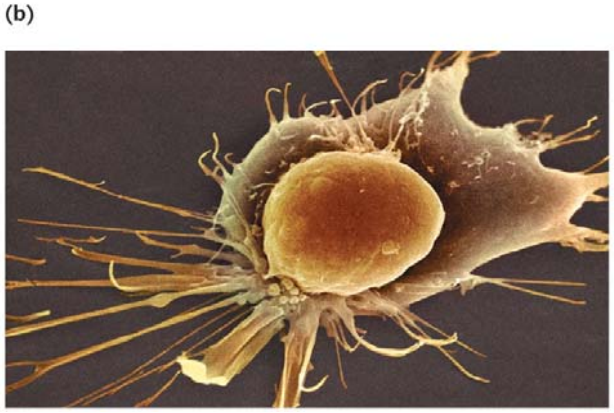
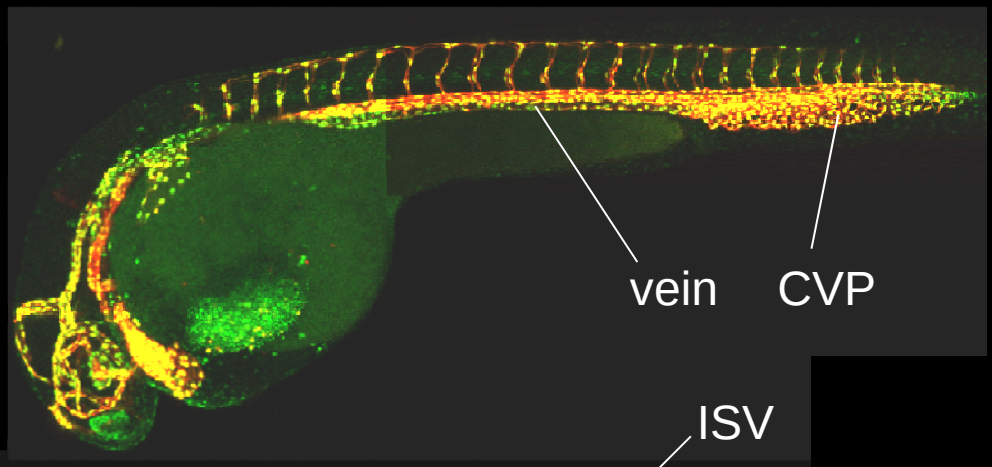
胚胎及發育生物學

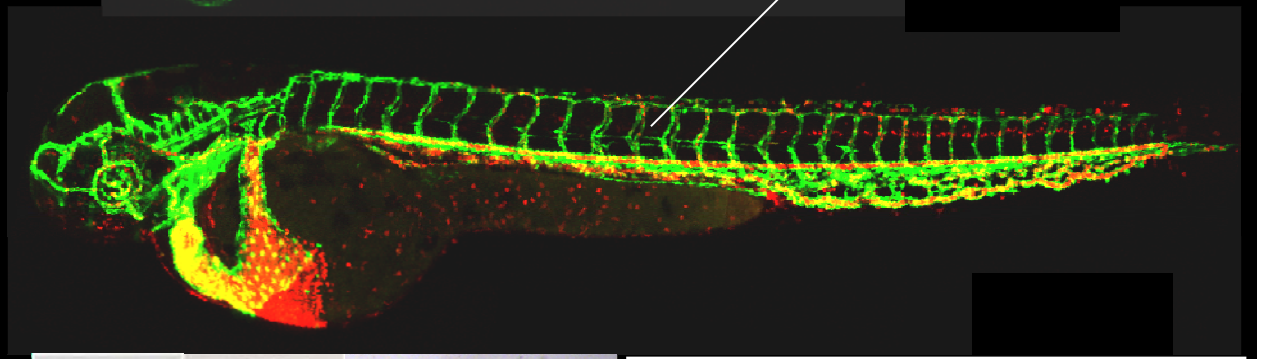
Embryogenesis, Developmental Biology and Stem Cell

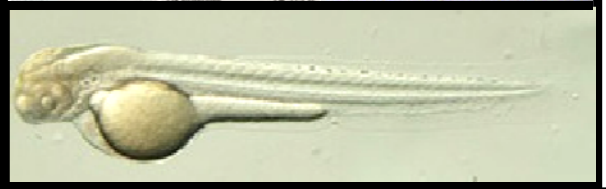
中山大學
生物科學系
吳長益



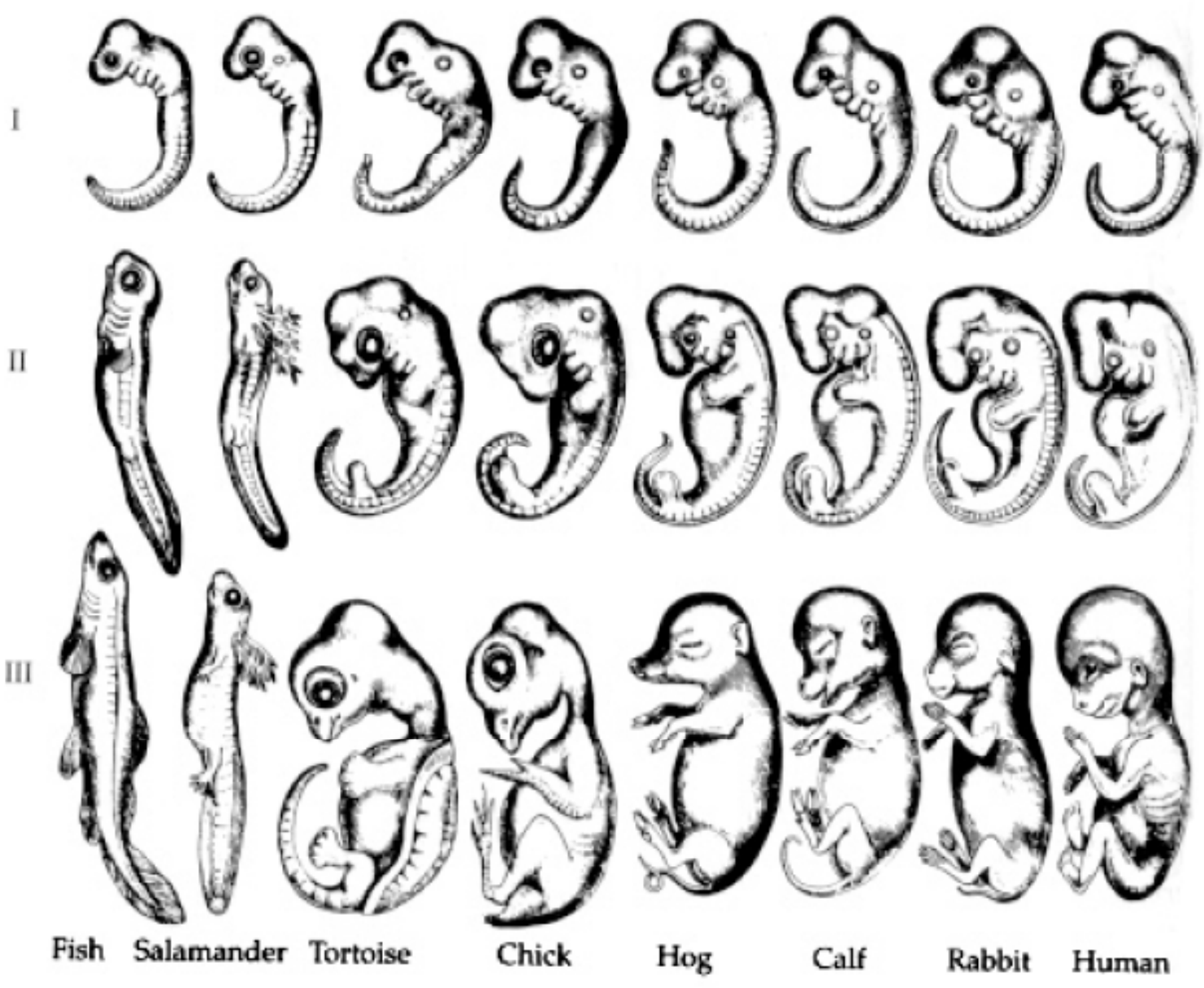
胚胎發育及幹細胞





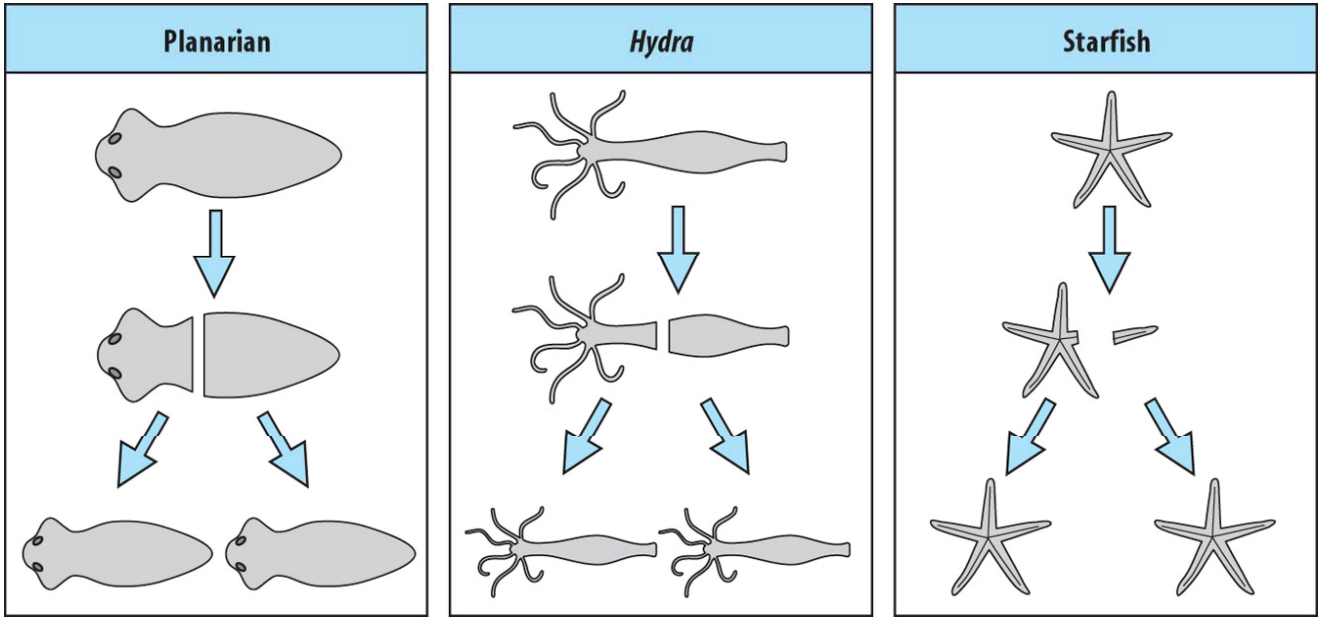


Embryos


I
II
III
Fish
Salamander
Tortoise
Chick
Hog
Calf
Rabbit
Human

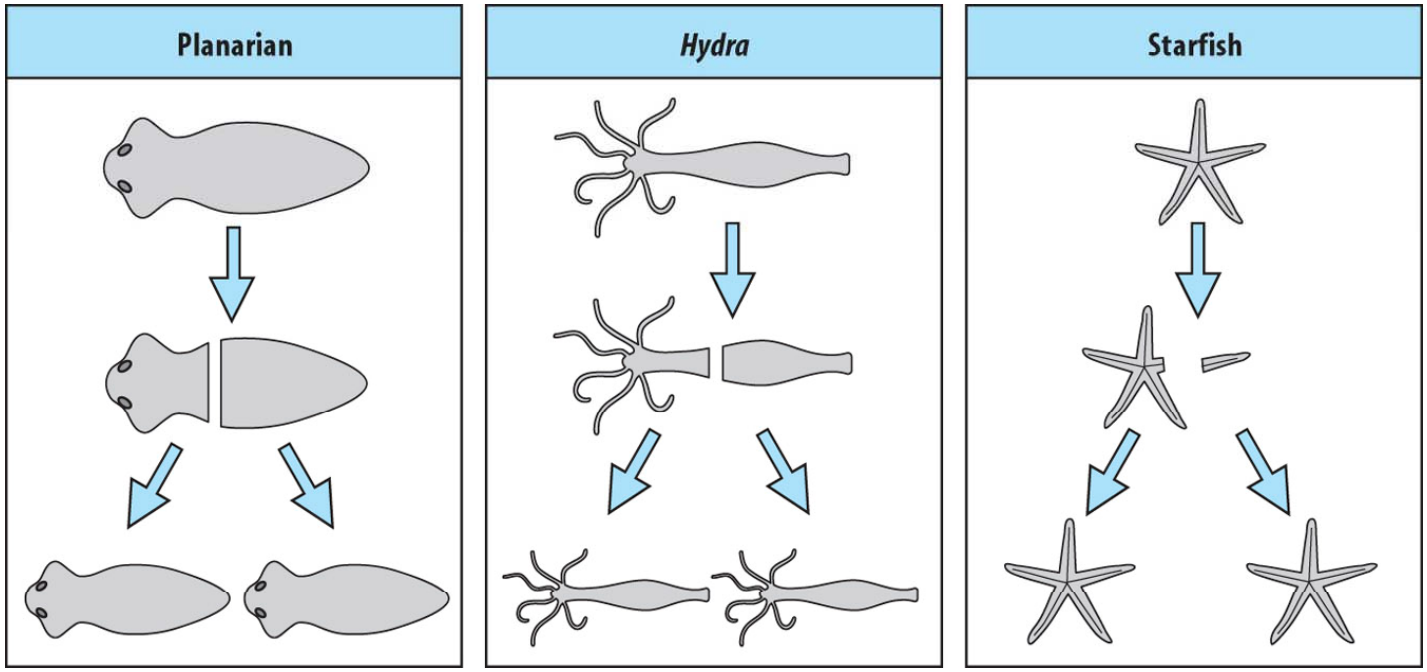
胚胎

複製/再生 —— 幹細胞



Outline

1. 胚胎學 (embryology) vs. 發育生物學 (developmental biology)
2. 模式生物 (model organisms)
3. 動物發育的主要階段
4. 發育過程之機制
5. 組織再生與幹細胞

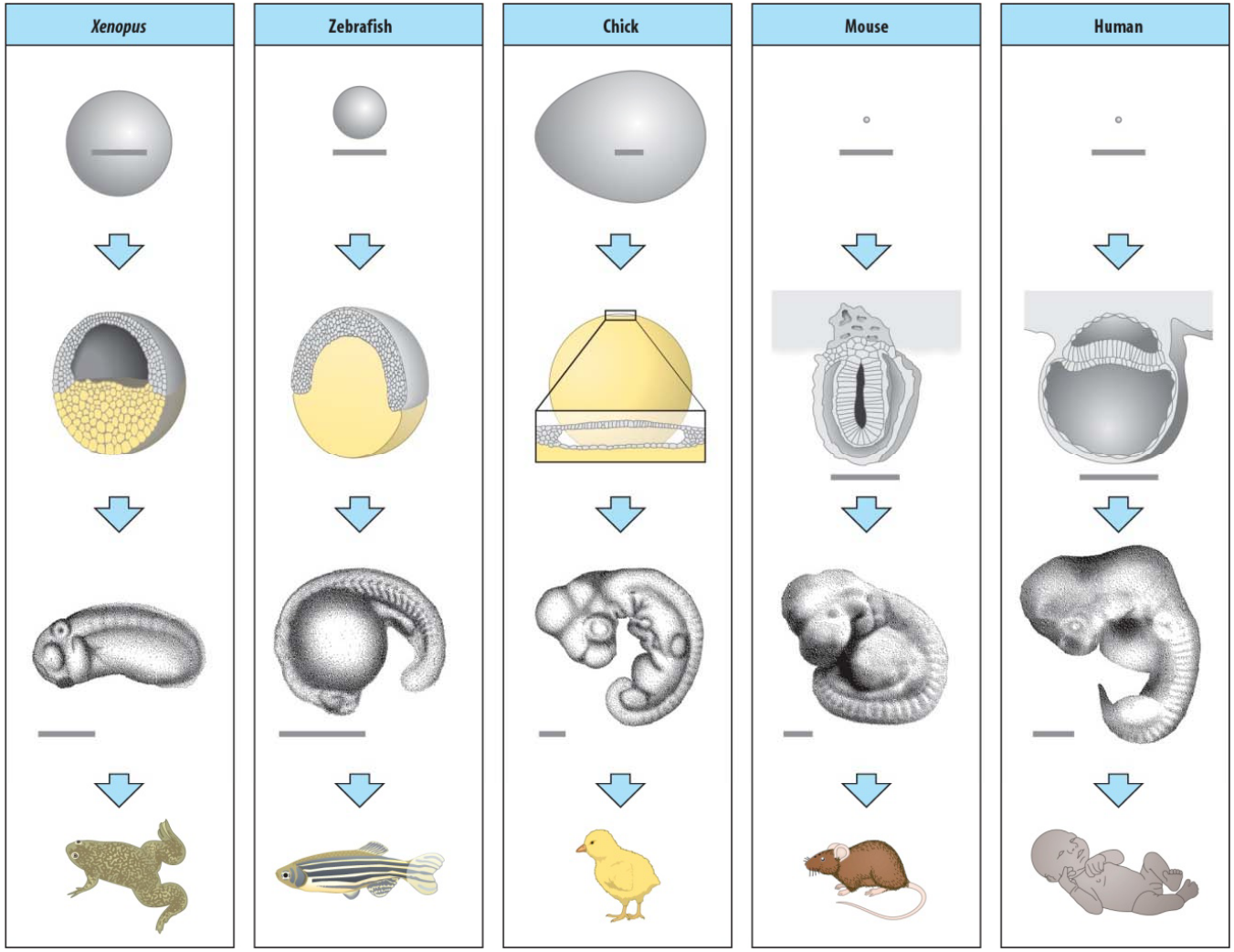


胚胎學 **(Embryology) :** The development of an embryo from the fertilized egg

偏重述敘的科學, 探討如何形成個體正確及完整形態的各個步驟。

發育生物學 **(Developmental Biology)** is to understand how multicellular organism develop

著重於分子和細胞生物學層次上的胚胎學。



何謂發育生物學？

·發育生物學(developmental biology) 源自於胚胎學(embryology)

·胚胎學：探討受精卵到出生的過程
(**A Body-Building Plan)**

·發育生物學包含：

胚胎學

+

個體生長、器官及組織受損的修復與再生、 老化、疾病的發生與治療等

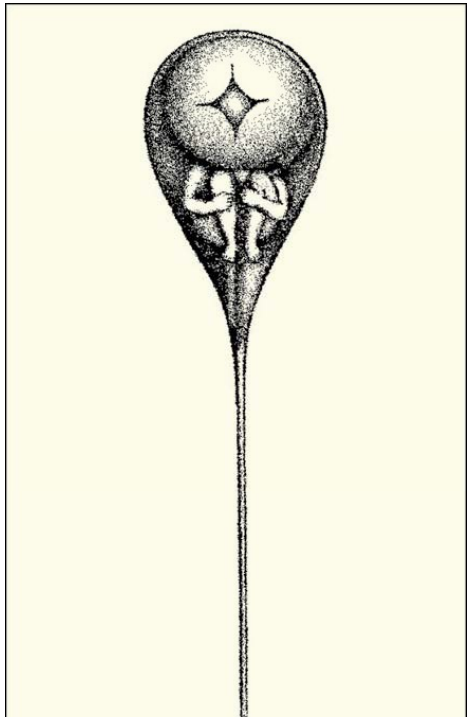
胚胎學上古老的爭論

Preformation theory (先成說)

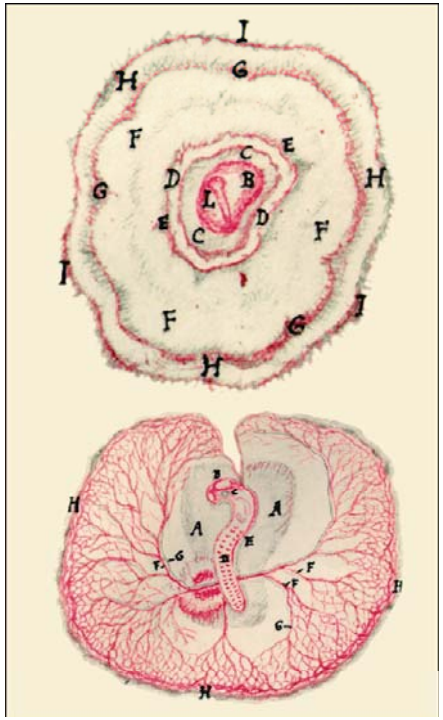
Epigenesis theory (漸成說)

胚胎的各部份是一開始就存在?

還是在發育過程中逐漸形成的？



An homunculus in the head of each sperm (1694)



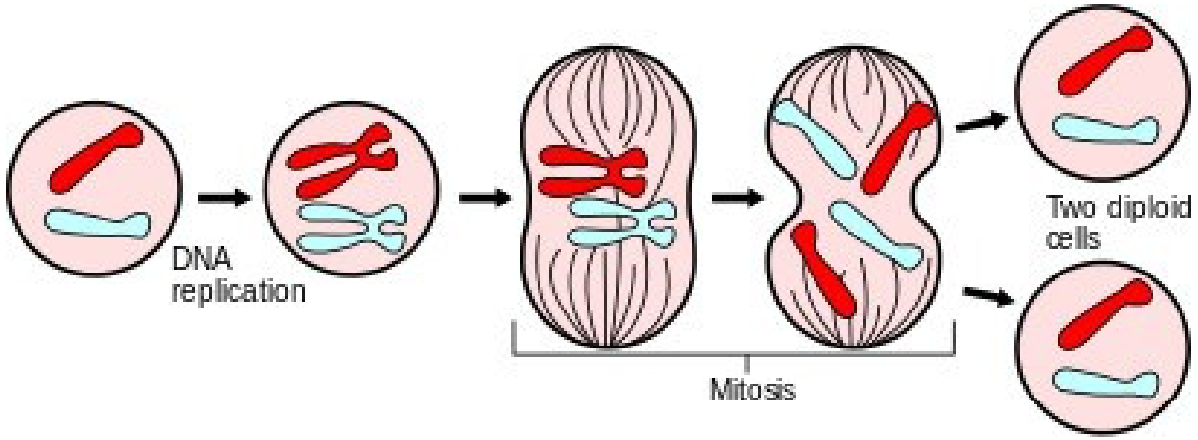
Malpighi's description of the chick embryo. (1673)

顯微鏡的發明

細胞學說的確立 (1820-1880)

基因概念的形成 (1900)

胚胎發育符合漸成說的理論



發育的觀念: A Life cycle of Frog

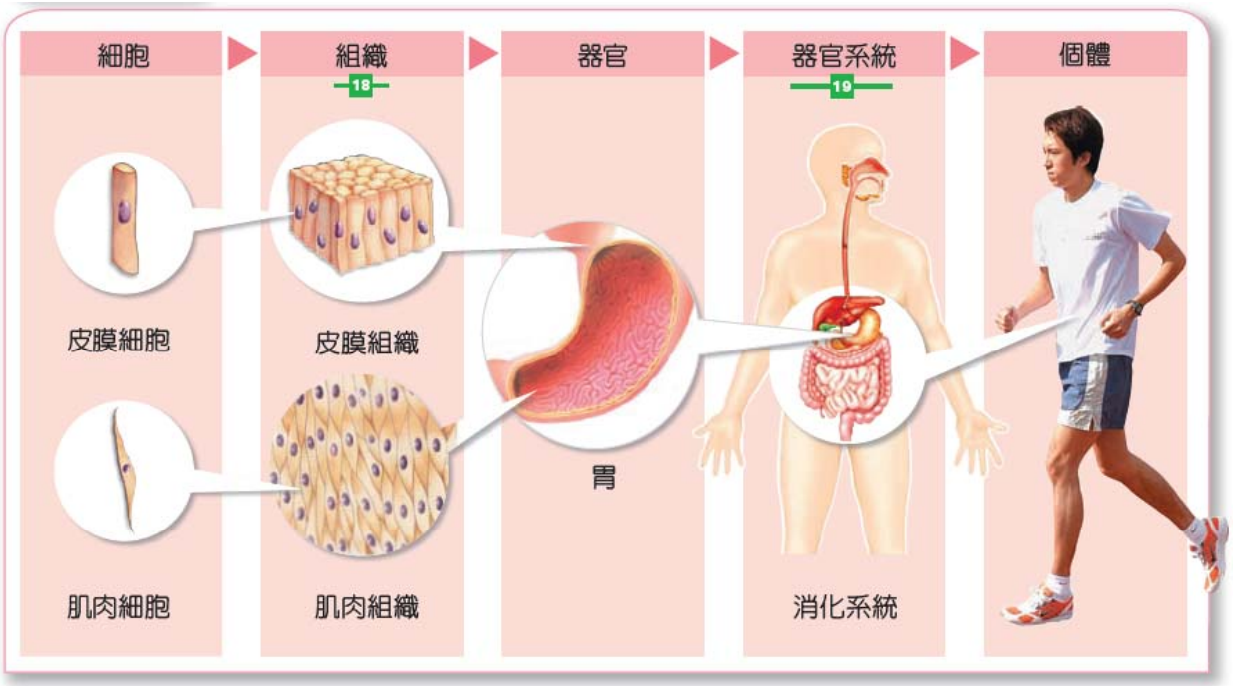
動物的發育（發育生物學研究的範疇）

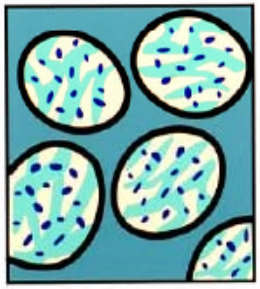
- 生命的週期，由單細胞至多細胞個體的過程

video

DEVELOPMENTAL BIOLOGY 10e, Figure 1.1

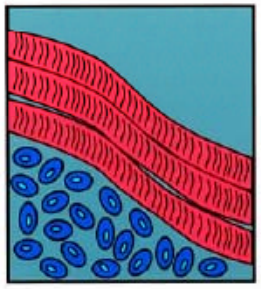
發育的三要素?



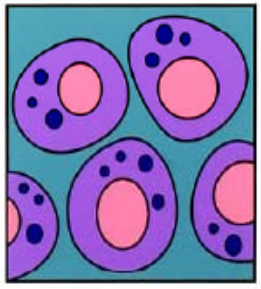


Bone marrow for leukemia & chemotherapy

Nerve cells for Parkinsons & Alzhiemer's disease



Heart muscle cells for heart disease



Pancreatic islet cells for diabetes

發育的三要素:

1. 生長/分裂 growth/cleavage

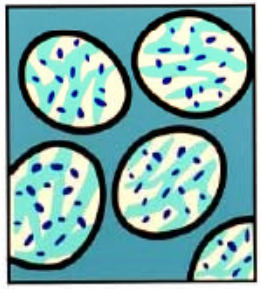
Increase in cell number
Increase in cell size

2. 分化 Differentiation

The fate of daughter cells

3. 形態發生 Morphogenesis

The formation of shapes and patterns



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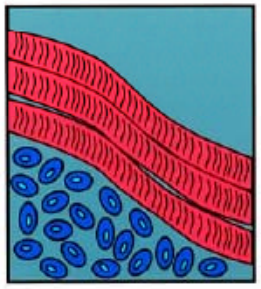

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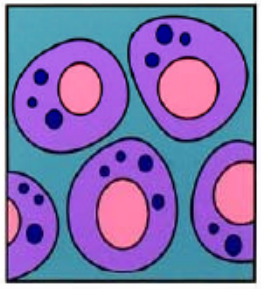

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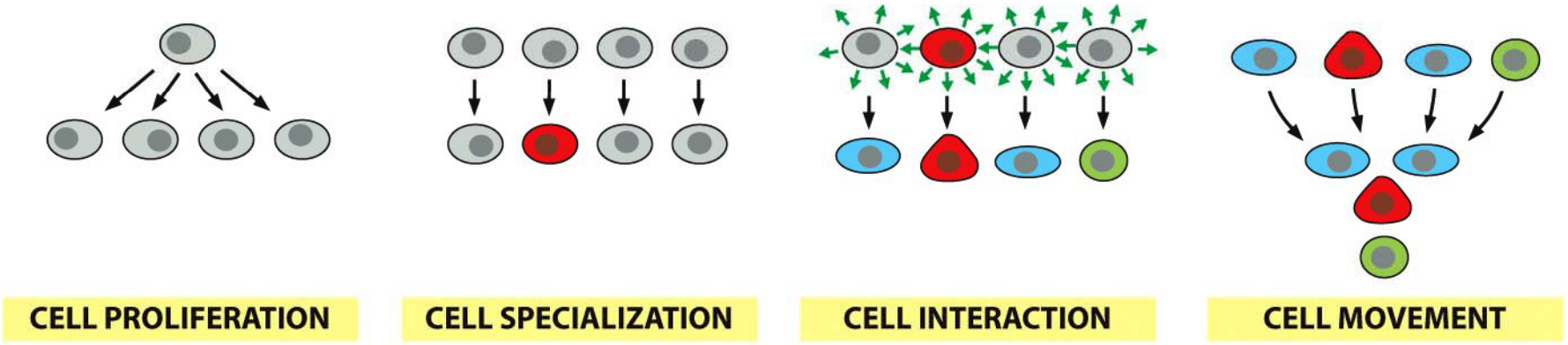
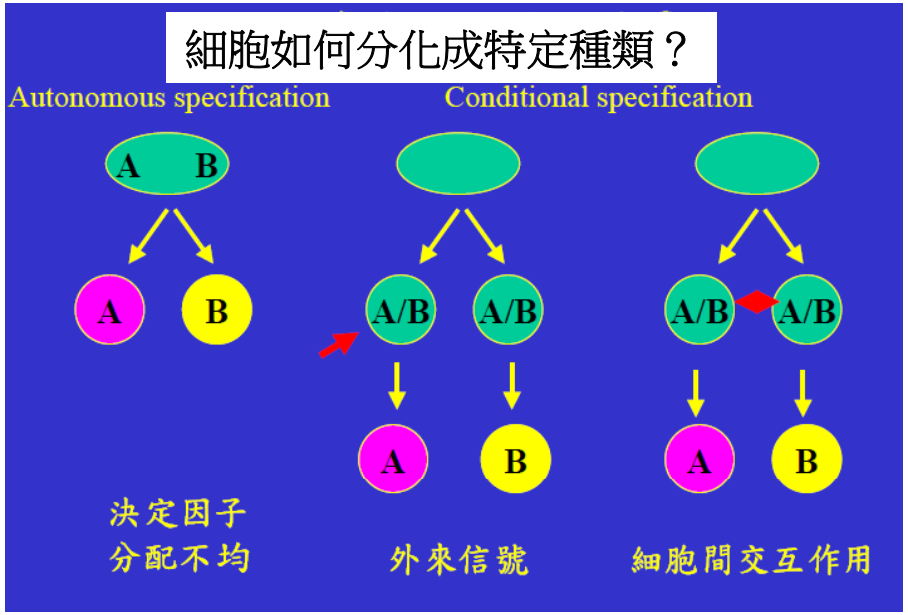


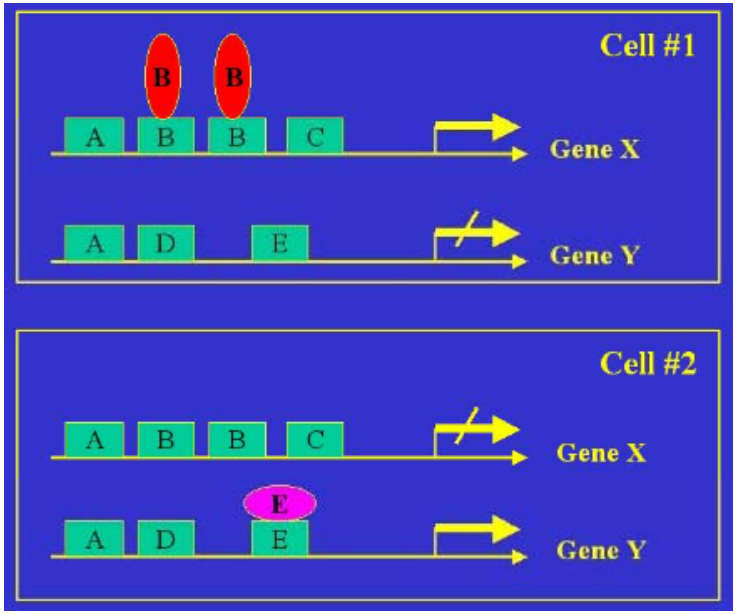
發育生物學的 (研究)中心主題:

細胞如何分化成特定種類？

細胞如何移動到特定位置？

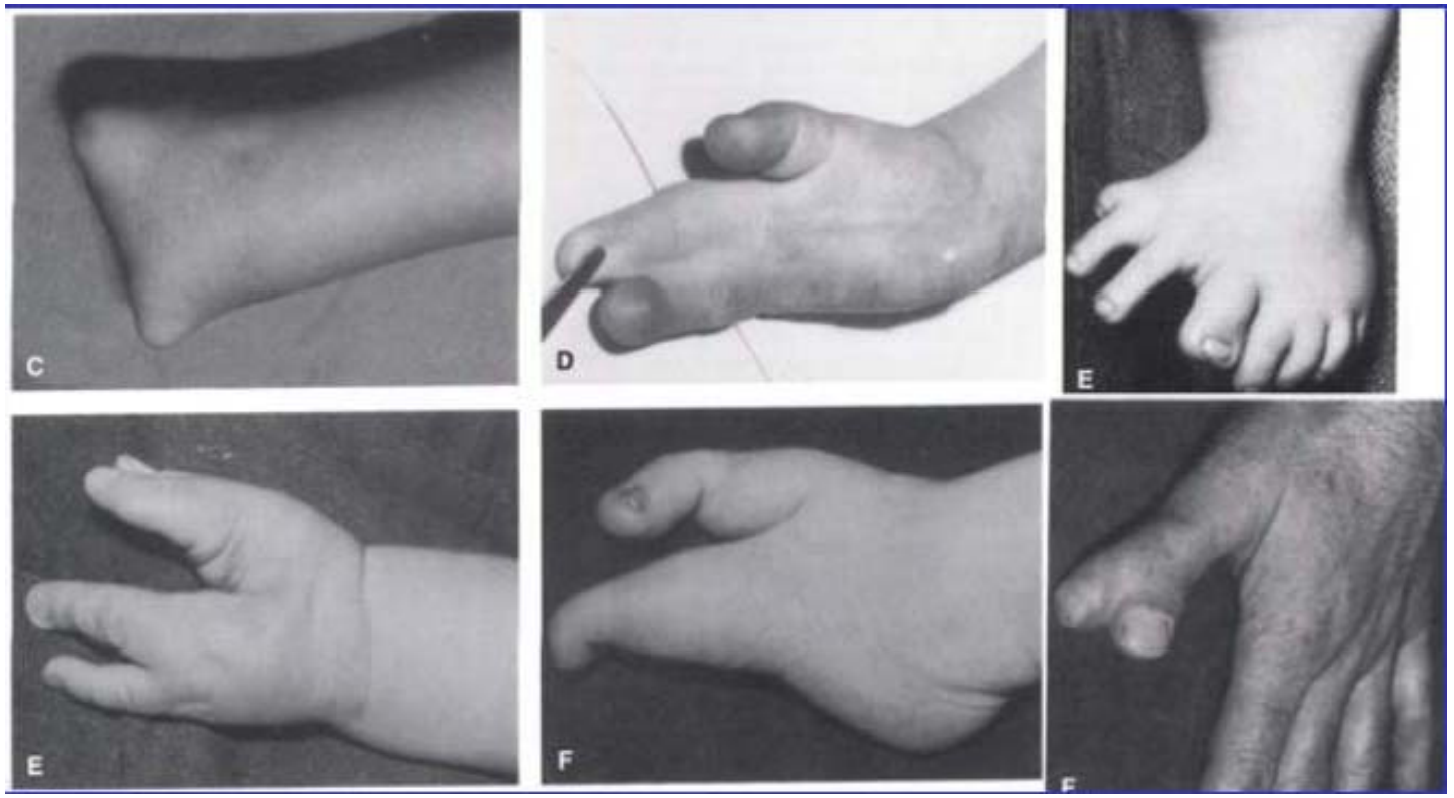
如何控制這些細胞發育成為不同類型的細胞組織？





What happen if genetic control goes wrong in limb development?

發育出問題, 有些會遺傳, 因為基因控制發育



1. 了解動物胚胎的發育(分子機制)

germ layers: ectoderm, mesoderm, endoderm

organogenesis

2. 了解發育生物學的研究發展及重要性

母體-胎兒保健, 預防新生兒缺陷

3. 發育生物學的相關應用

a.幹細胞 b.複製及器官再生 c.細胞凋零 d.老化 e. 癌症與疾病

Model organisms to study developmental biology
模式生物

– nematode (*C. elegans*) 線蟲
– fruit fly (*D. melanogaster*) 果蠅
– sea urchins 海膽
– South African Frog (*X. laevis*)
– Zebrafish (*D. Renio*)
– chick
– mouse
– plant (*A. thaliana*)

製造突變株:
看型態/性狀

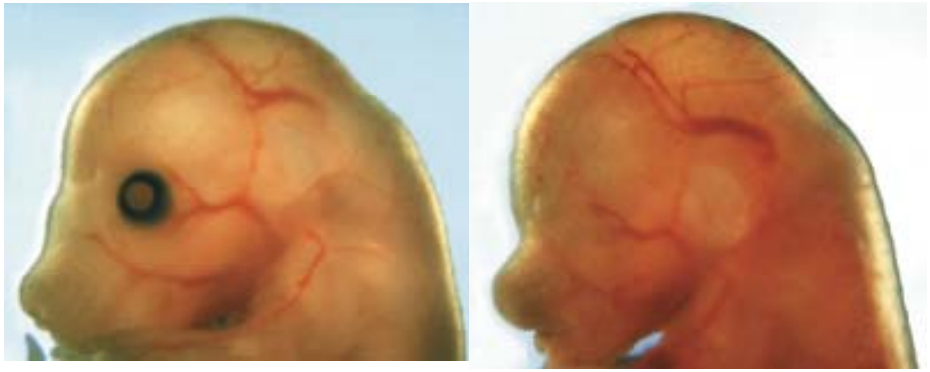
用以研究發育生物學, 人類疾病

Universal mechanisms of animal development

通用機制

小腦

Drosophila with mutant alleles of the *eyeless* gene



Mouse embryos with wild-type (L) and mutant (R) alleles of the *Pax-6* gene

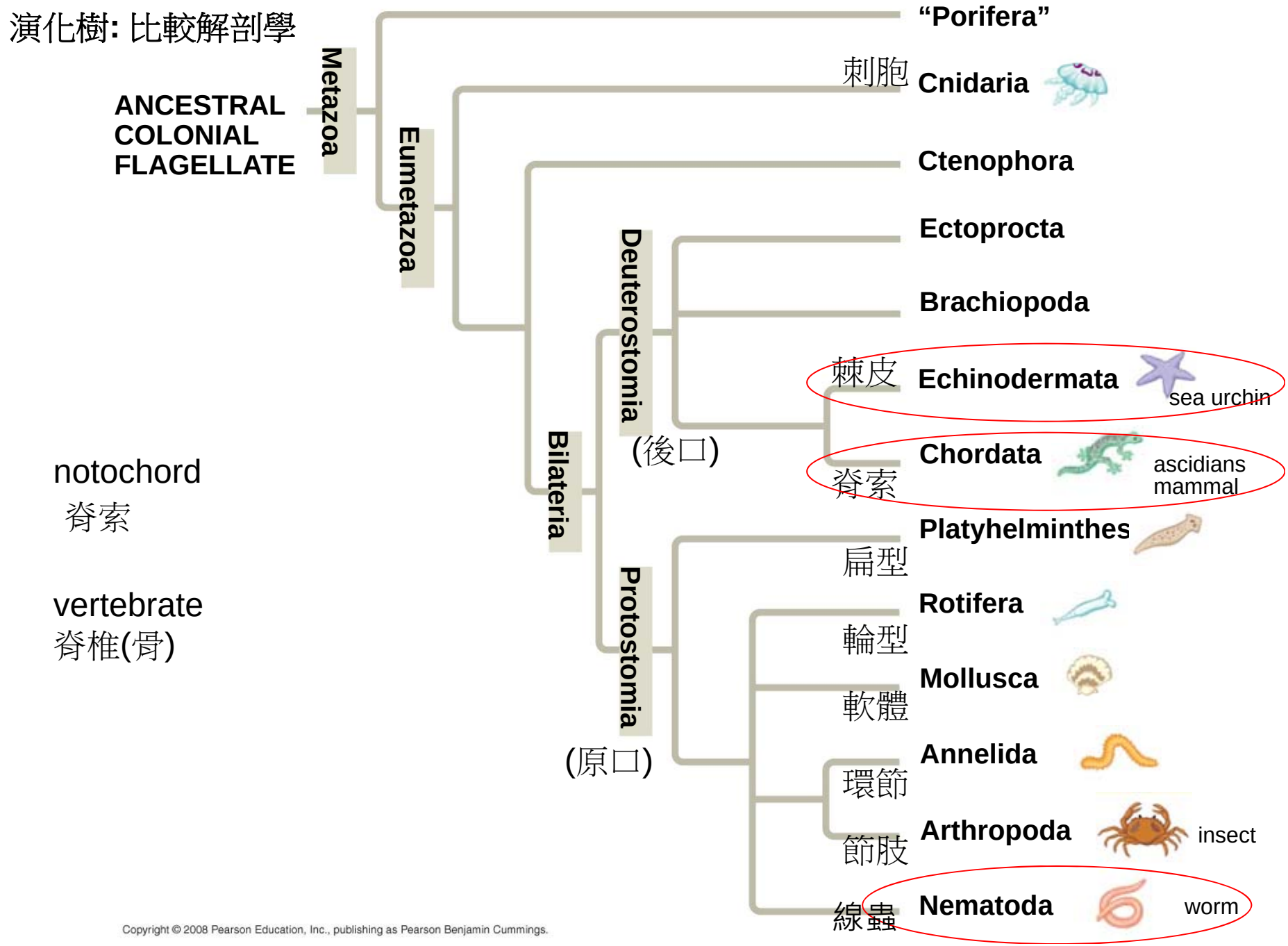
Fig. Homologous proteins functioning interchangeably in the development of mice and flies.

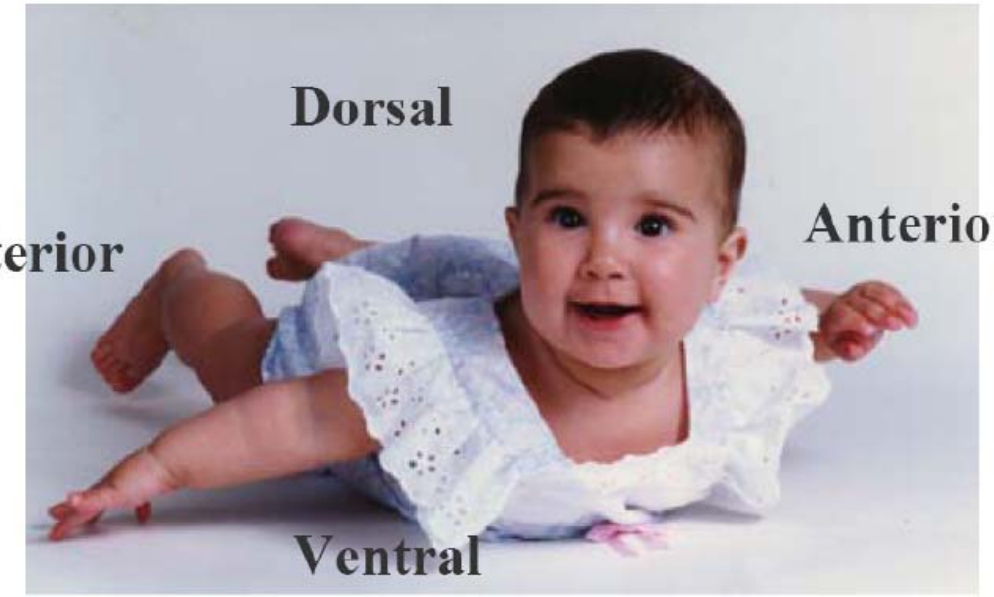
人類不利於作發育, 疾病模式之原因：

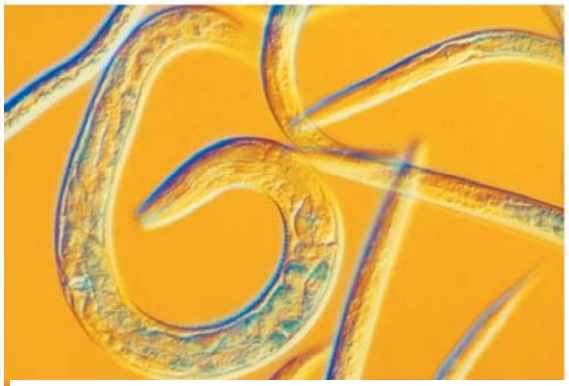
- 1.壽命長。
- 2.再生時間緩慢。
- 3.子代少。
- 4.極度異質性。
- 5.無法長期控制飼養方式及社經生活。
- 6.定量資料如飲食、飼養方面缺乏。
- 7.道德上的問題。

Comparative anatomy and Embryology provide clues to animal phylogeny

演化樹: 比較解剖學

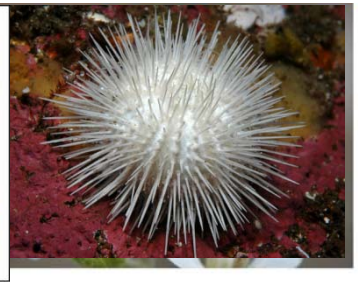




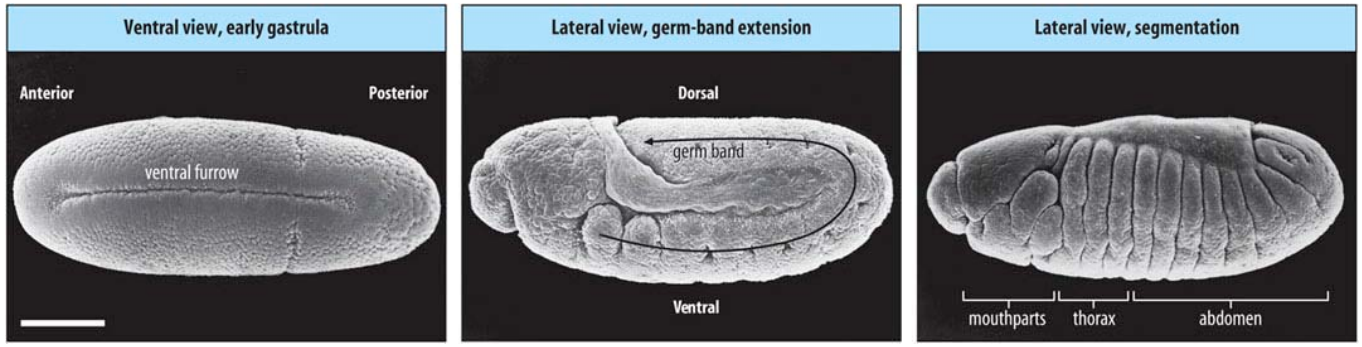


製造突變株:
看型態/性狀

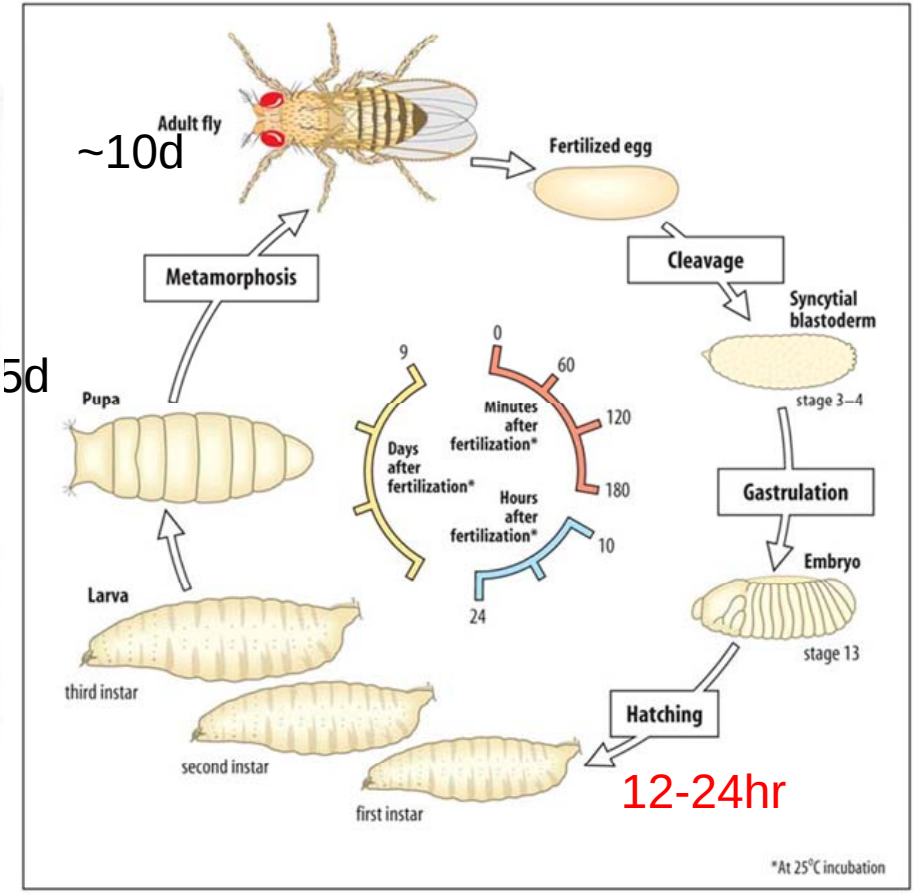
眼、四肢、胚胎過程



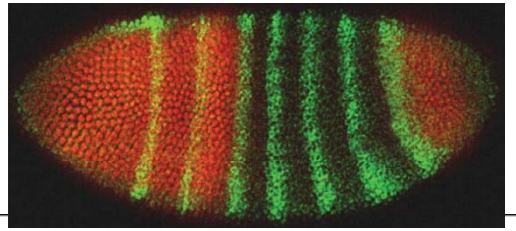
果蝇 fruit fly (*Drosophila melanogaster*)



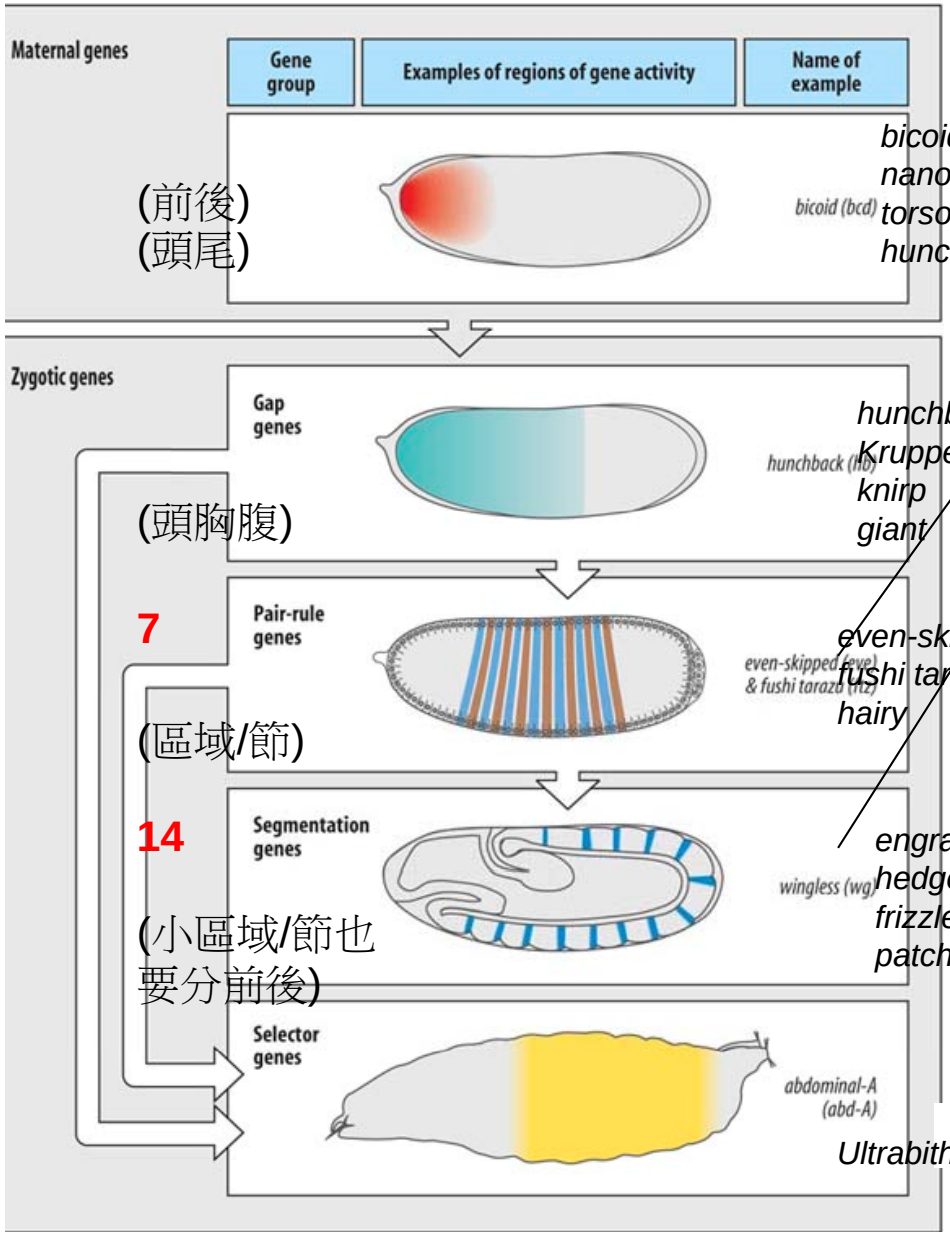
5d

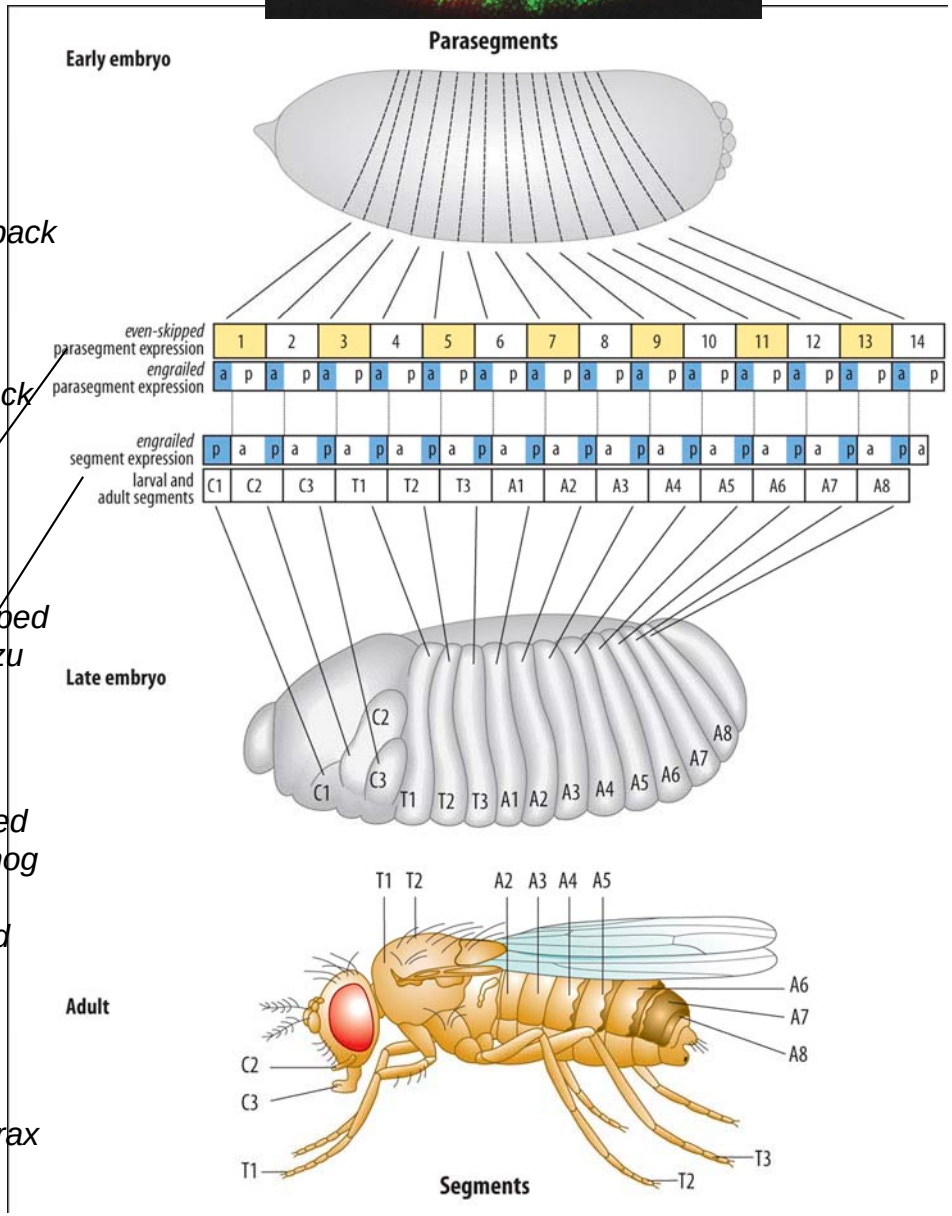


Body plan: To build a body

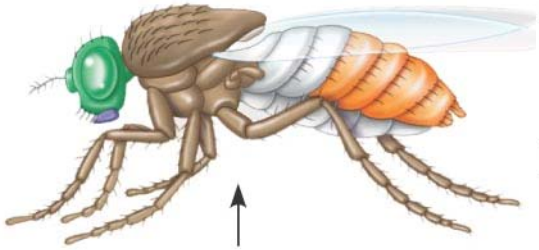


video





Adult fruit fly

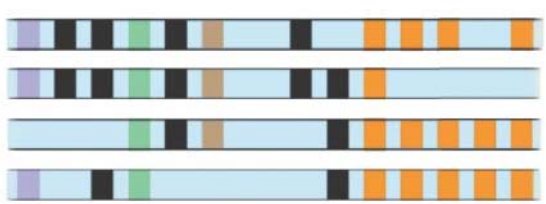


Fruit fly embryo (10 hours)

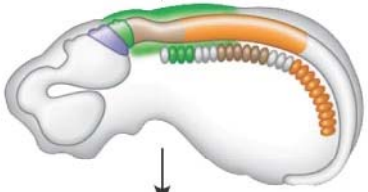
Fly chromosome

Homeobox genes

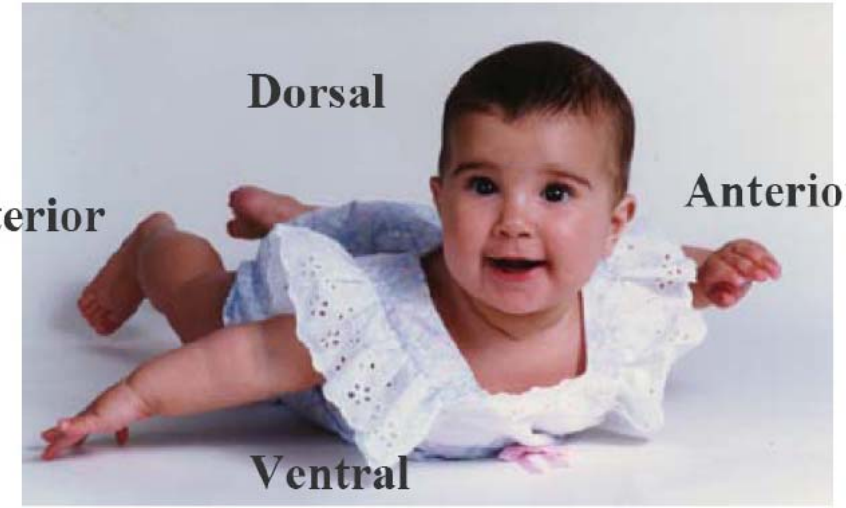
Mouse chromosomes

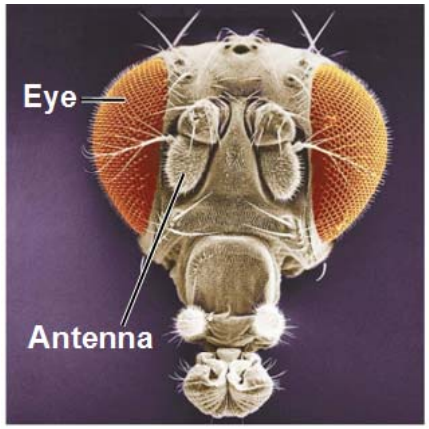


Mouse embryo (12 days)



Adult mouse



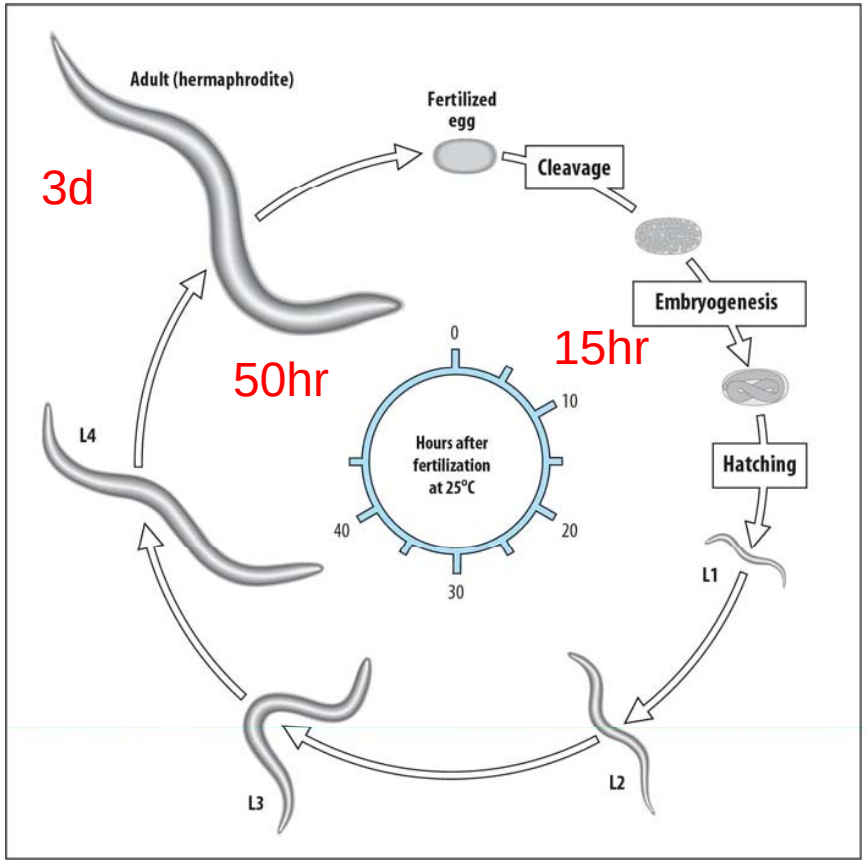


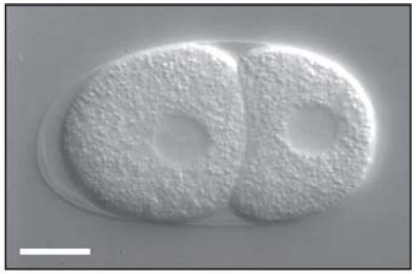
Wild type

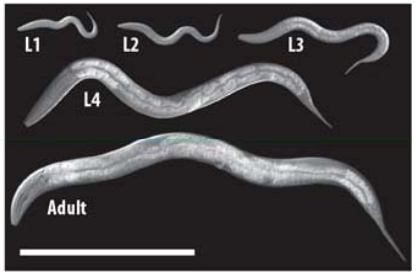
Mutant

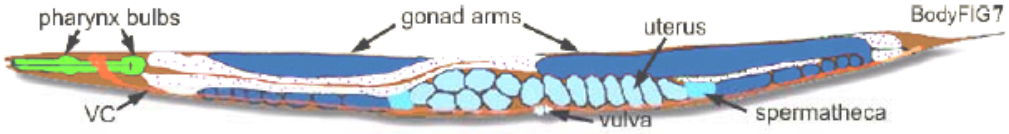
nematode (*Caenorhabditis elegans*)

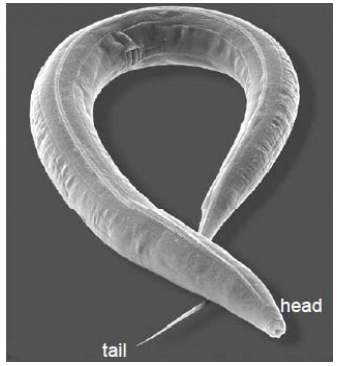
線蟲



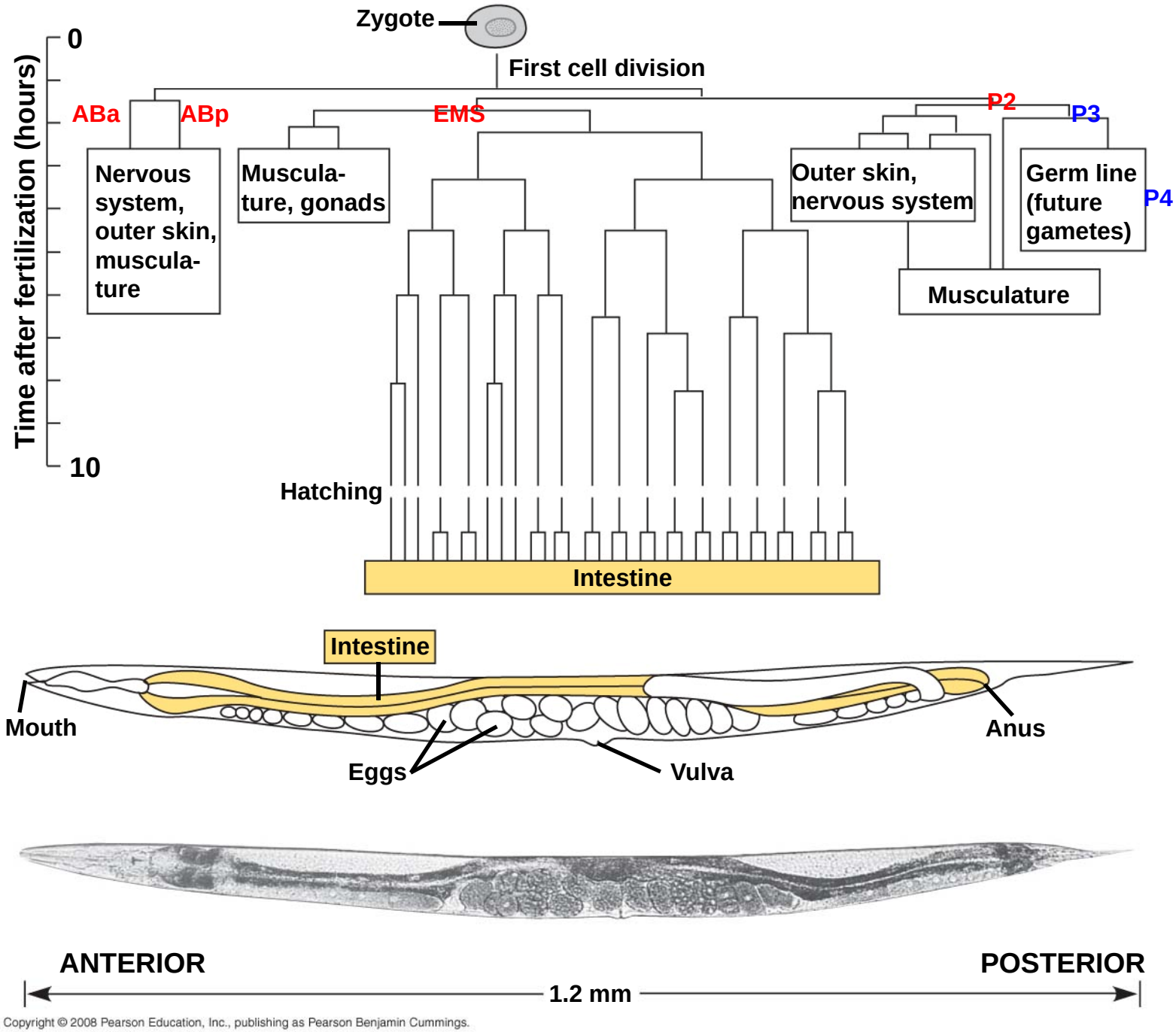


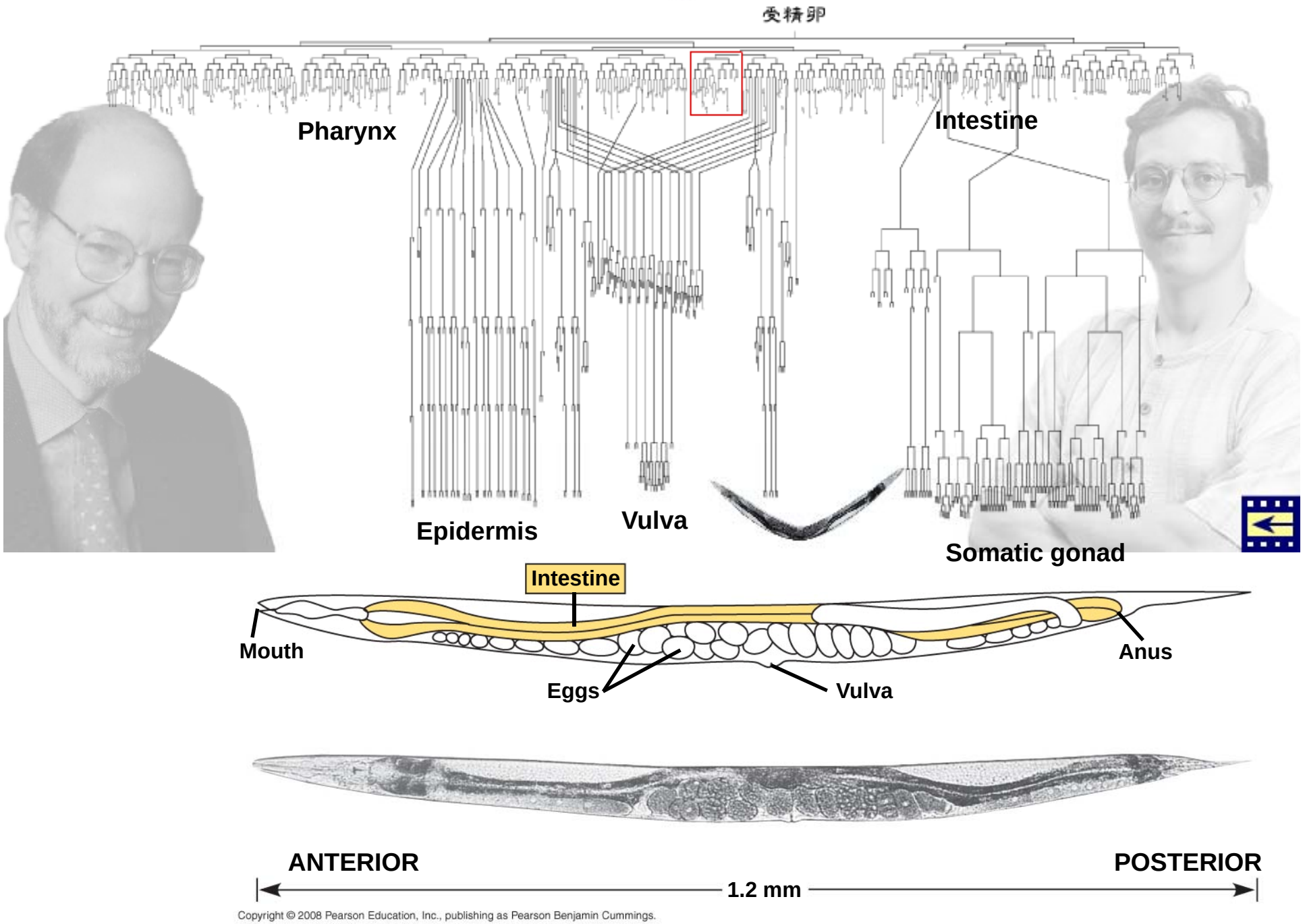






Nobel prizes: 2002 (lineage) Apoptosis, 2006 RNAi



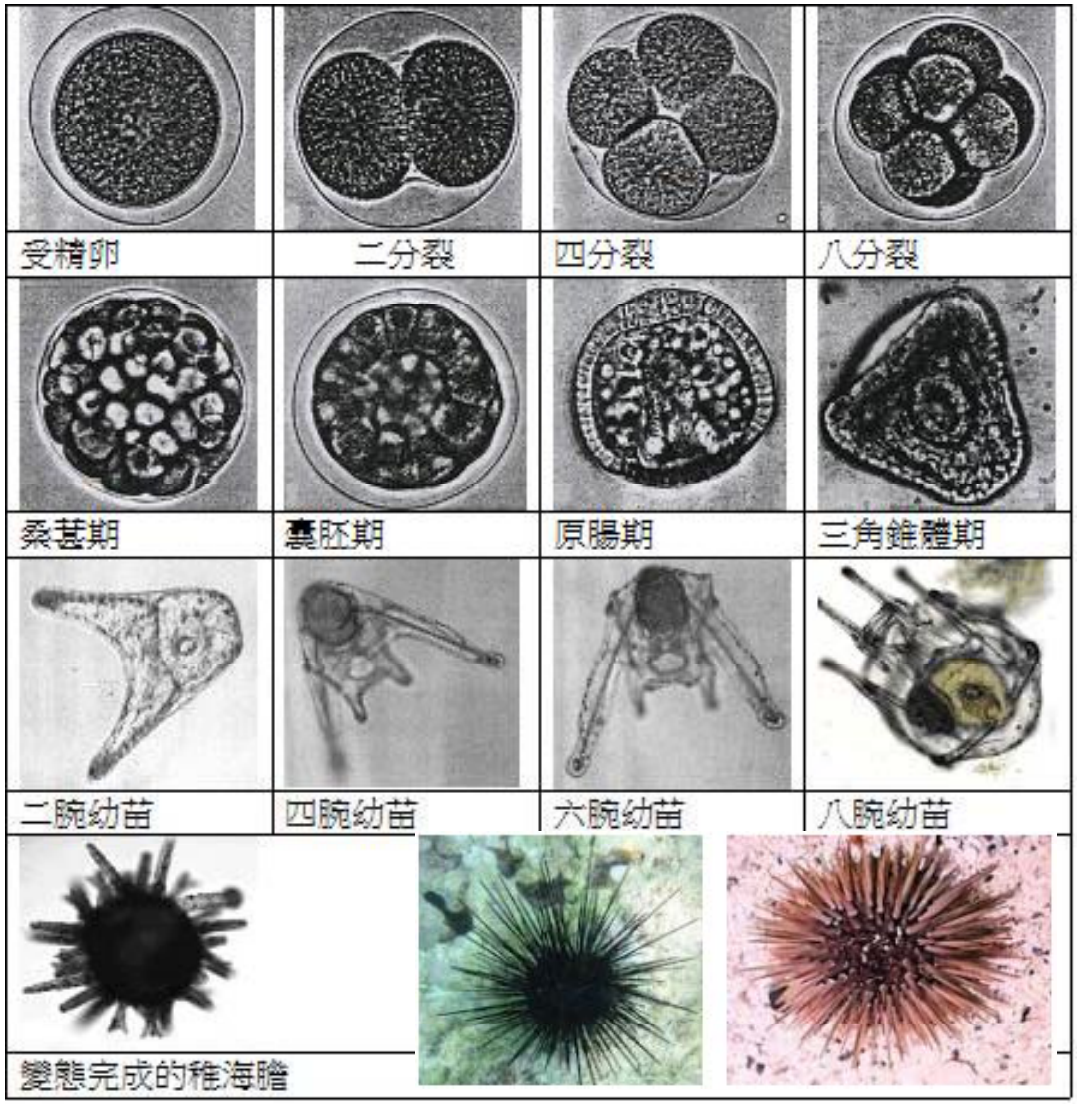


模式生物

– nematode (*Caenorhabditis elegans*)
– fruit fly (*Drosophila melanogaster*)
– sea urchins 海膽
– South African Frog (*Xenopus laevis*)
– Zebrafish (*Danio Renio*)
– chick
– mouse
– plant (*Arabidopsis thaliana*)

用以研究發育生物學, 人類疾病

Development of sea urchins

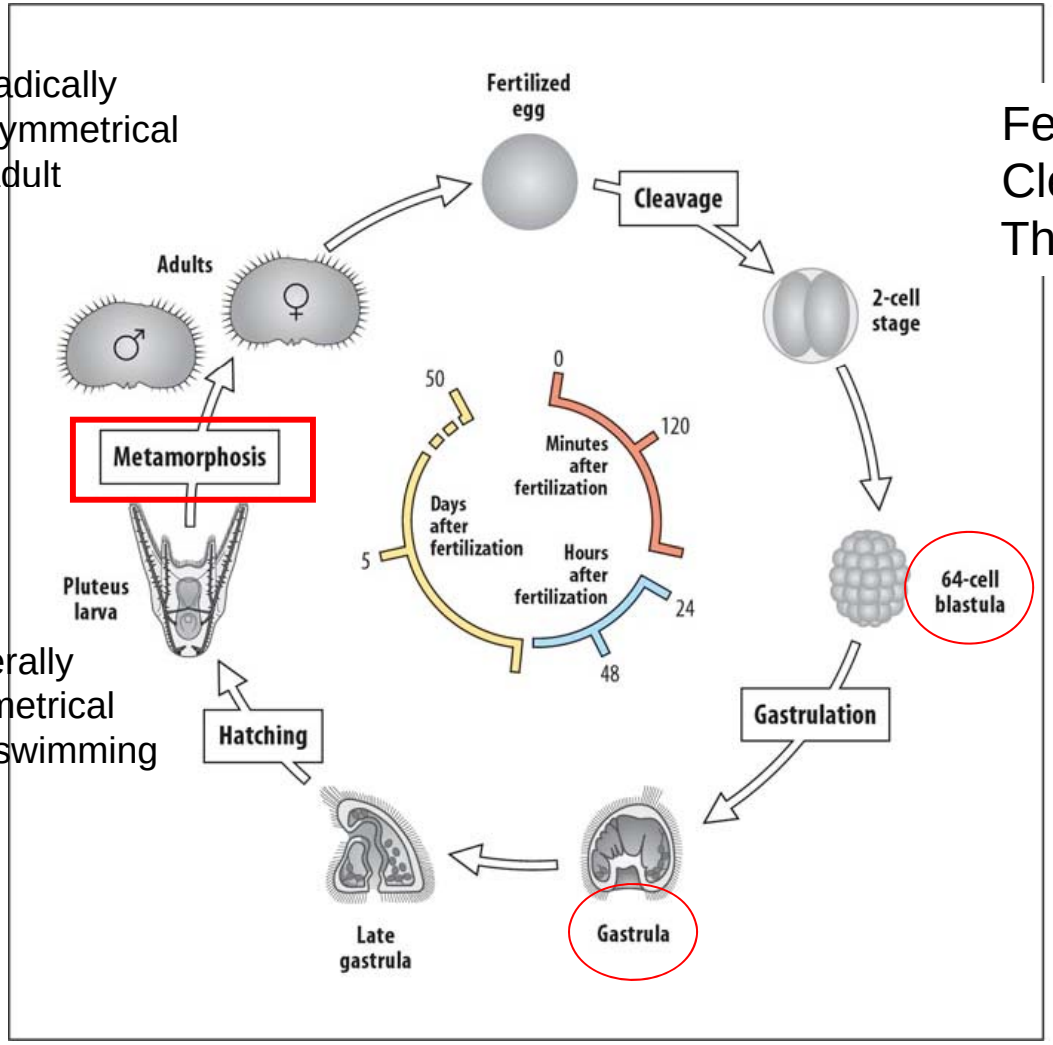


Sea urchin

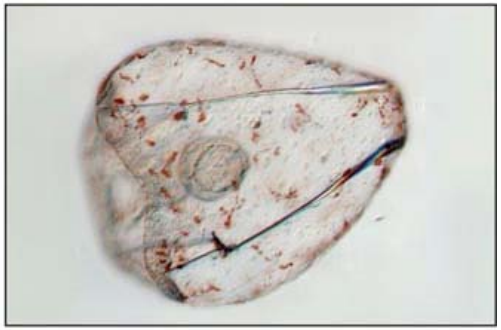
經典的動物發育研究材料之一

radically symmetrical adult

bilaterally symmetrical free-swimming larva

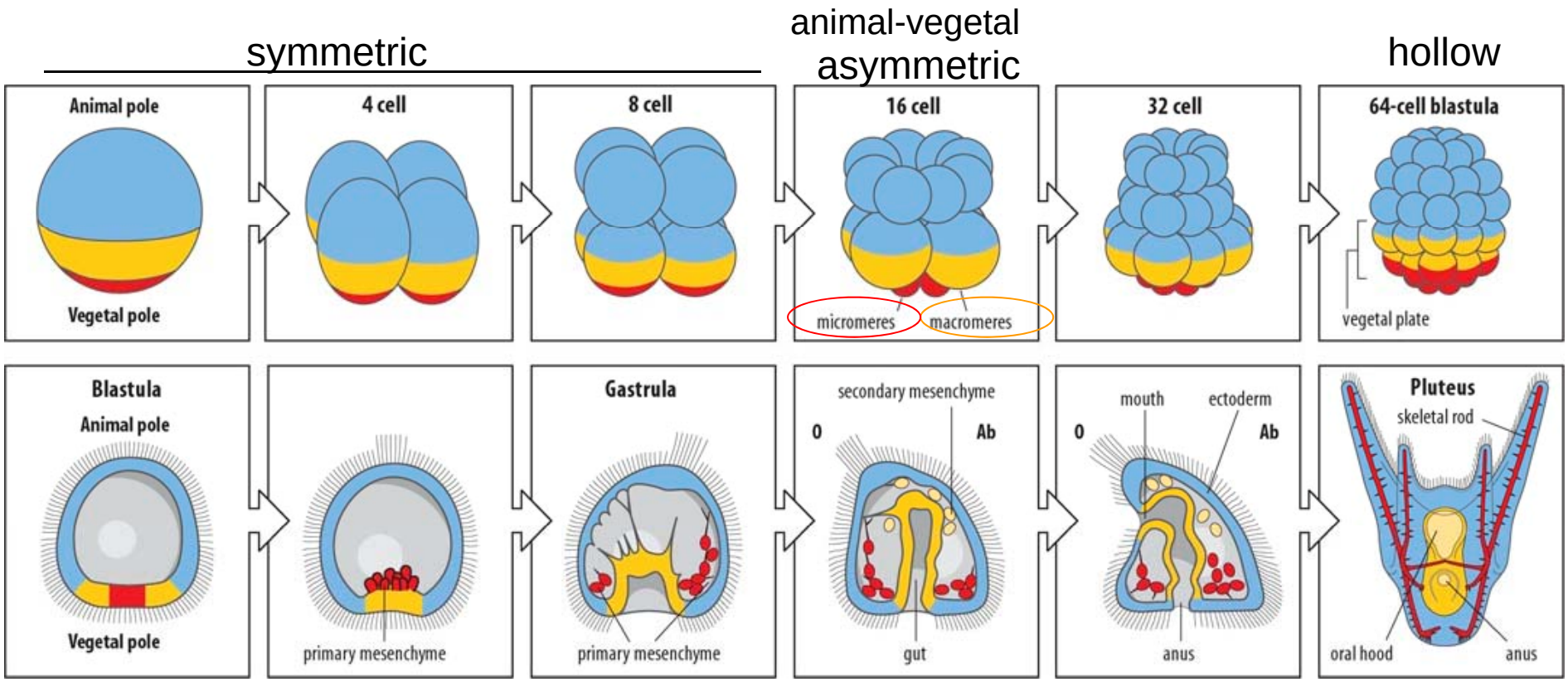


Fertilization
Cleavage
Three germ layers /gastrulation



The sea-urchin embryo develops into a free-swimming larva

Development of the sea urchin embryo.



初級間質

gut invaginate

二級間質

骨棒(中胚層)

Blue: prospective ectoderm

Yellow: endoderm

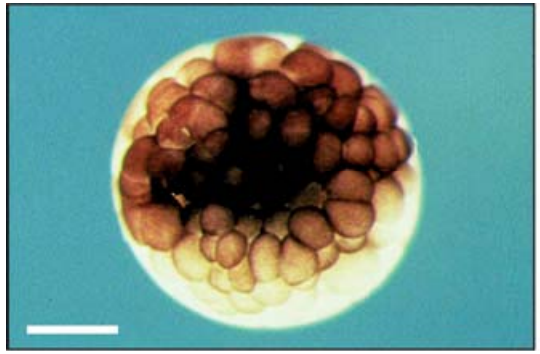
Red: mesoderm

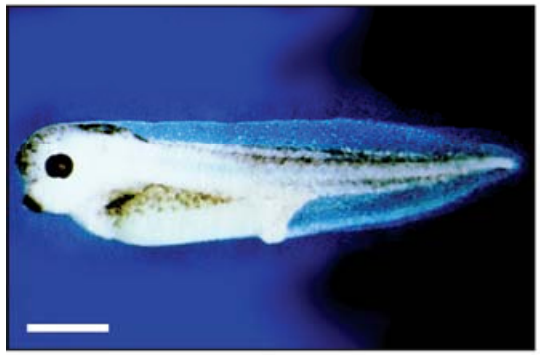
模式生物

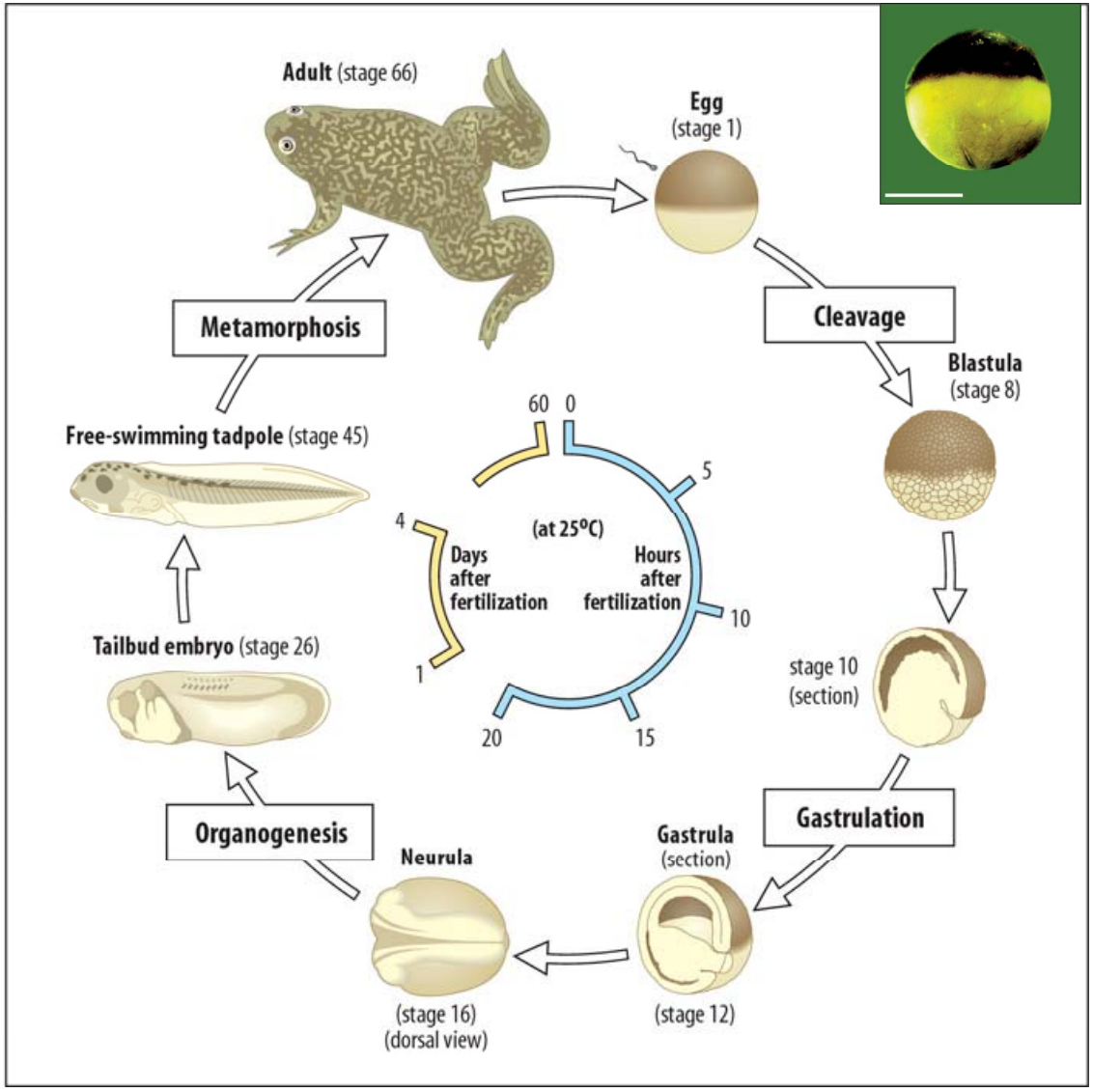
– nematode (*Caenorhabditis elegans*)
– fruit fly (*Drosophila melanogaster*)
無脊椎 → – sea urchins
– South African Frog (*Xenopus laevis*)
– Zebrafish (*Danio Renio*)
– chick
– mouse
– plant (*Arabidopsis thaliana*)

用以研究發育生物學, 人類疾病

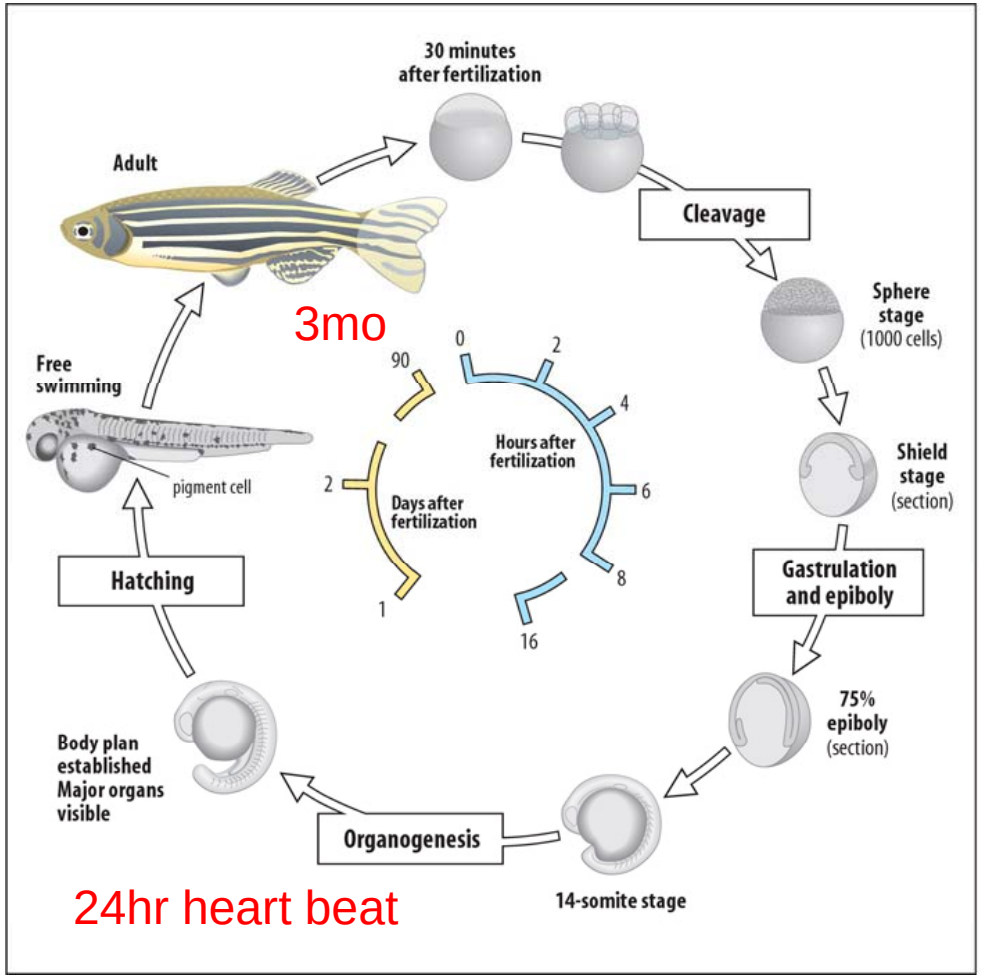
South African Frog (*Xenopus laevis*)

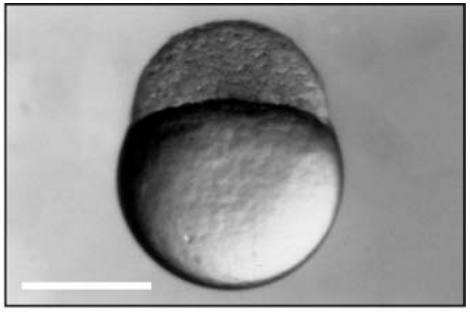


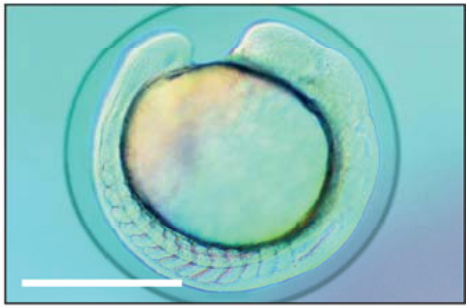


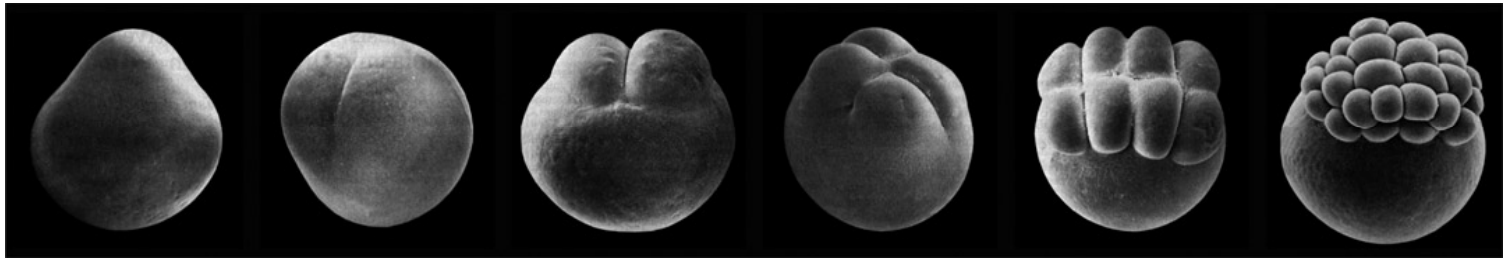


Zebrafish (*Danio Renio*)







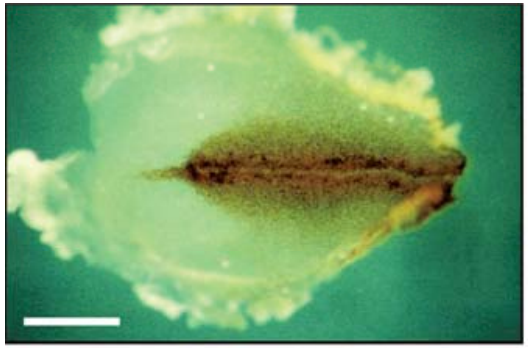


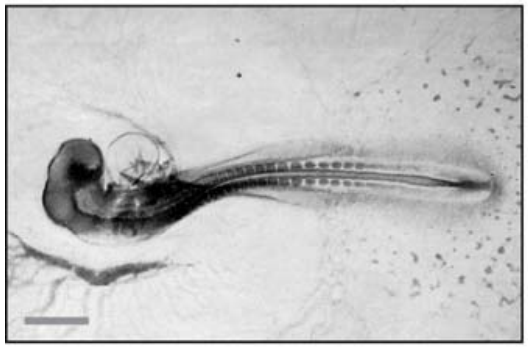
模式生物

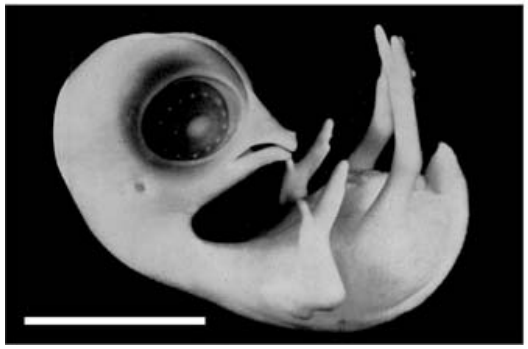
– nematode (*Caenorhabditis elegans*)
– fruit fly (*Drosophila melanogaster*)
– sea urchins
– South African Frog (*Xenopus laevis*)
– Zebrafish (*Danio Renio*)
– chick
– mouse
– plant (*Arabidopsis thaliana*)

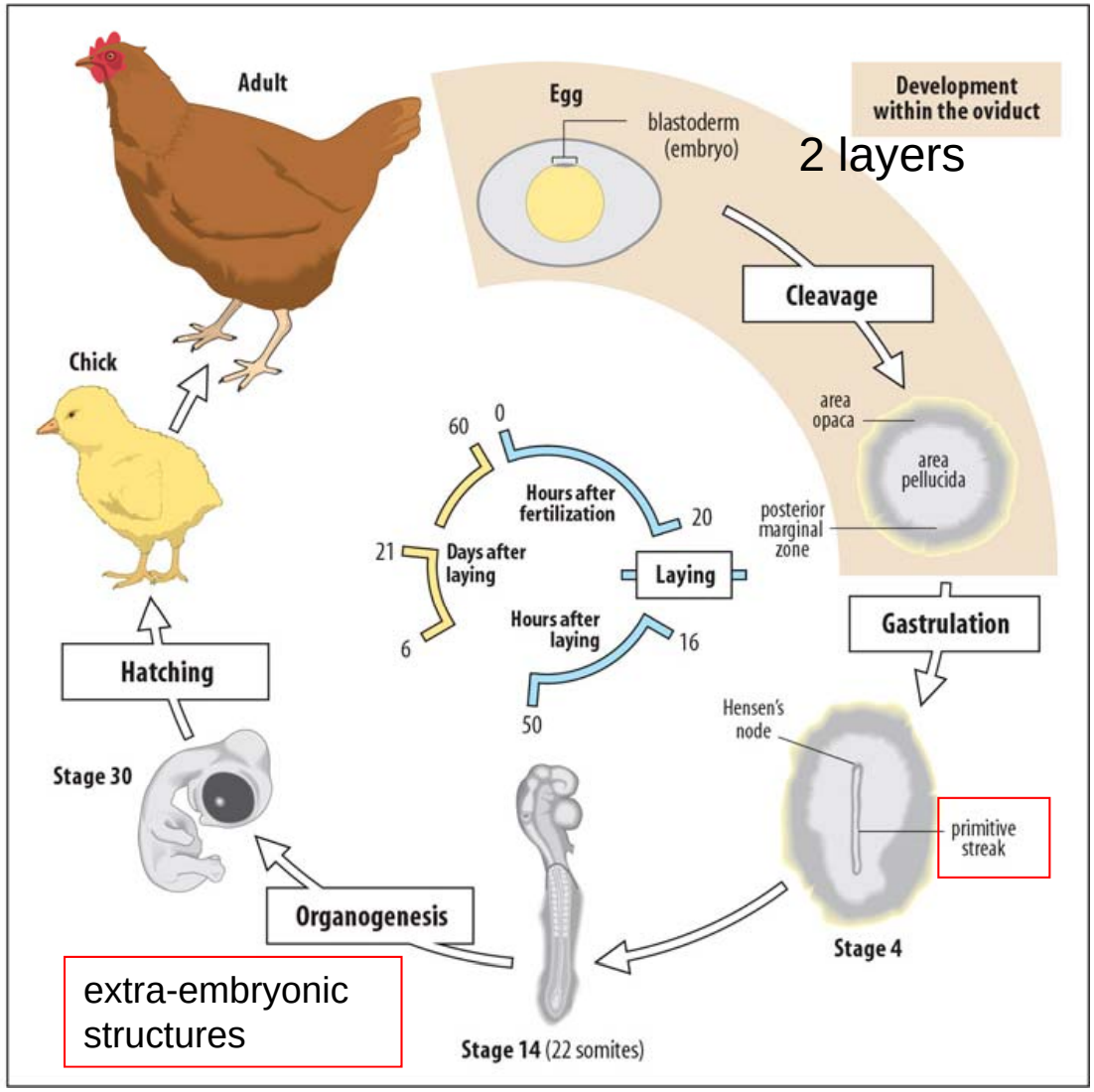
用以研究發育生物學, 人類疾病

Part 3 Life cycle of the chicken





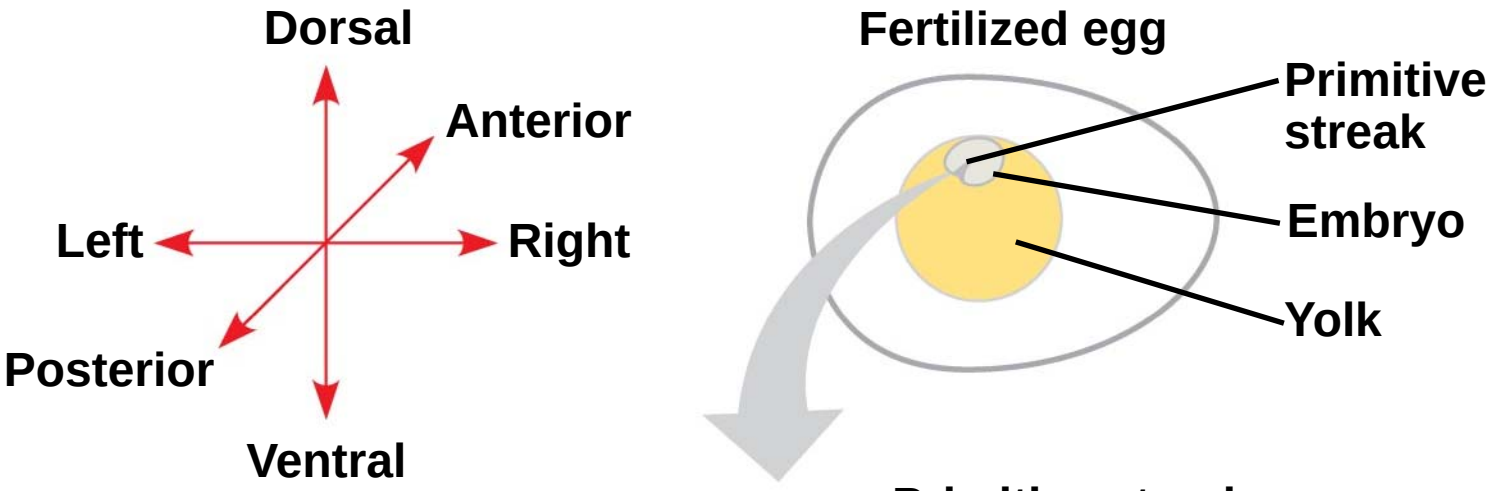


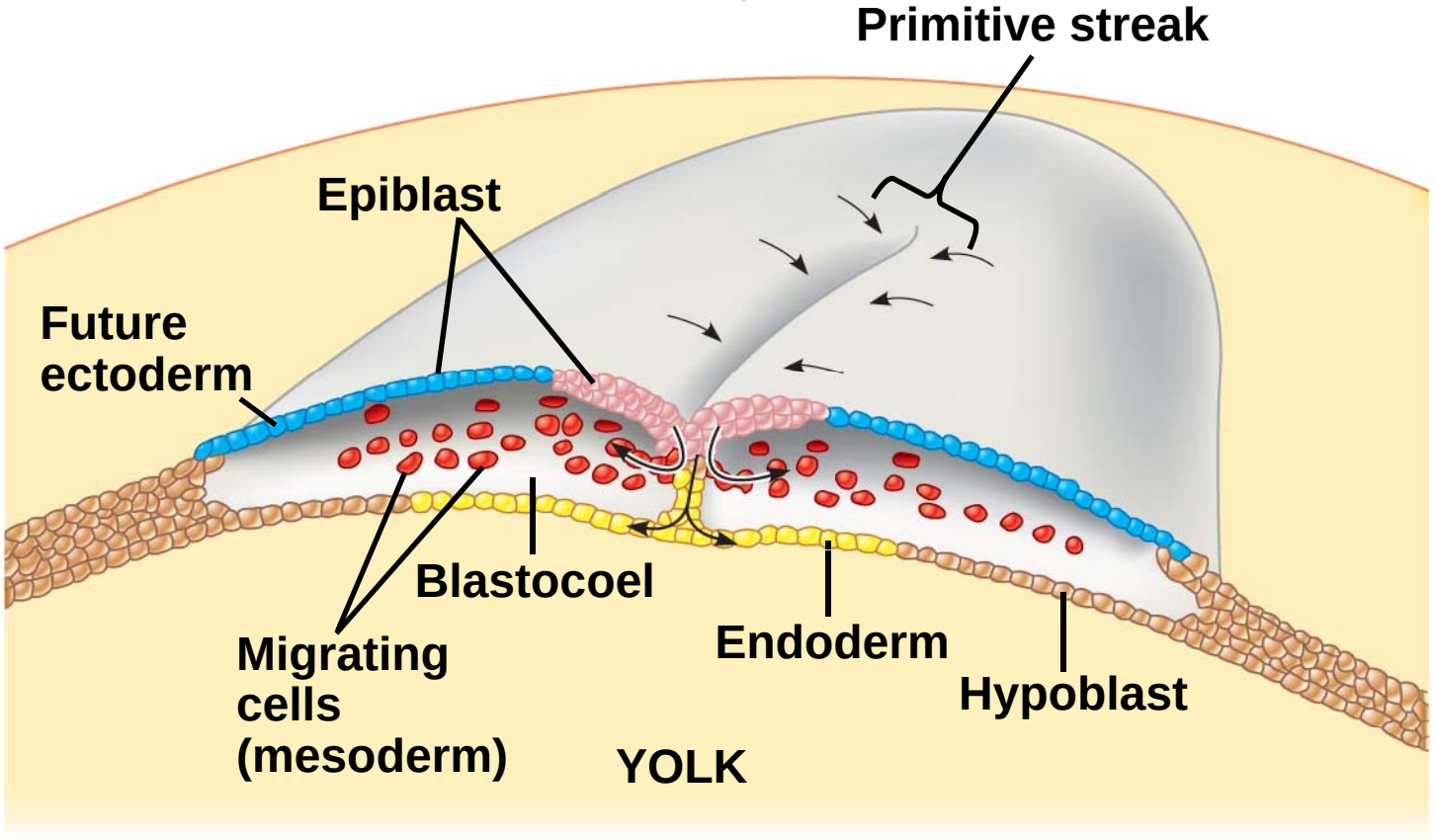


Birds and mammals resemble each other and different from frog in some important features of early development

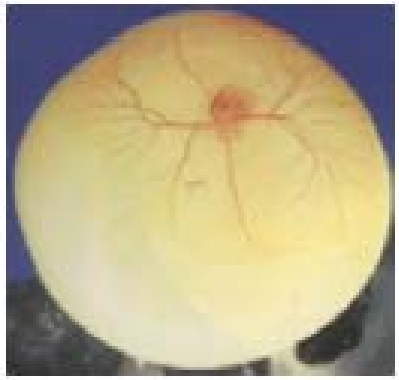
卵大 易取得 破殼 半透明 基因改造
具羊膜 (與哺乳類像)

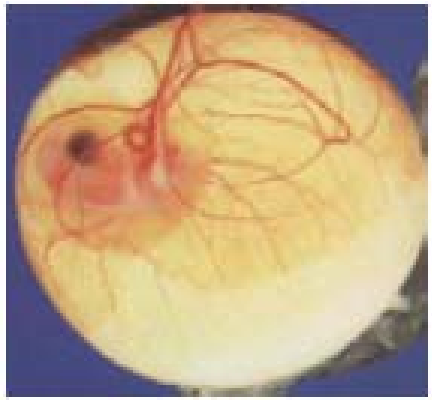
Fig. 47-11



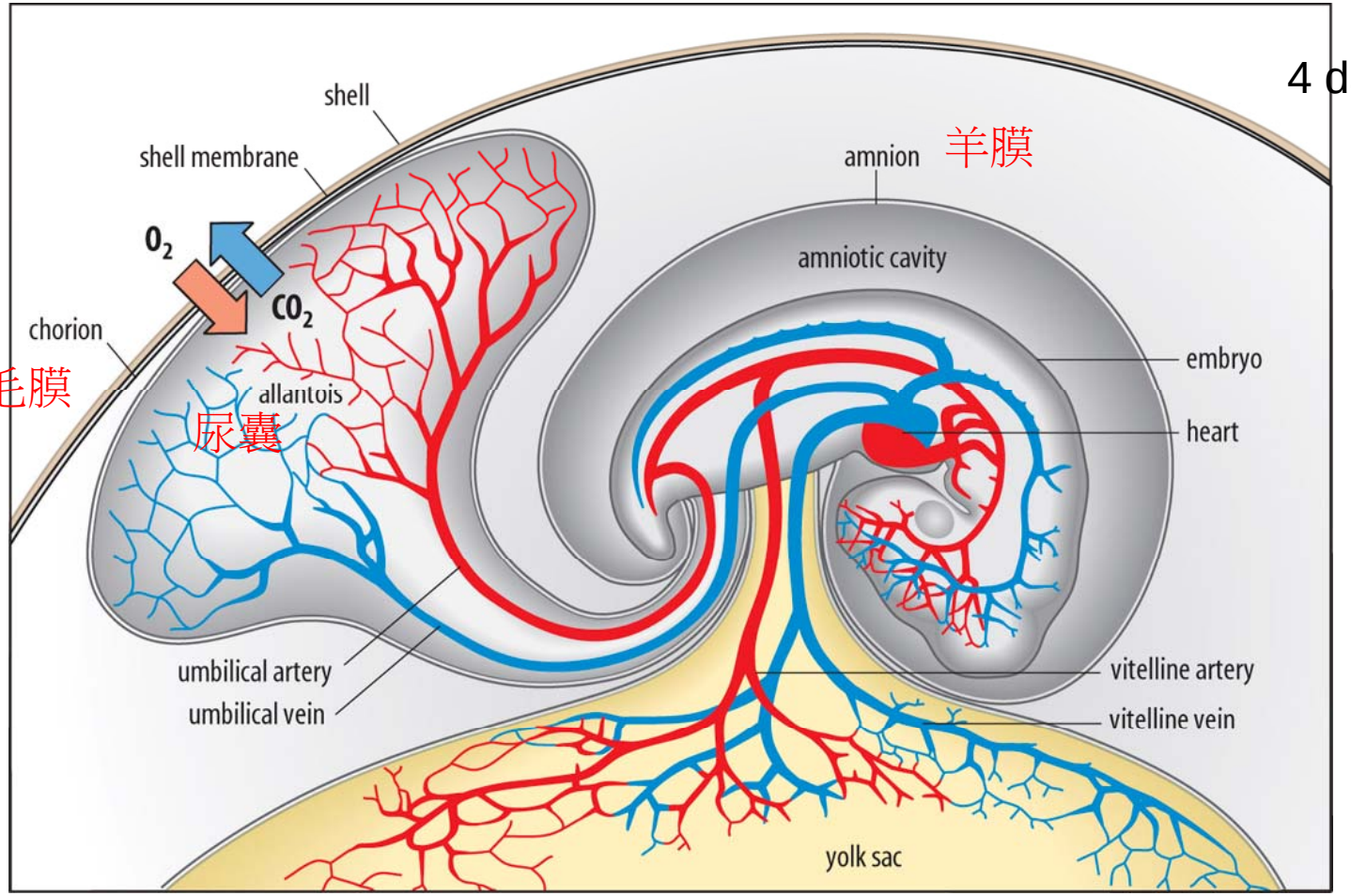


Chick **embryogenesis**





The extra-embryonic structure and circulation of the chick embryo



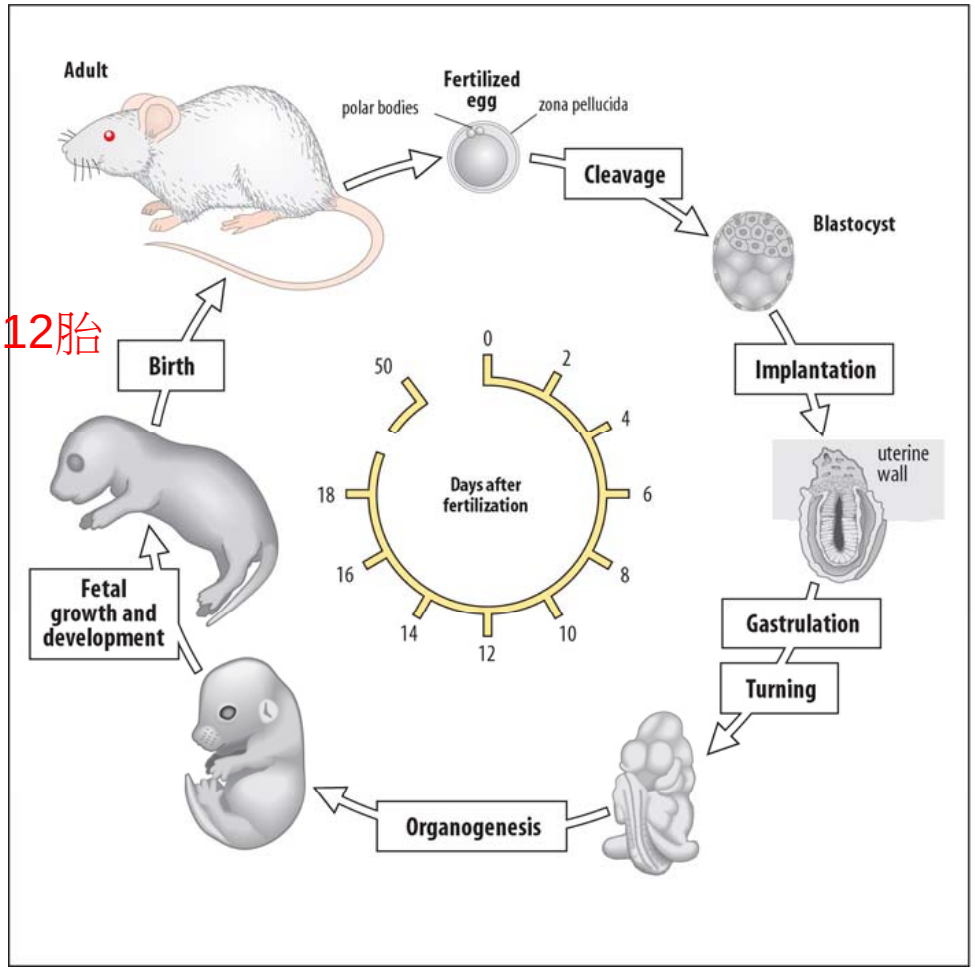
具羊膜 (與哺乳類像)

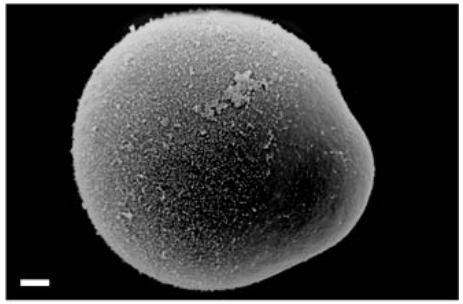
Amnion and amniotic cavity provide mechanical protection
Chorion maintain shell
Allantois bridge for oxygen and waste
Vitelline vein take nutrient form yolk to embryo
Umbilical vein take oxygen to embryo

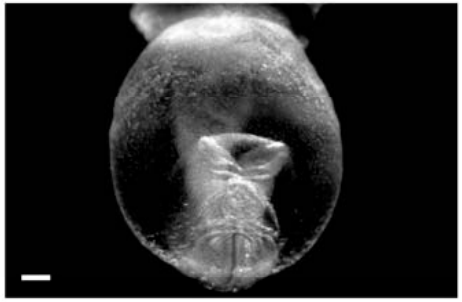
mouse

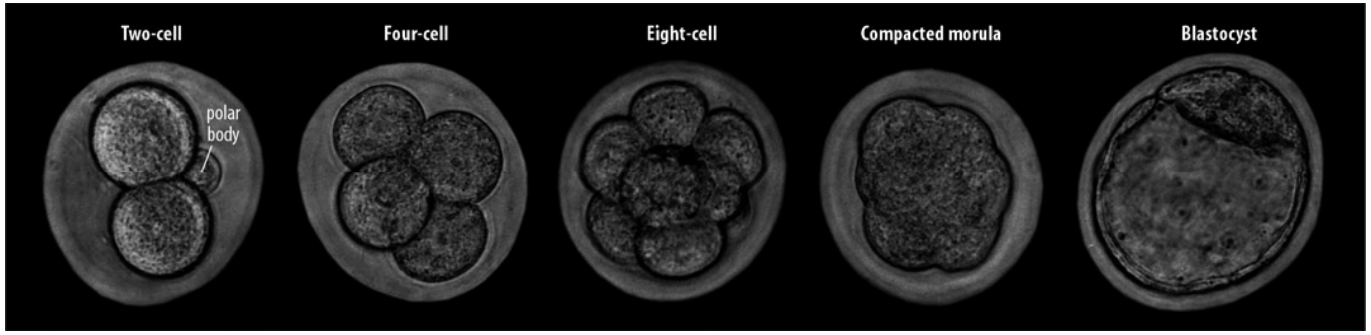
缺點?

19d, 8-12胎

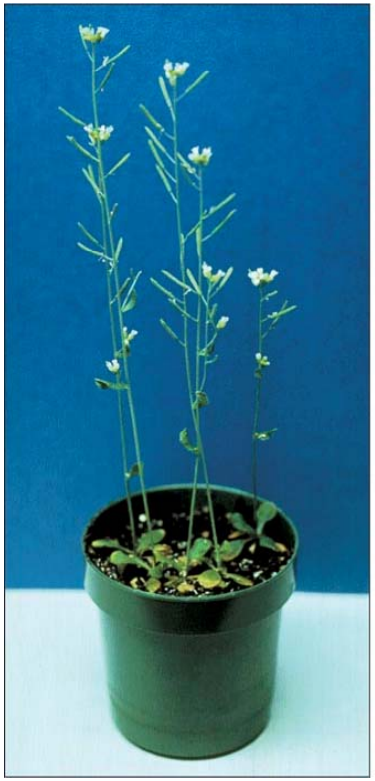


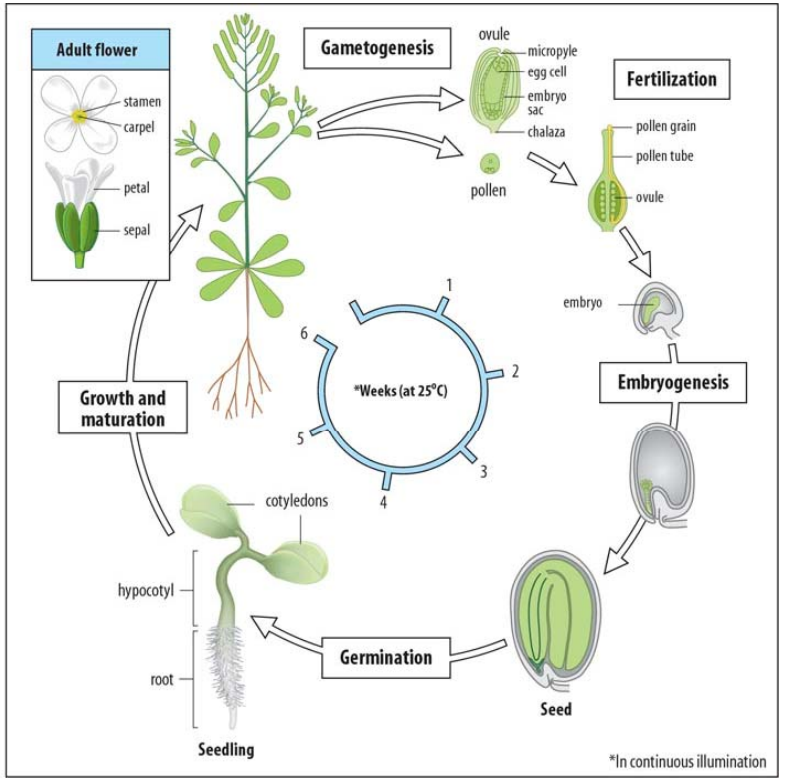


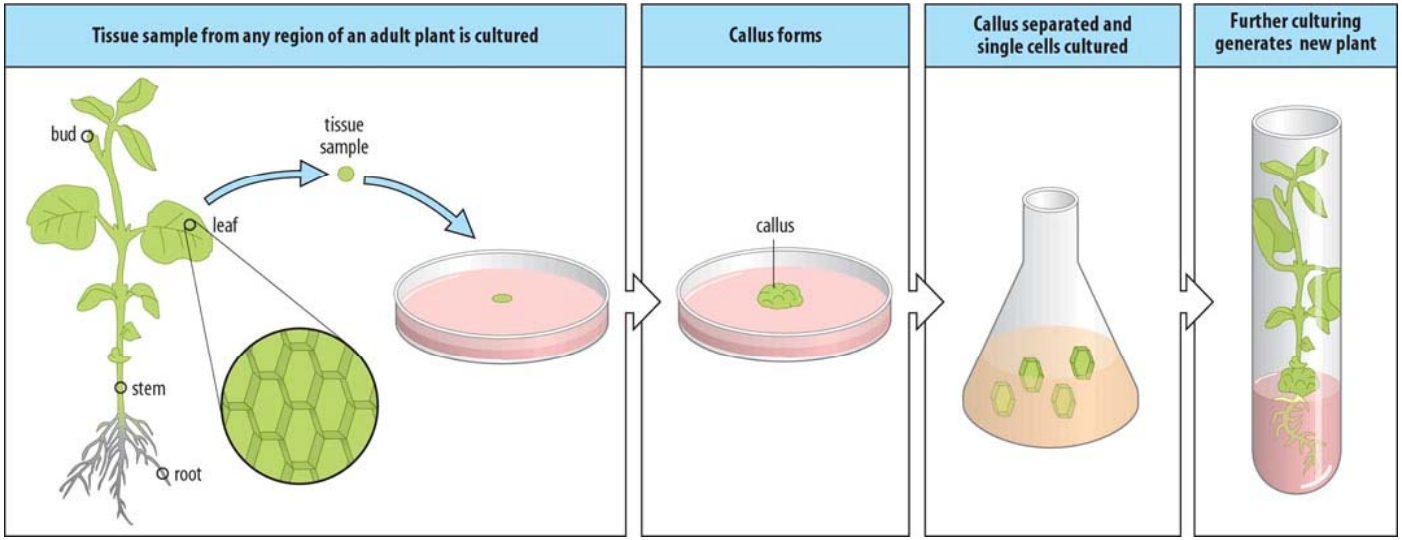




plant (*Arabidopsis thaliana*)



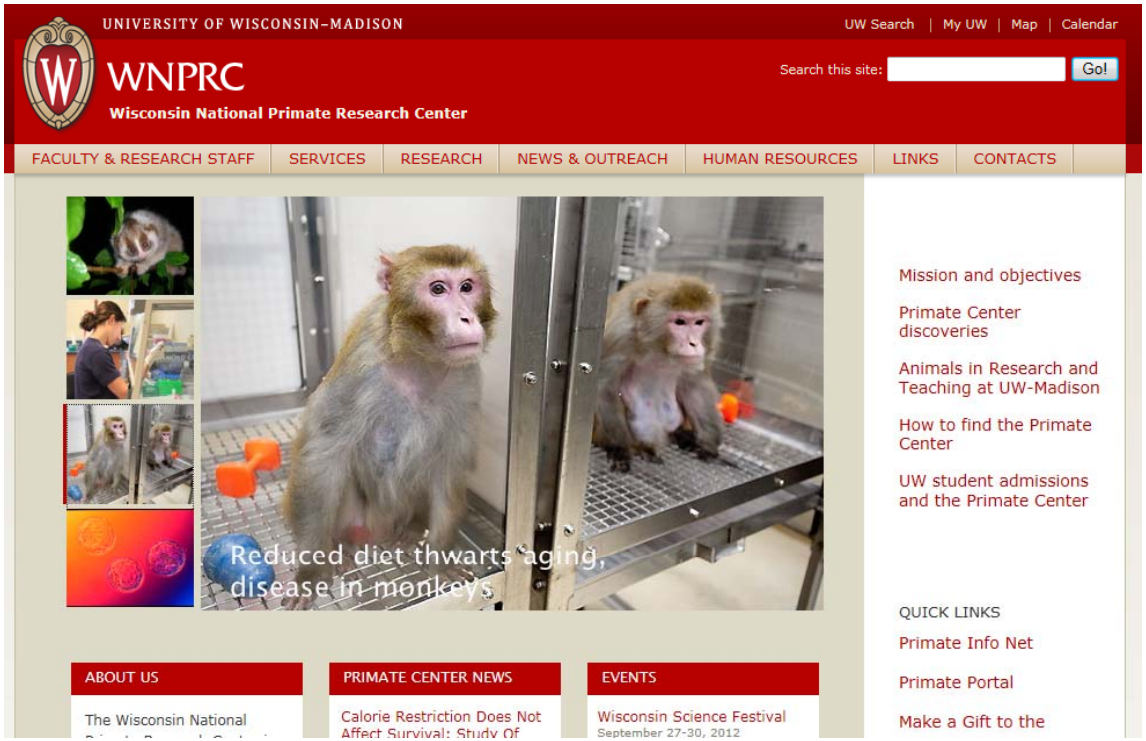




模式生物(動物)的特性

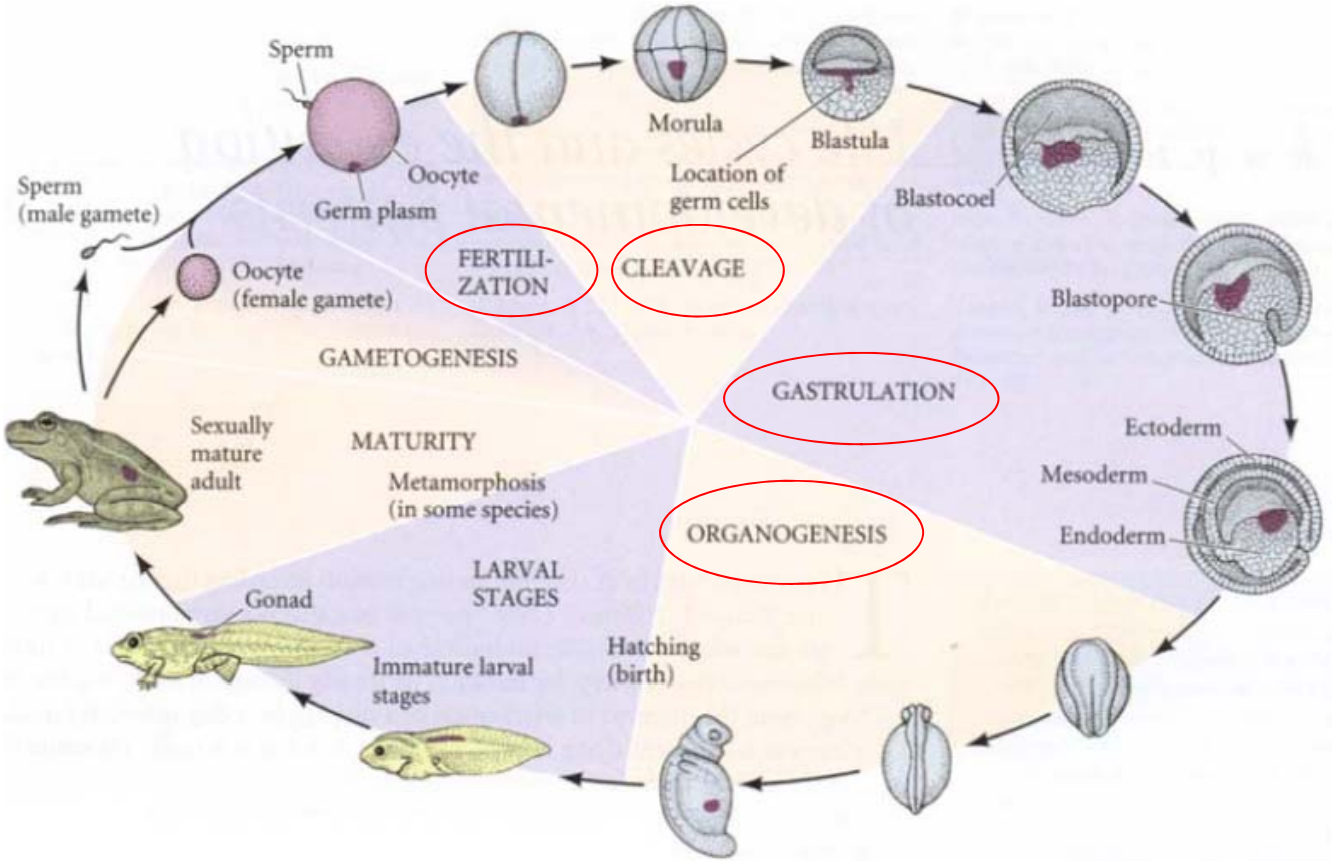
1. 與人類有相似處 (功能相似, 有基因保留性)
2. 易培養 (經費少, 空間小, 生長周期短, 繁殖快, 子代多)
3. 易於實驗操作 (體外受精, 胚體透明, 容易進行基因操控)
4. 資料多 (基因已解碼)

Primate
黑猩猩: HIV, HBV, Behavior, Learning

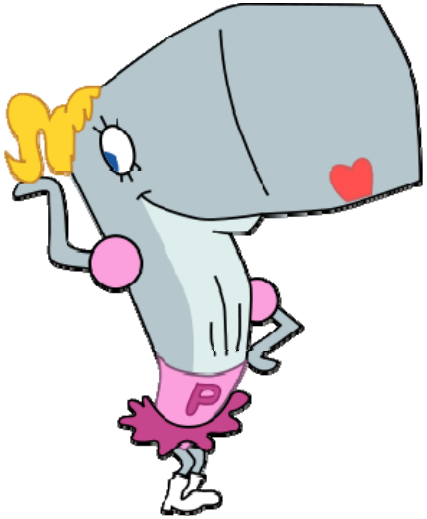


Outline

1. 胚胎學 (embryology) vs. 發育生物學 (developmental biology)
2. 模式生物 (model organisms)
3. **動物發育的主要階段**
4. **發育過程之機制**
5. **組織再生與幹細胞**



動物發育的主要階段



所有動物皆一樣?

動物發育的主要過程

1. 受精 (Fertilization)

2. 卵裂 (Cleavage)

cell division creates a hollow ball of cells called a blastula

3. 原腸化 (Gastrulation)

cells are rearranged into a three-layered gastrula

4. 神經 (Neurulation)

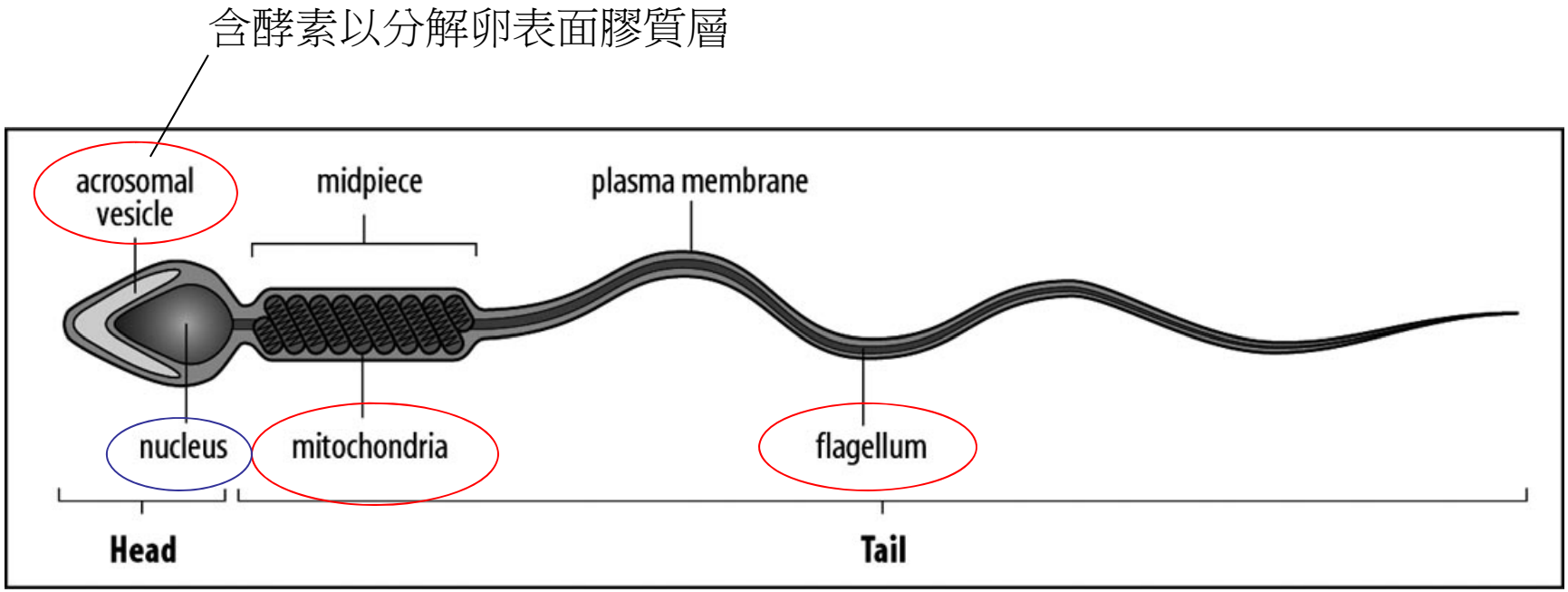
5. 器官生成 (Organogenesis)

the three layers interact and move to give rise to organs

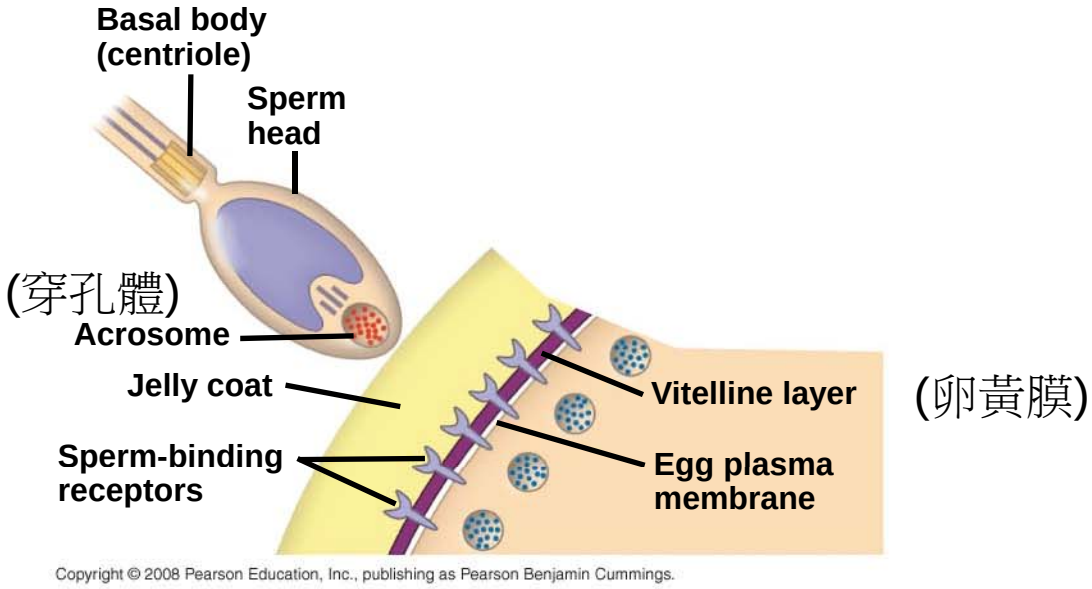
6. 個體生成 (Growth)

Fertilization

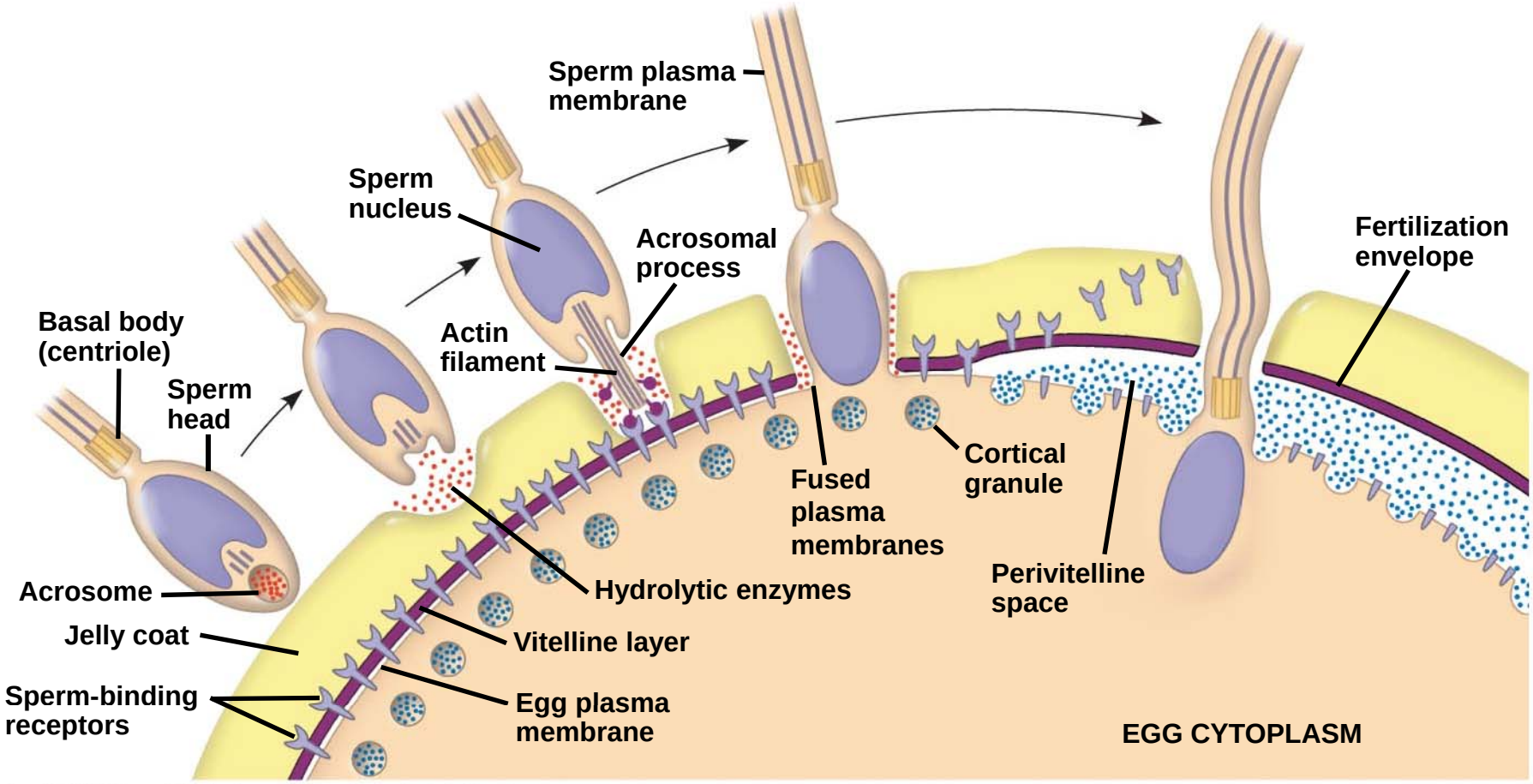
- Fertilization brings the haploid nuclei of sperm and egg together, forming a diploid zygote
- The sperm's contact with the egg's surface initiates metabolic reactions in the egg that trigger the onset of embryonic development



The acrosomal and cortical reactions during sea urchin fertilization



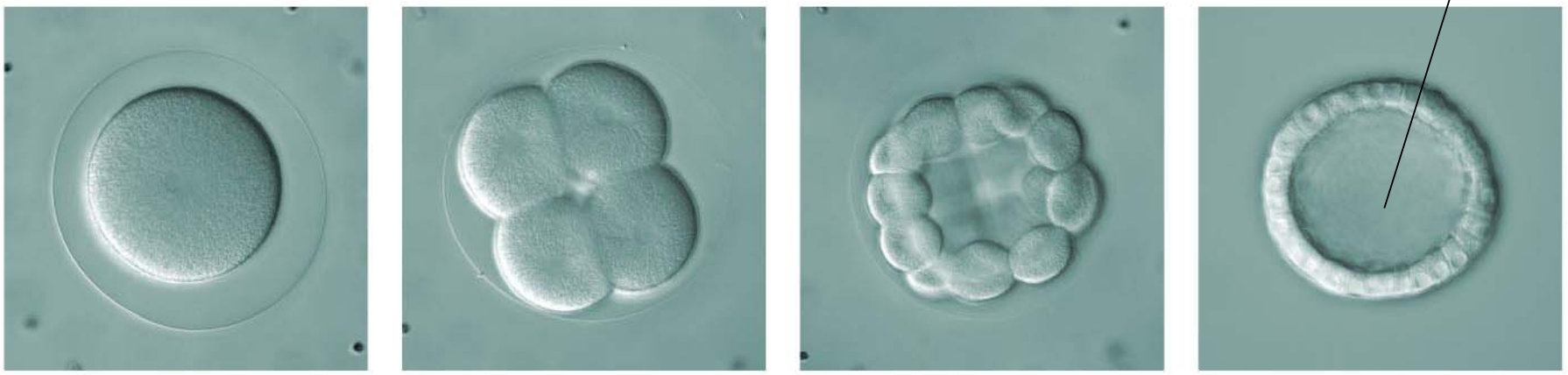
The acrosomal and cortical reactions during sea urchin fertilization



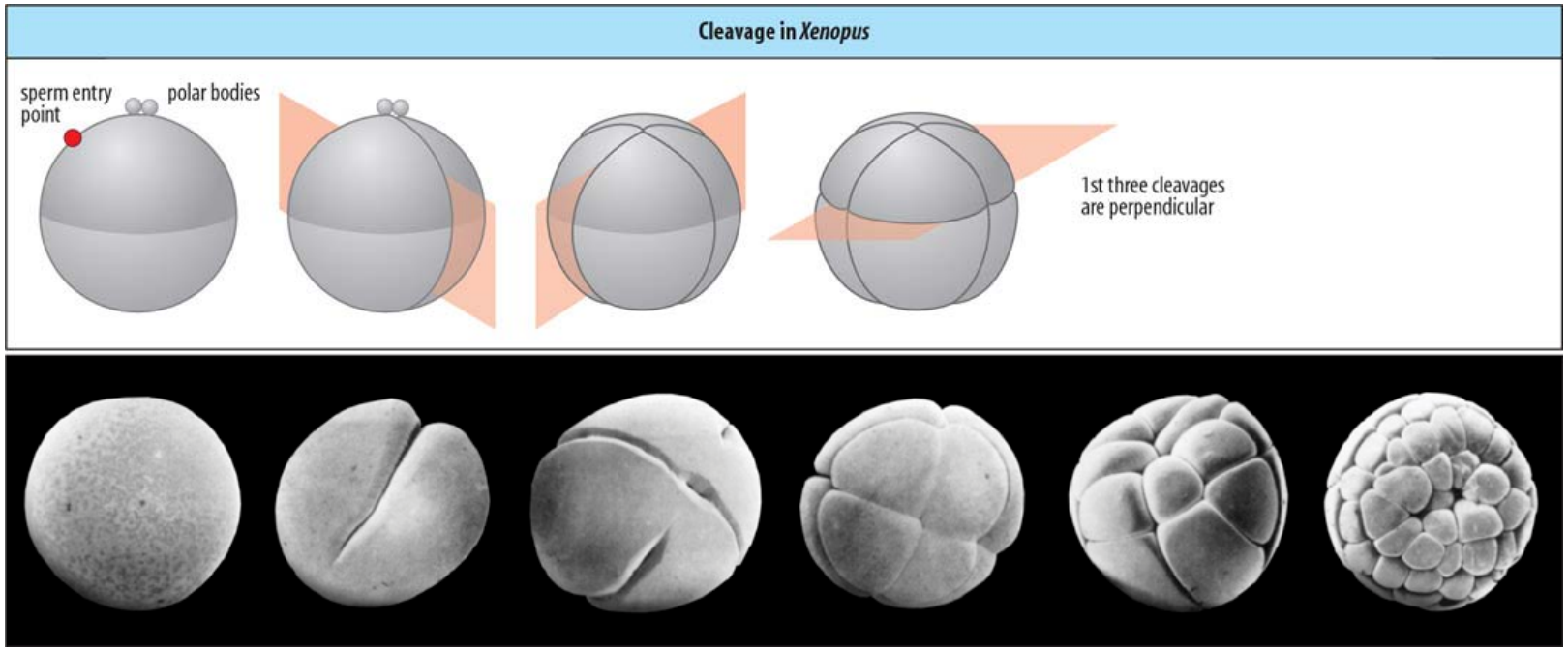
動物發育的主要過程

1. 受精 (Fertilization)
2. 卵裂 (Cleavage)
3. 原腸化 (Gastrulation)
4. 神經 (Neurulation)
5. 器官生成 (Organogenesis)
6. 個體生成 (Growth)

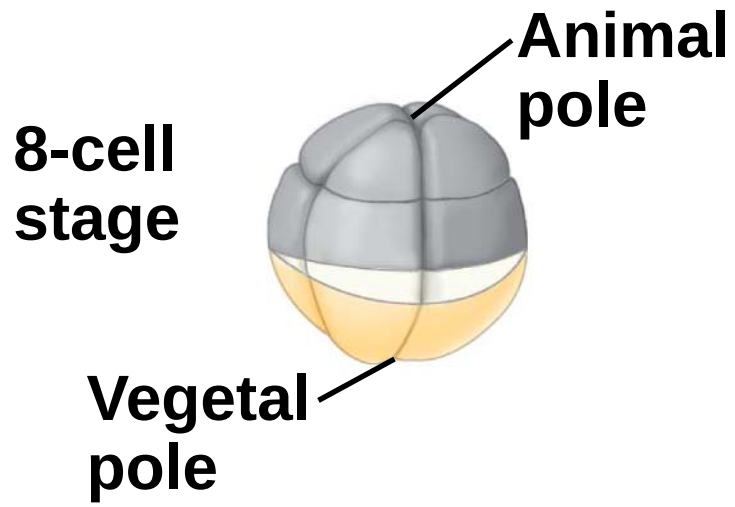
Cleavage



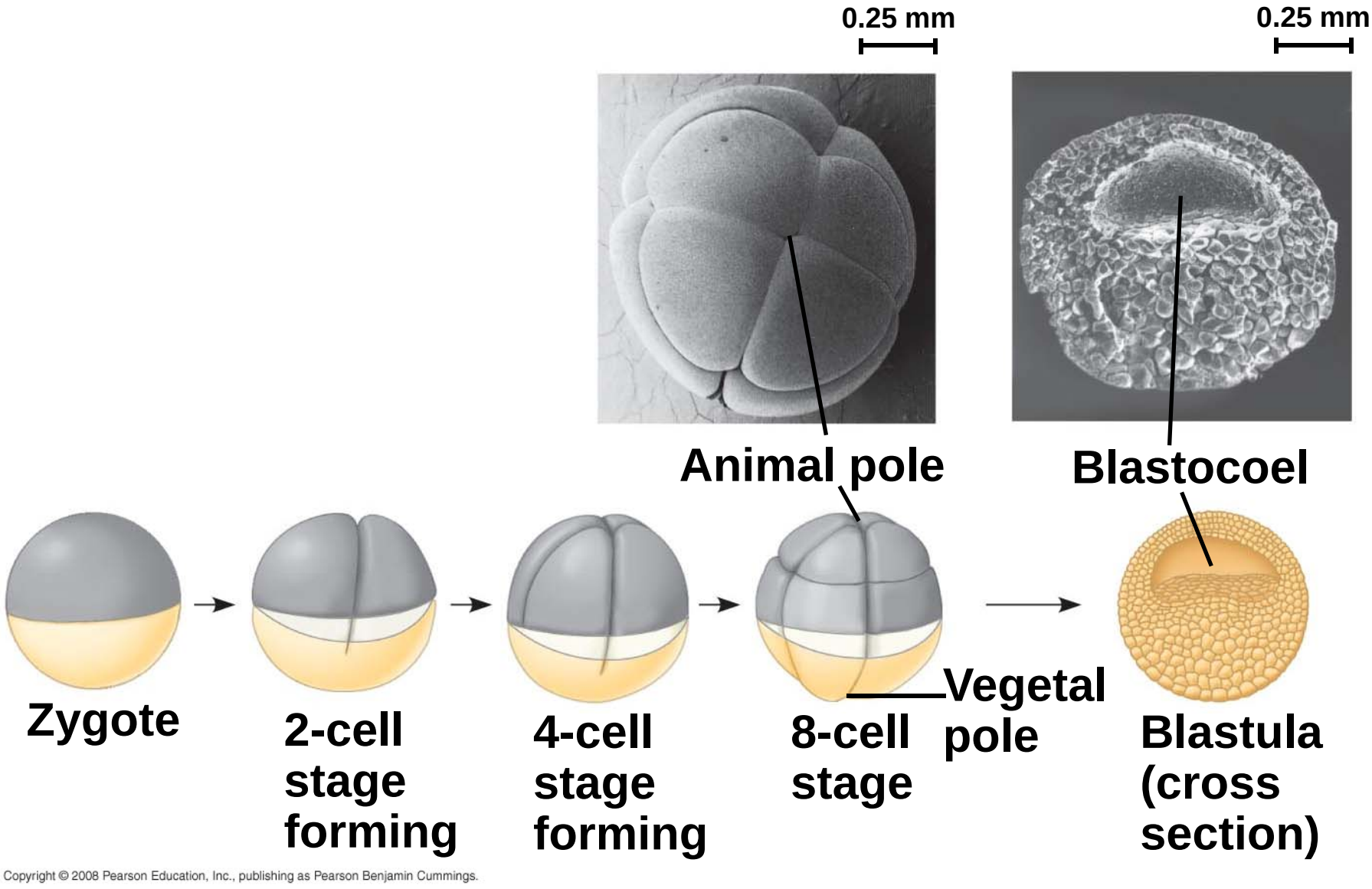
(a) Fertilized egg (b) Four-cell stage (c) Early blastula (d) Later blastula



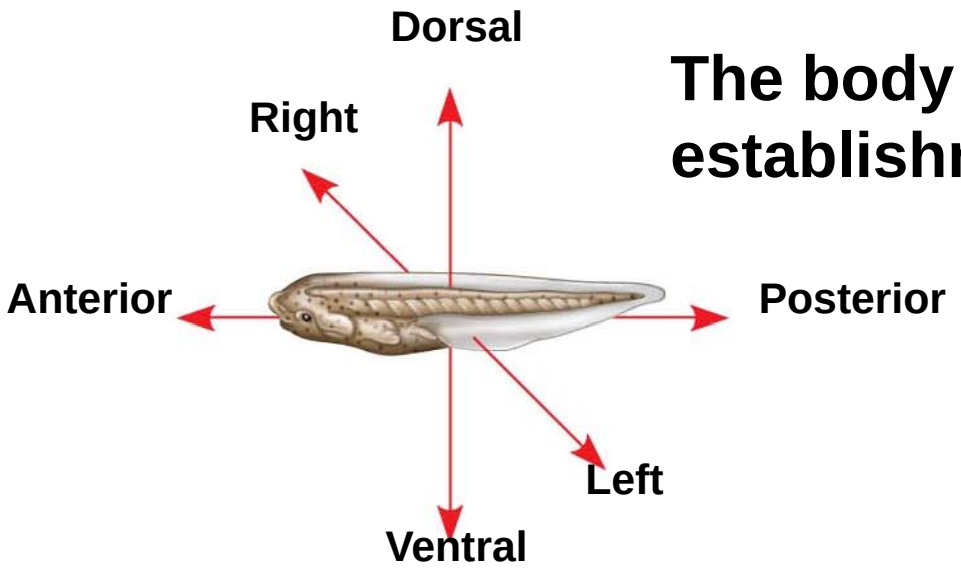
Cleavage in a frog embryo



Cleavage in a frog embryo

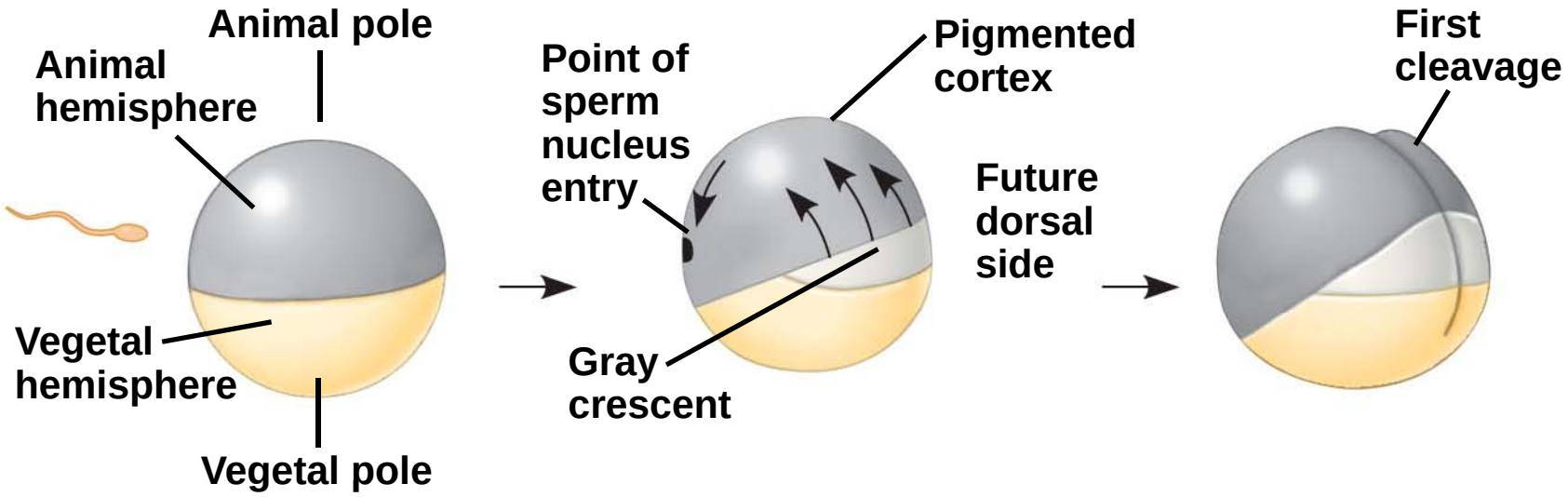


The body axes and their establishment in an amphibian



體軸
前/後軸(A/P axis)
背/腹軸(D/V axis)
左/右軸(L/R axis)

(a) The three axes of the fully developed embryo



(b) Establishing the axes

Fig. 47-23a

EXPERIMENT

方向性?

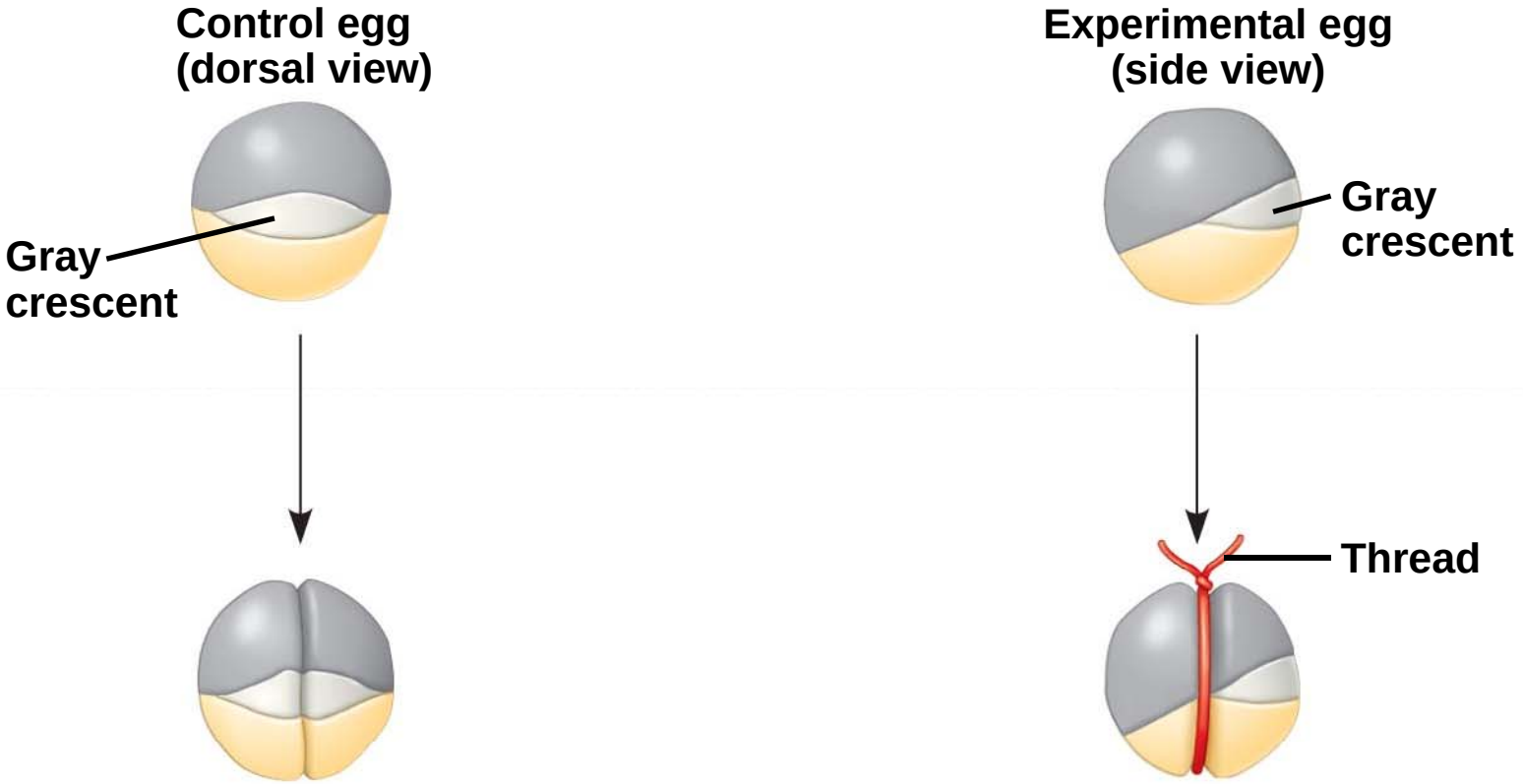
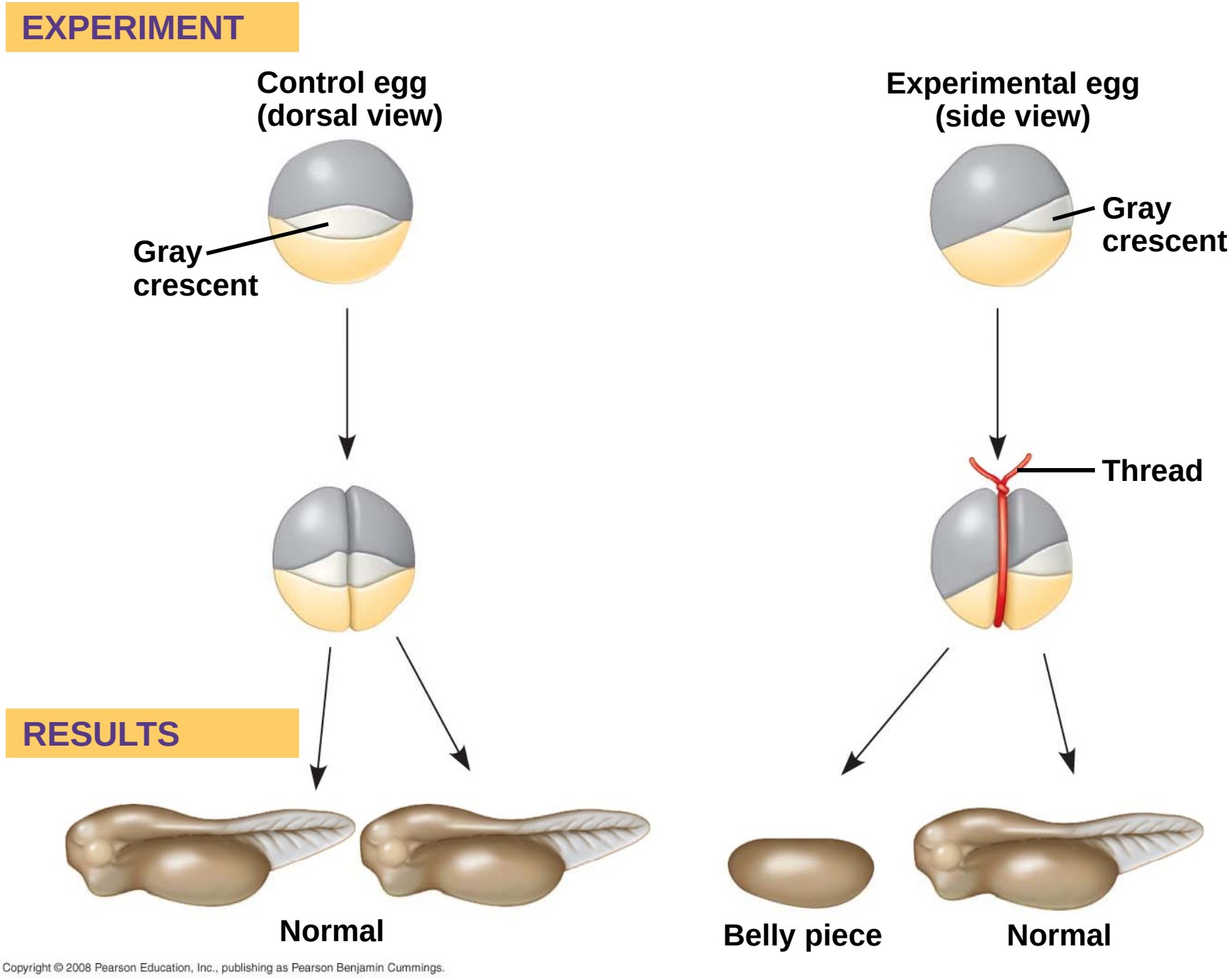


Fig. 47-23b



動物發育的主要過程

1. 受精 (Fertilization)
2. 卵裂 (Cleavage)
3. **原腸化 (Gastrulation)**
4. 神經 (Neurulation)
5. 器官生成 (Organogenesis)
6. 個體生成 (Growth)

大量細胞轉移
胚層生成
體軸建立

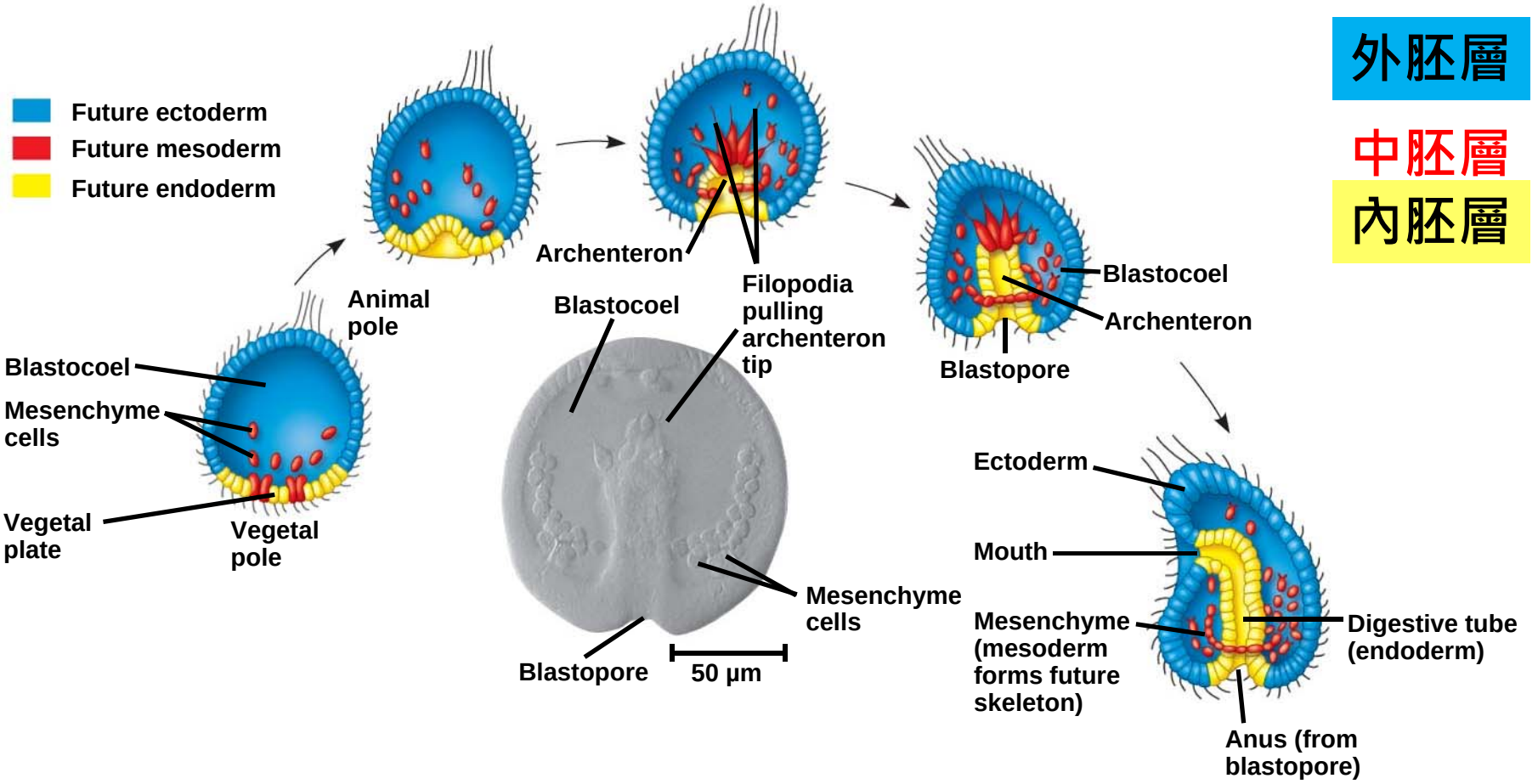
Gastrulation in a sea urchin embryo
原腸化

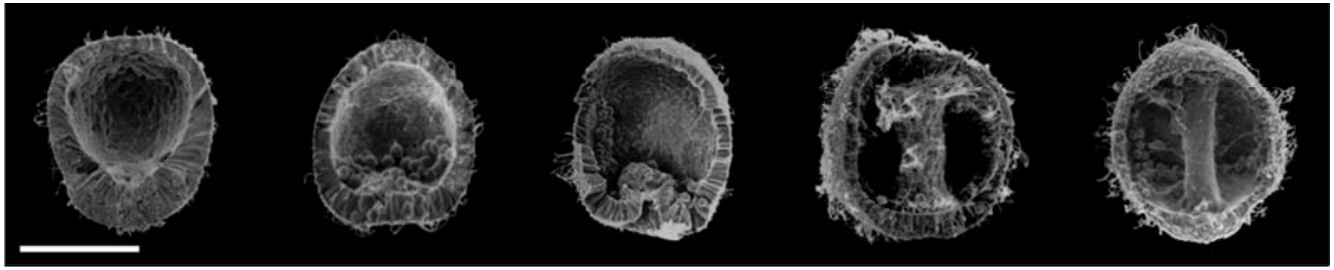
video

外胚層

中胚層

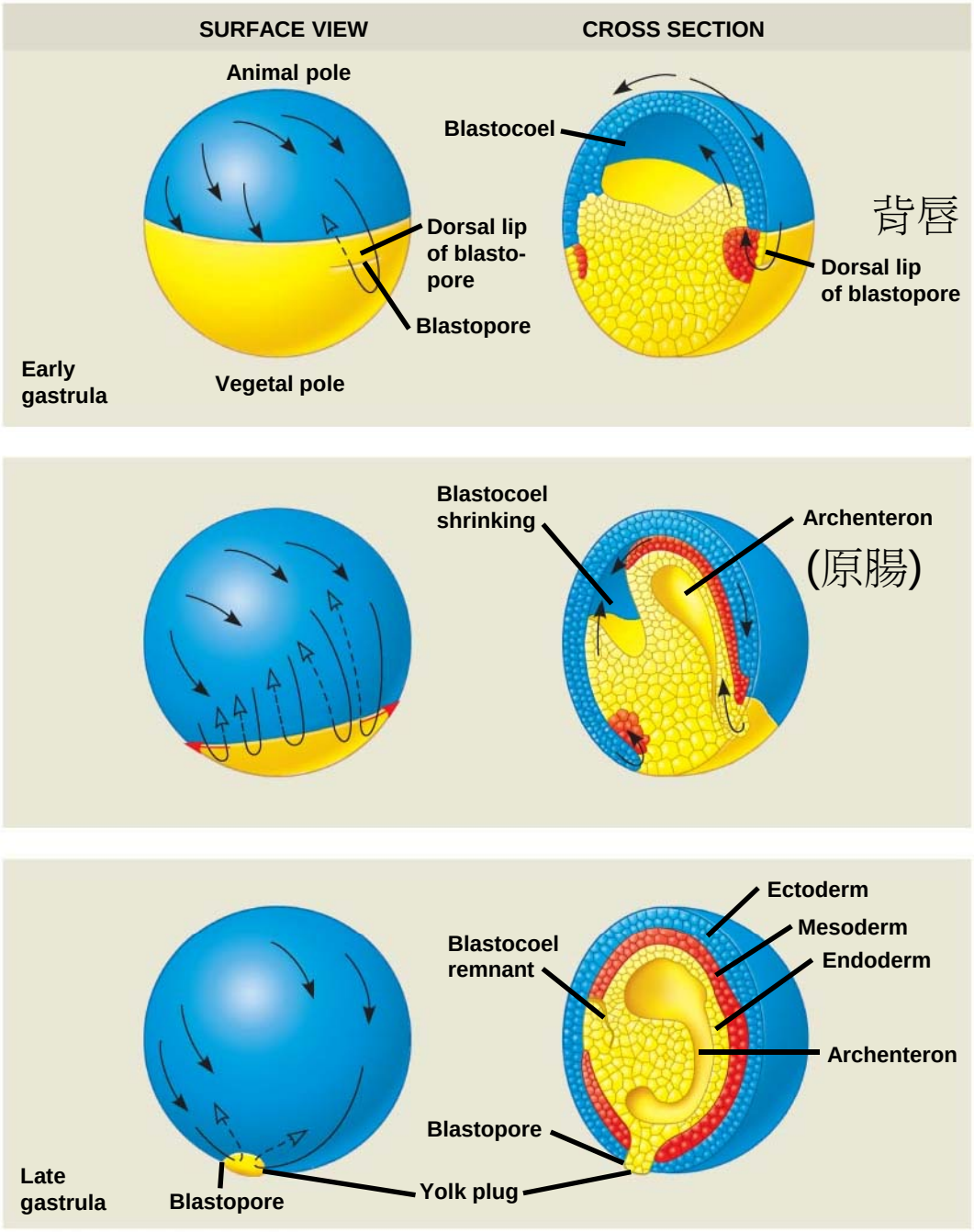
内胚層



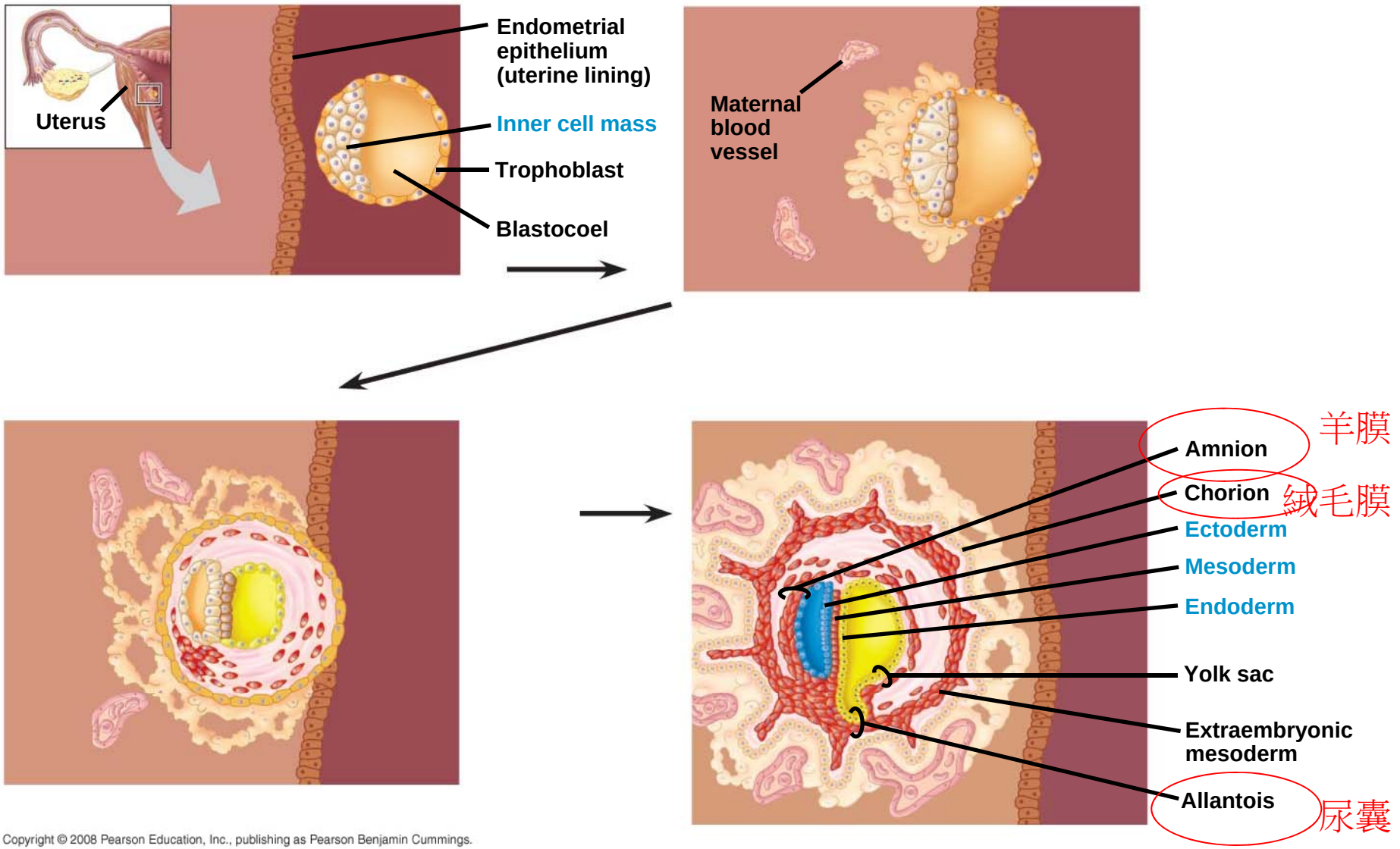


Gastrulation in the frog

- Cells of the **dorsal lip** originate in the **gray crescent** and **invaginate** to create the **archenteron** (原腸)
- Cells continue to move by **involution**
- These cells become the **endoderm and mesoderm**
- The blastopore encircles a **yolk plug** when gastrulation is completed
- **ectoderm, endoderm, and mesoderm**



Mammal (human)



胎盤素


白金胎盤素
森田藥粧
VEGETAL
PLACENTAL
Essence Mask
白金胎盤素拉花面膜
Peptide · EGF · Hyaluronic Acid
Platinum · Ceramide · Collagen · Elastin
docopp


「瑕疵 暗沉 斑點 通通掰掰」輕鬆遮瑕 完美出擊！
MICCOSMO
輕輕一抹 斑點 OUT!
純物理性防曬
溫和不刺激
立即擁有無瑕透明感嬰兒般白肌。
忙碌的早晨只需這一瓶就 OK! 上妝的同時也以胎盤素保養！
給想要修飾個人的斑斑點點…
卻又不想要厚重妝感的您。
空氣感薄透觸感，智慧遮蓋斑點！
新感覺BB霜！
自然膚色
SPF25 PA++
シミが隠せるBBクリーム
胎盤素白肌 BB 霜 28g
使用方法 使用化妝水後，取適量（紅豆大小）均勻塗在全臉。薄薄地塗上推開是不脫妝的關鍵，再以手指輕輕按壓。可與平時使用的蜜粉搭配。卸妝時以一般卸妝產品即可輕鬆卸除乾淨。
Point 1 忙碌的早晨也能瞬間擁有嬰兒般白肌
集合美容液、妝前乳、防曬霜、遮瑕膏、粉底，全方位智慧機能，添加＂超細滑 & 遮瑕粉末＂，如同慕斯狀的保濕觸感，極佳的延展性在肌膚上滑順的推開，簡單上妝不 NG!
什麼是＂超細滑 & 遮瑕粉末＂？
比尼龍柔軟的神奇微粒子粉末，具高度遮瑕力，輕輕塗一層就能呈現透明感妝感，實現了兼具遮瑕力與自然妝感。
超細滑 & 遮瑕粉末
Before
After
Point 2 添加日本國產 100% 胎盤素，滋潤感維持一整天
奢華添加高保濕效果的胎盤素精華，另外添加了膠原蛋白及玻尿酸，賦予肌膚彈力光澤，上妝同時維持肌膚滋潤。
BB 霜成分
Point 3 抵擋紫外線！ 敏弱性肌膚也可安心使用！
不添加化學性防曬劑，是一款專為敏感肌打造無添加配方，添加防汗防水配方，保護肌膚遠離紫外線，預防因日曬引起的傷害，貼膚力佳。
（無香料、合成色素、礦物油、防腐劑、酒精）的 BB 霜。


胎盤素原液
Placentasa Extract

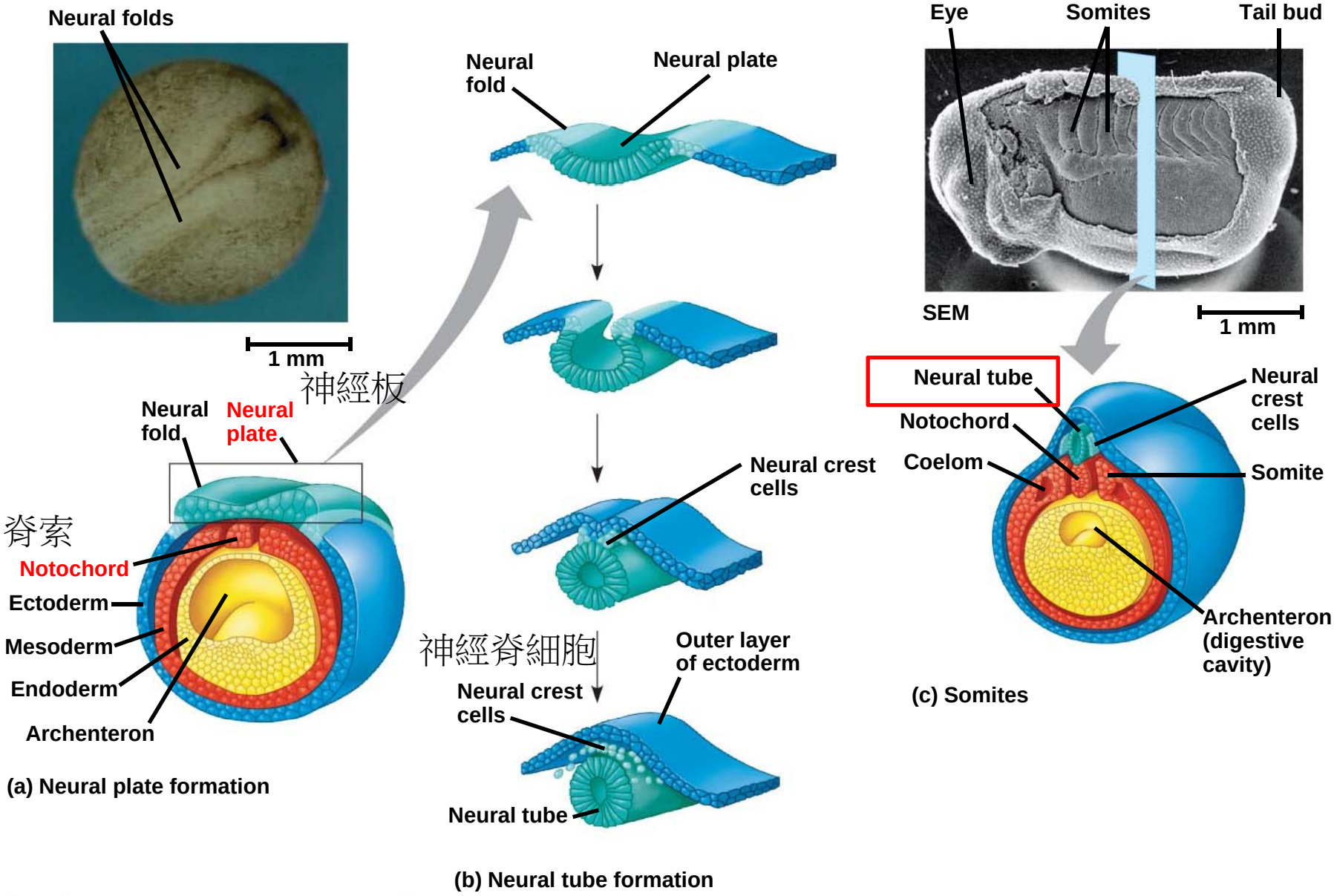

JCare
潤コラ
胎盤素
プラセンタ
胶原蛋白
コラーゲン
果汁饮
ドリンク
净含量 400ml(50ml×8支)


植物胎盤素
精華化妝水

動物發育的主要過程

1. 受精 (Fertilization)
2. 卵裂 (Cleavage)
3. 原腸化 (Gastrulation)
4. **神經 (Neurulation)**
5. 器官生成 (Organogenesis)
6. 個體生成 (Growth)

neurulation (神經管的生成)



動物發育的主要過程

1. 受精 (Fertilization)
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3. 原腸化 (Gastrulation)
4. 神經 (Neurulation)
5. **器官生成 (Organogenesis)**
6. 個體生成 (Growth)

外胚層	中胚層	內胚層
ECTODERM	**MESODERM**	**ENDODERM**
• Epidermis of skin and its derivatives (including sweat glands, hair follicles) • Epithelial lining of mouth and anus • Cornea and lens of eye • Nervous system • Sensory receptors in epidermis • Adrenal medulla • Tooth enamel • Epithelium of pineal and pituitary glands	• Notochord • Skeletal system • Muscular system • Muscular layer of stomach and intestine • Excretory system • Circulatory and lymphatic systems • Reproductive system (except germ cells) • Dermis of skin • Lining of body cavity • Adrenal cortex	• Epithelial lining of digestive tract • Epithelial lining of respiratory system • Lining of urethra, urinary bladder, and reproductive system • Liver • Pancreas • Thymus • Thyroid and parathyroid glands

Germ Layers:

Ectoderm,
Mesoderm,
Endoderm

外胚層
中胚層
內胚層

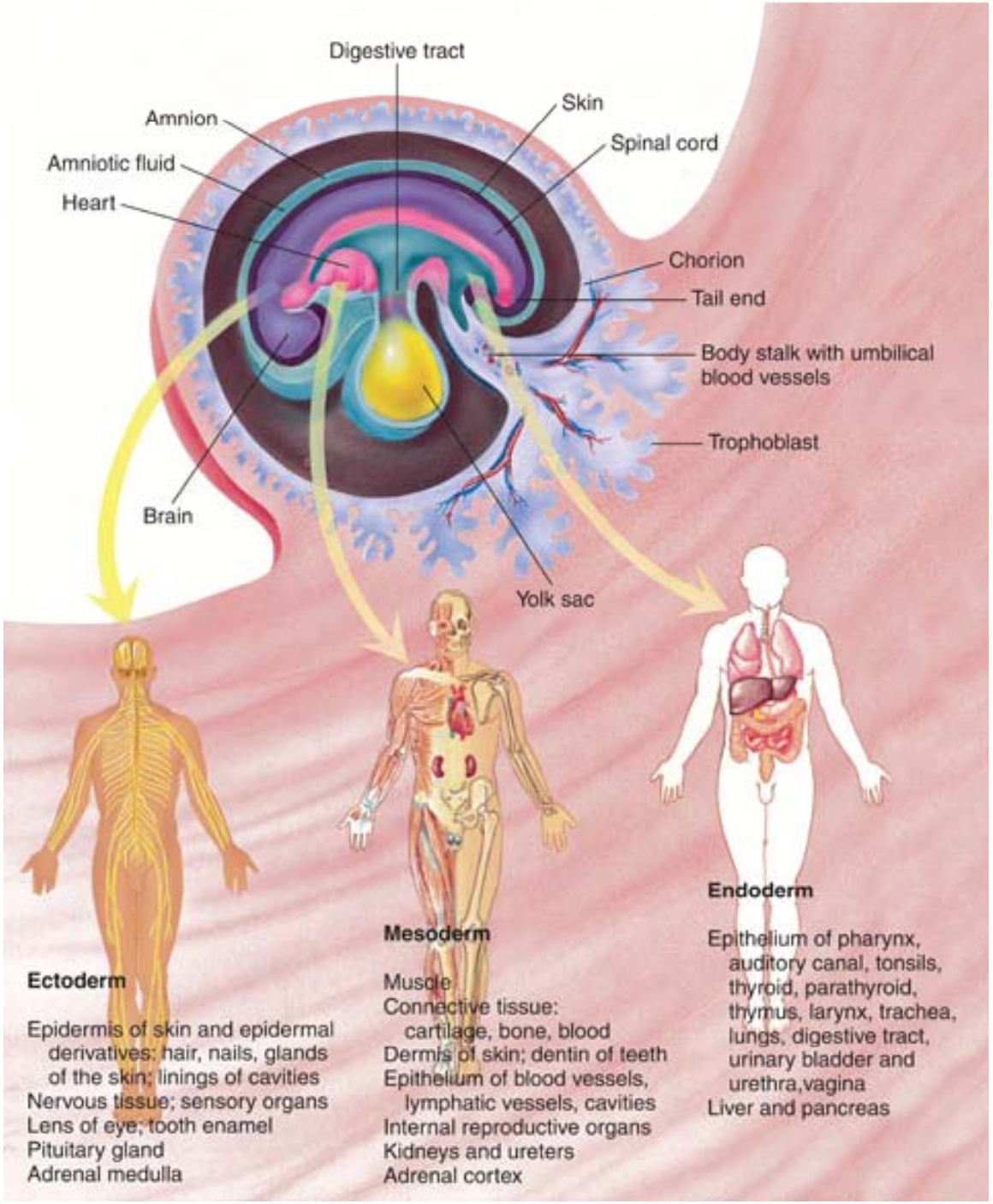
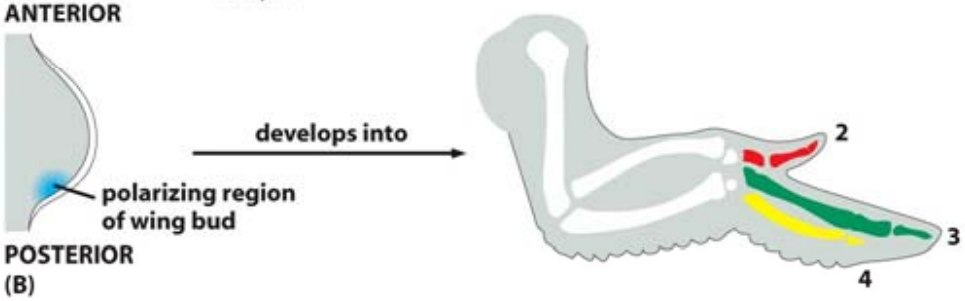


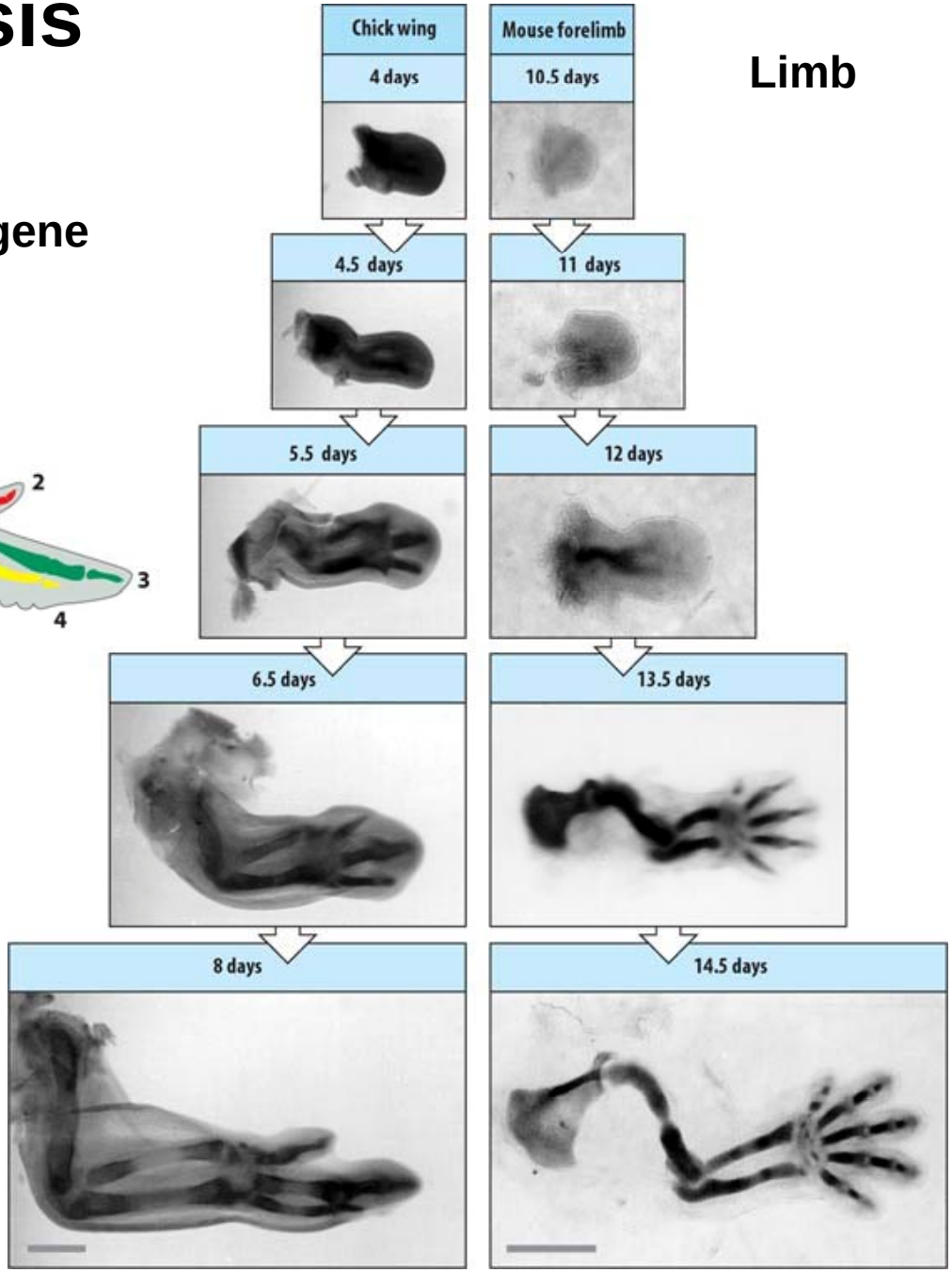
Figure 3.15 The primordial embryo. When the three basic layers of the embryo form at gastrulation, many cells become "fated" to follow a specific developmental pathway. However, each layer probably retains stem cells as the organism develops. Under certain conditions, these cells may produce daughter cells that can specialize as many cell types.

Organogenesis

Expression of
Sonic hedgehog gene



Limb

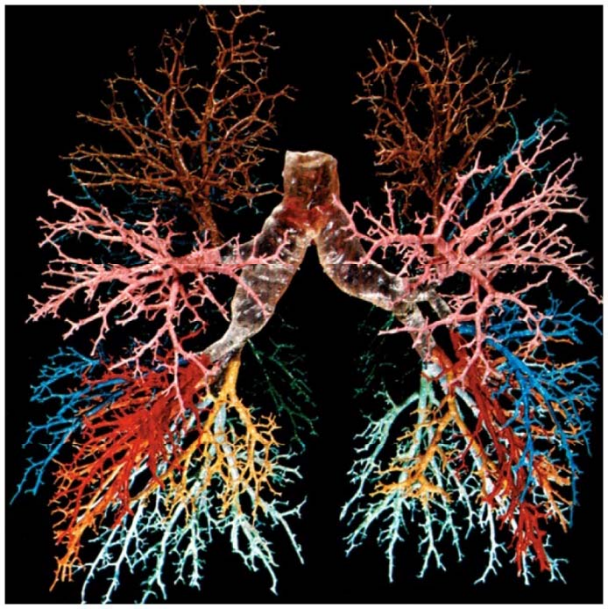


thalidomide 「沙利竇邁」

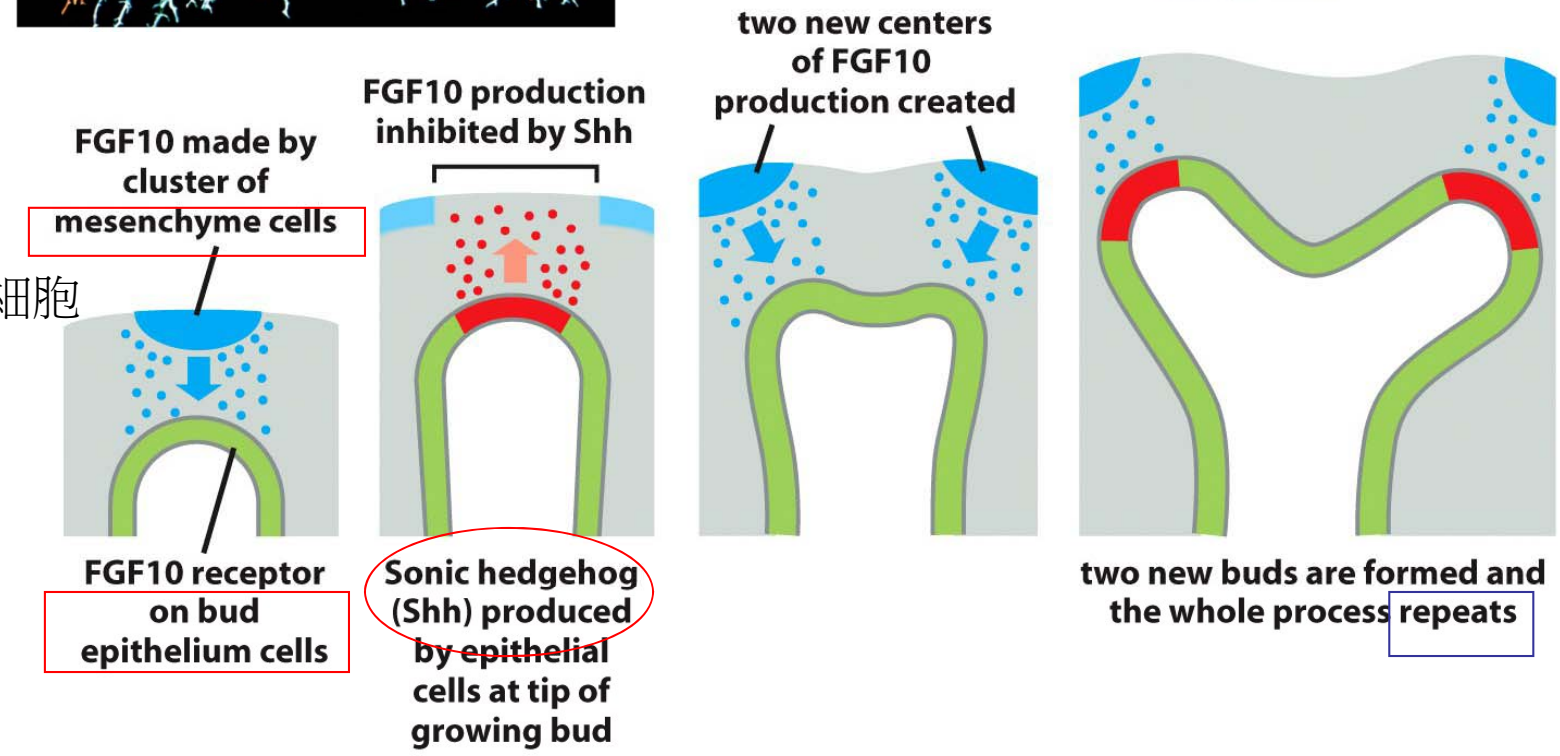
在1997年，統計發現人類的新生兒中有2%的是畸形，這些缺陷的產生，有些是來自基因，另外的大宗，可能來自環境因子抑制了發育的過程。以1961年Lenz和Mcbride發現為例，他們證明一種用來鎮定孕婦憂鬱的藥(thalidomide)，會使新生兒四肢發育不全。Nowack(1965)研究發現，這藥物會在懷孕初期的20~36天左右，對四肢的發育產生抑制的作用，當時藥物包括台灣的遠東地區都有販售，因此可看見現年約40~50歲世代，有許多這樣的例子出現，造成許多悲劇與社會的成本，

Effect of reduced or no FGF10

Figure 22-44a
Molecular Cell Biology, Sixth Edition



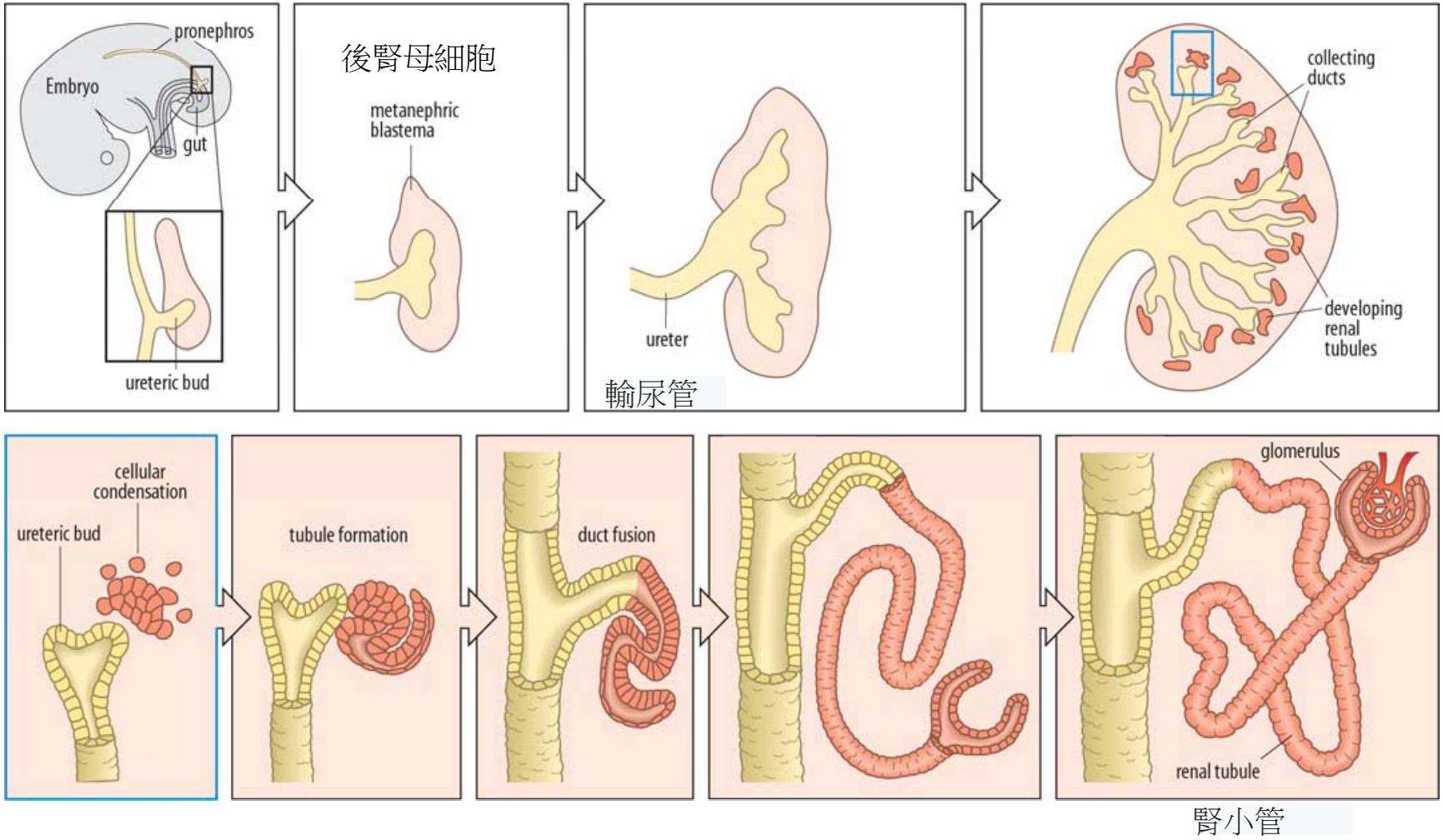
Branching morphogenesis of lung mediated by FGF10 and Shh signaling



間質幹細胞

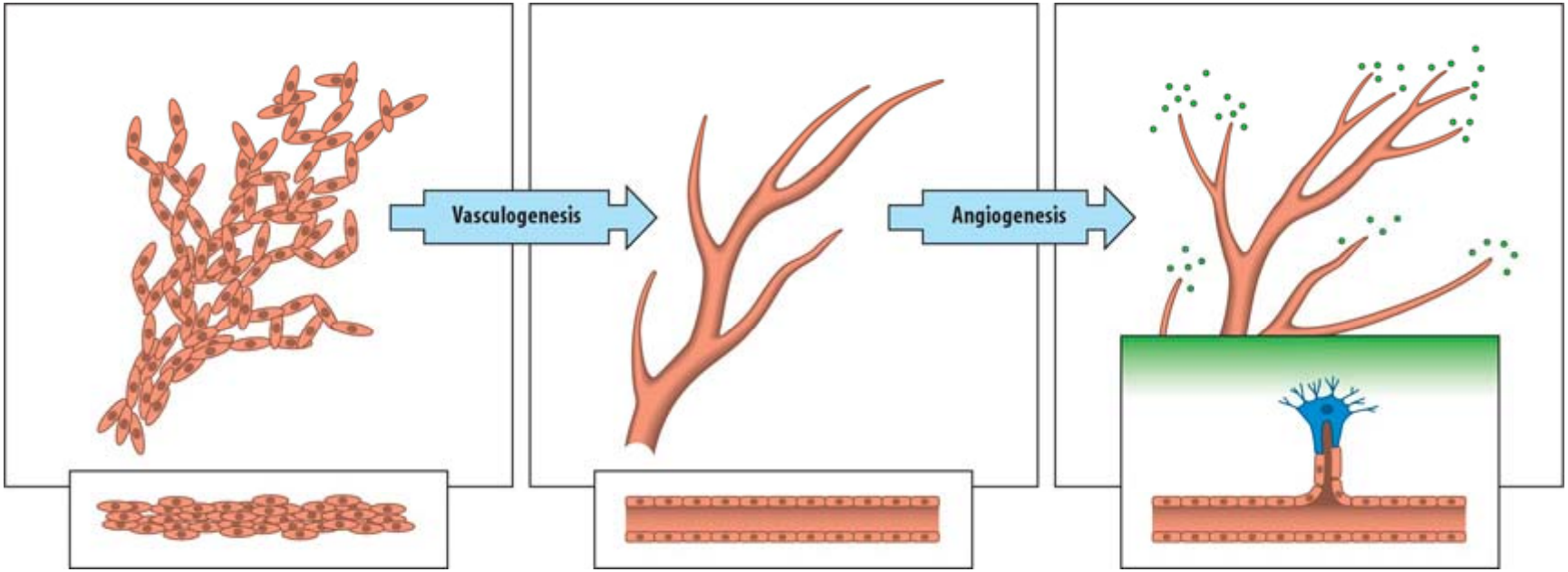
(参考用)

kidney


pronephros
Embryo
gut
ureteric bud
後腎母細胞
metanephric blastema
ureter
輸尿管
collecting ducts
developing renal tubules
cellular condensation
ureteric bud
tubule formation
duct fusion
glomerulus
renal tubule
腎小管

(参考用)

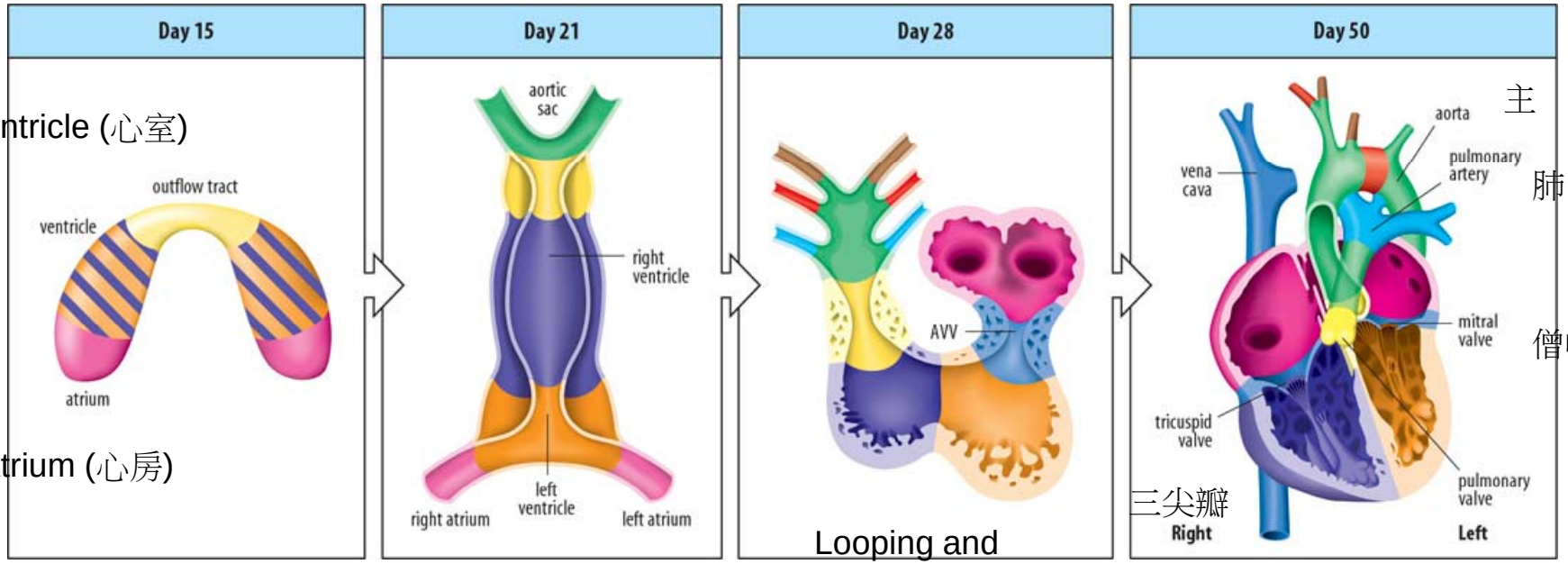
Blood vessels



Angiogenesis and cancer

(參考用)

Schematic of human heart development



Ventricle (心室)

Atrium (心房)

主

肺

僧帽瓣

三尖瓣

Left side: Pitx2

Looping and partitioning

BMP→ Nkx2.5 Transcription factor (7 activating regions and 3 repressor regions)

Retinoic acid

GATA

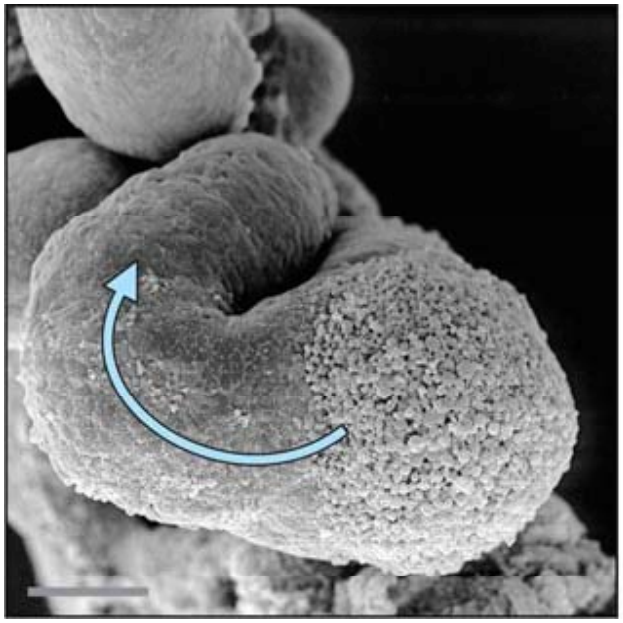
Turn cardiac cell differentiation gene expression

Organ handedness in vertebrates

In the mouse, the **iv gene** controls the handedness of internal organs.
In **iv mutants**, organ handedness is random and some individuals show heterotaxis where normal and inverted organs are found in one animal.

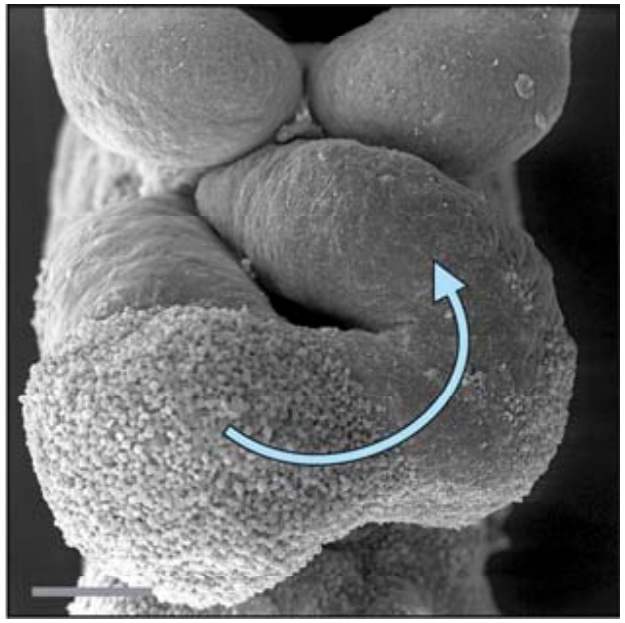
Heterotaxis (內臟易位): The organs of inverted normal and asymmerty are present in the same animal

Normal



It loops to the right

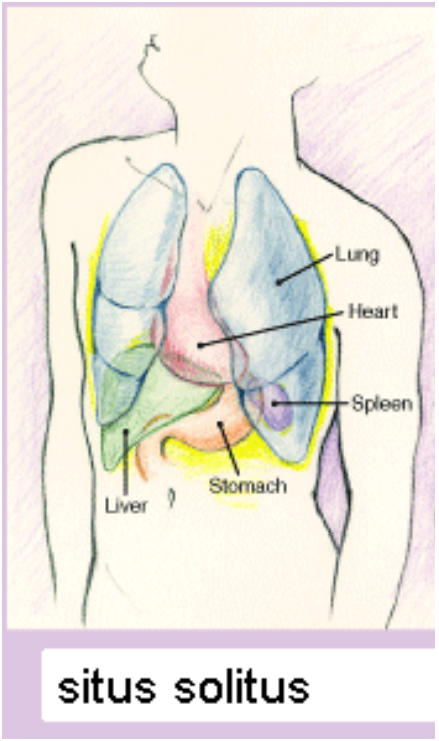
iv mutant



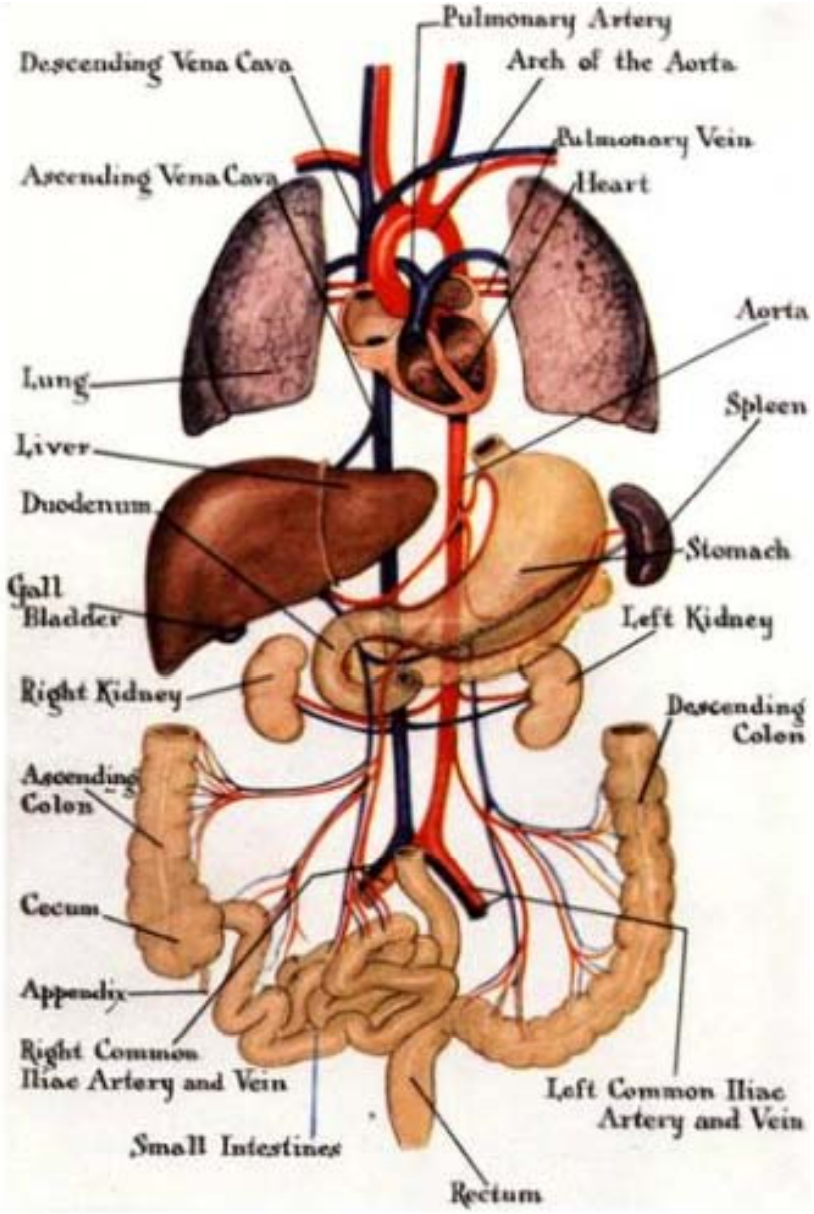
It loops to the left

The condition, *situs inversus*, found in 1 in 10,000 people, is a mirror reversal of the 'handedness' of the internal organs.

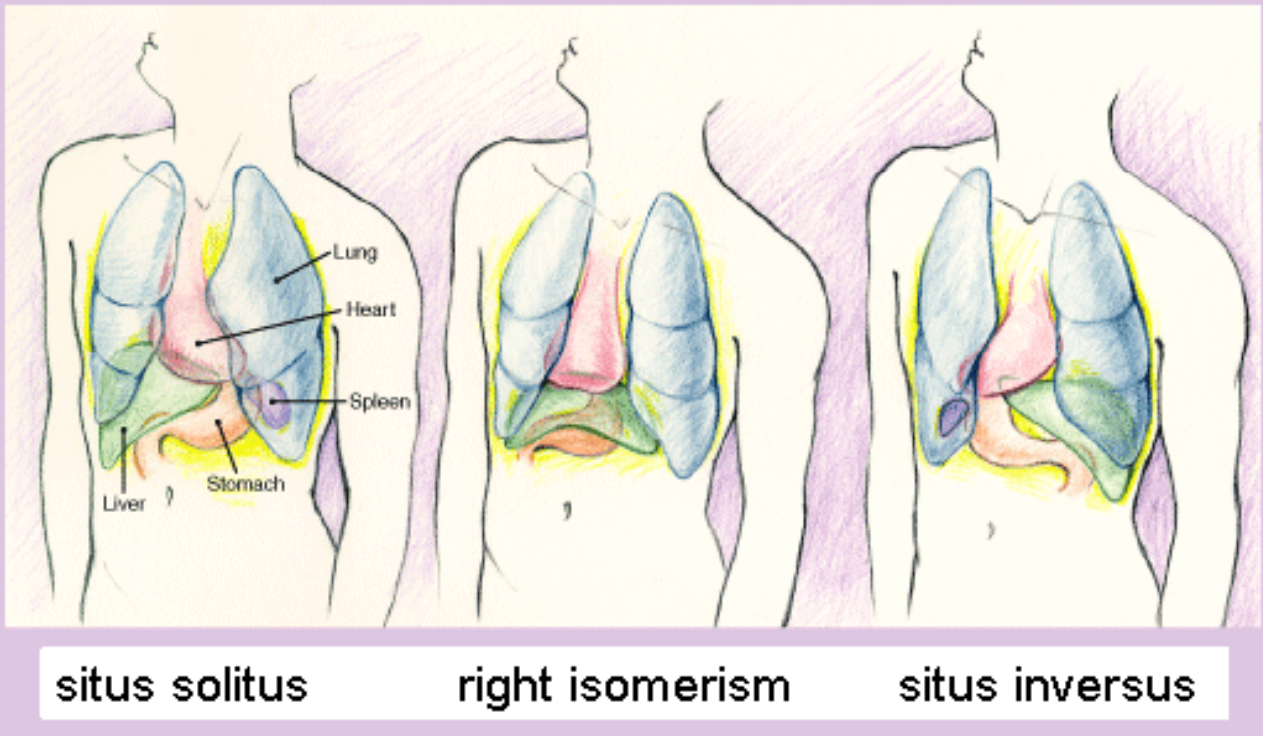
器官轉位



心臟偏左,
肺葉左二,右三葉,
腹腔右邊的器官是肝臟, 膽囊,
腹腔左側的器官是脾臟, 胃



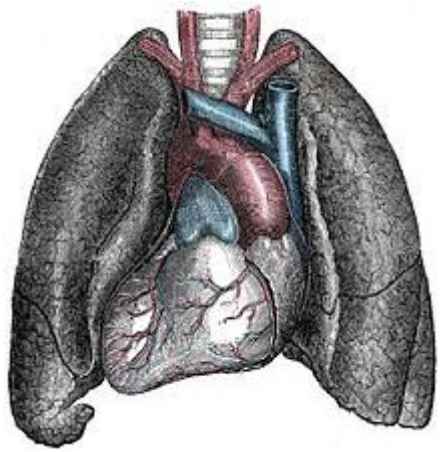
The condition, *situs inversus*, found in 1 in 10,000 people, is a mirror reversal of the 'handedness' of the internal organs.



心臟偏左,
肺葉左二,右三葉,
腹腔右邊的器官是肝臟, 膽囊,
腹腔左側的器官是脾臟, 胃

兩邊都是右邊的臟器

器官整個左右相反



Situs inversus causes the positions of the heart and lungs to be mirrored.

動物發育的主要過程

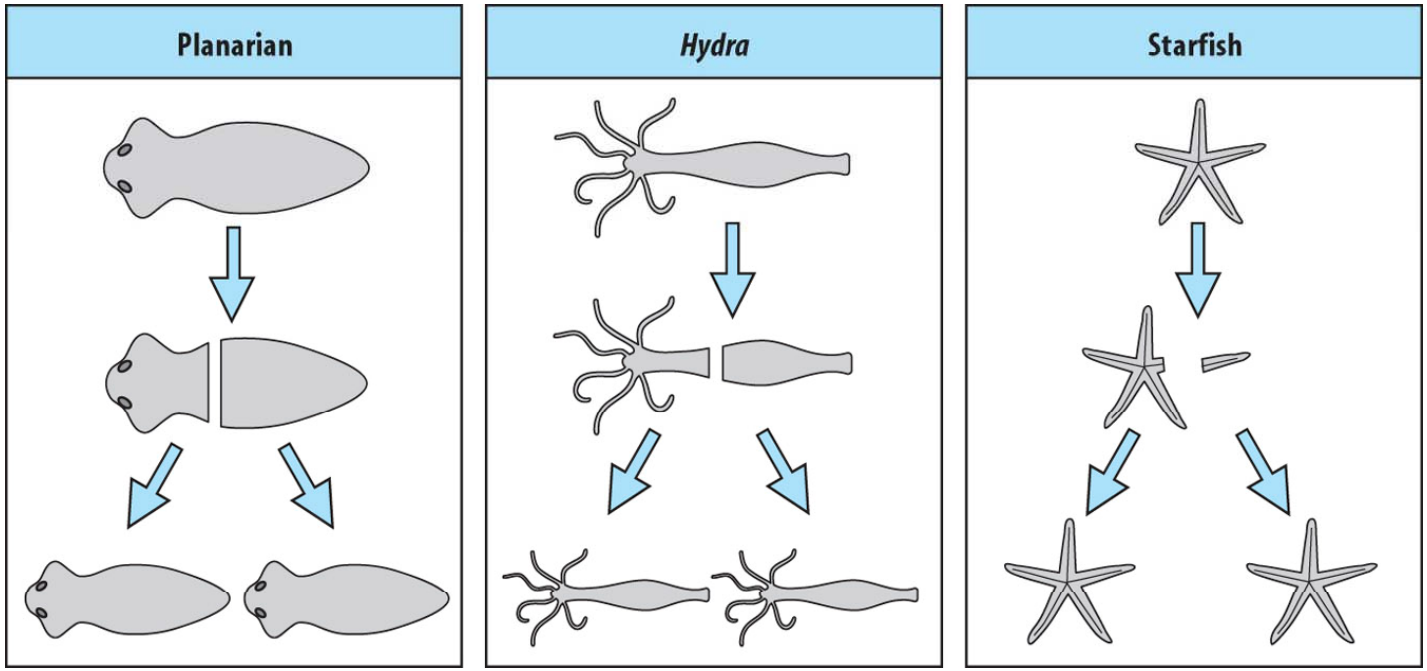
1. 受精 (Fertilization)
2. 卵裂 (Cleavage)
3. 原腸化 (Gastrulation)
4. 神經 (Neurulation)
5. 器官生成 (Organogenesis)
6. 個體生成 (Growth)

Pattern/ hair, spots, stripe

?

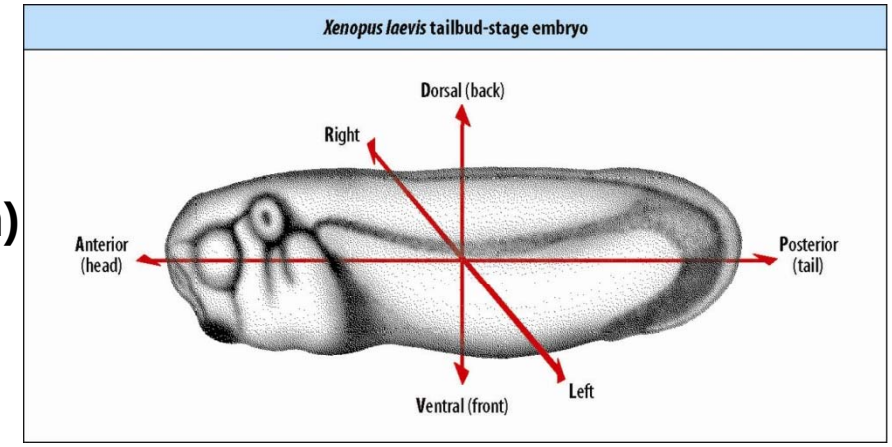
Outline

1. 胚胎學 (embryology) vs. 發育生物學 (developmental biology)
2. 模式生物 (model organisms)
3. 動物發育的主要階段
4. **發育過程之機制**
5. **組織再生與幹細胞**



發育過程包括

Pattern formation (body plan)
Morphogenesis (型態)
Cell differentiation (分化)
Growth (生長)

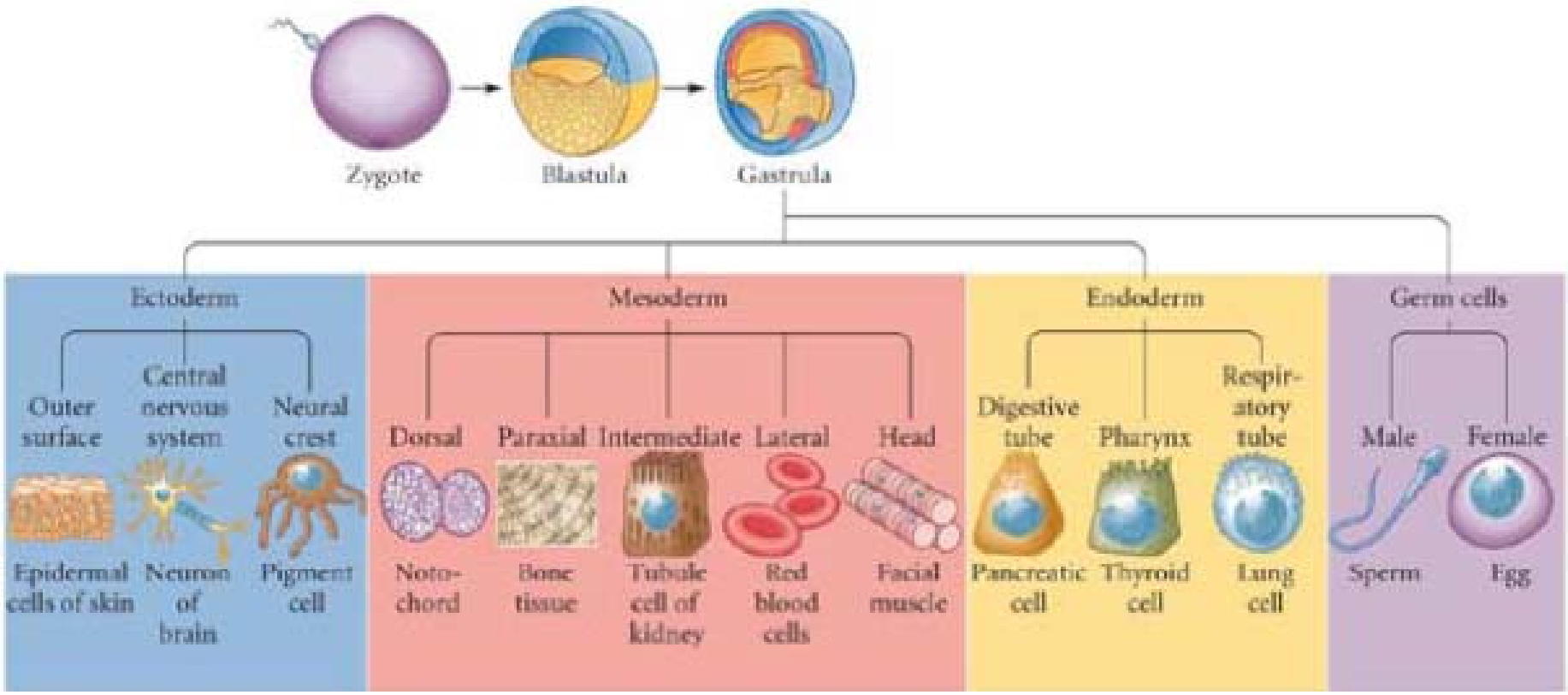


體軸
前/後軸(A/P axis)
背/腹軸(D/V axis)
左/右軸(L/R axis)

4.發育過程之機制

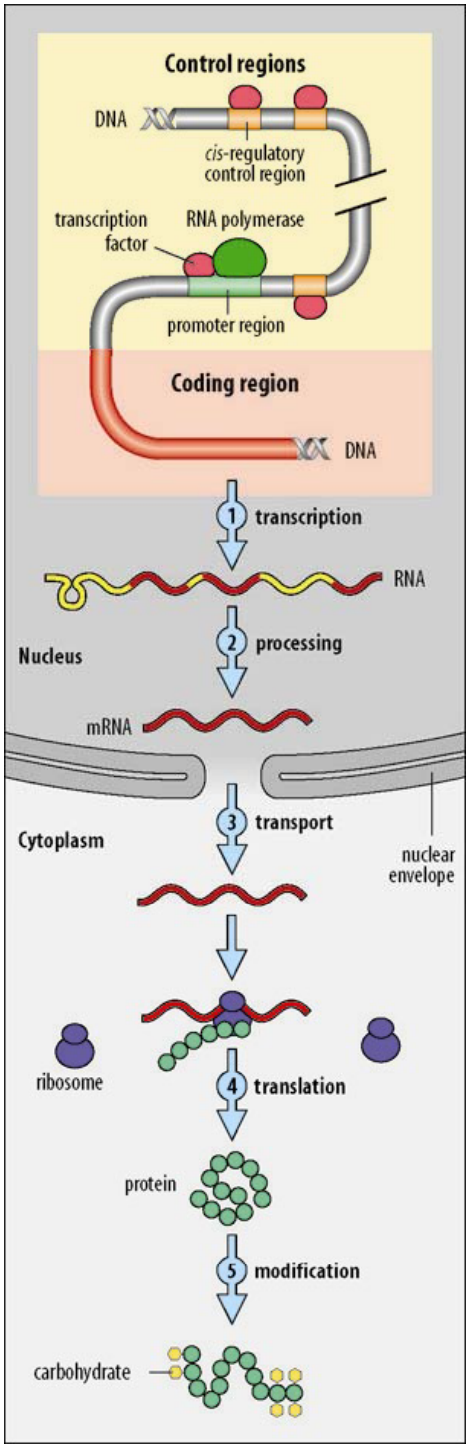
1. **Differential gene expression/signaling (基因表現)**
2. **Cell fate determination** 細胞命運決定
3. **Induction** 誘導
4. **Pattern formation**
    a. **Positional information**
    b. **Lateral inhibition**
5. **Asymmetric division (不對稱分化)**

4.1. Differential gene expression causes cell differentiation



Representative cell types of a vertebrate

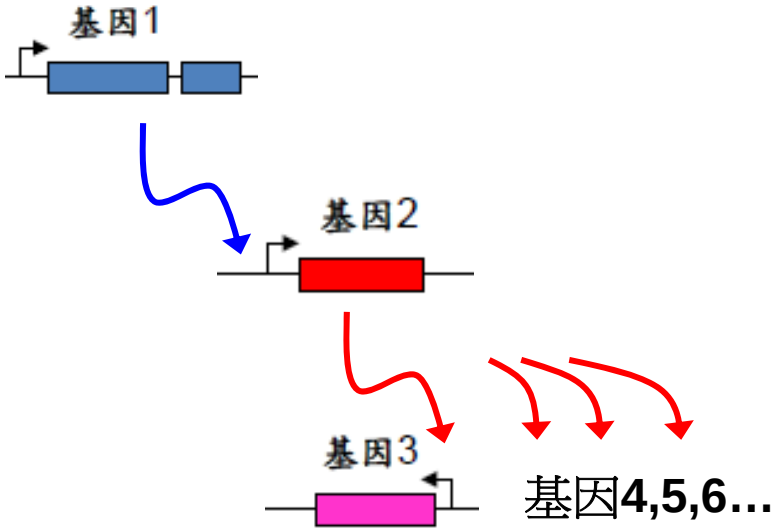
人類有**100億cells, 250**種不同類型的細胞
線蟲**952 cells.**



Gene expression and protein synthesis

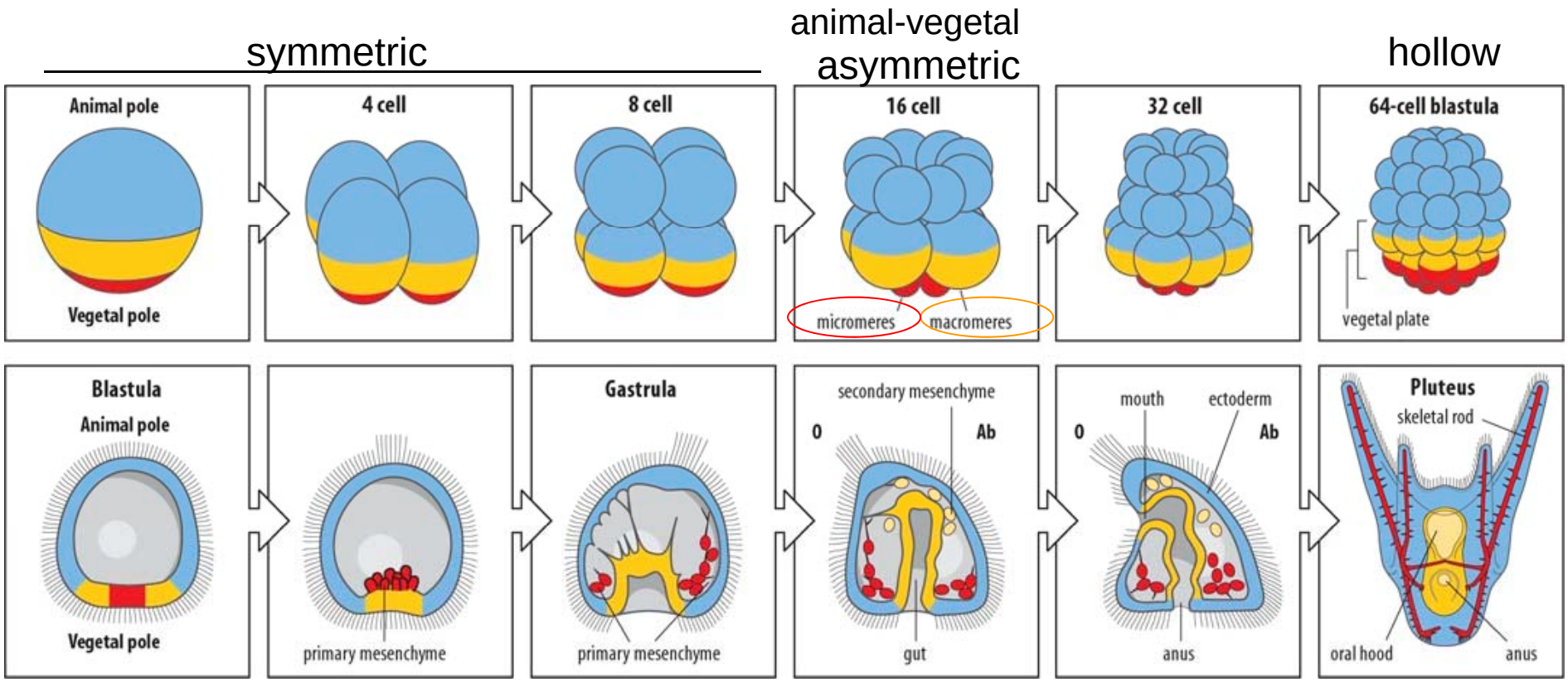
In the early development of *Drosophila*, at least 60 genes are directly involved in pattern formation to form segments.

In C. elegant, at least 50 genes are needed to specify vulva (reproductive structure). About 9% of the genes (1722/ 20,000) are involved in development.



基因如何調控呢?

Development of the sea urchin embryo.



初級間質

gut invaginate

二級間質

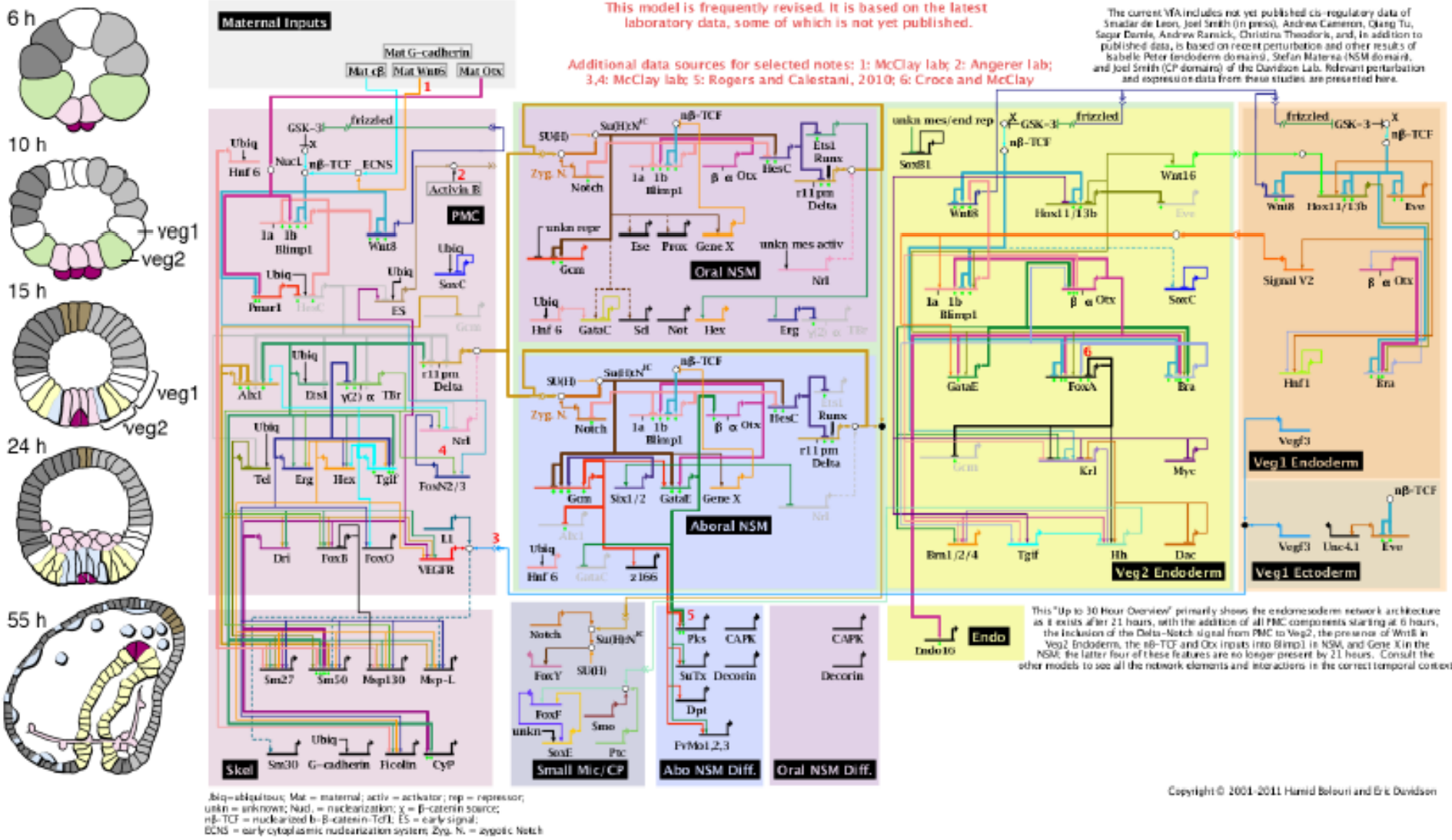
骨棒(中胚層)

Blue: prospective ectoderm

Yellow: endoderm

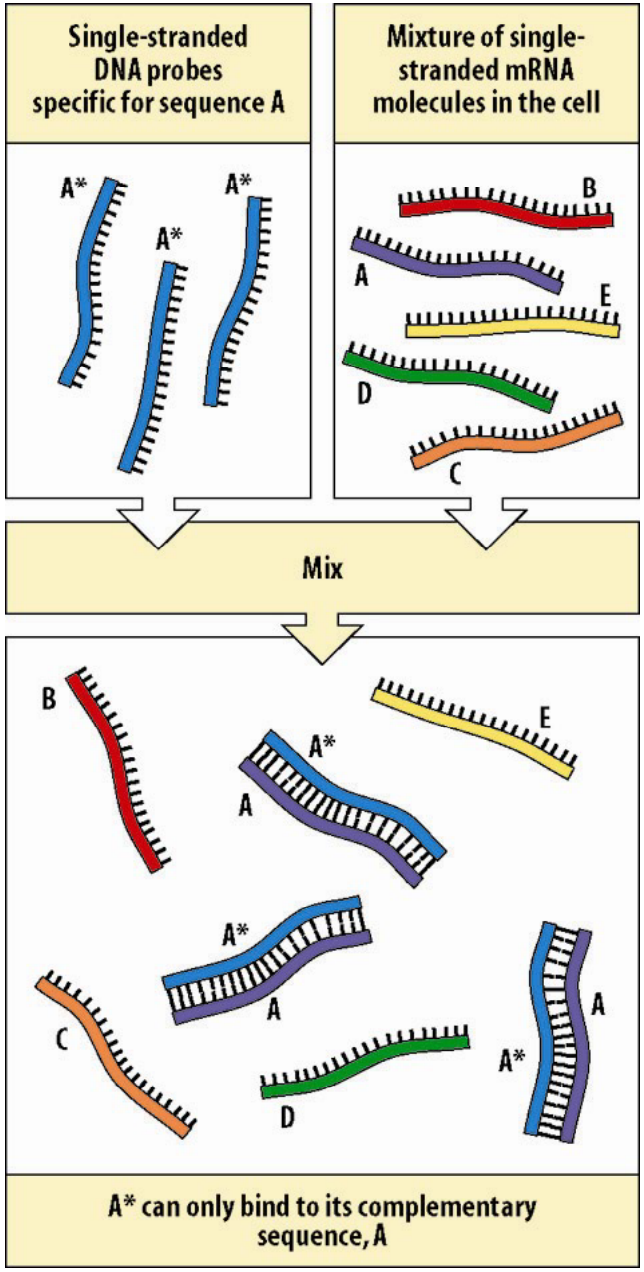
Red: mesoderm

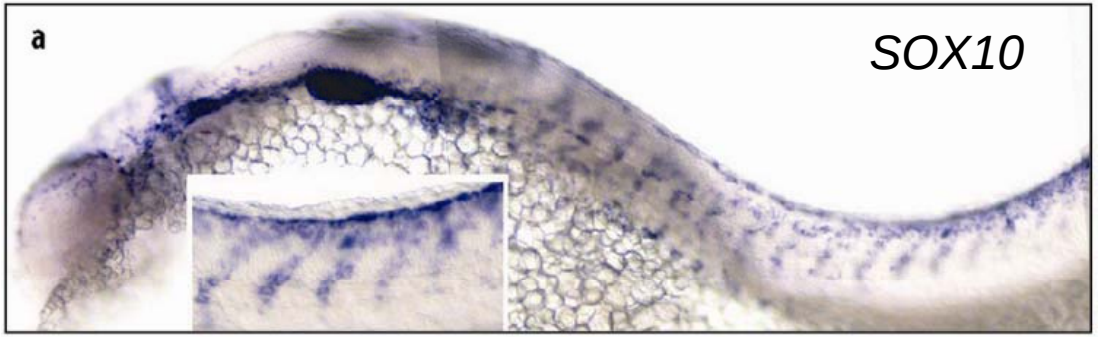
海膽胚胎的中內胚層發育基因調控網路

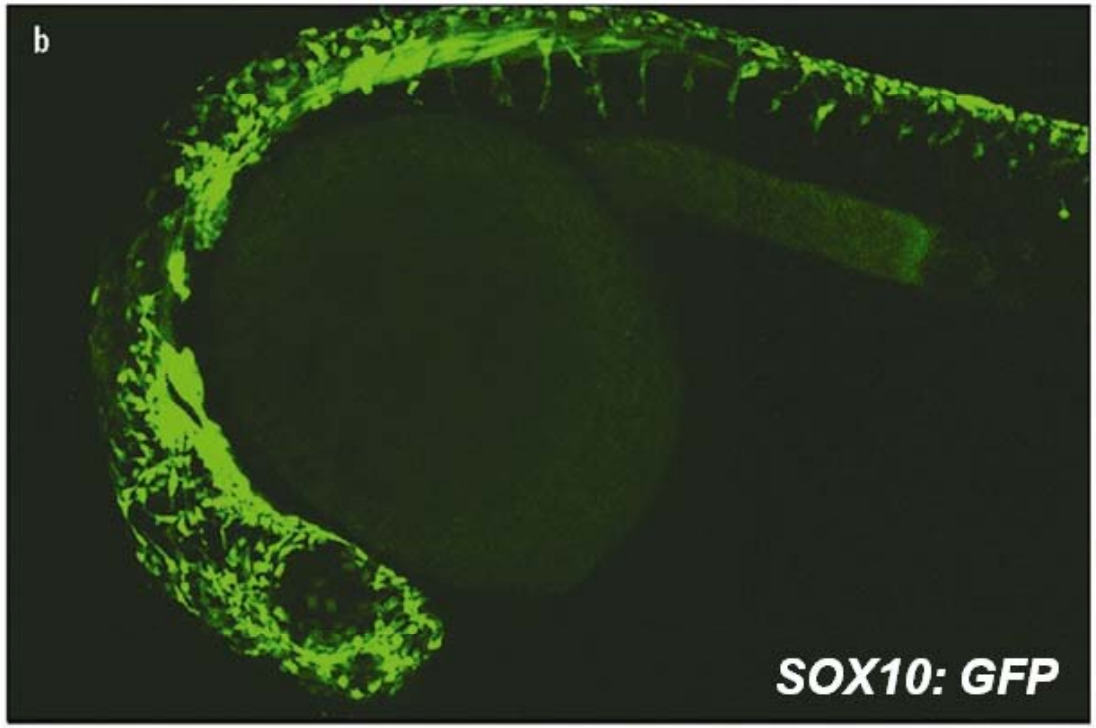


http://sugp.caltech.edu/endomes/#EndoNetworkDiagrams

Study (tracking) gene expression in embryos

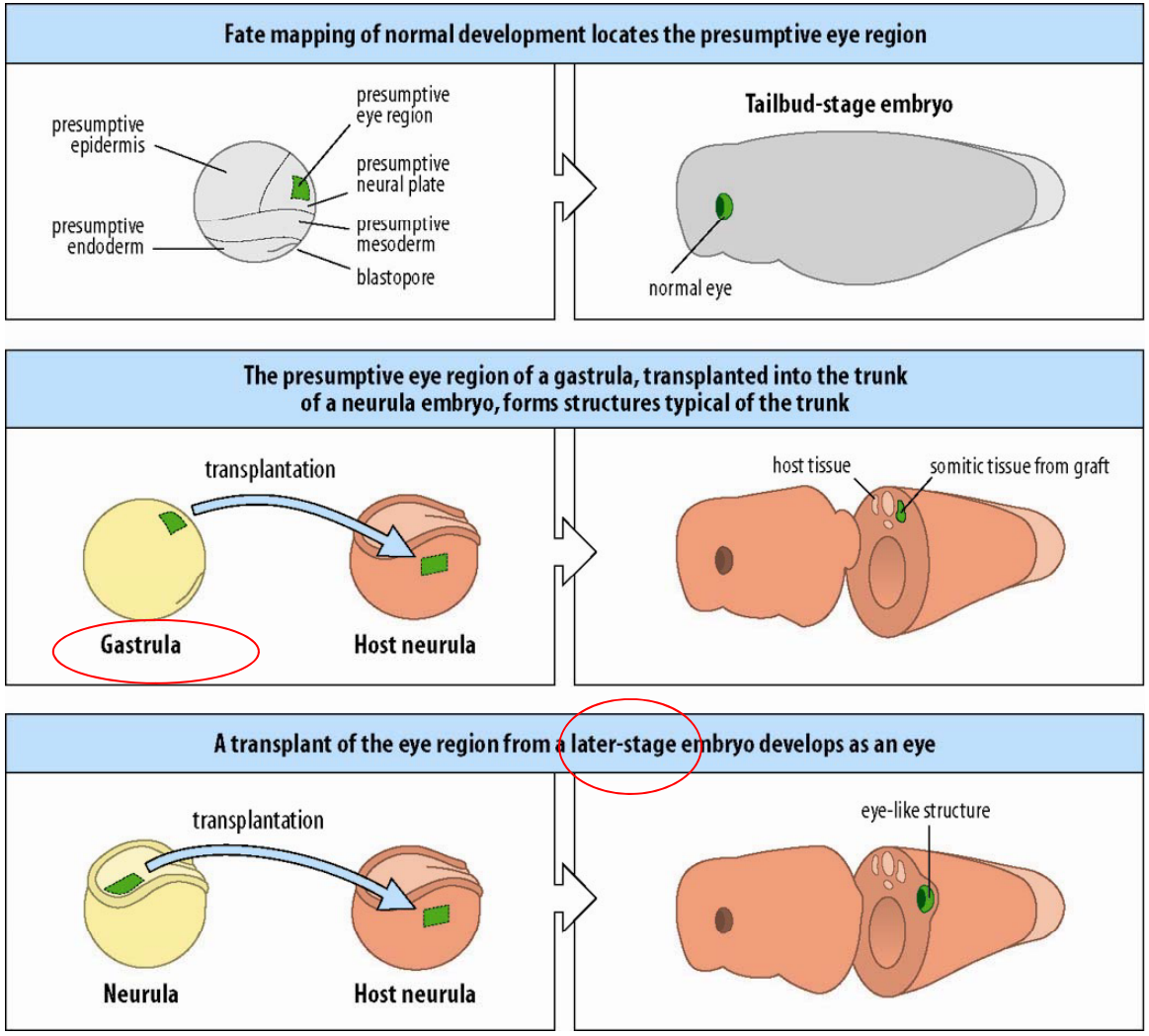






4.2. Cell fate determination

Cell transplantation

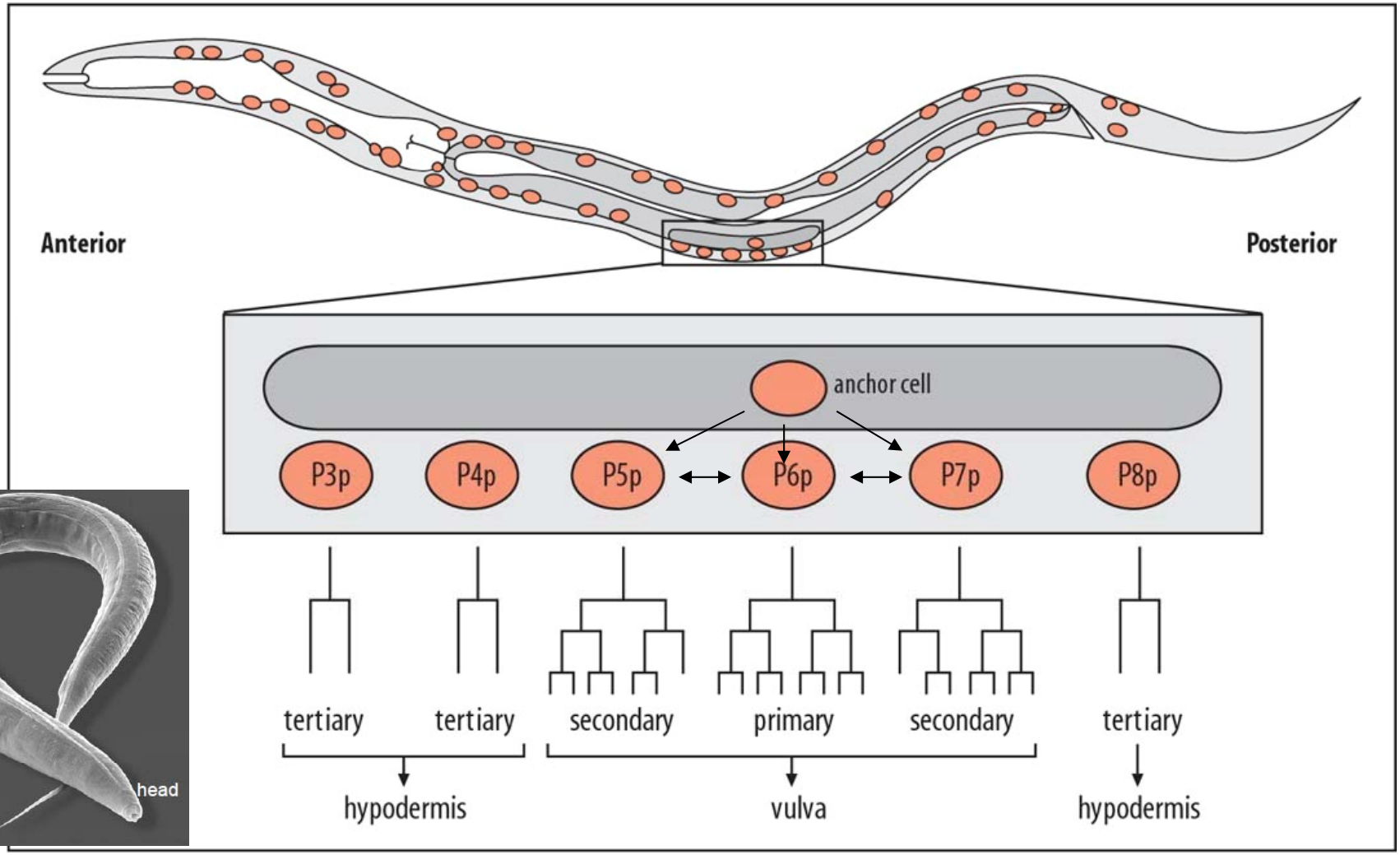


earlier stage: not determined

later stage: determined

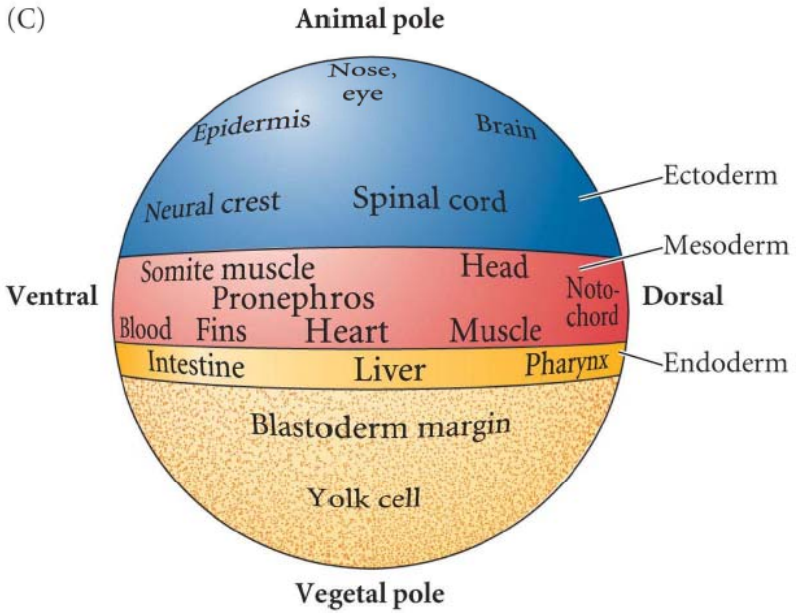
2. Cell fate determination

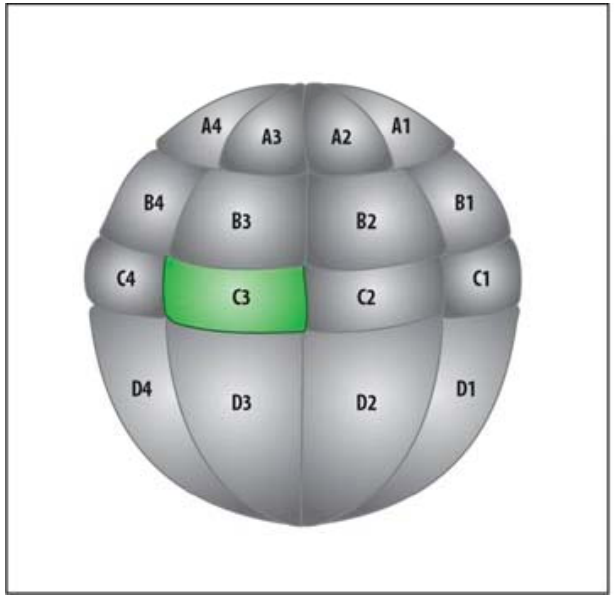
Cell-linage analysis

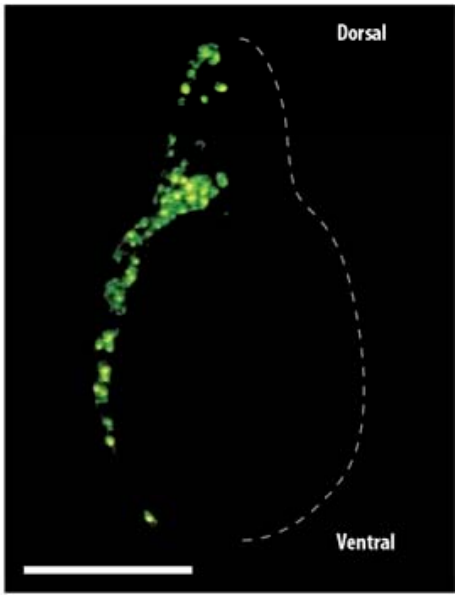


4. 2. Cell fate determination

GFP labeled or Laser caged





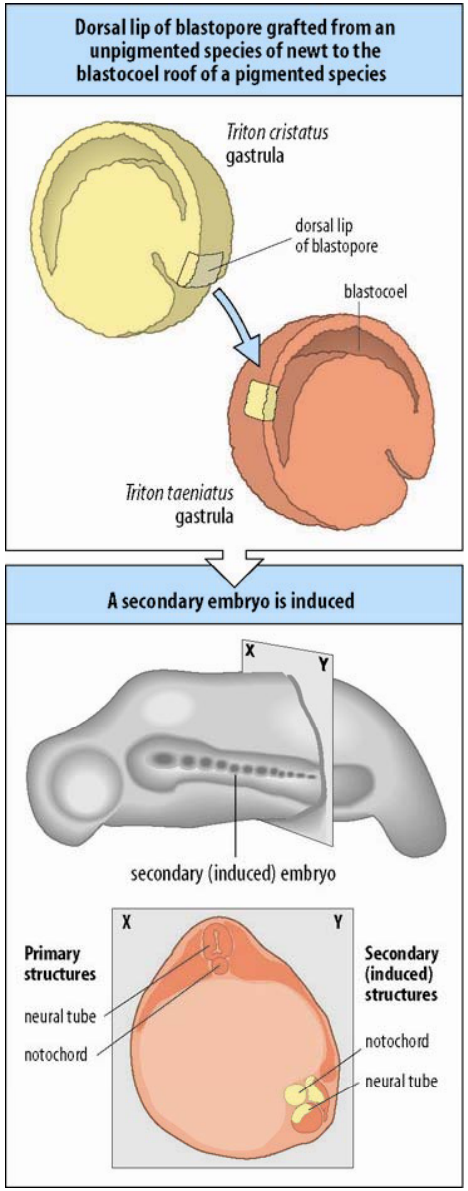


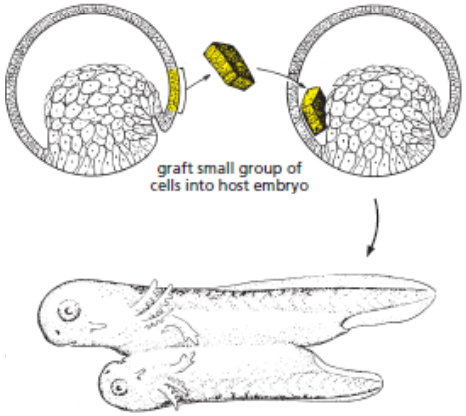
3. Induction

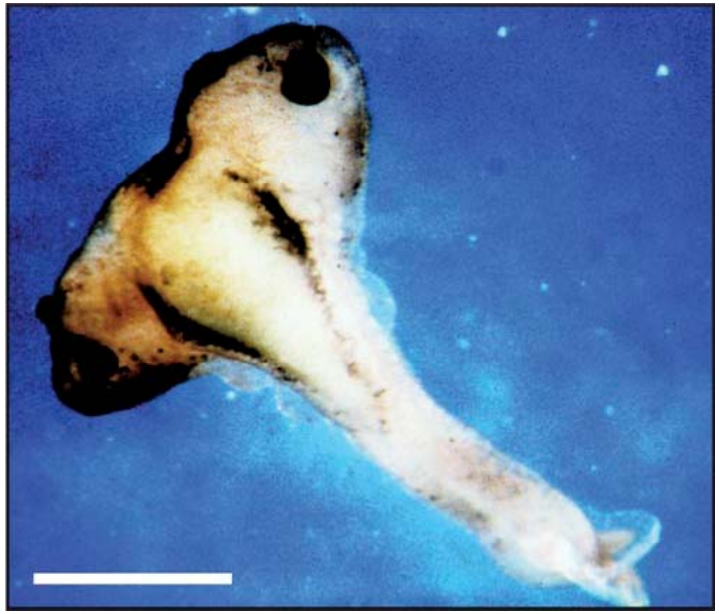
One group of cells could determine the development of neighboring cells

Spemann and Mangold experiment

(Spemann organizer, 1935 Nobel Prize**)**







The vertebrate eye develops from the neural tube and the ectoderm of the head

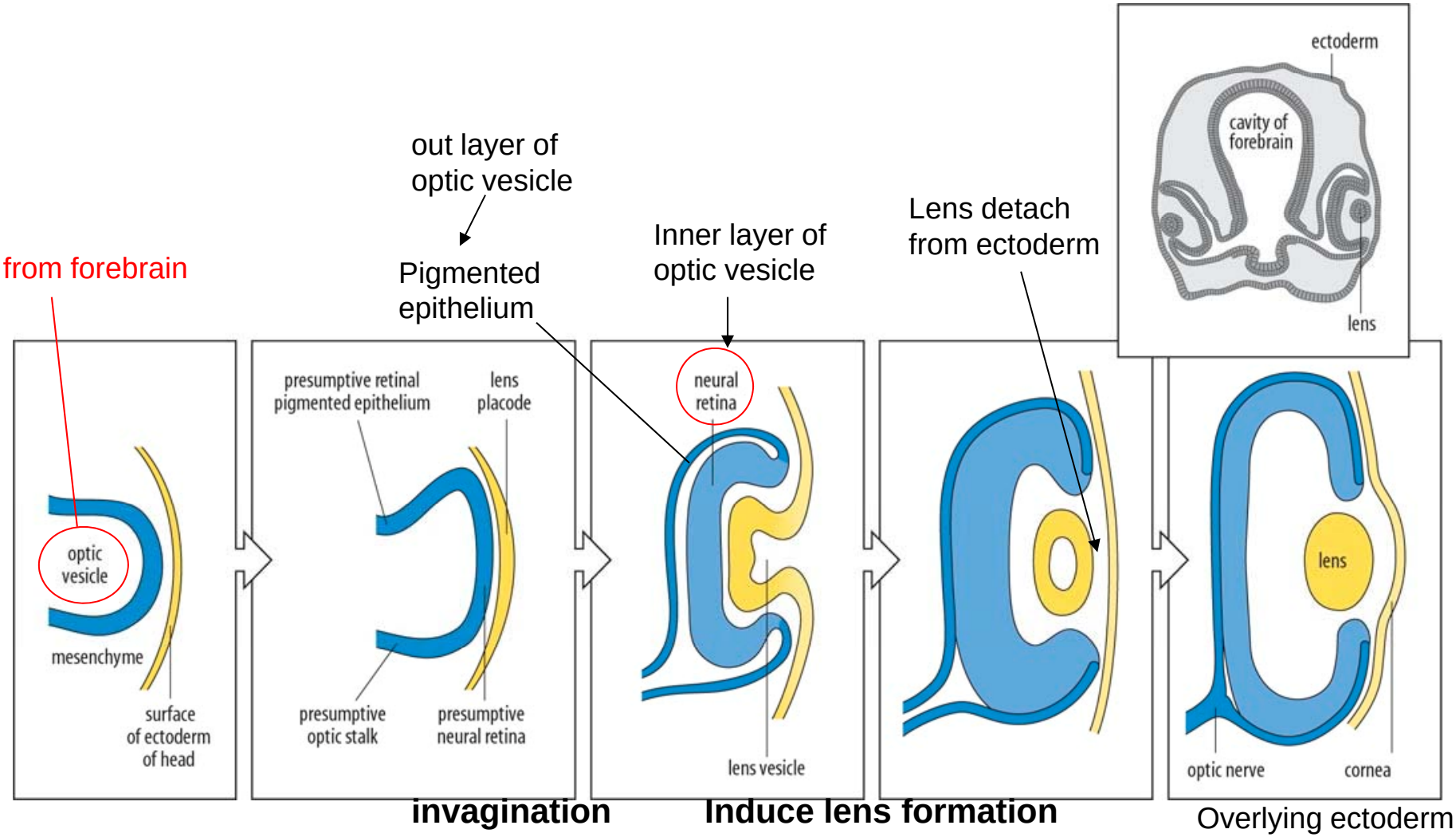
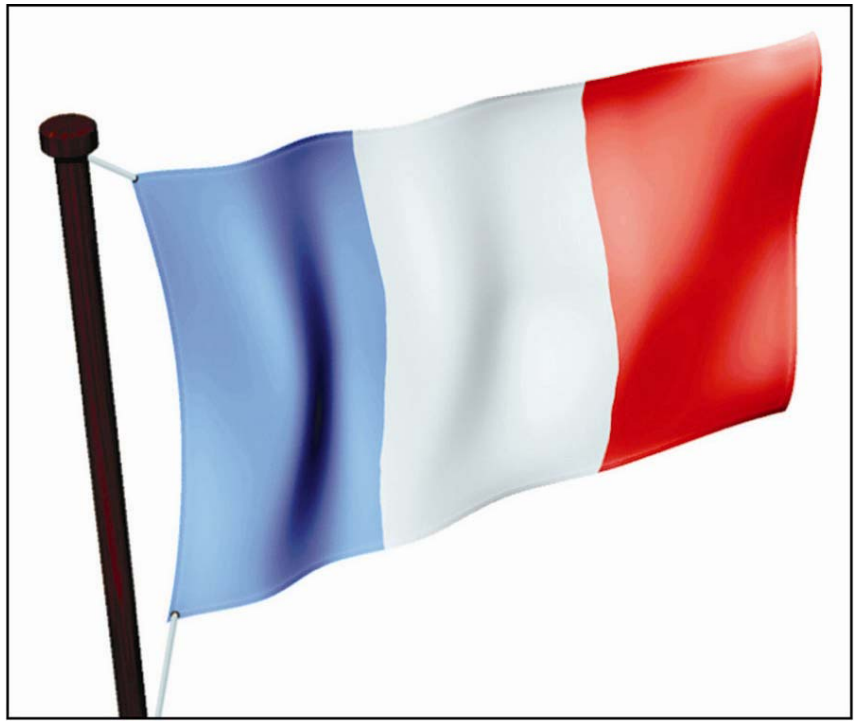


Fig. The main stages in the development of the vertebrate eyes

4. Pattern formation

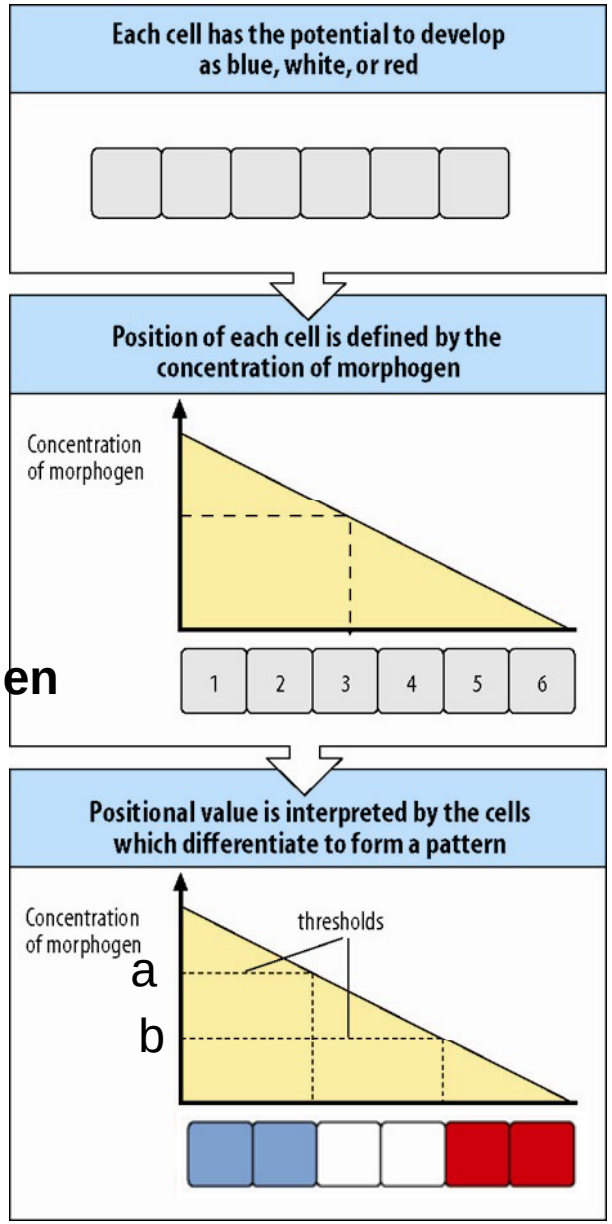
a. Positional information



4. Pattern formation

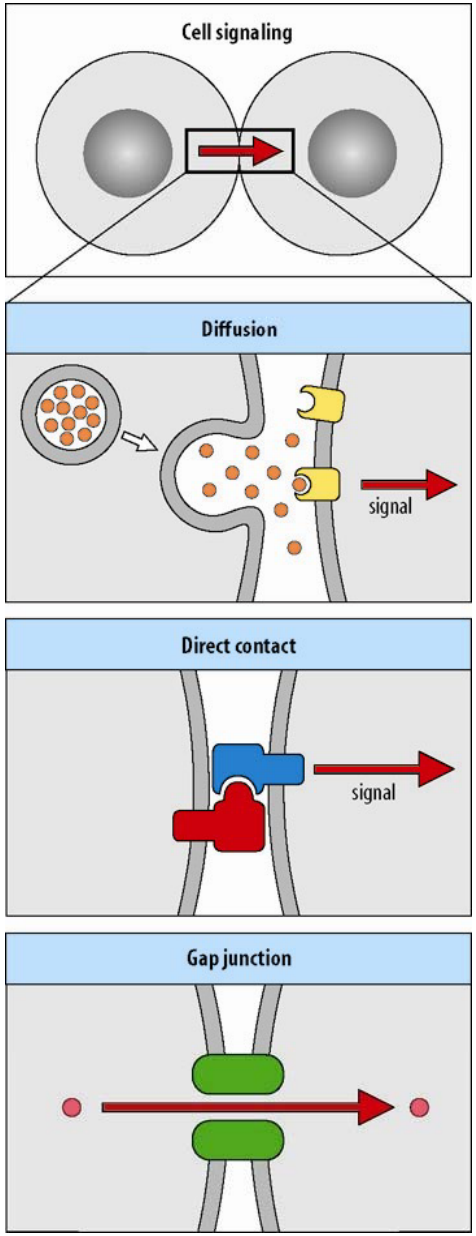
a. Positional information

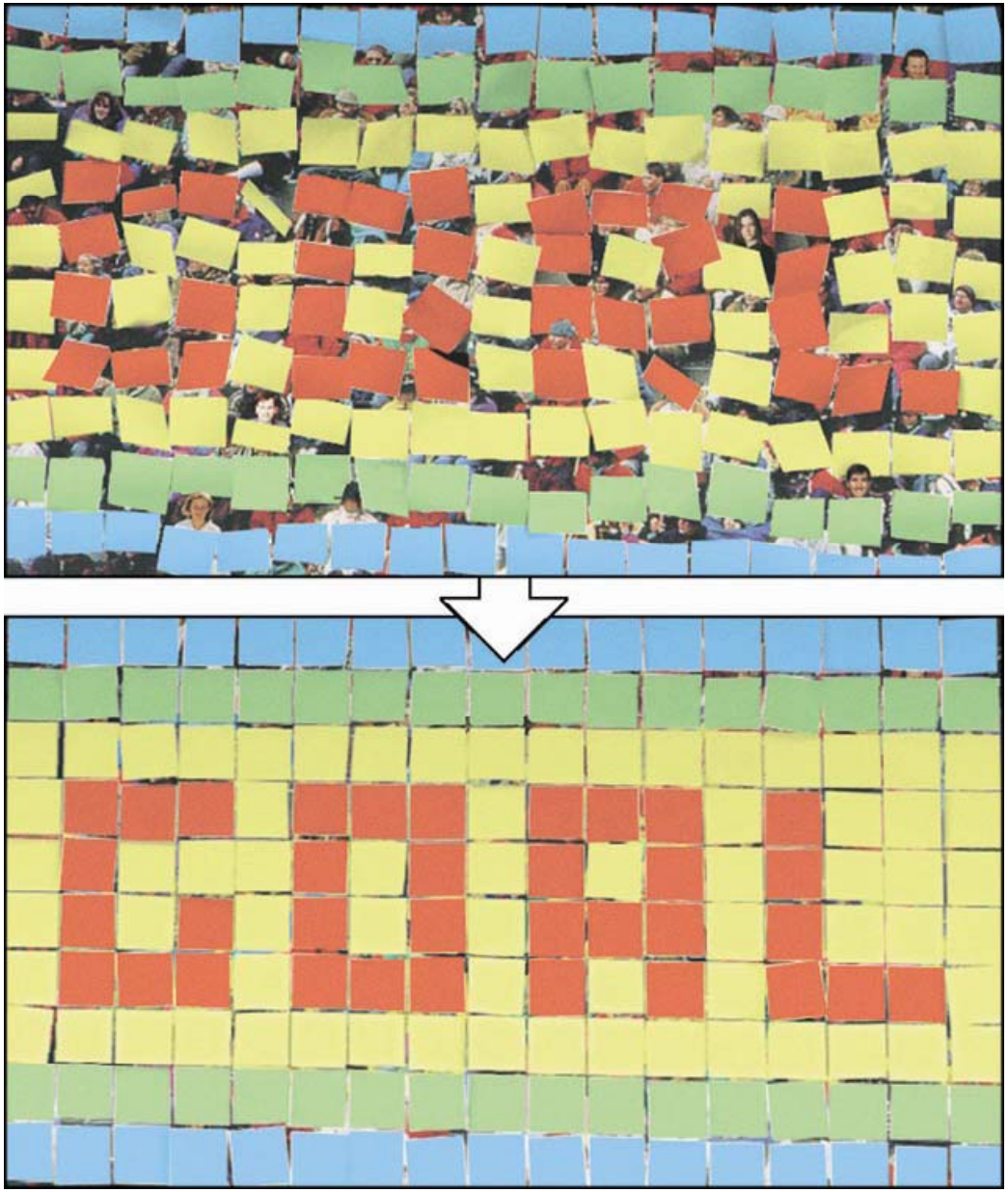
(生長因子)
Morphogen gradient



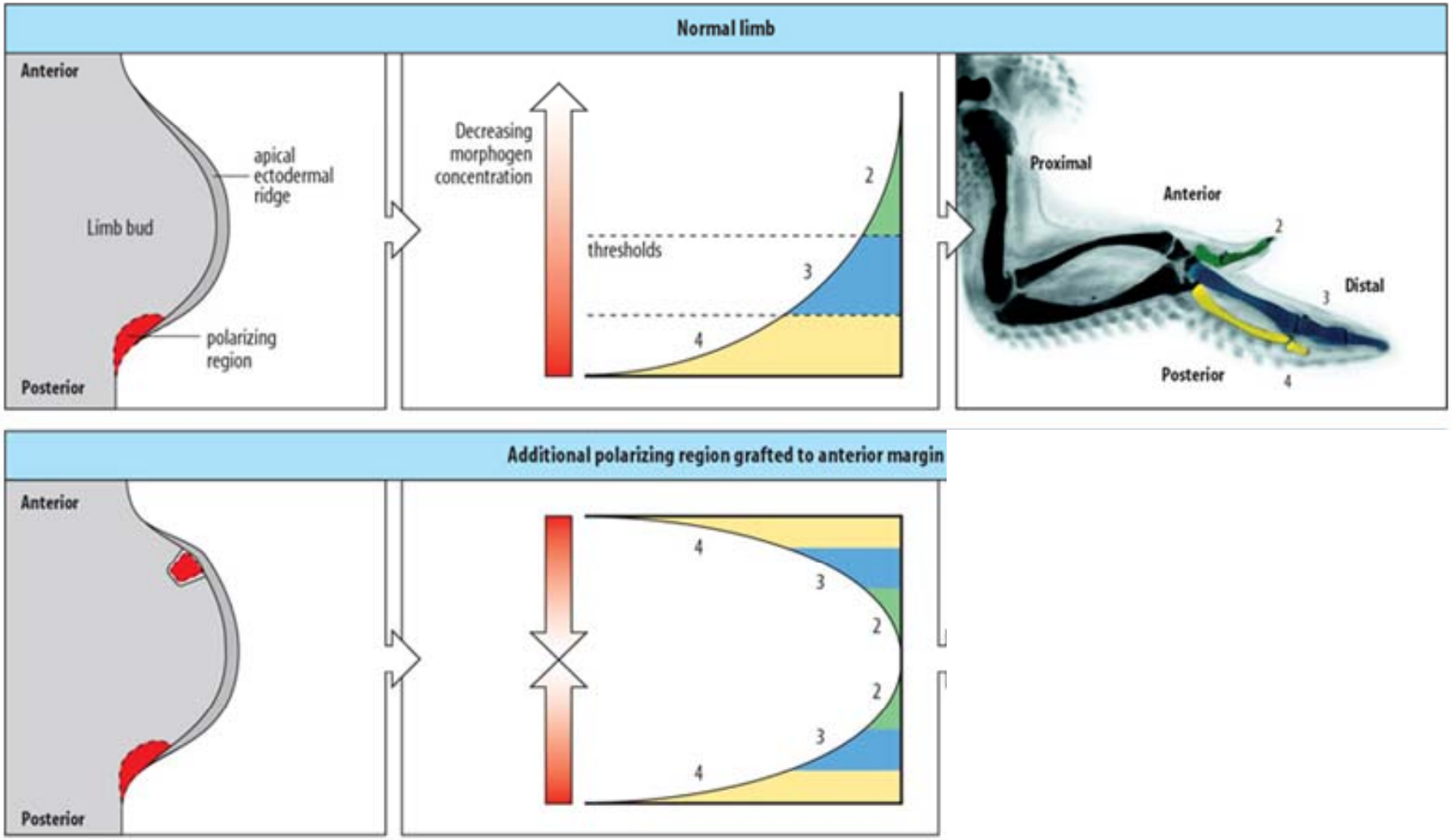
Set >a : Blue
<b : Red

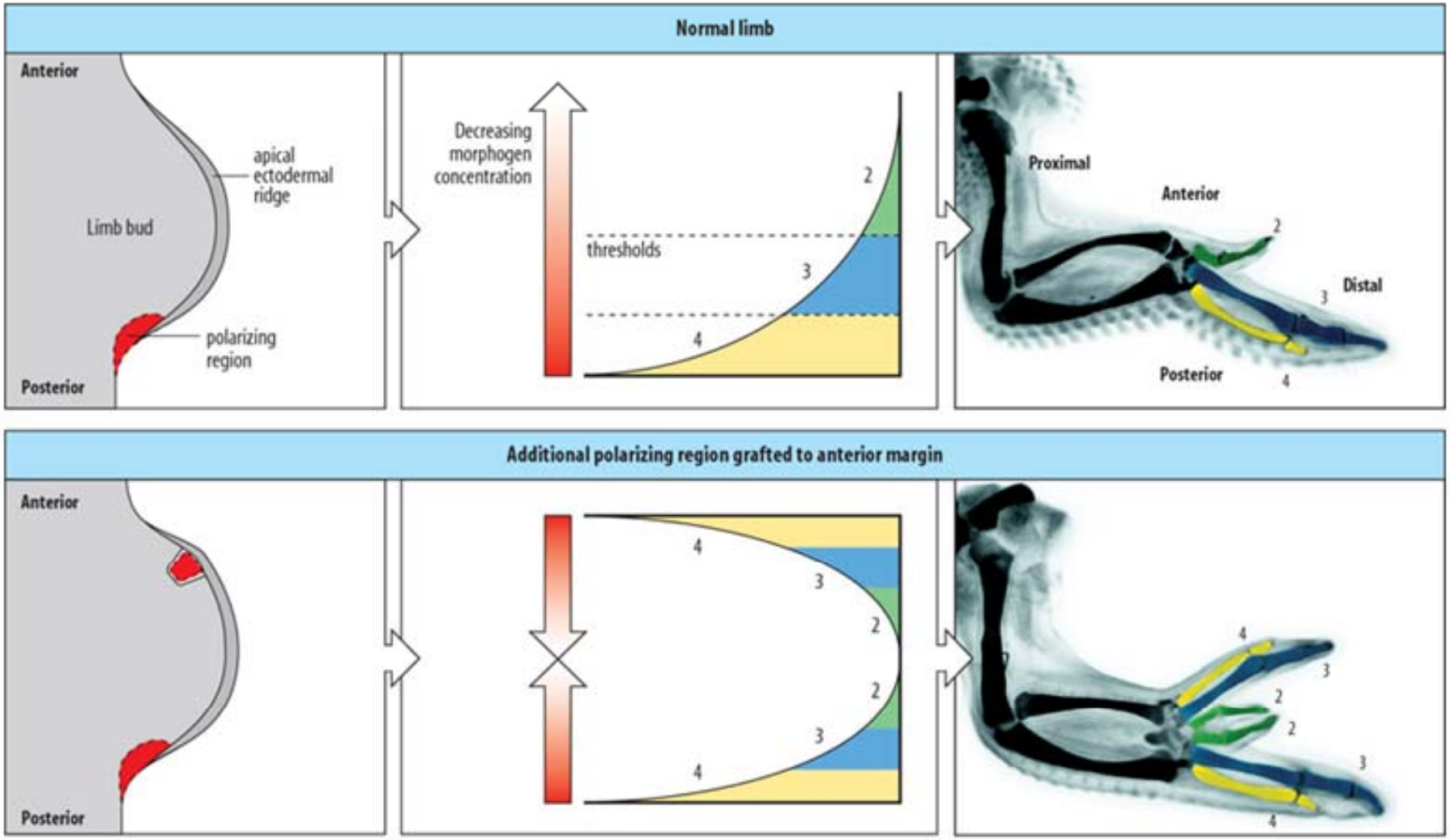
cell-cell communication





2D


Normal limb
Anterior
apical ectodermal ridge
Limb bud
polarizing region
Posterior
Decreasing morphogen concentration
thresholds
2
3
4
Proximal
Anterior
2
3
Distal
Posterior
4
Additional polarizing region grafted to anterior margin
Anterior
Posterior
4
3
2
2
3
4


Normal limb
Anterior
apical ectodermal ridge
Limb bud
polarizing region
Posterior
Decreasing morphogen concentration
thresholds
2
3
4
Proximal
Anterior
Distal
Posterior
Additional polarizing region grafted to anterior margin
Anterior
Posterior

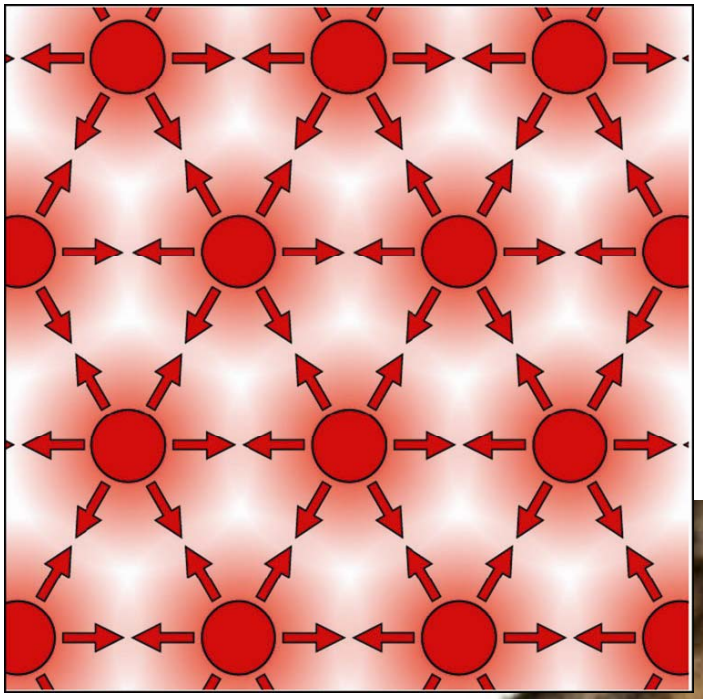
Synpolydactyly (SPD), caused by mutations in *HOXD 13*, is characterized by extra fingers and toes and bone abnormalities in the hands and feet

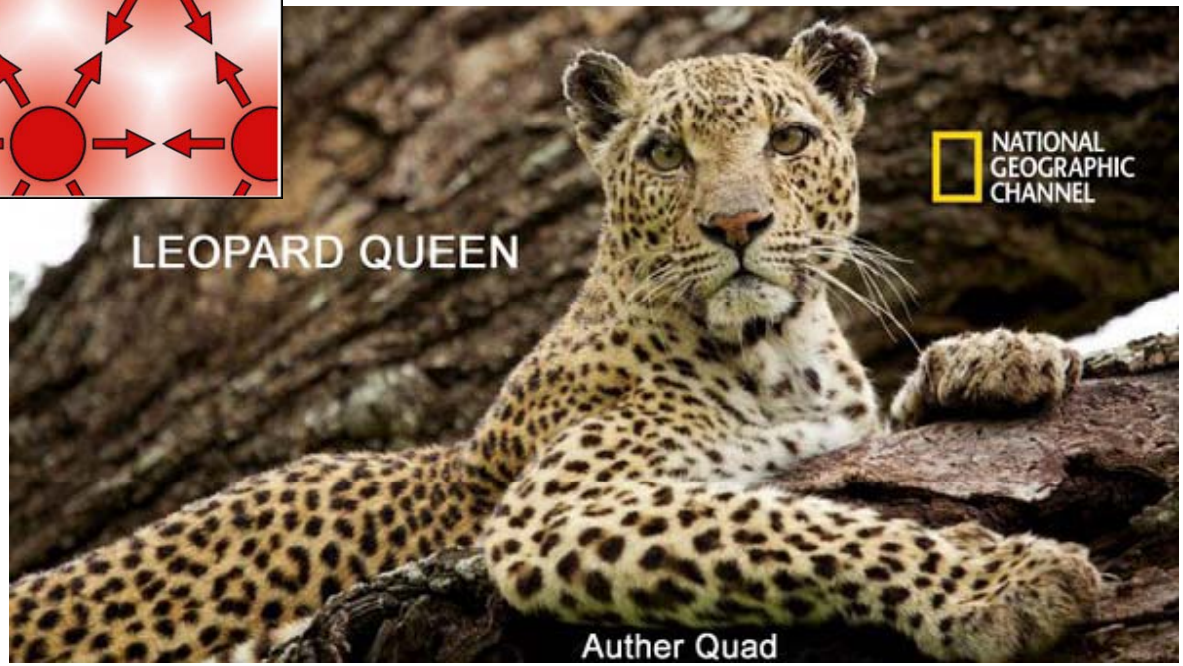
Mutations that affect antero-posterior patterning can cause polydactyly. With **preaxial polydactyly** has mutations in the *SHH* gene

4. Pattern formation (spacing patterns)

b. Lateral inhibition

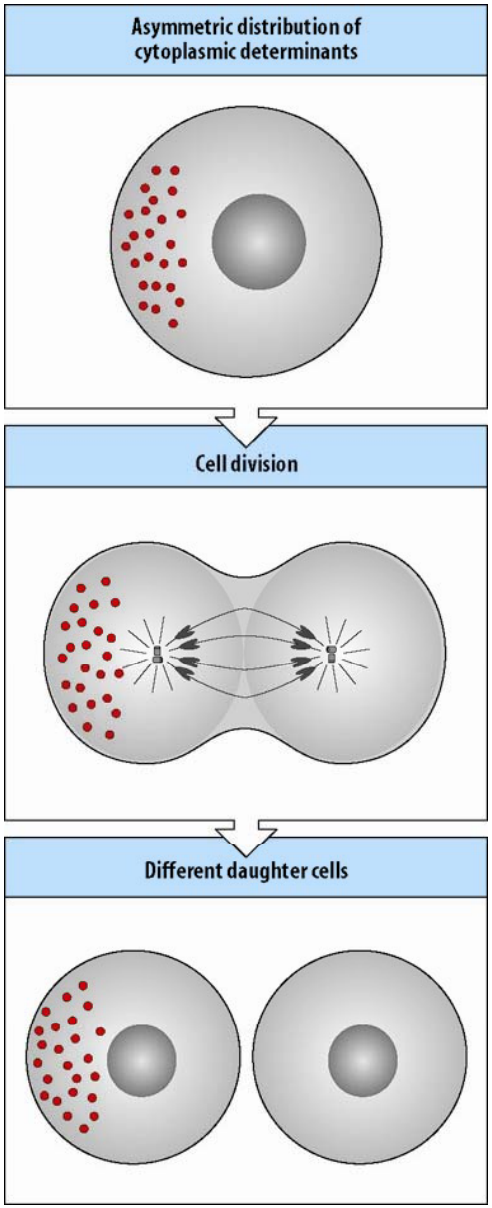
Bird’s skin, animal’s spots

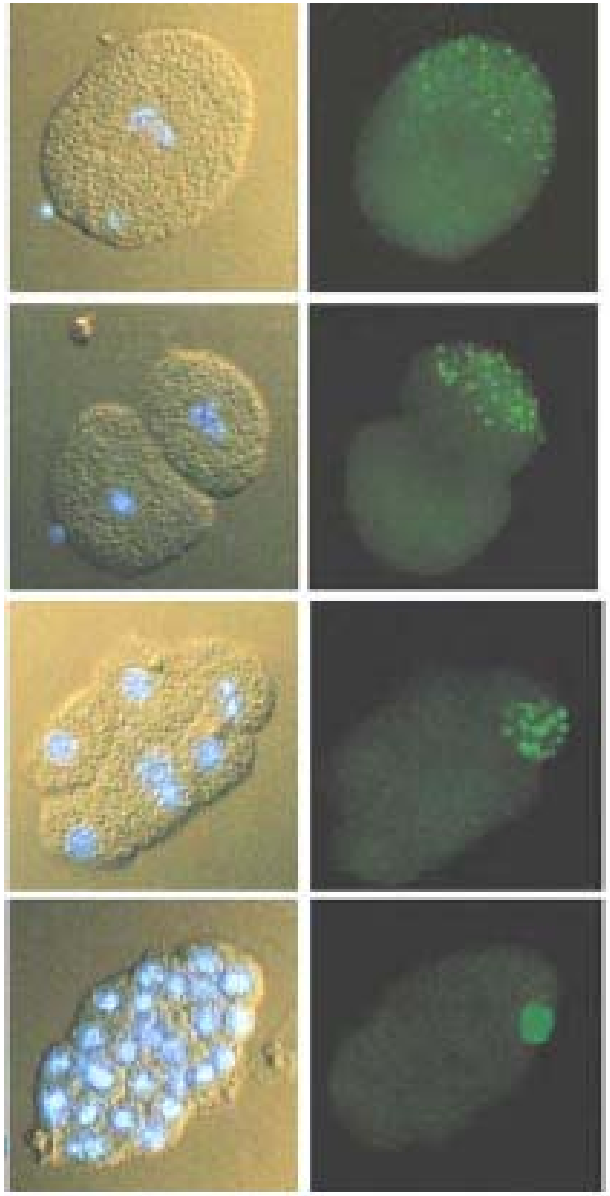


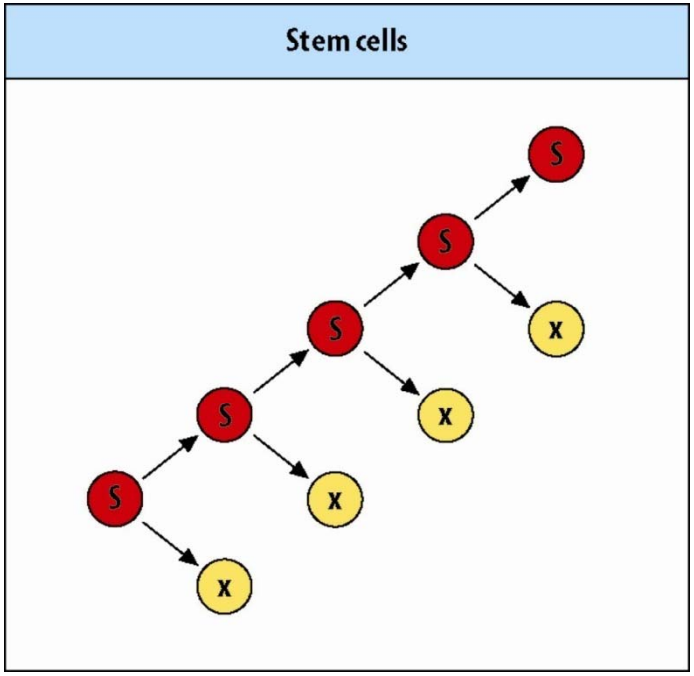


5. Asymmetric division

Cytoplasmic determinant





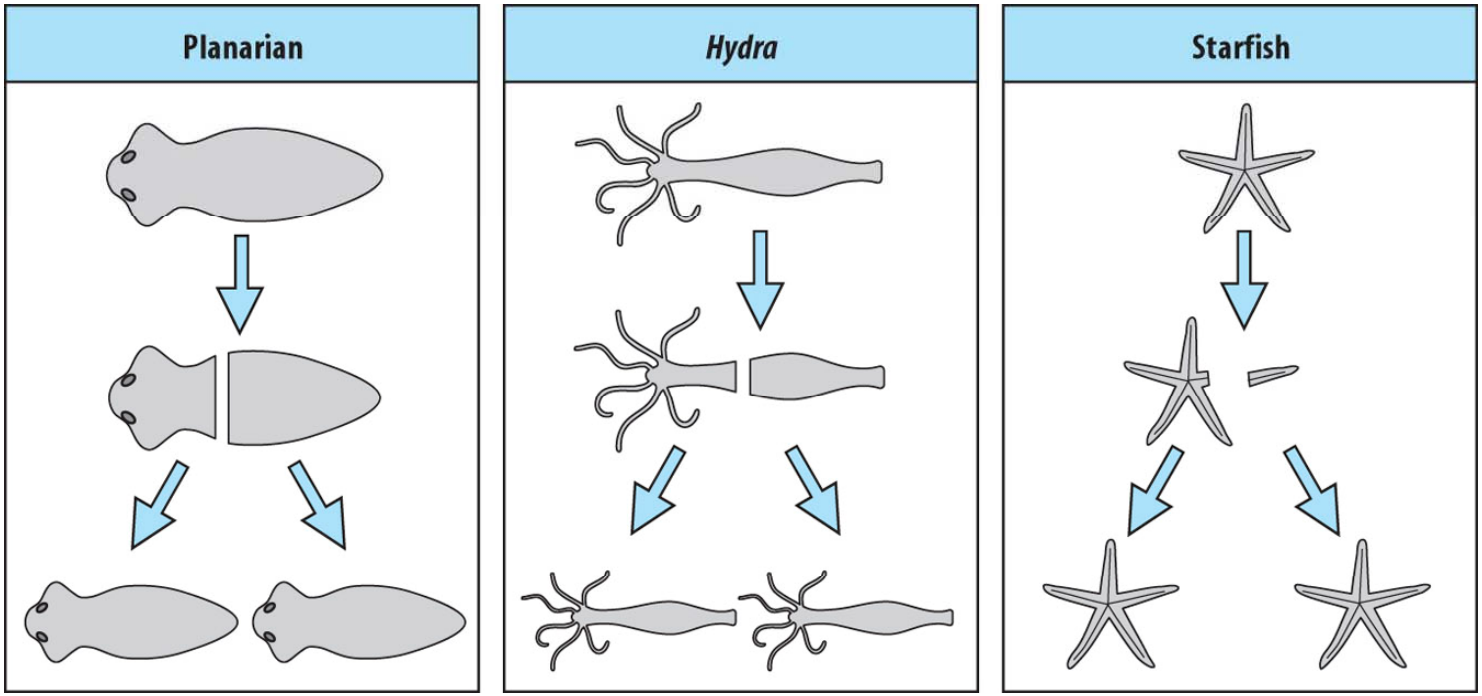


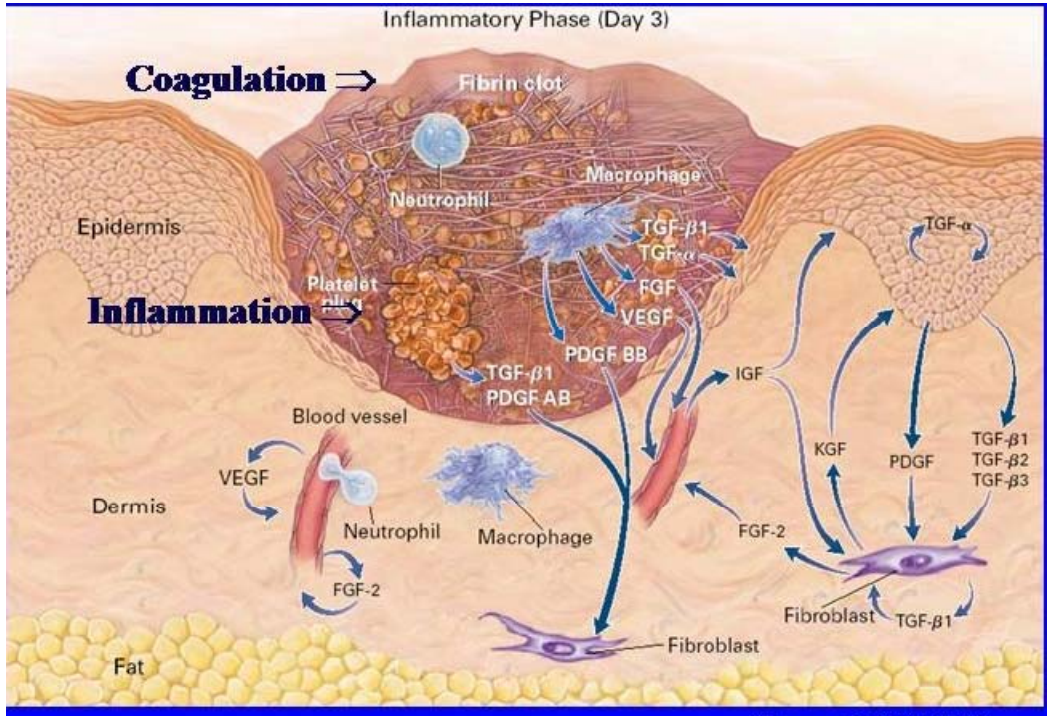
germline cell marker (green)

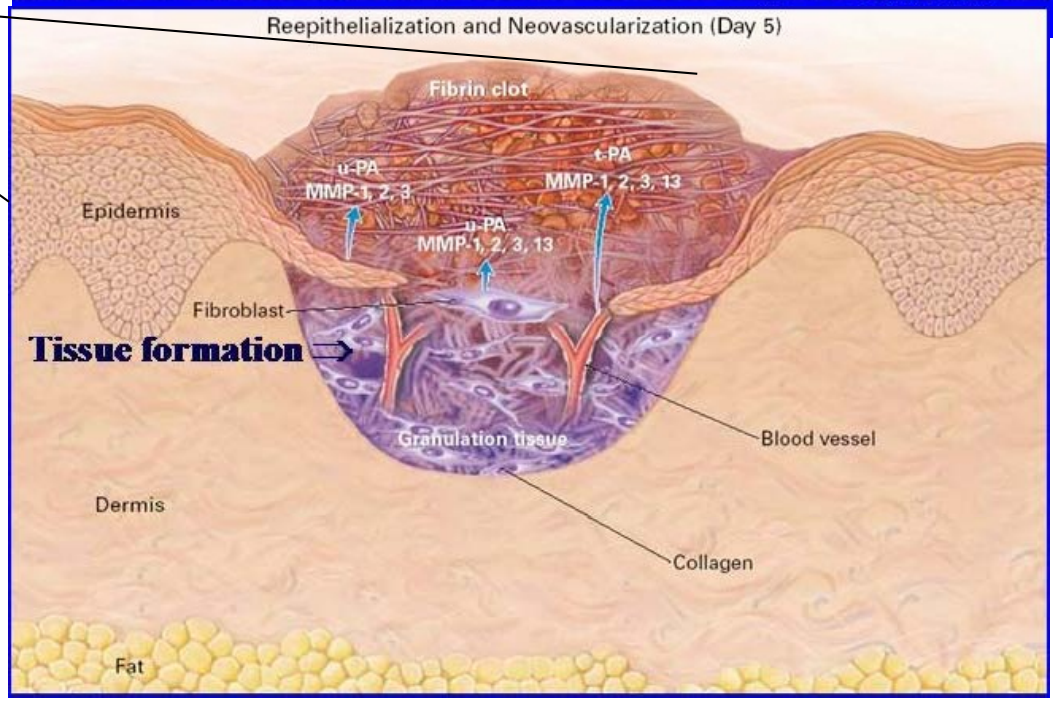
Cell nuclear (blue)

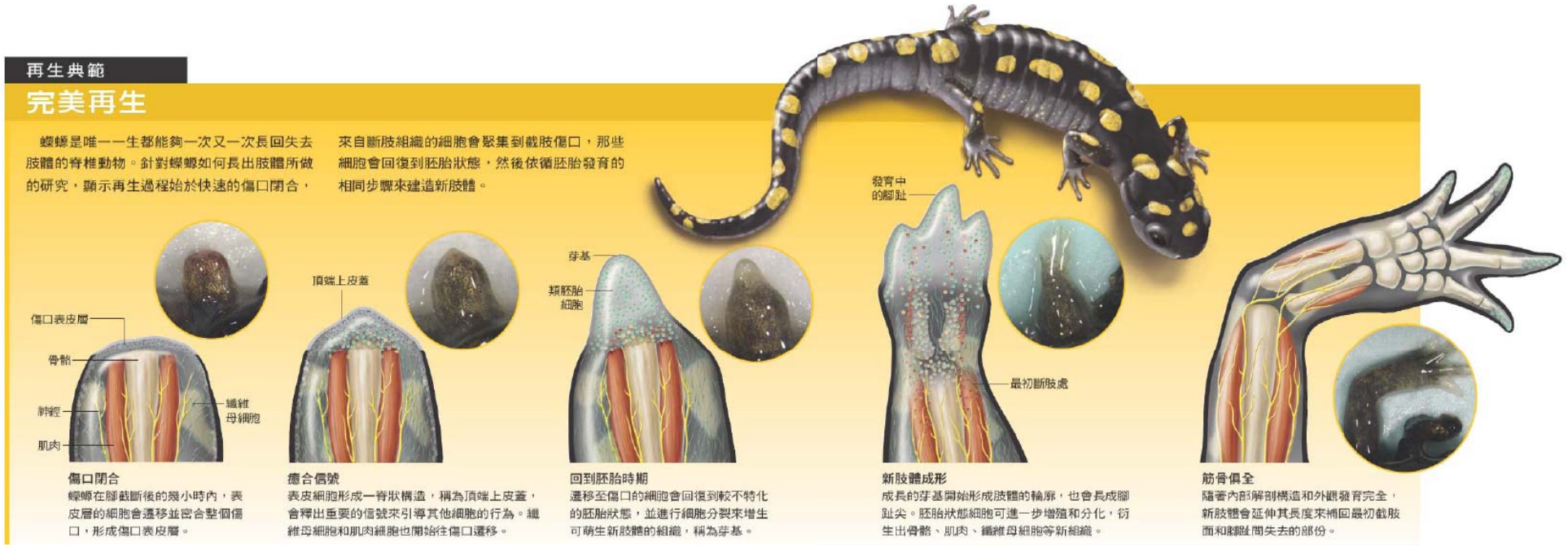
Outline

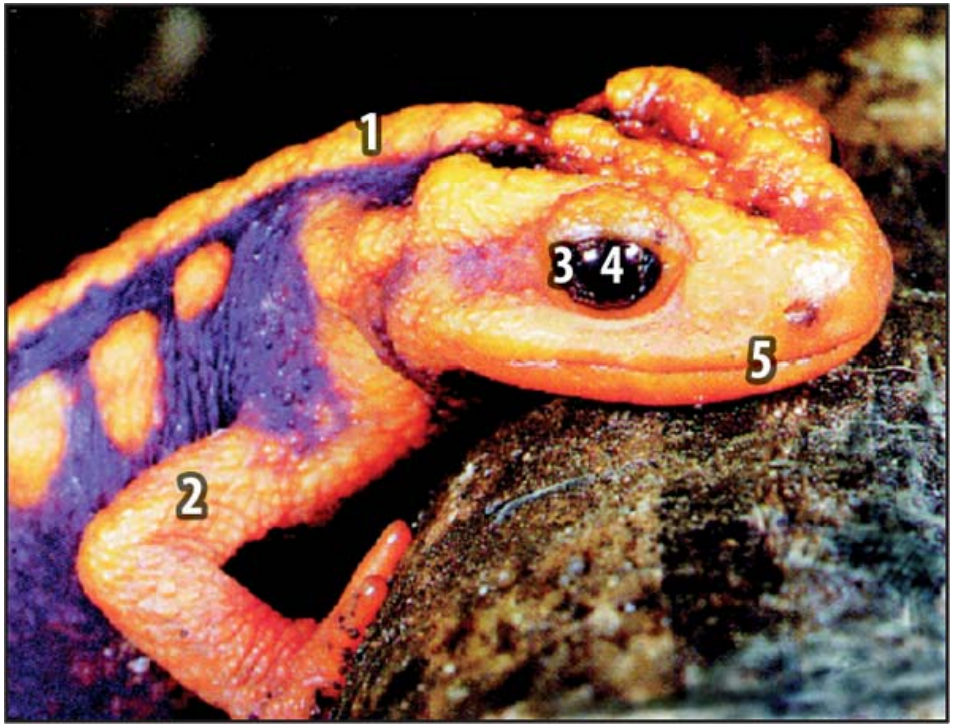
1. 胚胎學 (embryology) vs. 發育生物學 (developmental biology)
2. 模式生物 (model organisms)
3. 動物發育的主要階段
4. 發育過程之機制
5. **組織再生與幹細胞**



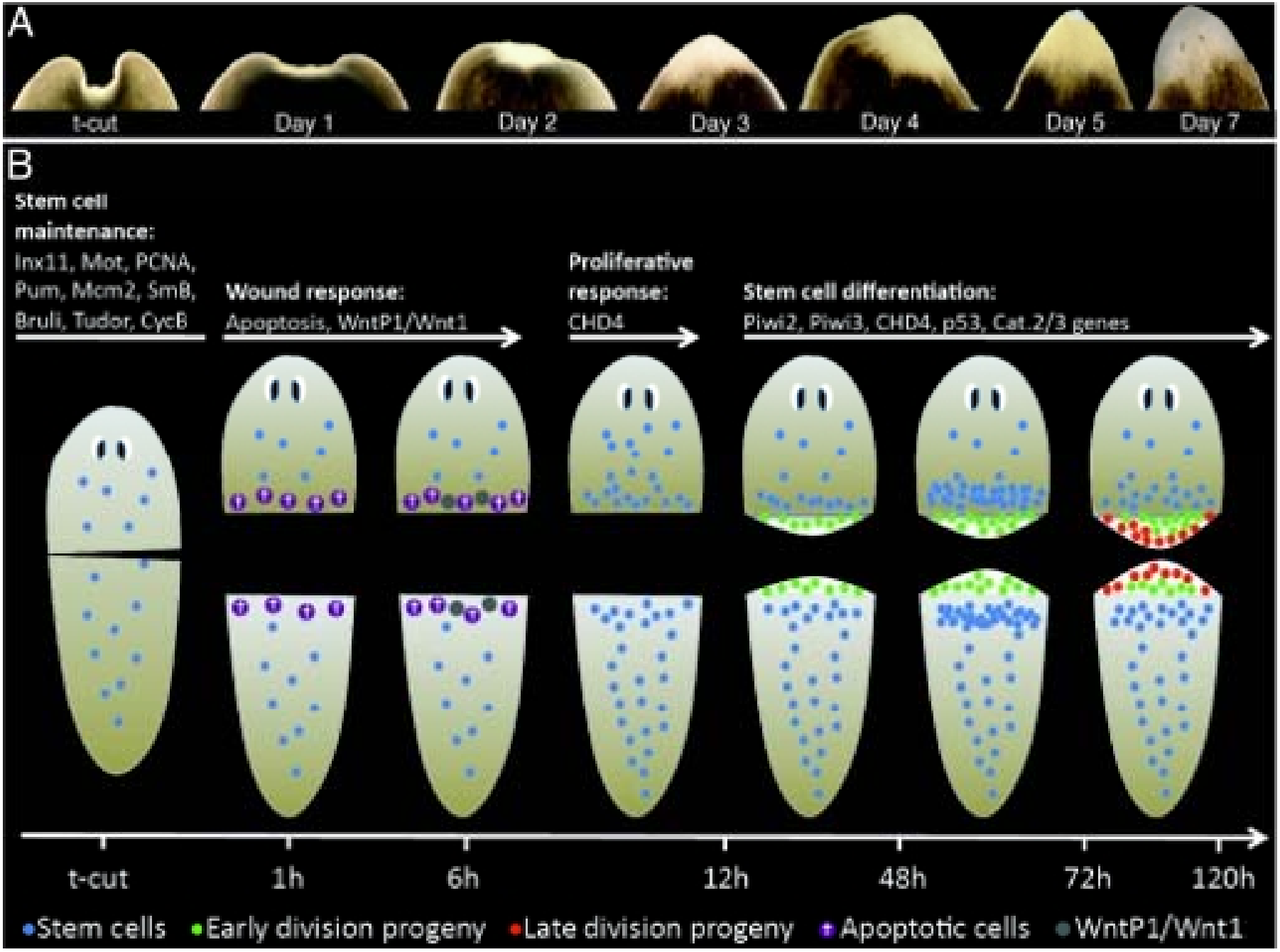

Inflammatory Phase (Day 3)
Coagulation
Fibrin clot
Neutrophil
Macrophage
Epidermis
TGF-β1
TGF-α
Platelet
FGF
Inflammation
VEGF
PDGF BB
TGF-β1
PDGF AB
IGF
TGF-α
Blood vessel
KGF
PDGF
TGF-β1
TGF-β2
TGF-β3
VEGF
Dermis
Neutrophil
Macrophage
FGF-2
FGF-2
Fibroblast
TGF-β1
Fibroblast
Fat


Reepithelialization and Neovascularization (Day 5)
Fibrin clot
u-PA
MMP-1, 2, 3
t-PA
MMP-1, 2, 3, 13
Epidermis
u-PA
MMP-1, 2, 3, 13
Fibroblast
Tissue formation
Granulation tissue
Blood vessel
Dermis
Collagen
Fat





The capacity for regeneration in urodele amphibians (newt)
(1) Dorsal crest, (2) limbs, (3,4) retina and lens, (5) jaw, and tail



幹細胞

1.甚麼是幹細胞

2.幹細胞來源

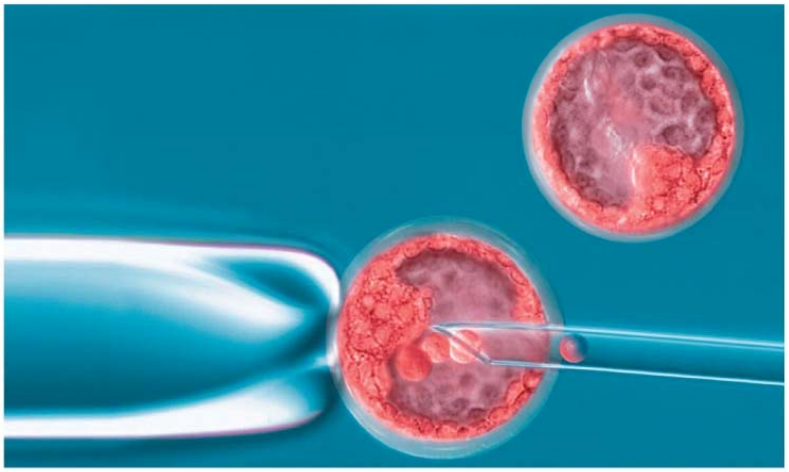
a. 成體幹細胞 (adult stem cell):
骨髓，成體週邊血 (取得極為困難)

b. 胚胎幹細胞 (embryonic stem cell):
胚胎，臍帶血 (取得容易)

3. 幹細胞之運用 (複製, 組織再生)

4. 幹細胞研究之道德探討

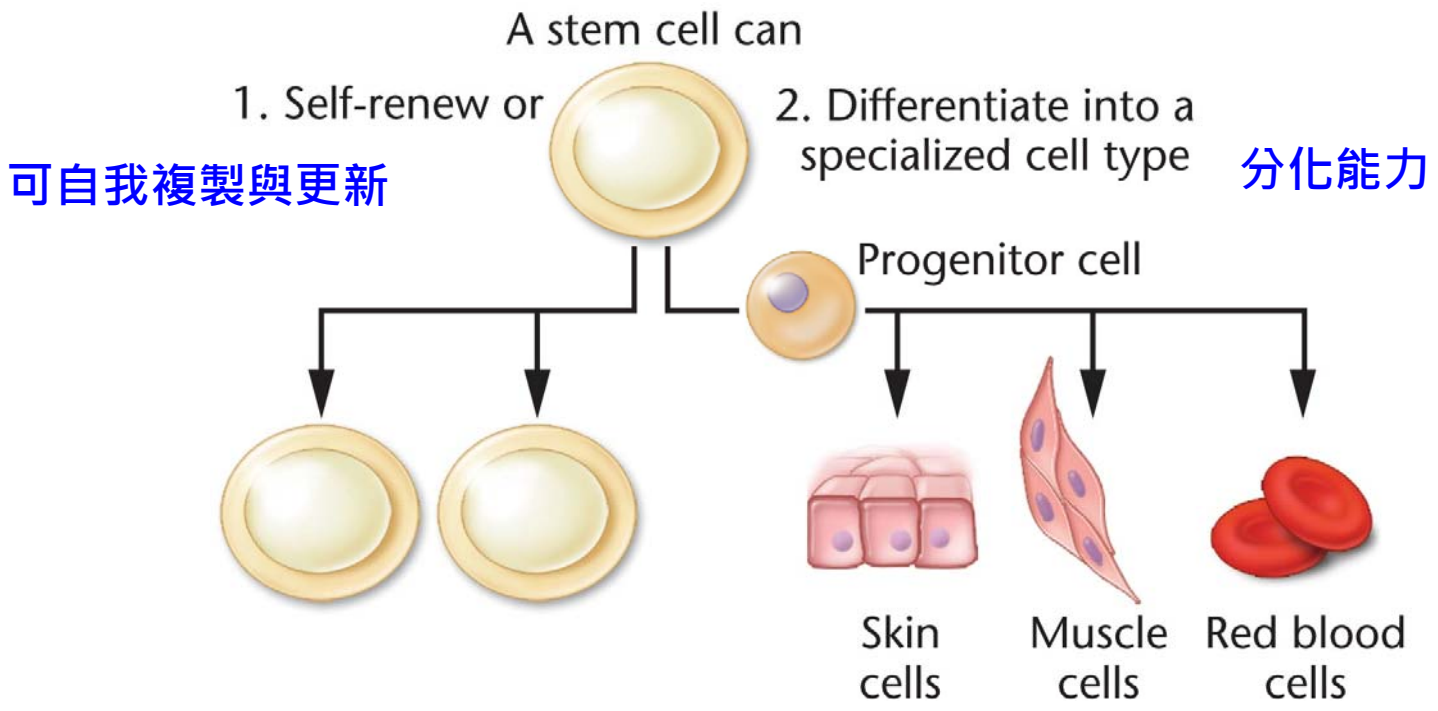
(a)



(b)

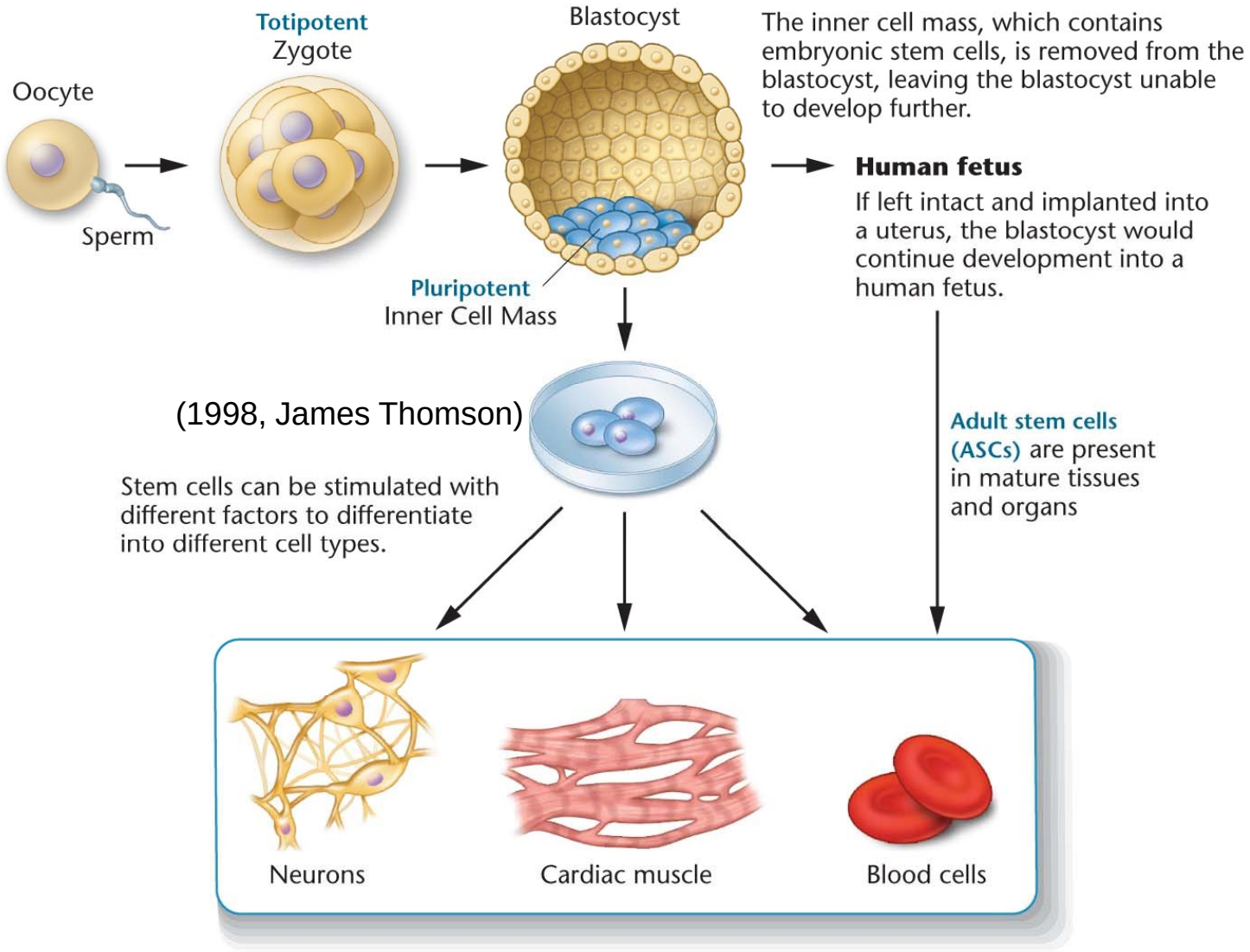
What Are Stem Cells?

- Stem cells share two basic characteristics that make them distinctive from other cell types : **self-renewal** and **differentiation** into specialized cell types

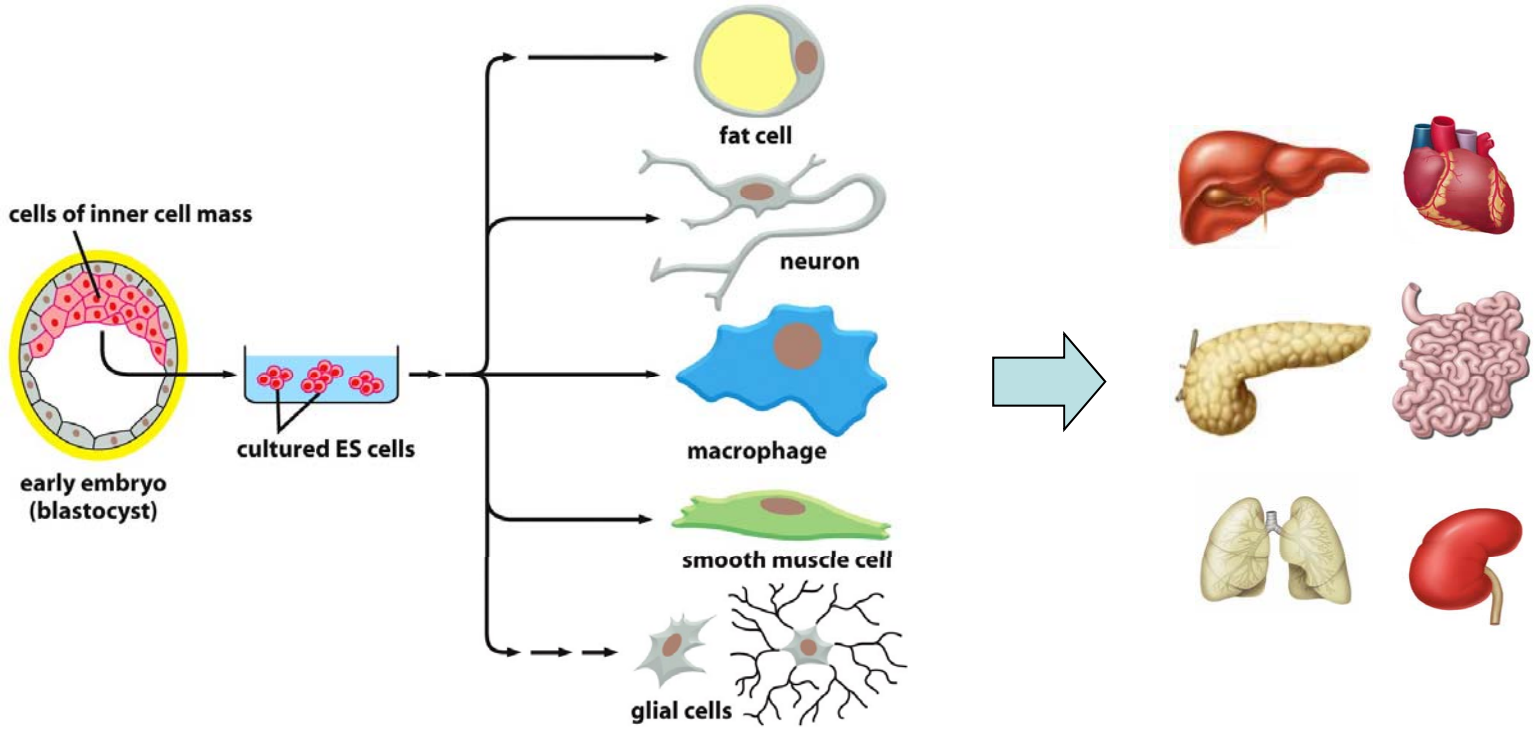


幹細胞來源之一　　胚胎幹細胞

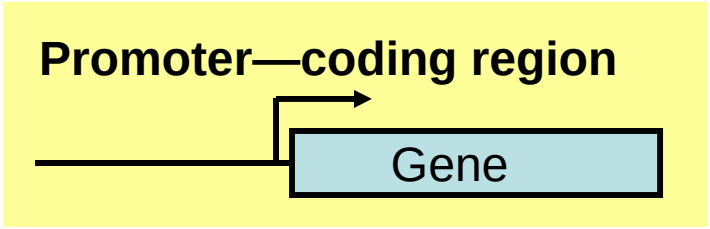
human embryonic stem cells (hESCs)



Cell differentiation (細胞分化)

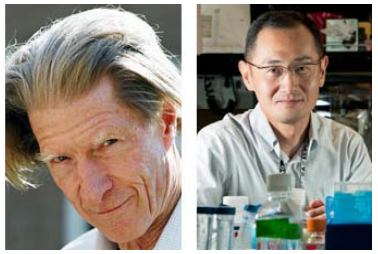


How to control the cell differentiation?
differential expression of gene?



Can differentiated cells reverse to ES cells? 返老還童?

The Nobel Prize in Physiology or Medicine 2012
Sir John B. Gurdon, Shinya Yamanaka



SCNT vs iPS

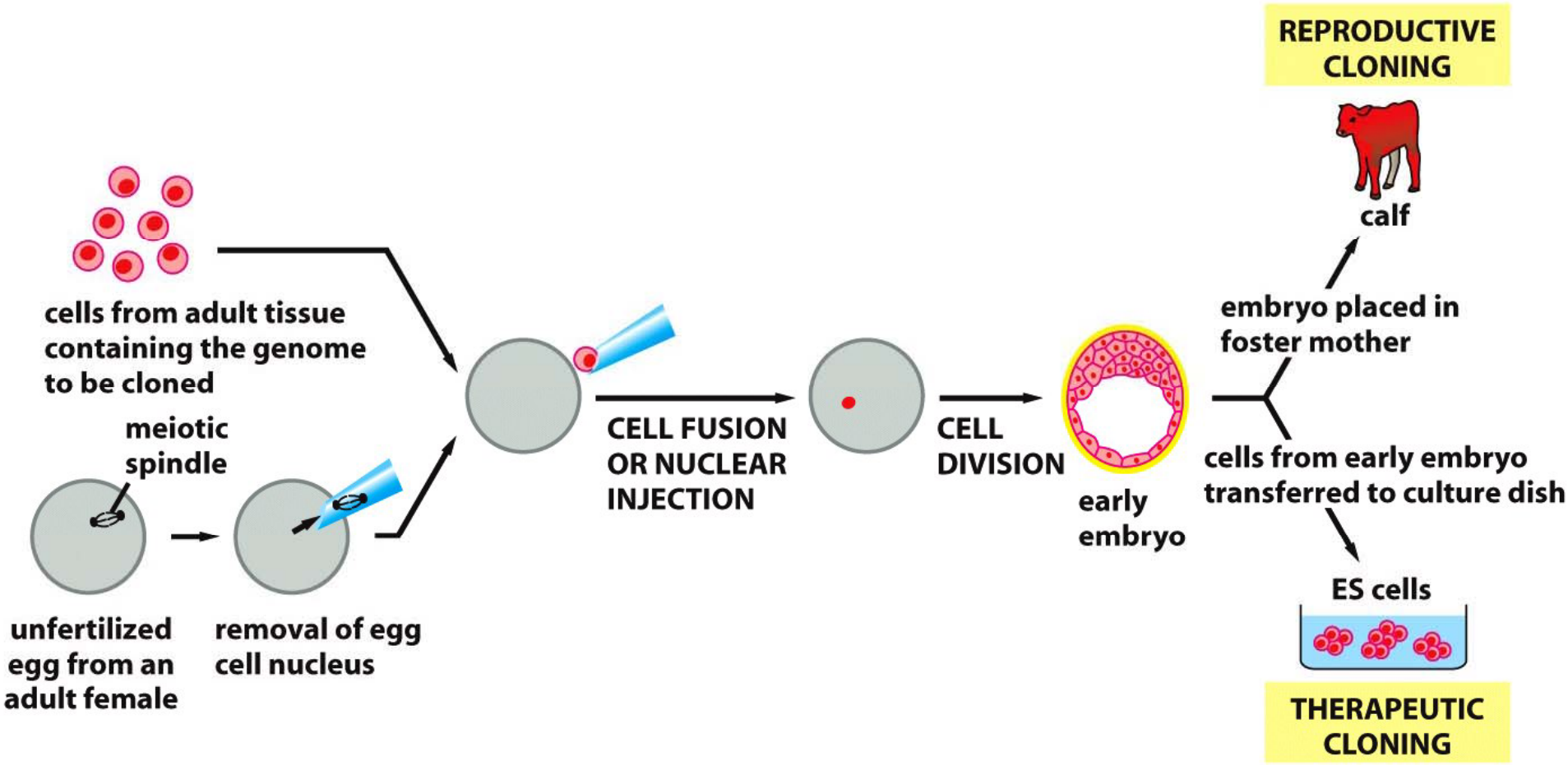
Somatic Cell Nuclear Transfer (體細胞核移殖)

SCNT

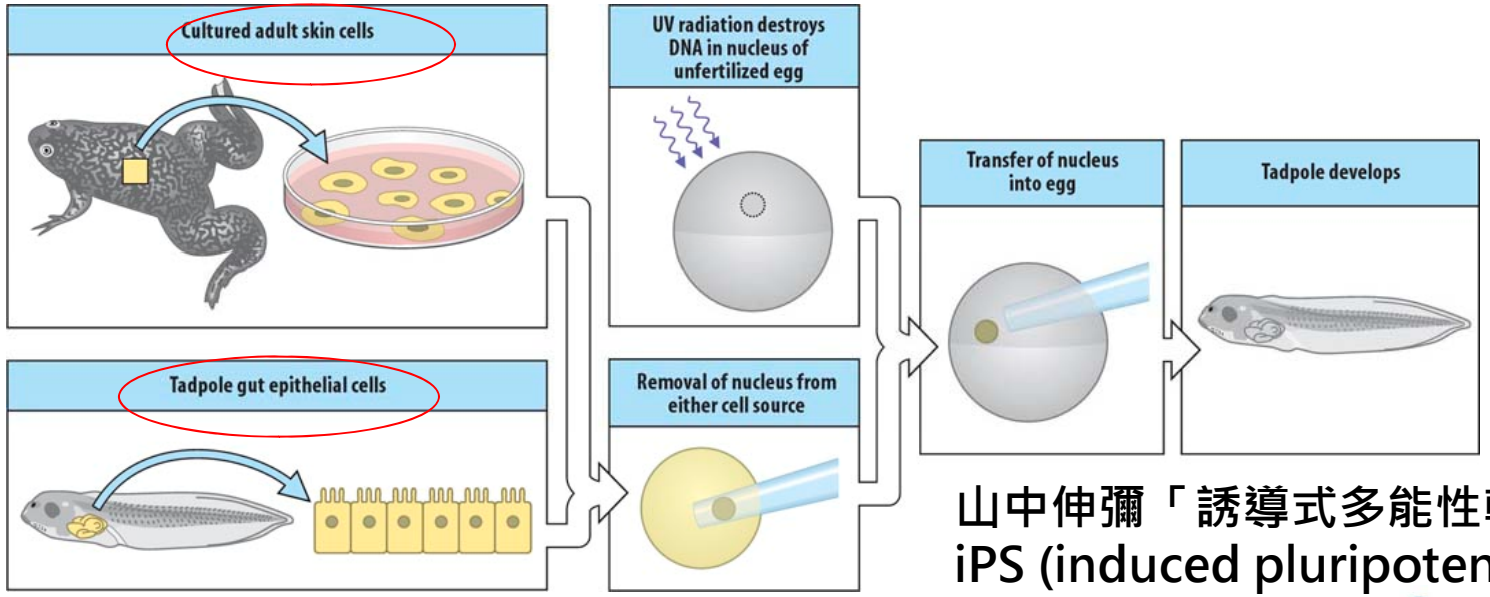
複製動物
•1997年2月27日英國Roslin研究所科學家於Nature雜誌上首先發表複製羊桃莉(Dolly)複製成功

Nature 385: 810

Somatic Cell Nuclear Transfer (體細胞核移殖)

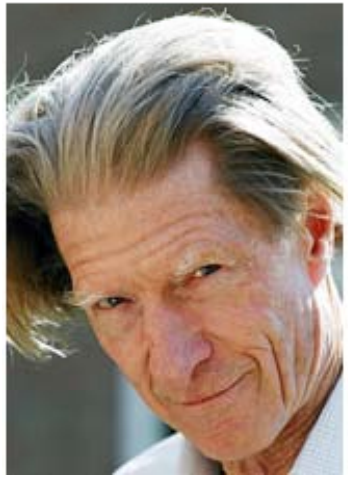


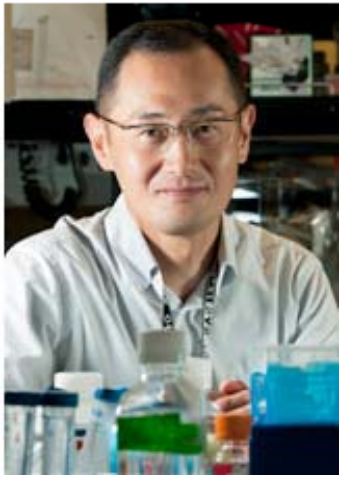
Somatic cell nuclear transplantation (SCNT) by John Gurdon

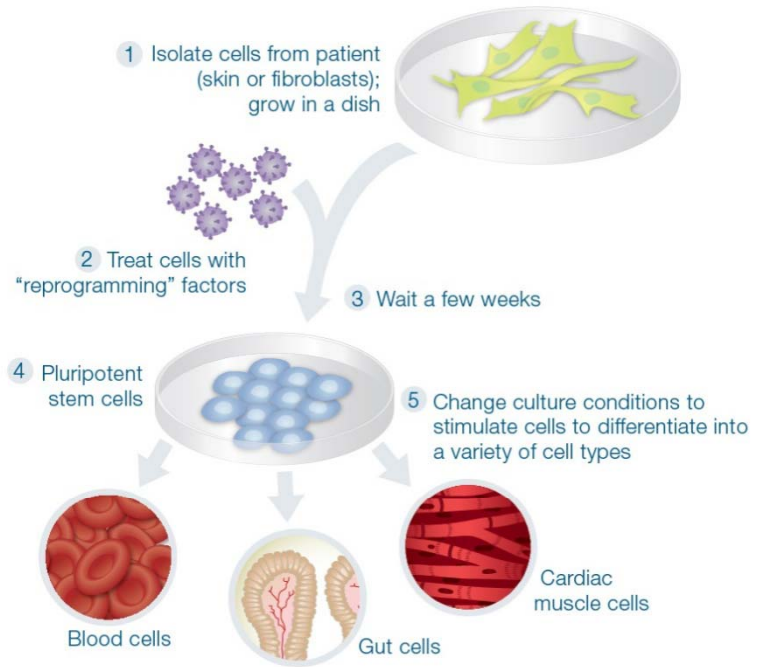


山中伸彌「誘導式多能性幹細胞」
iPS (induced pluripotent stem cells)

The Nobel Prize in Physiology or Medicine 2012
Sir John B. Gurdon, Shinya Yamanaka

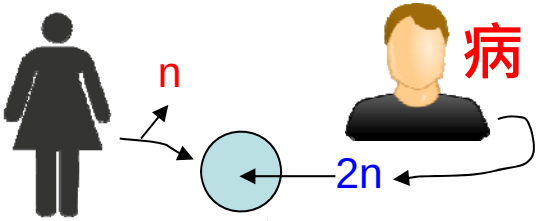






複製人與器官複製

代理孕母



inner cell mass

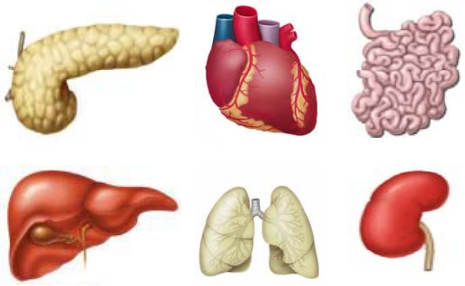
幹細胞
(分裂)

體外培養

生命之開始
(法律定義)

幹細胞 (分化)

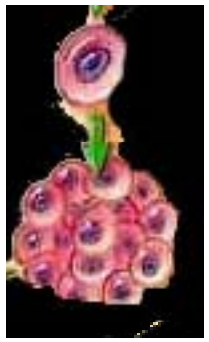
合法？合理？



器官複製（使用動物）

取得胚胎幹細胞

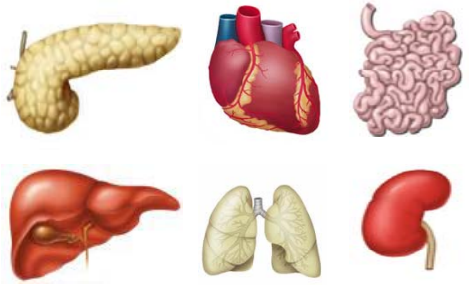
代理孕母

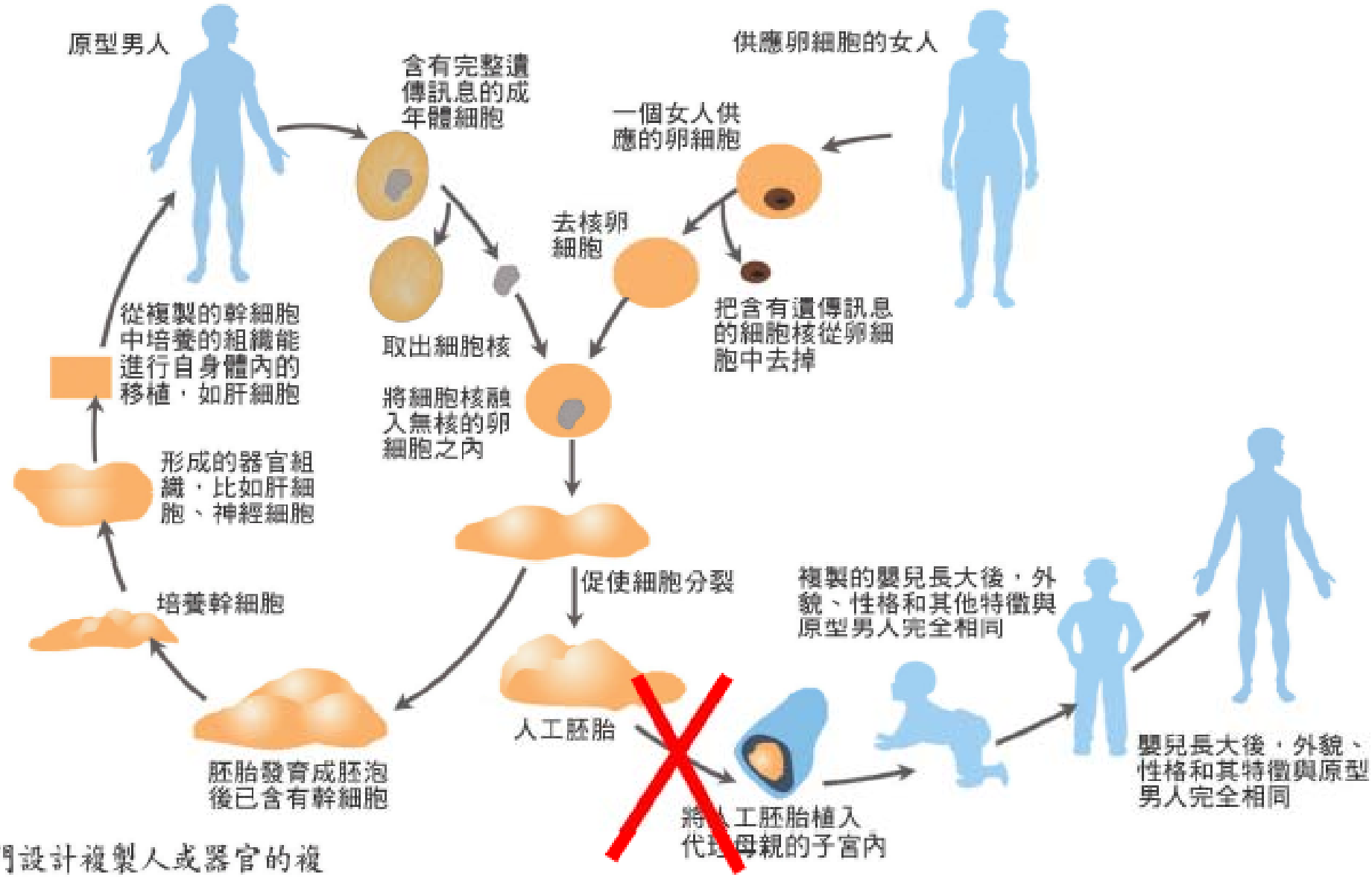


生命之開始
(法律定義)

幹細胞 (分化)

合法？合理？

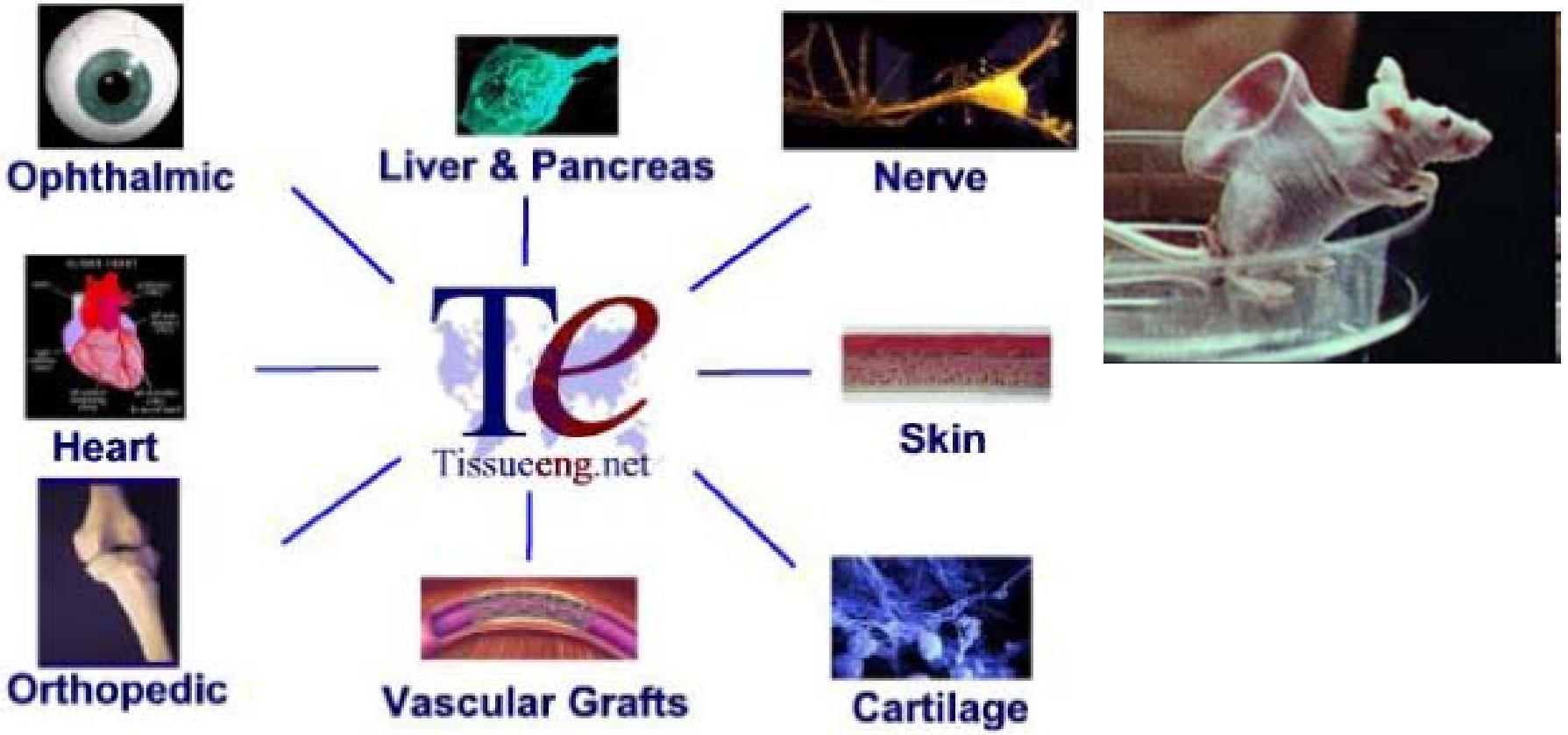




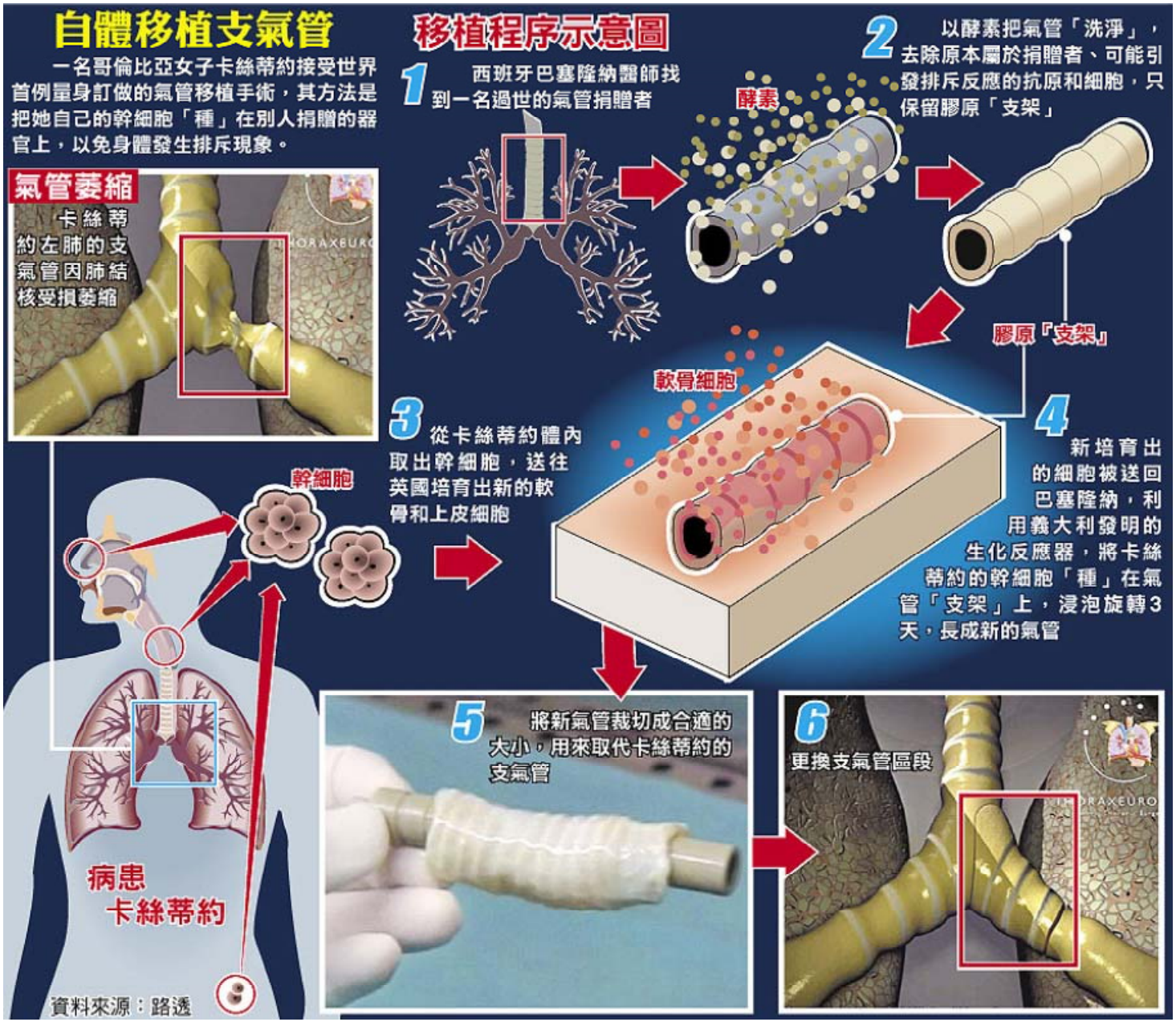
專門設計複製人或器官的複製技術與步驟

組織工程(Tissue Engineering)

- 皮膚移植（燒燙傷、美容）
- 器官再造
  - 1997 Dr. Charles Vacanti (University of Massachusetts)
    利用小鼠製造人工義耳: 以可吸收性聚合物製造耳朵形狀，以牛膠原細胞包覆, 埋放到裸鼠皮下，生長成人形耳朵
  - 其他可能應用：膀胱、軟骨、血管...等



2008 自體幹細胞培育氣管移植



regenerative medicine (再生醫學)

- Scientists working in regenerative medicine are also optimistic about their ability to produce viable organs from stem cells
- **Sheets of skin** and other organs such as the **urinary bladder** have been created *in vitro*

QUESTIONS?

Summary

1. 胚胎學 (embryology) vs. 發育生物學 (developmental biology)
2. 模式生物 (model organisms)
3. 動物發育的主要階段
4. 發育過程之機制
5. 組織再生與幹細胞