dermis (skin)

"**Somite formation** in all **vertebrates** proceeds from the **anterior** (cranial) to the **posterior** (caudal) end in a predetermined temporal sequence."



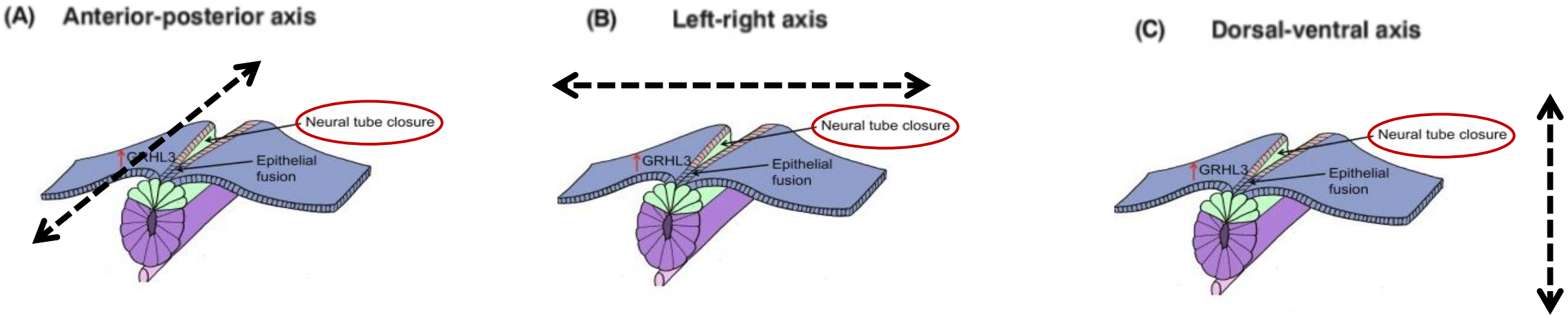
Neurulation establishes the neural tube



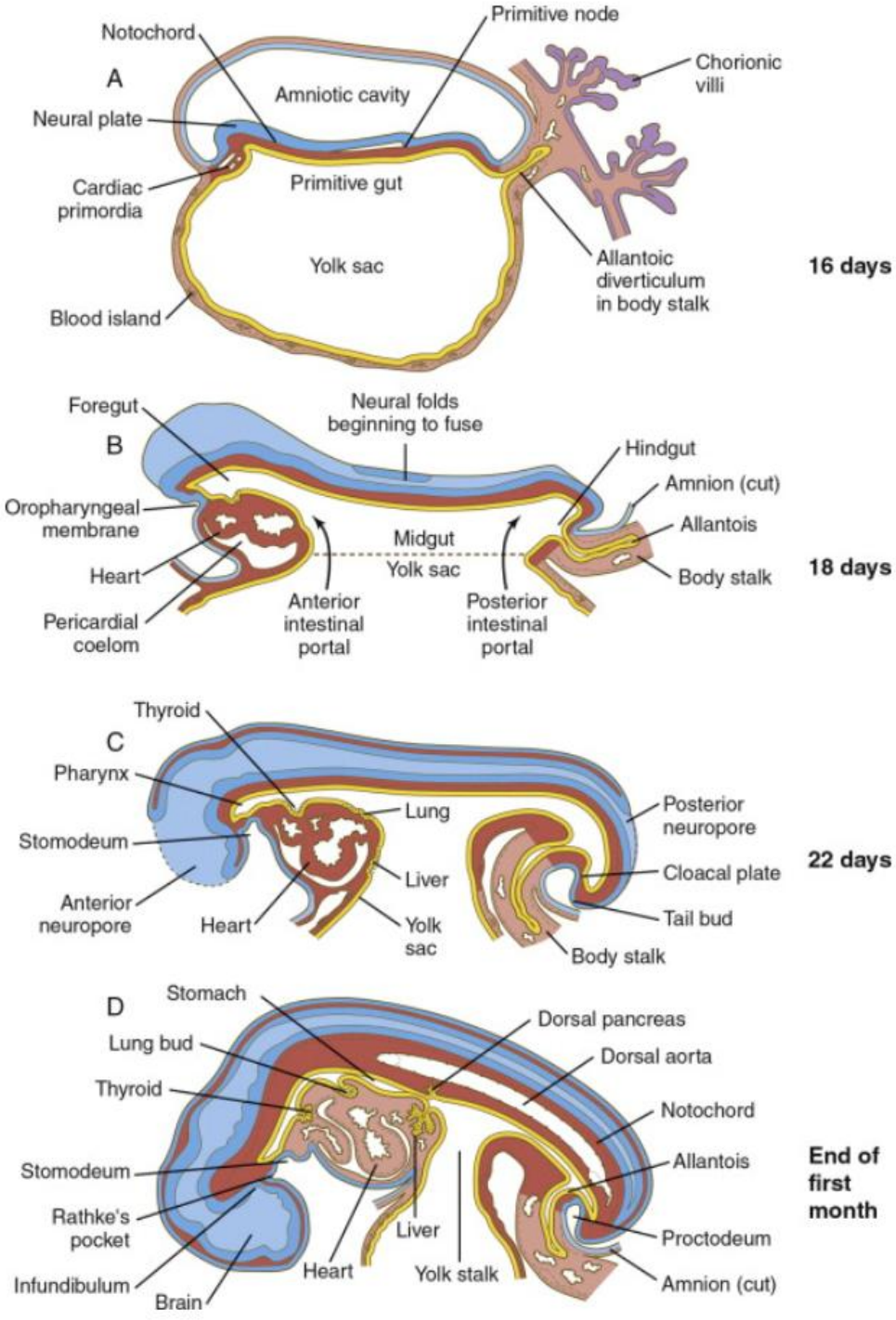


Establishing the body axes

The body plan is organised around three principal anatomical axes:



- The **anterior–posterior axis** extends from the head region toward the tail.
- The **dorsal–ventral axis** distinguishes the back from the belly.
- The **left–right axis** separates the two lateral sides and permits asymmetric organ positioning.
- Positional information along these axes allows cells with similar genomes to acquire different identities.
- The axes are progressively specified before and during gastrulation and refined during organogenesis.
- **Correct organ formation requires both cell-type specification and correct spatial orientation**.



Folding of the embryo

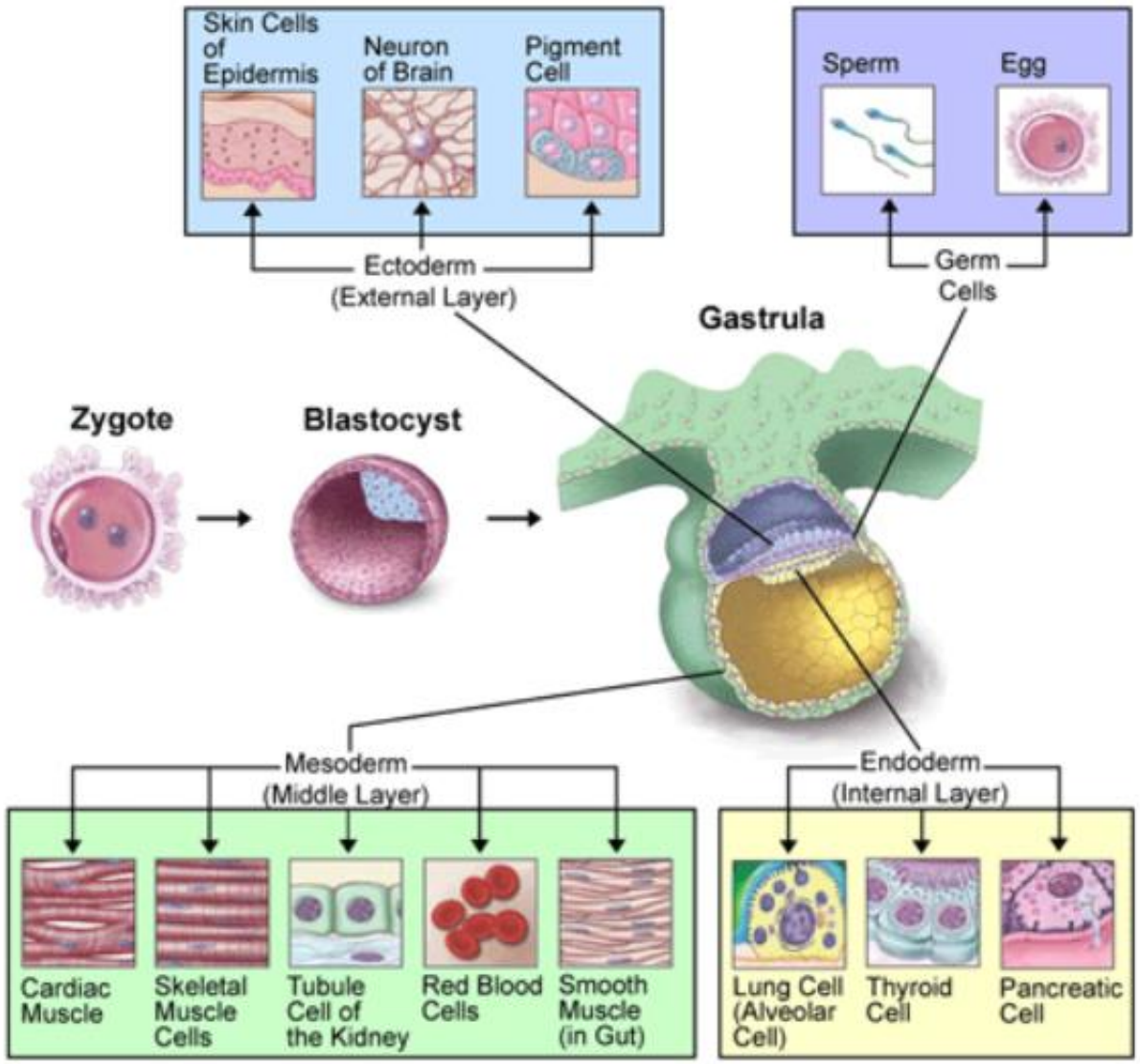
- During early development, the embryo undergoes **two major folding processes**: **cephalocaudal folding** (head-to-tail) and **lateral folding** (side-to-side). These movements transform the flat embryonic disc into a three-dimensional structure, partially enclosing the **endoderm-lined cavity** within the embryo. This enclosed cavity becomes the **primitive gut tube**, the precursor of the entire digestive system.

- At the **cranial end**, the primitive gut tube forms a closed, blind-ended region called the **foregut**. At the **caudal end**, a similar blind-ended region called the **hindgut** develops. These segments will later differentiate into specific components of the **digestive** and **respiratory** systems.

- The **midgut**, located between the foregut and hindgut, remains temporarily connected to the **yolk sac** through the **vitelline duct (yolk stalk)**. This connection supports early nutrient exchange before the yolk sac regresses as the placenta becomes the primary source of nourishment.

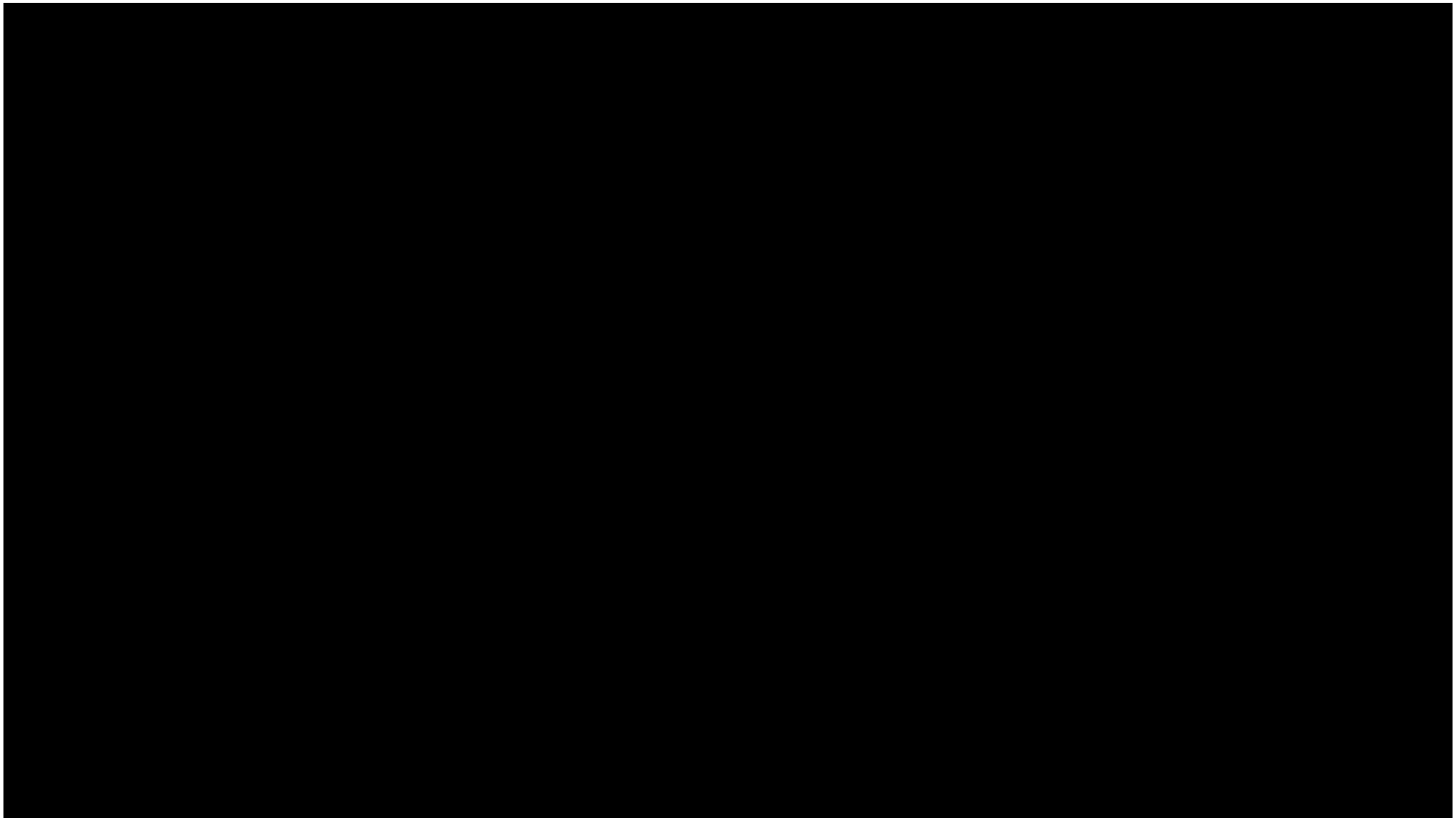
- The formation of the primitive gut is a critical step in embryogenesis, establishing the foundational structure from which the **gastrointestinal tract** and its associated organs will arise. Understanding these early folding events explains the spatial organization and later specialization of the digestive system.

Cell differentiation: the generation of diversity



- **Cell differentiation** is the process through which **cells acquire specialised molecular, structural** and **functional properties.**
- **Most somatic cells contain** essentially the **same genome** but express different combinations of genes.
- **Differential gene expression** produces distinct repertoires of RNA and protein.
- These **molecular differences** determine cellular **architecture**, **metabolism, communication** and **physiological function.**
- Differentiation is progressive and **may include intermediate states** before a mature phenotype is reached.
- ***Differentiation explains cellular diversity;***
- ***Morphogenesis explains how diverse** cells are **organised into functional structures**.*

From Fertilization to Blastocyst



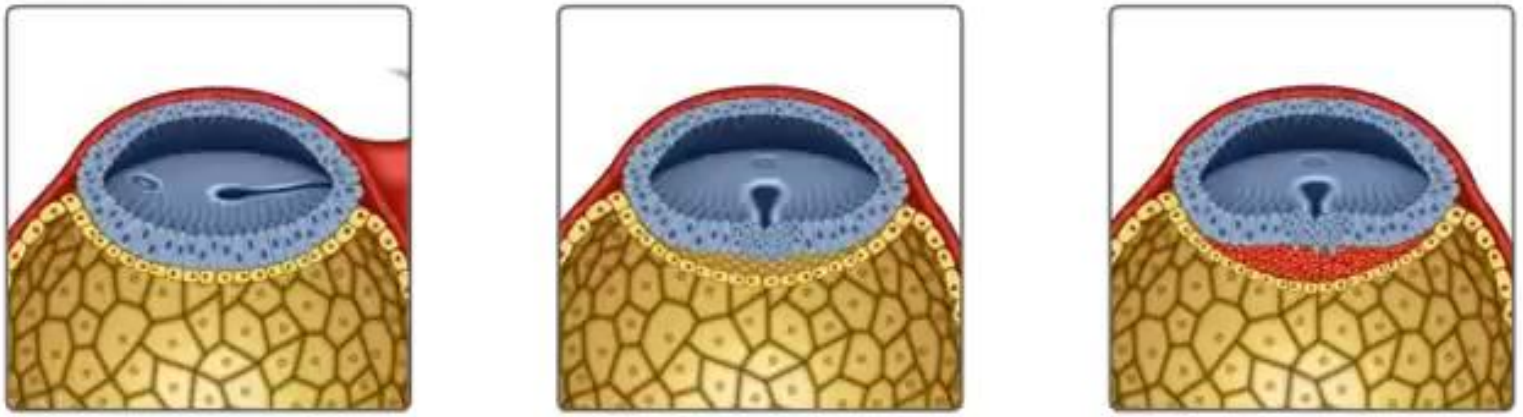
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Gatrulation

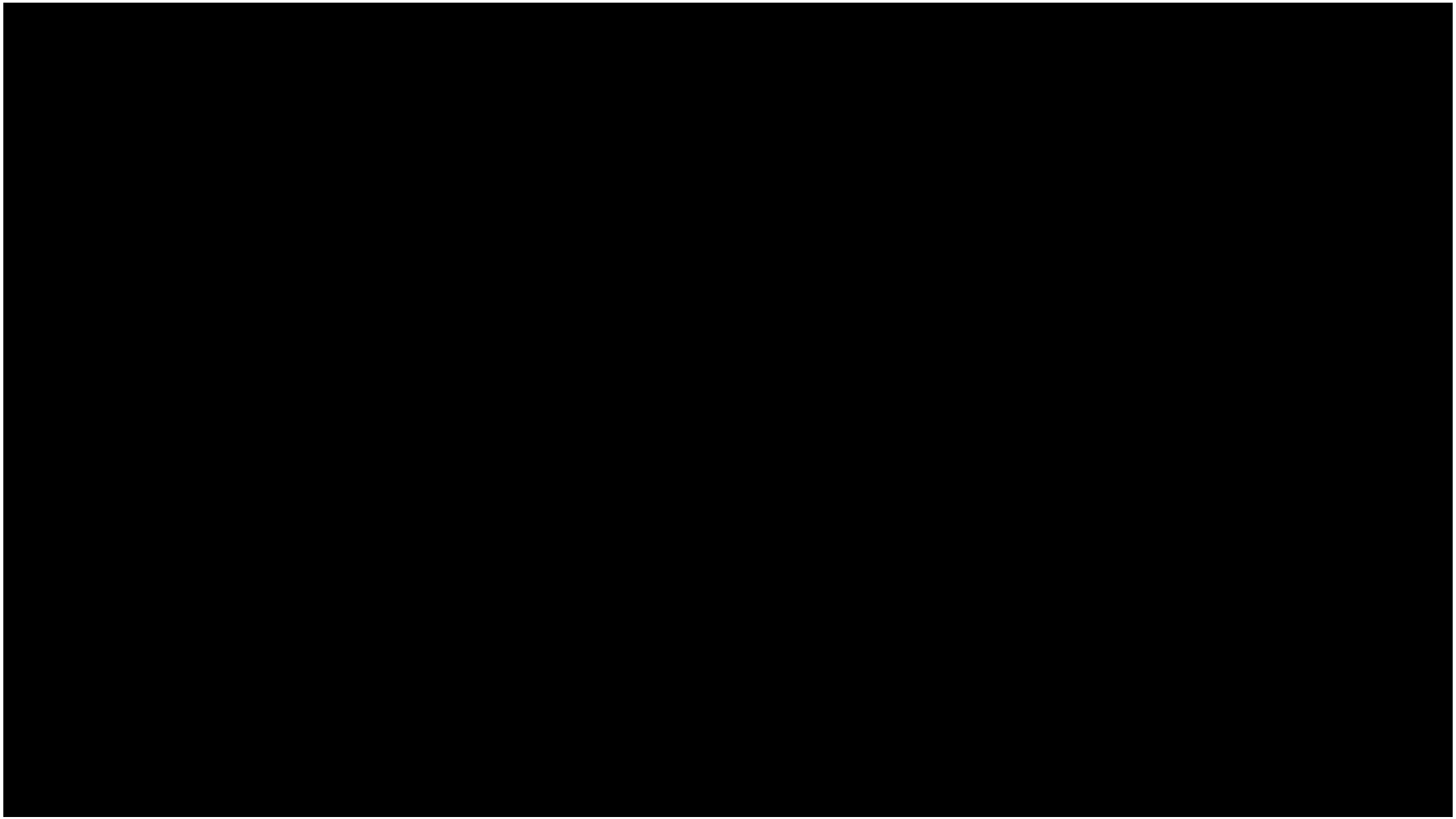
Gastrulation

Gastrulation is the process whereby the bilaminar embryonic disc undergoes reorganization to form a trilaminar disc.



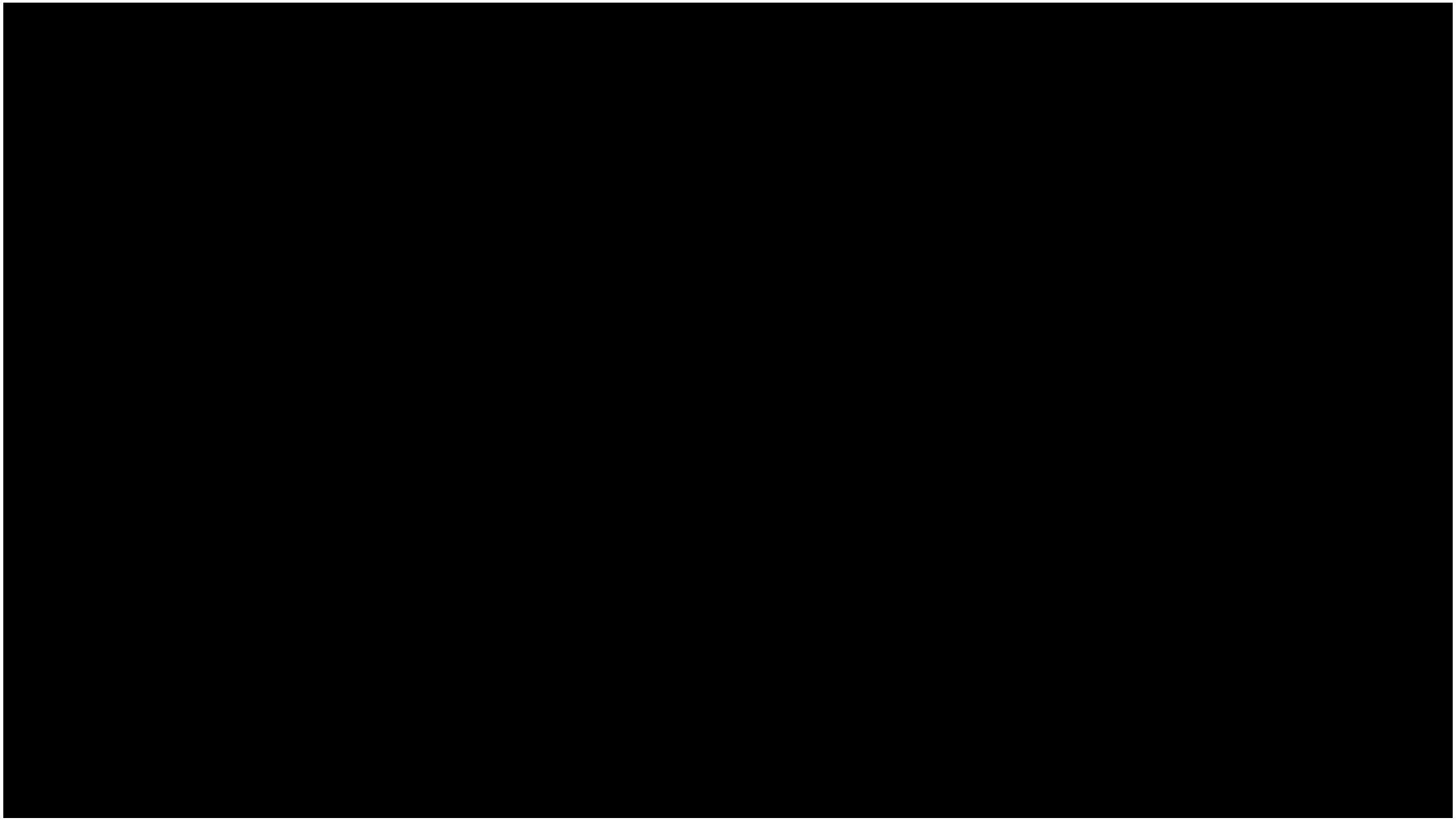
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How the Primitive Streak is formed



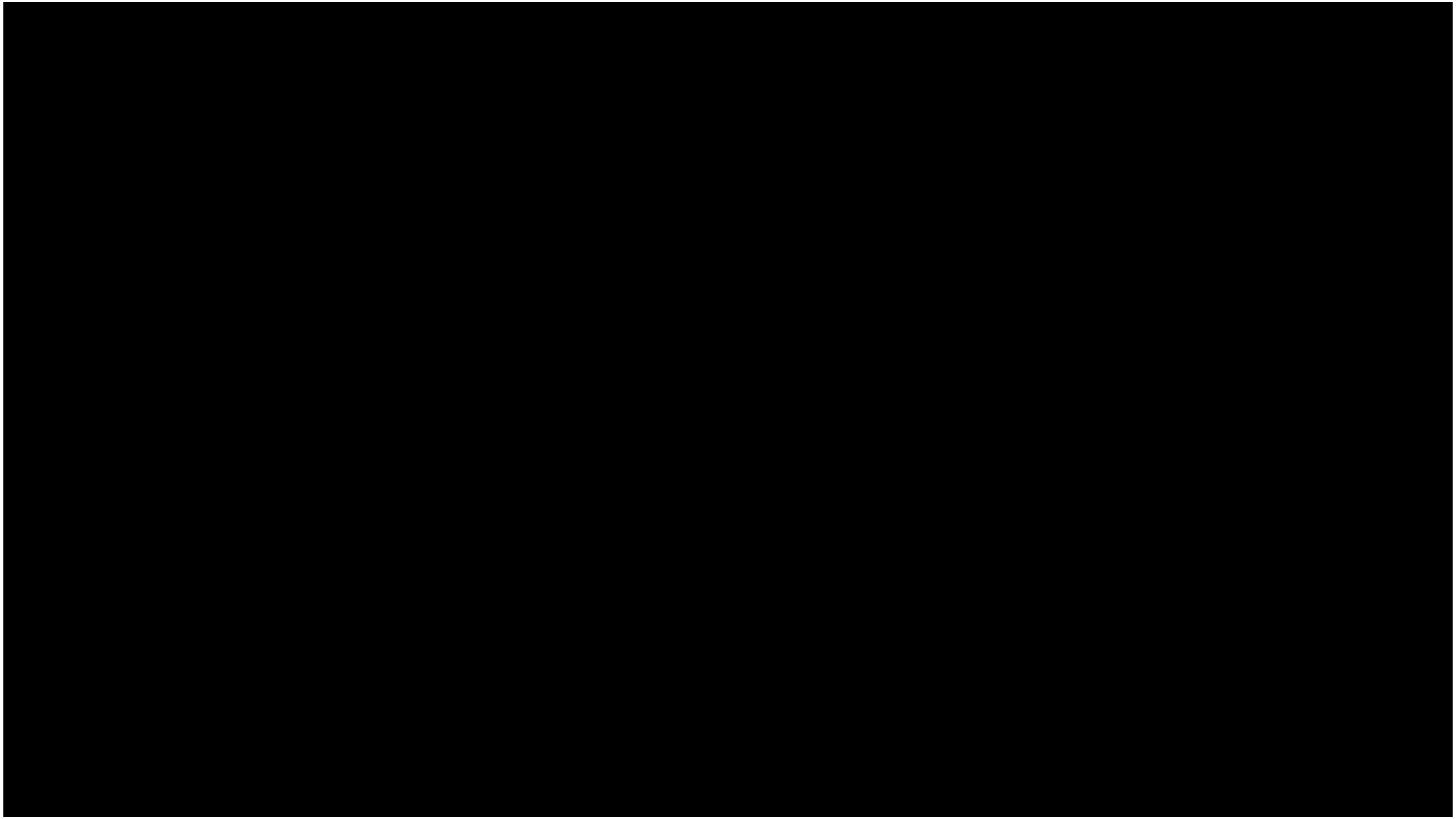
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Notochord Formation



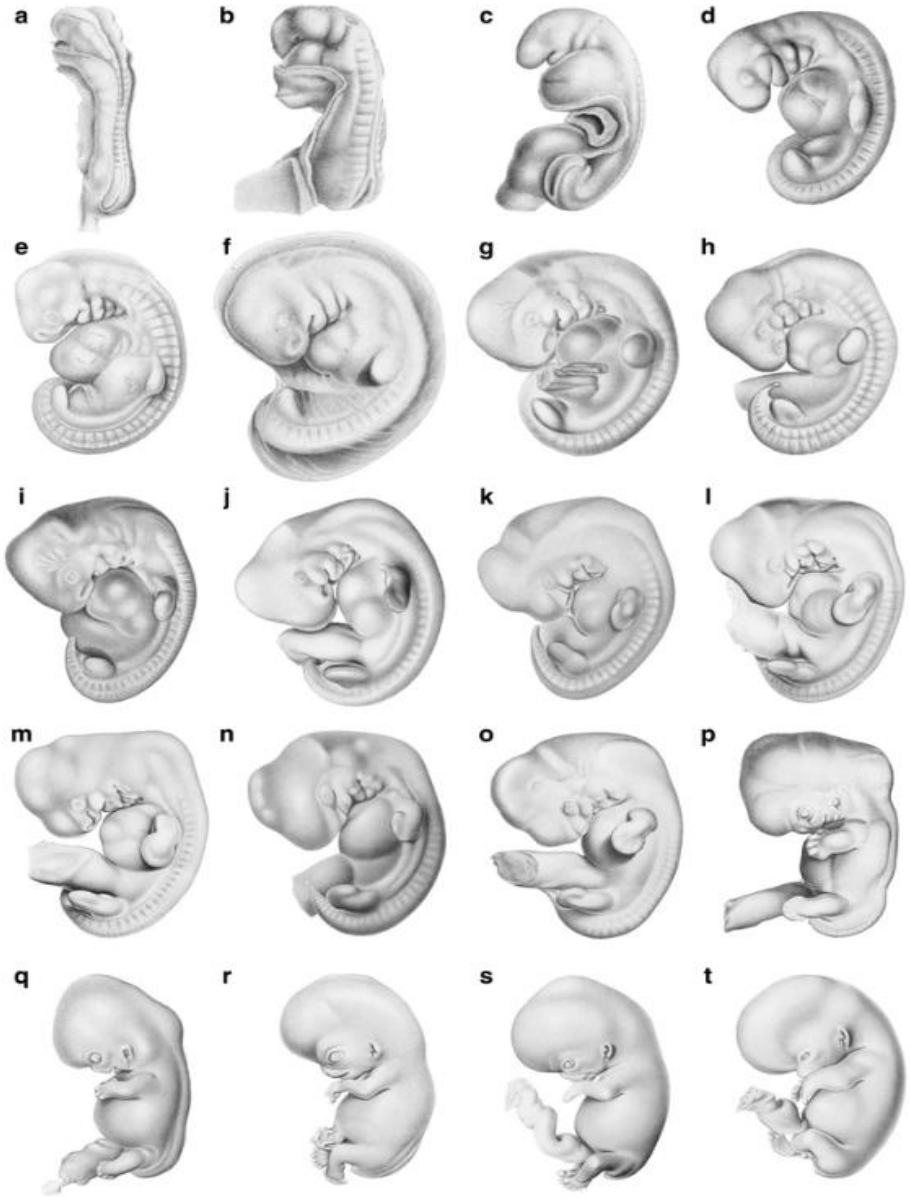
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Neurolation



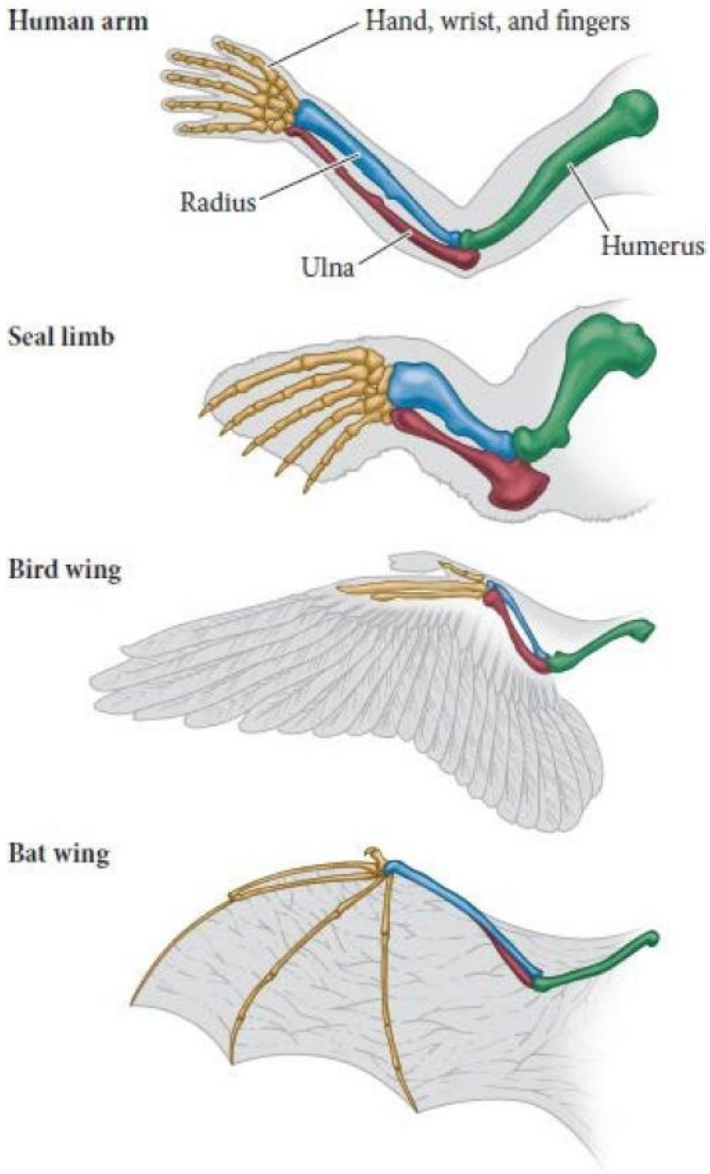
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Morphogenesis: the generation of form



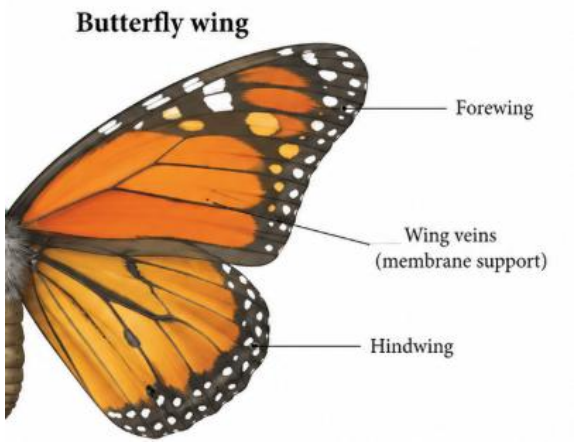
- **Morphogenesis** is the process through which cells and tissues **generate organised anatomical form**.
- It depends on regulated **changes in cell shape, polarity**, **adhesion** and **cytoskeletal organisation**.
- **Cells may migrate** individually or as coordinated epithelial sheets.
- **Differential proliferation** and **programmed cell death** can expand, reduce or separate developing structures.
- **Tissue folding, invagination, elongation, branching** and **fusion** create **three-dimensional organs**.
- Morphogenesis **changes the spatial arrangement of cells** *without necessarily changing their identities*.
- **Developmental defects** may arise when correctly specified cells fail to reach or construct the correct structure.

Morphogenesis: homologous vs analogous



Homologous structures are those whose underlying similarity arises from their being derived from a common ancestral structure:

- *the wing of a bird and the arm of a human are homologous, both having evolved from the forelimb bones of a common ancestor*

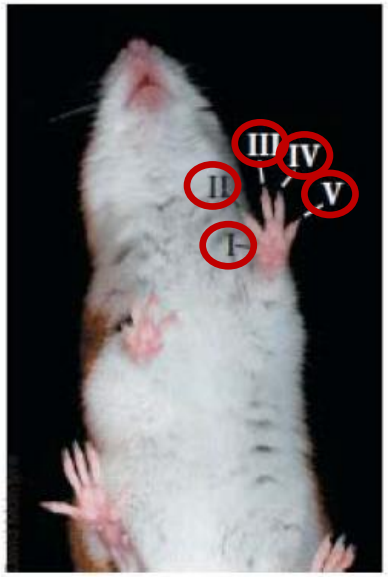


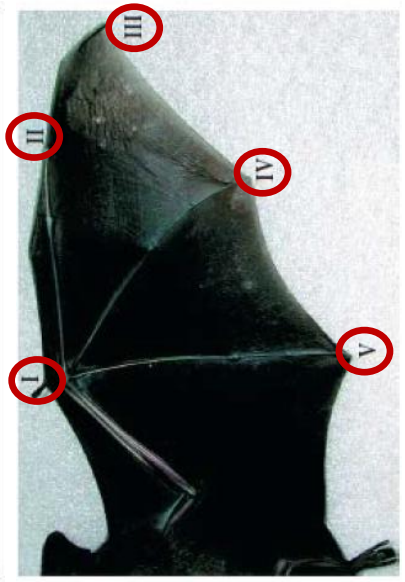
Analogous structures are those whose similarity comes from their performing a similar function rather than their arising from a common ancestor:

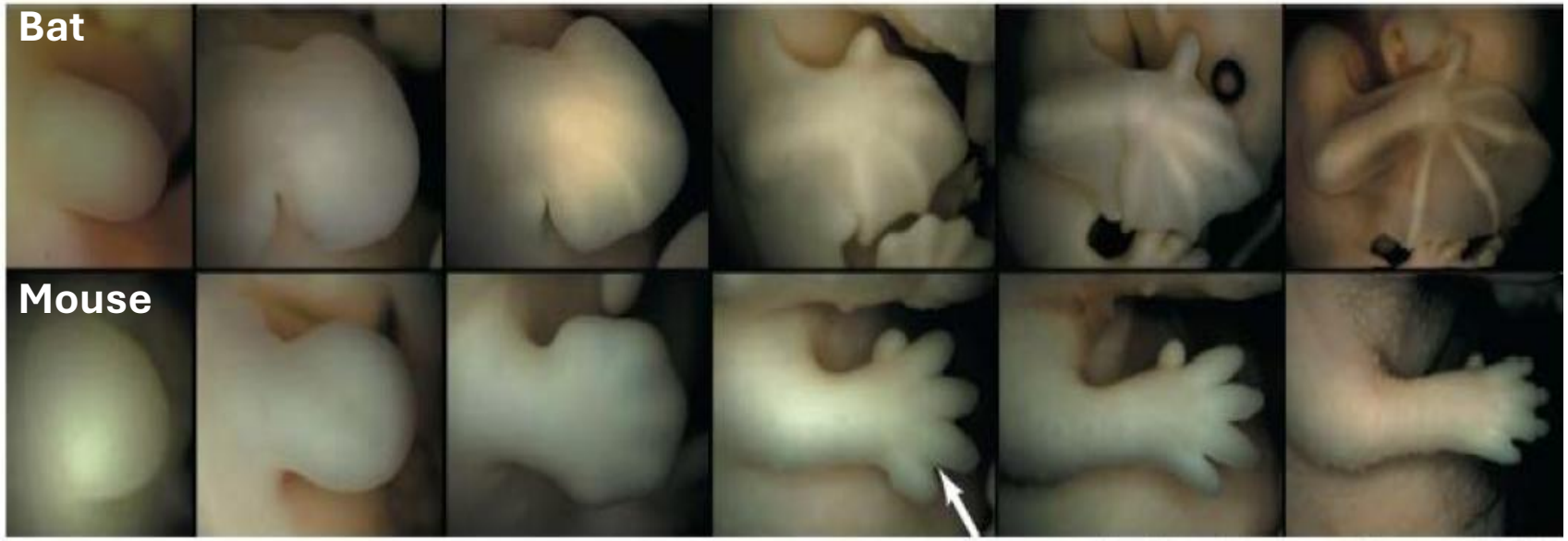
- *the wing of a butterfly and the wing of a bird are analogous; the two share a common function (and thus both are called wings), but the bird wing and insect wing did not arise from a common ancestral structure*

Morphogenesis: when death is part of the formation

- **Evolutionary change often arises through changes in developmental processes**
- Bat and mouse forelimbs begin from a broadly similar embryonic plan, including **digits initially connected by interdigital tissue**.
- **In mice**, genetic signals trigger **apoptosis of the interdigital cells**, **separating the digits** and producing free fingers adapted for grasping and manipulation.
- **In bats**, genetic signals inhibit apoptosis so that **interdigital cell death is reduced or prevented**.
- At the same time, signals that promote **digit elongation and cartilage growth** are enhanced, producing the elongated fingers that support the wing membrane.





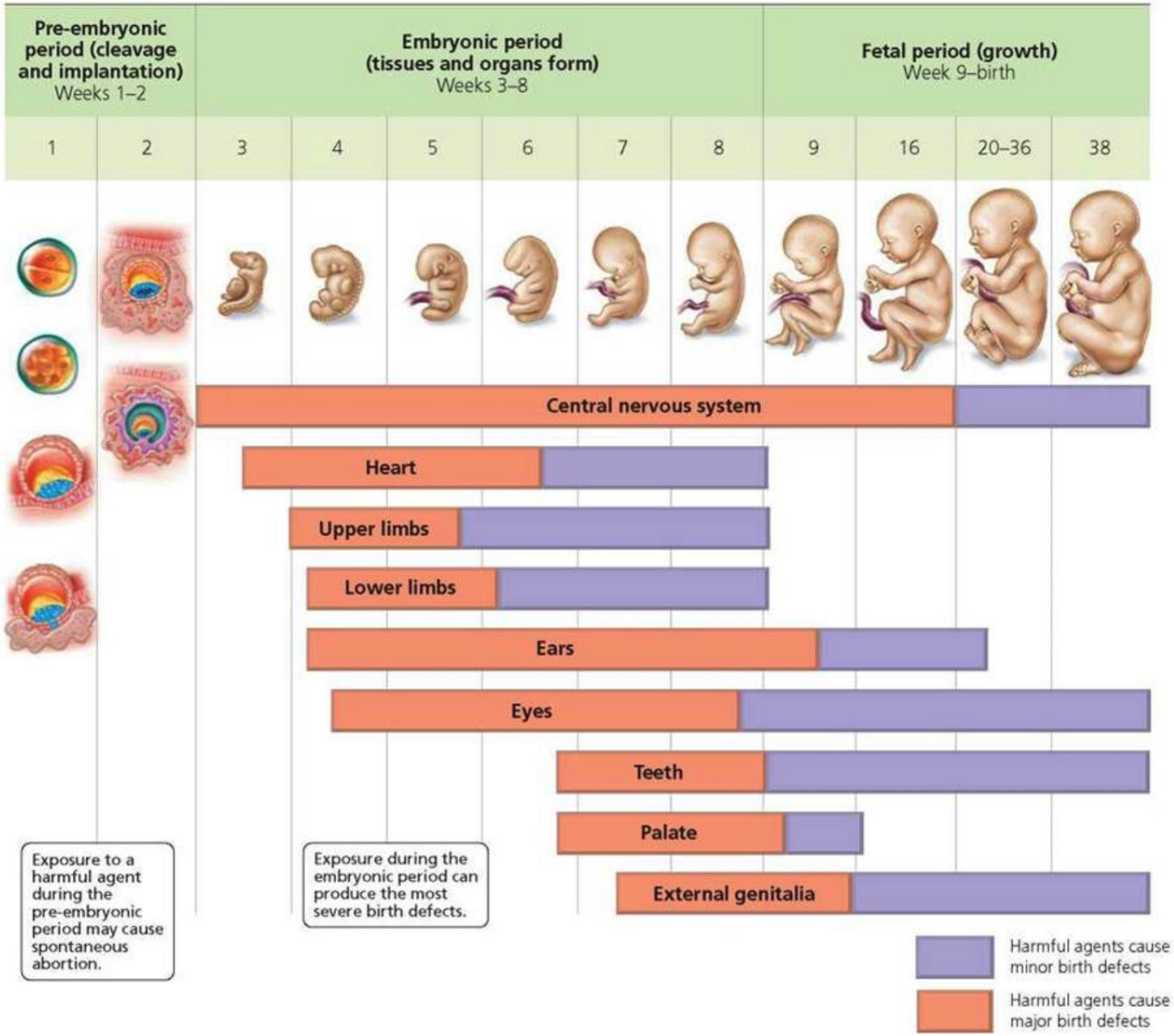


Organogenesis builds functional structures

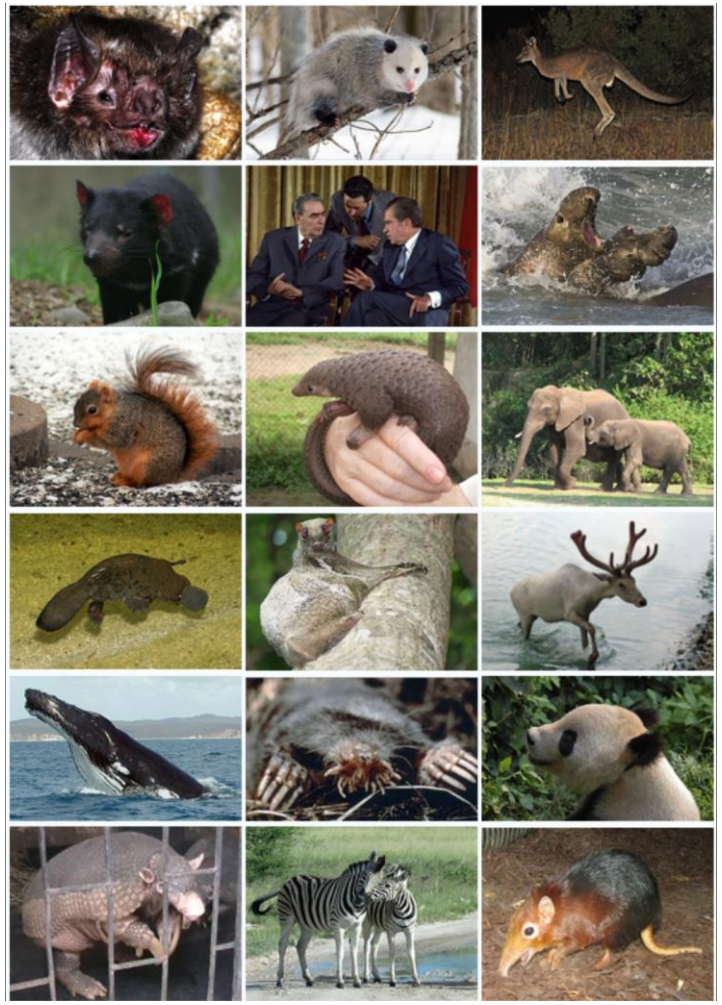
- **Organogenesis** begins after germ-layer organisation and converts embryonic tissues into organ primordia.
- **Cells communicate** through inductive signals that specify which structures form at particular positions.
- **Tissue folding, branching, fusion** and **separation** generate complex three-dimensional architecture.
- **Cells may migrate long distances** from their site of origin to their final destination.
- **Proliferation, differentiation** and **programmed cell death** refine organ size and shape.
- Most organs contain **interacting derivatives of two or more germ layers**.
- *Early organs may begin functioning while their anatomical development is still incomplete*.



Organogenesis builds functional structures



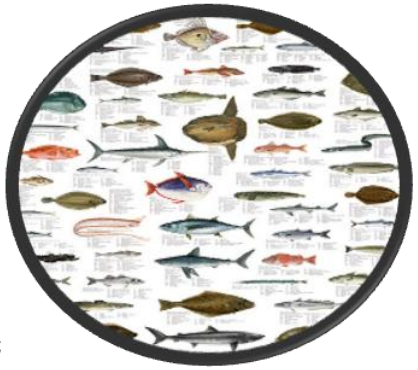
Hatching and Birth



Viviparous The new organism is brought into the world through live birth.

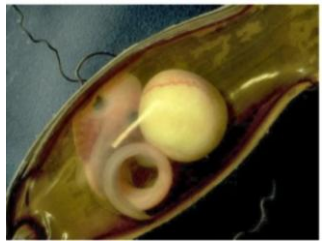


Oviparous Embryonic development occurs inside an egg laid in the external environment.

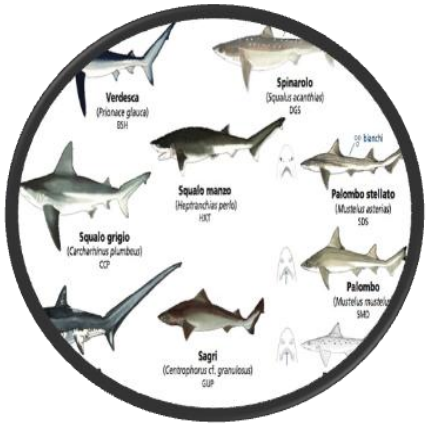






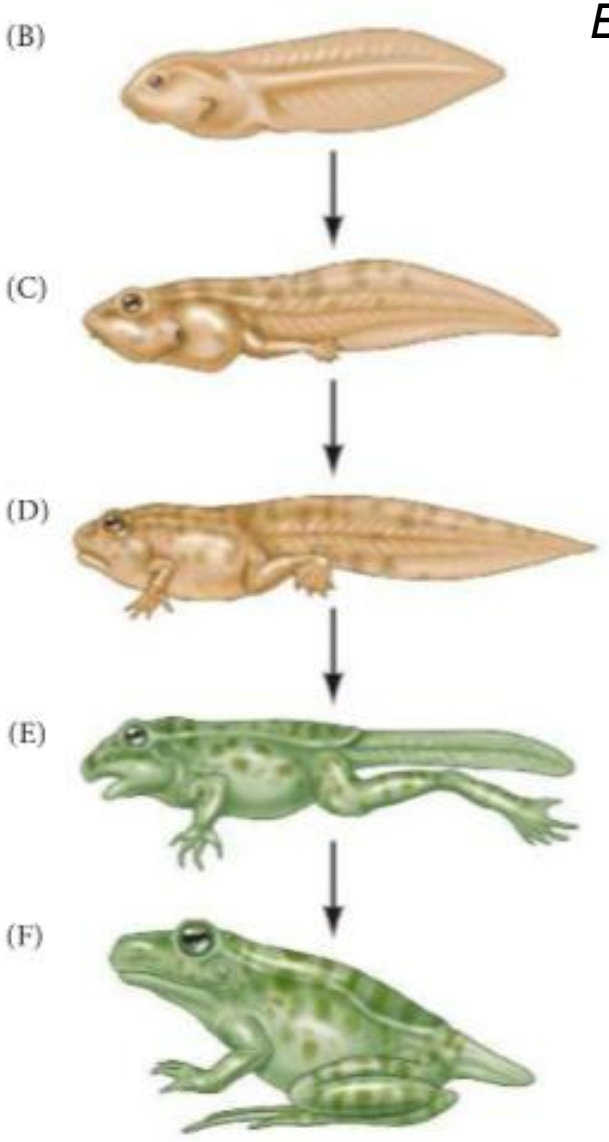


Ovoviviparous Embryonic development occurs inside an egg that hatches within the mother's body.





Postnatal Development and Metamorphosis



Birth or hatching does not mark the end of development

- Juvenile organisms commonly undergo continued growth, tissue maturation and changes in physiology.
- A **larva** is a postembryonic stage that may differ markedly from the sexually mature adult.
- **Metamorphosis** transforms a larval body into the adult form through coordinated tissue growth, remodelling and degeneration.
- **In amphibians**, **thyroid hormones coordinate changes** in limbs, tail, intestine, respiratory organs and craniofacial structures.
- **Environmental conditions may influence** the timing and rate of metamorphosis.
- **Mammals** show less dramatic metamorphosis but **still undergo extensive postnatal development and sexual maturation**.



What is a model organism?

- A **model organism** is an **experimentally tractable species** selected to answer a defined biological question.
- A model **is not assumed to reproduce every aspect** of another species, including humans.
- Its value depends on whether the **relevant developmental mechanism is conserved** and **experimentally accessible**.
- Model organisms **permit controlled observation**, **perturbation** and **replication**.
- Shared strains, genome resources, staging systems and experimental protocols increase their scientific usefulness.
- *The research question must determine the model; the availability of a familiar model should not determine the question.*



Model organisms in Developmental biology

Why do developmental biologists use multiple models?

- No single organism provides maximum accessibility, genetic power, and relevance for every question.
- Different models offer complementary experimental advantages.
- External embryos favor direct imaging and manipulation, whereas mammalian models provide closer physiological relevance to humans.
- Comparative studies distinguish conserved mechanisms from species-specific adaptations.
- A mechanism discovered in one model can be tested in another to evaluate its generality.
- Some organisms are selected because they display exceptional traits such as regeneration, diapause, or rapid ageing.
- Strong conclusions often emerge from converging genetic, cellular, and comparative evidence obtained in multiple systems.

How is a model organism selected?

- **Size and husbandry:** Can sufficient numbers of adults be housed and bred efficiently?
- **Generation time:** How rapidly can experimental crosses and multigenerational studies be completed?
- **Embryo accessibility:** Can embryos be collected, observed, labelled, or manipulated?
- **Genomic tractability:** Are the genome, gene-expression resources, and genome-editing methods available?
- **Phylogenetic position:** Is the organism biologically relevant to the mechanism or comparison being studied?
- **Experimental manipulability:** Can genes, cells, tissues, or signals be removed, transplanted, or activated?
- **Community resources:** Are standard strains, staging series, databases, and validated protocols available?

Model organisms in Developmental biology



Ambystoma mexicanum



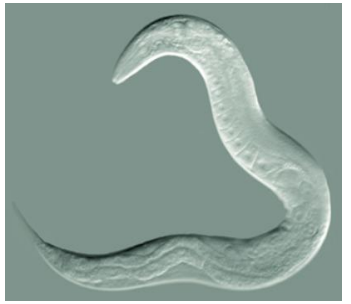
Danio Renio



Strongylocentrotus purpuratus



Mus Musculus



Caenorhabditis elegans



Xenopus Laevi



Nothobranchius furzeri

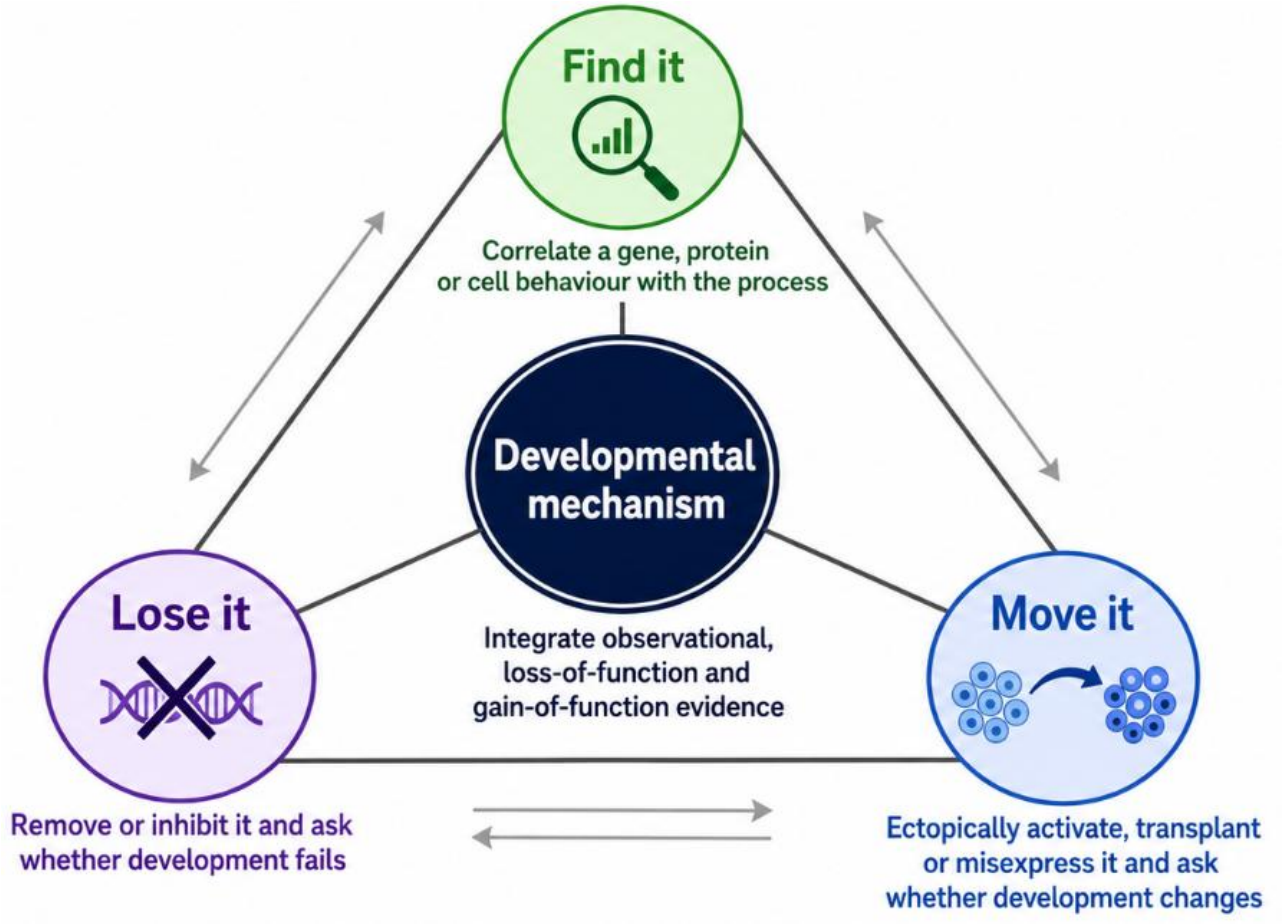


Drosophila Melanogaster

Model organisms in Developmental biology

GROUP	MODEL ORGANISM	MAIN ADVANTAGES	TYPICAL DEVELOPMENTAL USES
INVERTEBRATES Simple body plans, short life cycles and powerful genetic tools	 ***Drosophila melanogaster*** (fruit fly)	• Short generation time • Powerful genetics • Many mutants and transgenic tools • Low cost and easy maintenance	• Pattern formation • Segmentation • Axis specification • Neurogenesis
	 ***Caenorhabditis elegans*** (nematode)	• Transparent body • Invariant cell lineage • Rapid life cycle • Simple anatomy	• Cell lineage • Cell fate specification • Apoptosis • Nervous system development
	 ***Strongylocentrotus purpuratus*** (sea urchin)	• External fertilization • Synchronous development • Transparent embryos • Abundant gametes and embryos	• Fertilization • Cleavage • Cell specification • Gastrulation
FISH Vertebrates with external development and high experimental accessibility	 ***Danio rerio*** (zebrafish)	• External fertilization • Transparent embryos • Rapid development • Vertebrate body plan	• Live imaging • Organogenesis • Cell migration • Cardiovascular and neural development
	 ***Nothobranchius furzeri*** (turquoise killifish)	• Very short life cycle • Embryonic diapause • Rapid ageing • Growing genomic resources	• Developmental timing • Diapause • Ageing • Environmental adaptation
AMPHIBIANS Large embryos and remarkable regenerative capacities	 ***Xenopus laevis*** (African clawed frog)	• Large embryos • Easy microinjection • Surgical manipulation • Robust embryology	• Gastrulation • Axis formation • Induction • Early vertebrate development
	 ***Ambystoma mexicanum*** (axolotl)	• High regenerative capacity • Large embryos and tissues • Vertebrate context • Laboratory breeding feasible	• Regeneration • Limb development • Patterning • Tissue plasticity
MAMMALS Closest physiology to humans and mammalian-specific processes	 ***Mus musculus*** (mouse)	• Mammalian physiology • Strong genetic tools • Similarity to human development • Numerous resources and protocols	• Implantation • Placentation • Organogenesis • Gene function in mammals

Experimental logic in developmental biology



- Developmental **research commonly begins by observing** when and where a biological event occurs.
- Observation **generates a hypothesis** about the cells, genes or signals that may regulate that event.
- **Experimental perturbation** is then required to distinguish correlation from causation.
- A **loss-of-function** experiment can test whether a component is necessary.
- A **gain-of-function or transplantation** experiment can test whether it is sufficient in a defined context.

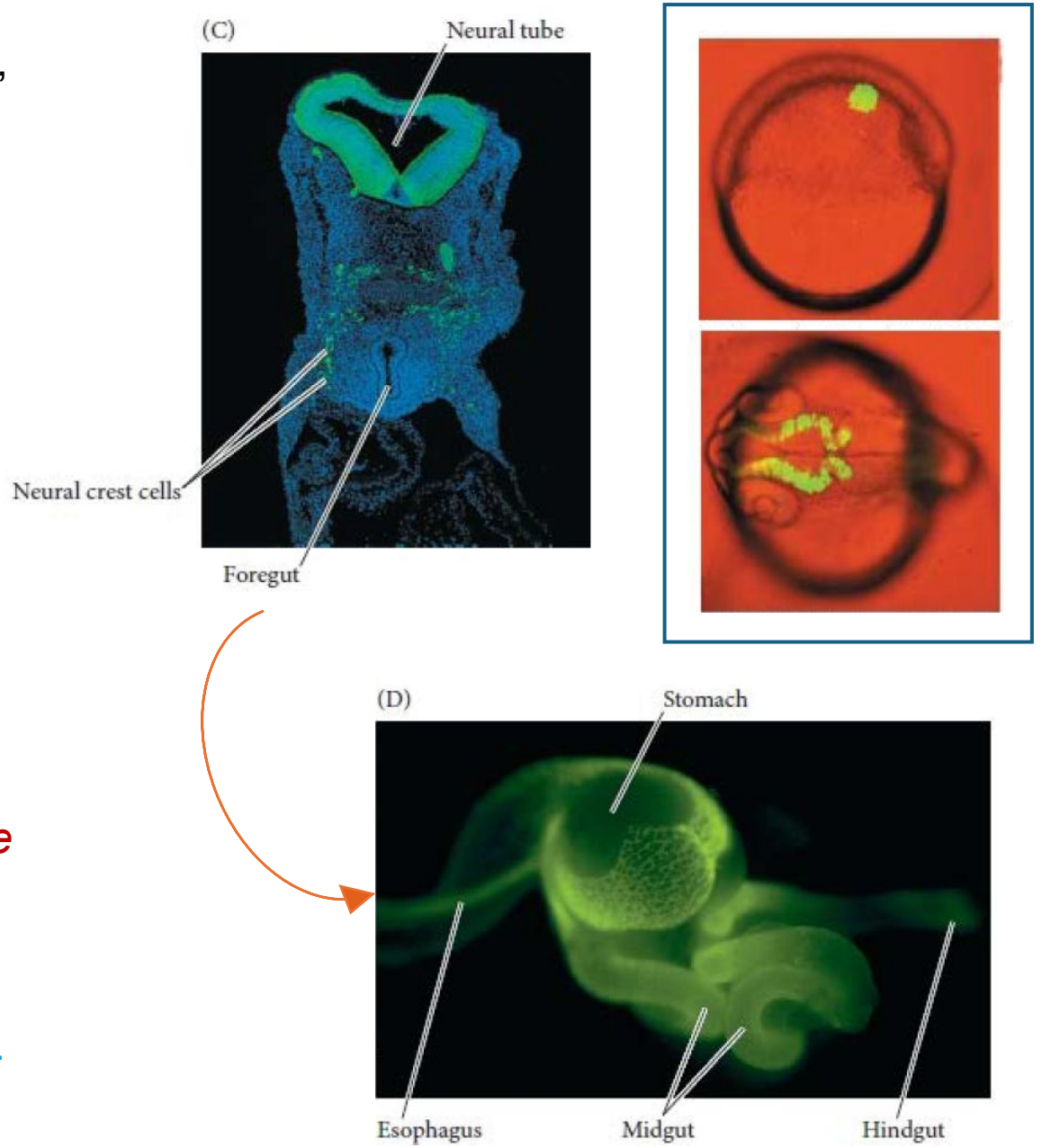
- **Appropriate controls are required** to separate specific developmental effects from toxicity, damage or experimental artefacts.
- The logic can be summarised as **find it, lose it, move it**.

Find it: locate the candidate mechanism

- A **find-it** experiment **identifies where** and **when** a **cell**, **gene product or developmental event is present**.
- **Whole embryos can be observed** by **bright-field**, **fluorescence**, **confocal** or **time-lapse microscopy**.
- **RNA localisation** can be detected by **in-situ hybridisation** or **transcript-specific reporters**.
- **Proteins** can be **detected using antibodies**, **fluorescent tags** or **activity-sensitive probes**.
- **Cell populations can be marked with dyes or** genetically encoded **fluorescent proteins**.

❑ *Spatiotemporal correlation can identify strong candidate regulators.*

❑ *However, the presence of a molecule does not by itself prove that it causes the observed developmental event.*



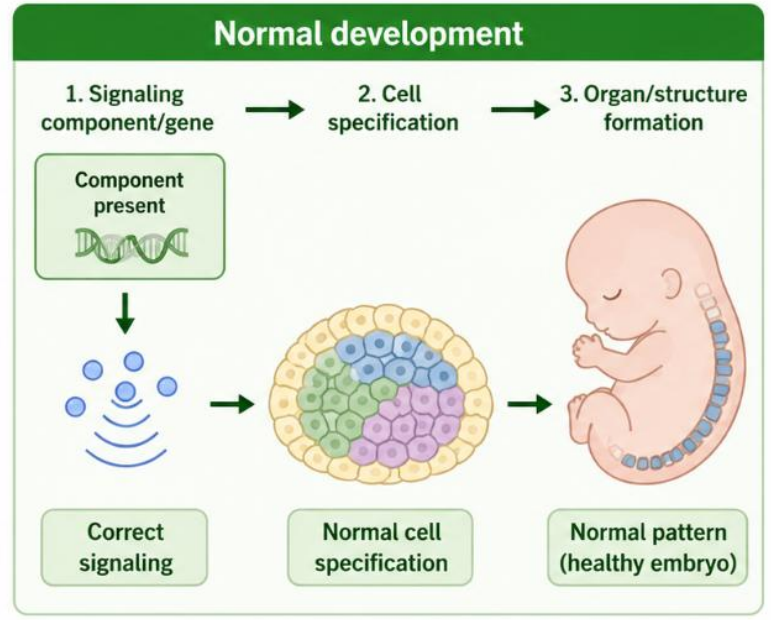
Lose it: test necessity

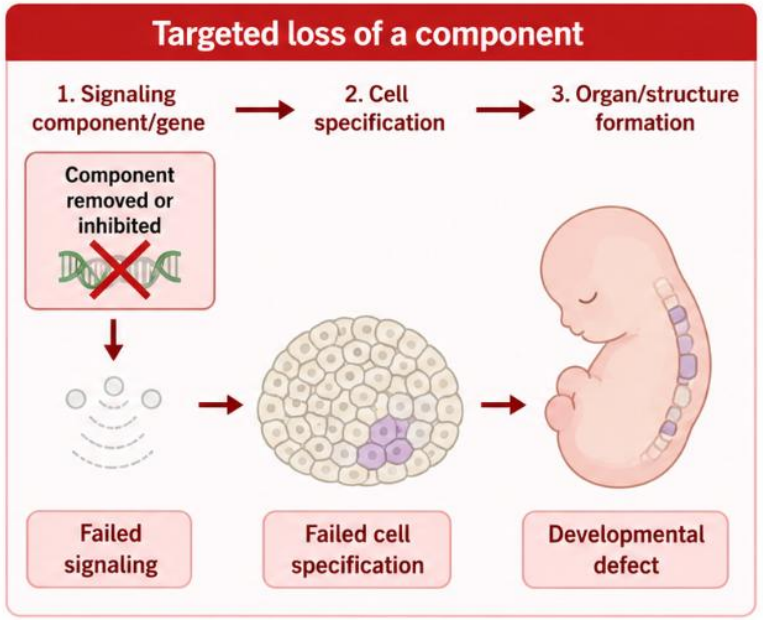
- A **lose-it** experiment **removes** or **reduces a candidate developmental component**.
- **Genes may be disrupted by mutation** or genome editing, whereas **RNA or protein function** can be **reduced** by other targeted methods.
- **Cells and tissues** may be **surgically removed** or selectively ablated.
- **Chemical inhibitors** can block a signalling pathway or cellular process.

❑ *If the developmental process fails after the component is removed, the component may be necessary*.

❑ *Interpretation requires controls for off-target effects, toxicity, incomplete inhibition and developmental delay.*

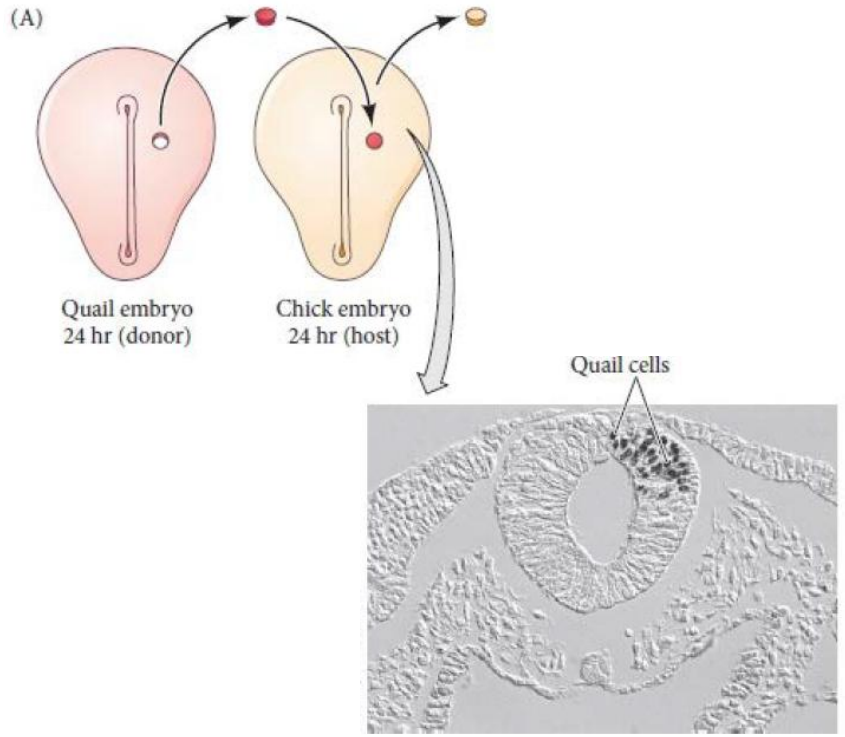
❑ *Absence of a phenotype does not prove irrelevance because redundant mechanisms may compensate for the loss.*



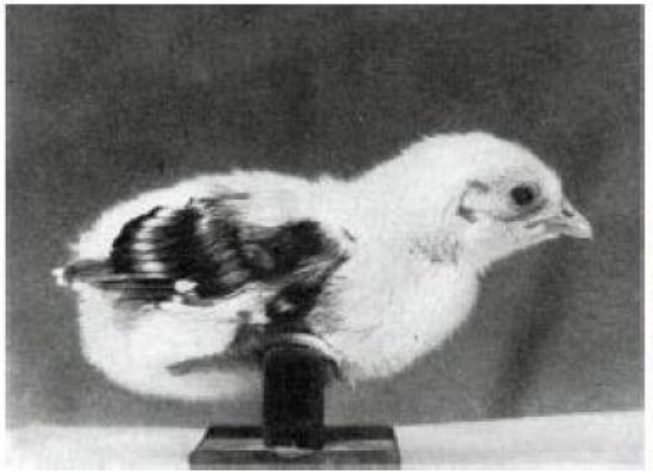


Experimental logic in developmental biology

- A **move-it** experiment **changes the position**, **amount or timing** of **a candidate developmental component**.
- **Cells or tissues can be transplanted** into a new embryonic location.
- **Genes can be expressed ectopically** or **activated earlier** than normal.
- Purified **signals** or signal-producing cells **can be introduced into a new region**.



- ❑ *If the introduced component initiates the predicted response, it may be sufficient in that experimental context*.
- ❑ *A negative result may indicate that the recipient tissue is not competent to respond*.
- ❑ *Gain-of-function results do not establish that the component normally acts alone or at the ectopic location*.



Direct observation and developmental staging

- Direct observation establishes the **normal sequence, timing** and **variability of developmental events**.
- **Embryos are classified** using **developmental stages** defined by **reproducible anatomical features**. Staging is often **more informative than chronological age** because developmental rate varies with temperature and environment.
- **Time-lapse imaging** reveals cell divisions, migrations and tissue rearrangements that static images cannot show.
- **Naturally pigmented blastomeres can occasionally be followed** without adding an experimental label.

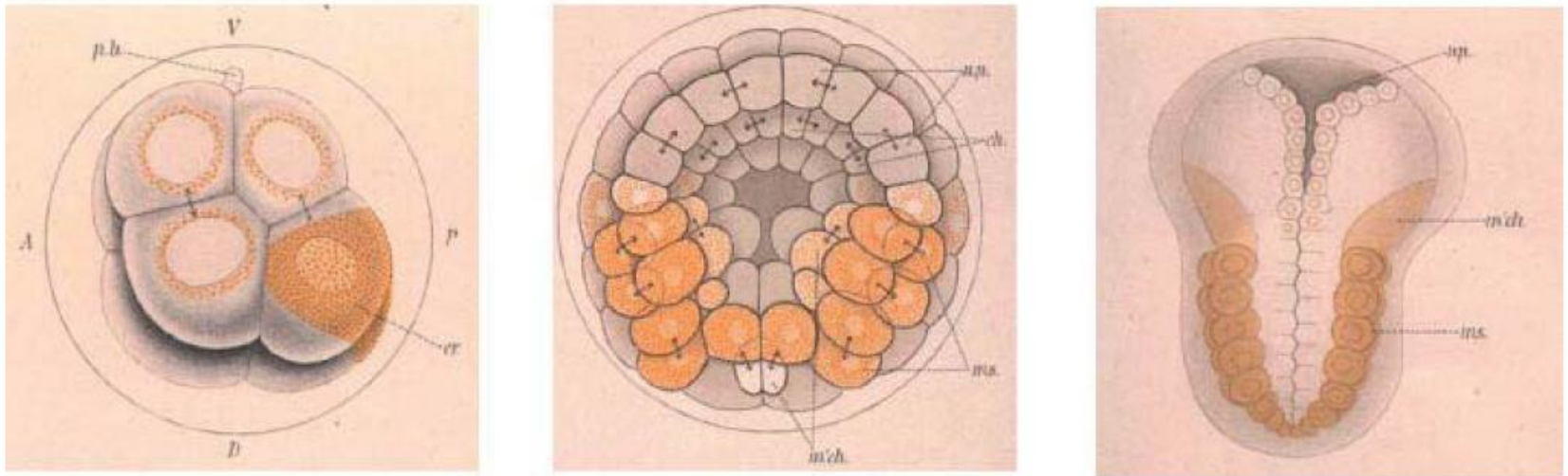


FIGURE 1.13 The fates of individual cells. Edwin Conklin mapped the fates of early cells of the tunicate *Styela partita*, using the fact that in embryos of this species, many of the cells can be identified by their different-colored cytoplasms. Yellow cytoplasm marks the cells that form the trunk muscles. (A) At the 8-cell stage, two of the eight blastomeres contain this yellow cytoplasm. (B) Early gastrula stage, showing the yellow cytoplasm in the precursors of the trunk musculature. (C) Early larval stage, showing the yellow cytoplasm in the newly formed trunk muscles. (From E. G. Conklin. 1905. *J Acad Nat Sci Phila* 13: 1–119.)

Cell labelling, fate maps and lineage tracing

Cell labelling allows a cell or embryonic region to be followed as development proceeds

- **Vital dyes** label living cells **without immediately destroying them**.
- **Fluorescent molecules** provide greater sensitivity but may become **diluted during repeated cell divisions**.
- Reliable labels must be stable, detectable and sufficiently non-toxic to preserve normal development.

- A **fate map** describes the tissues normally produced by cells located in different embryonic regions.
- A **cell lineage** records the actual sequence of cell divisions and ancestry connecting a cell with its descendants.
- Fate does not necessarily equal determination: a labelled cell may adopt a different fate if its environment is experimentally changed.

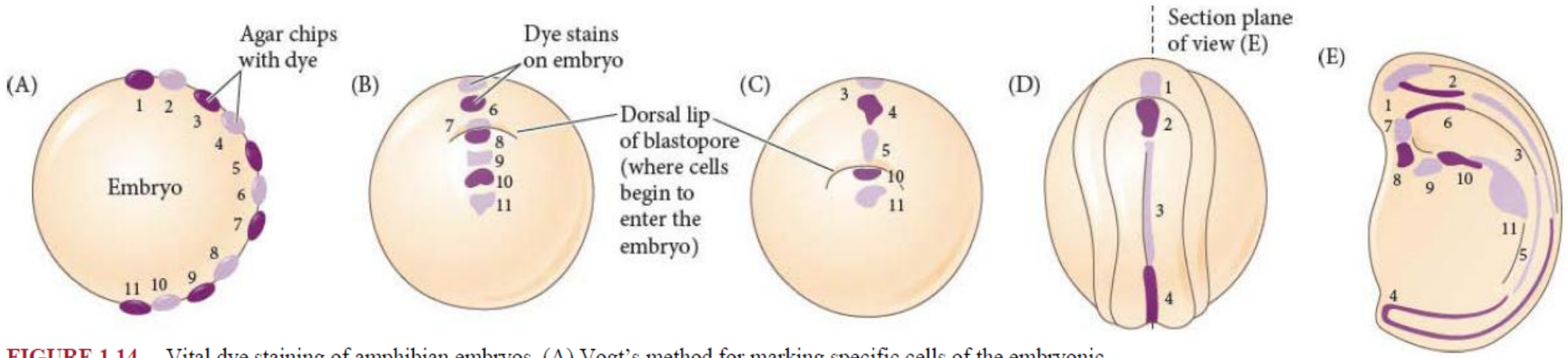


FIGURE 1.14 Vital dye staining of amphibian embryos. (A) Vogt's method for marking specific cells of the embryonic surface with vital dyes. (B–D) Dorsal surface views of stain on successively later embryos. (E) Newt embryo dissected in a medial sagittal section to show the stained cells in the interior. (After W. Vogt. 1929. *W. Roux' Archive f. Development*

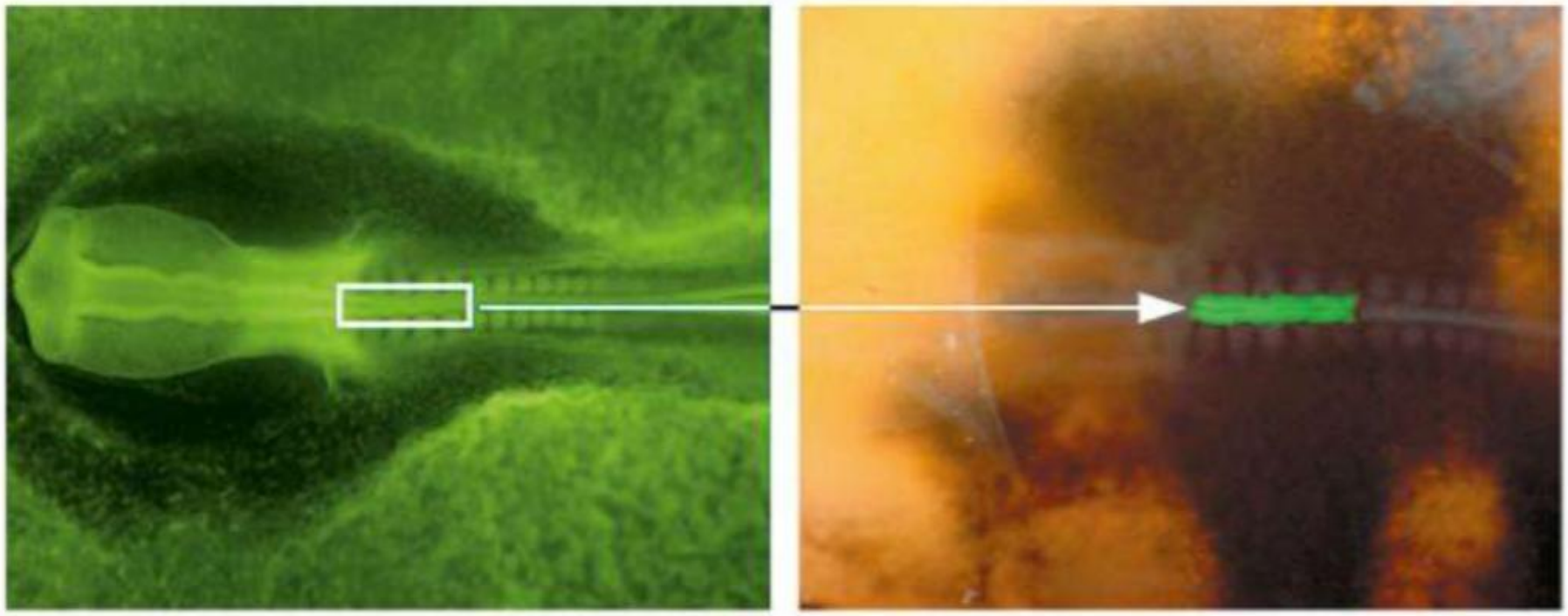
Genetic labelling and manipulation

- **Genetic labels** provide **more persistent identification** of cells and their descendants. **Transgenic fluorescent** proteins such as **GFP** can **mark** selected cell populations **in living embryos**.

- Genetic lineage tracing can label a progenitor and **permanently record** its descendants. Genome editing **can disrupt a developmental gene** or introduce a reporter into a defined genomic location.

- **Cell-type and time-specific regulatory sequences** allow reporters to be expressed only in defined tissues.

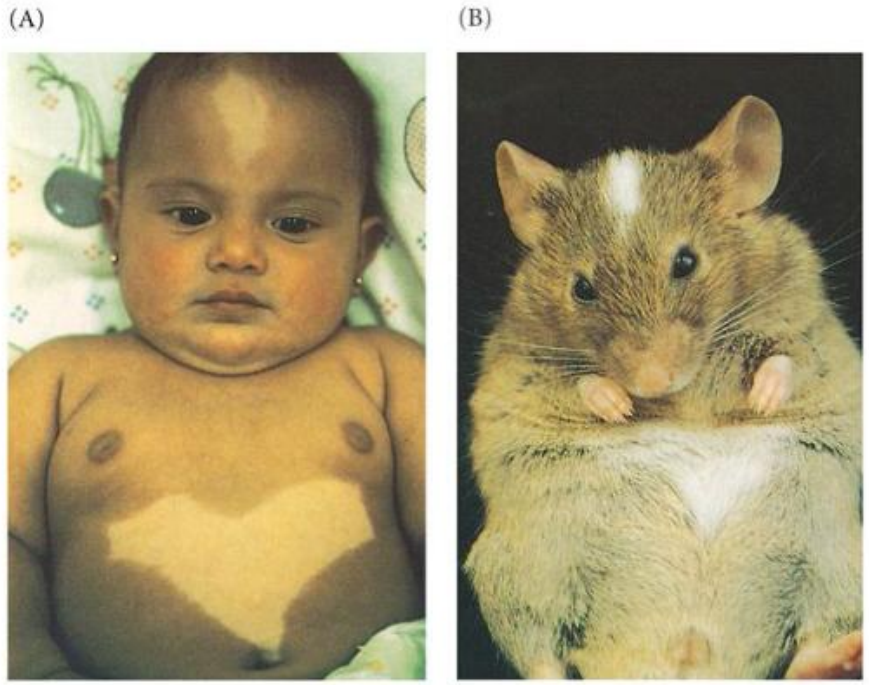
- **Chimeric embryos** contain cells originating **from genetically distinguishable donors and hosts**.



Congenital Abnormalities of Embryo Development

- Between 2 and 5% of live births show observable anatomical abnormalities.
- In the lack of experimental data…birth defects help us understand normal human development.
- Some birth defects are produced by mutant genes or chromosomal abnormalities, while others are produced by environmental factors.
- Genetic defects: malformations – often appear as syndromes
  Use of animal models to identify genetic, cellular and molecular basis of human syndromes.
  Ex: kit mutation leading to piebaldism
- Environmental defects: disruptions
  Responsible agents: teratogens – chemicals, viruses, radiation
  Ex: thalidomide leadind to phocomelia

- Piebaldism- dominant mutation on gene Kit. Includes anemia, sterility, unpigmented regions of the skin and hair, deafness, and absence of nerves that cause peristalsis in the gut.



DEVELOPMENTAL BIOLOGY, Eighth Edition, Figure 1.15 © 2006 Sinauer Associates, Inc.

Medical embryology and teratology

- **Medical embryology** applies developmental principles to **human reproduction**, **prenatal development** and **congenital anomalies**.
- Developmental disorders may have **genetic, environmental or multifactorial** causes.
- A **teratogen** is **an environmental agent capable of disrupting development** and **producing structural** or **functional abnormalities**.
- Teratogenic effects depend on dose, exposure duration, developmental timing and genetic susceptibility.
- **Different organs** have **different critical windows** during which they **are especially vulnerable**.
- **Thalidomide** provided a historically important demonstration that exposure timing determines which structures are affected.



FIGURE 1.27 A developmental anomaly caused by an environmental agent. (A) Phocomelia, the lack of proper limb development, was the most visible of the birth defects that occurred in many children born in the early 1960s whose mothers took the drug thalidomide during pregnancy. These children are now middle-aged adults; this photograph is of Grammy-nominated German singer Thomas Quasthoff. (B) Thalidomide disrupts different structures at different times of human development. (B, data from E. Nowak. 1965. *Humangenetik* 1: 516–536; graph after N. Vargesson. 2015. *Birth Defects Res C Embryo Today* 105: 140–156, and references therein.)