The later development in xenopus and zebrafish

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outline

- Ectoderm

  1) neural tube formation and differentiation
  2) neural crest cells
  3) eye development

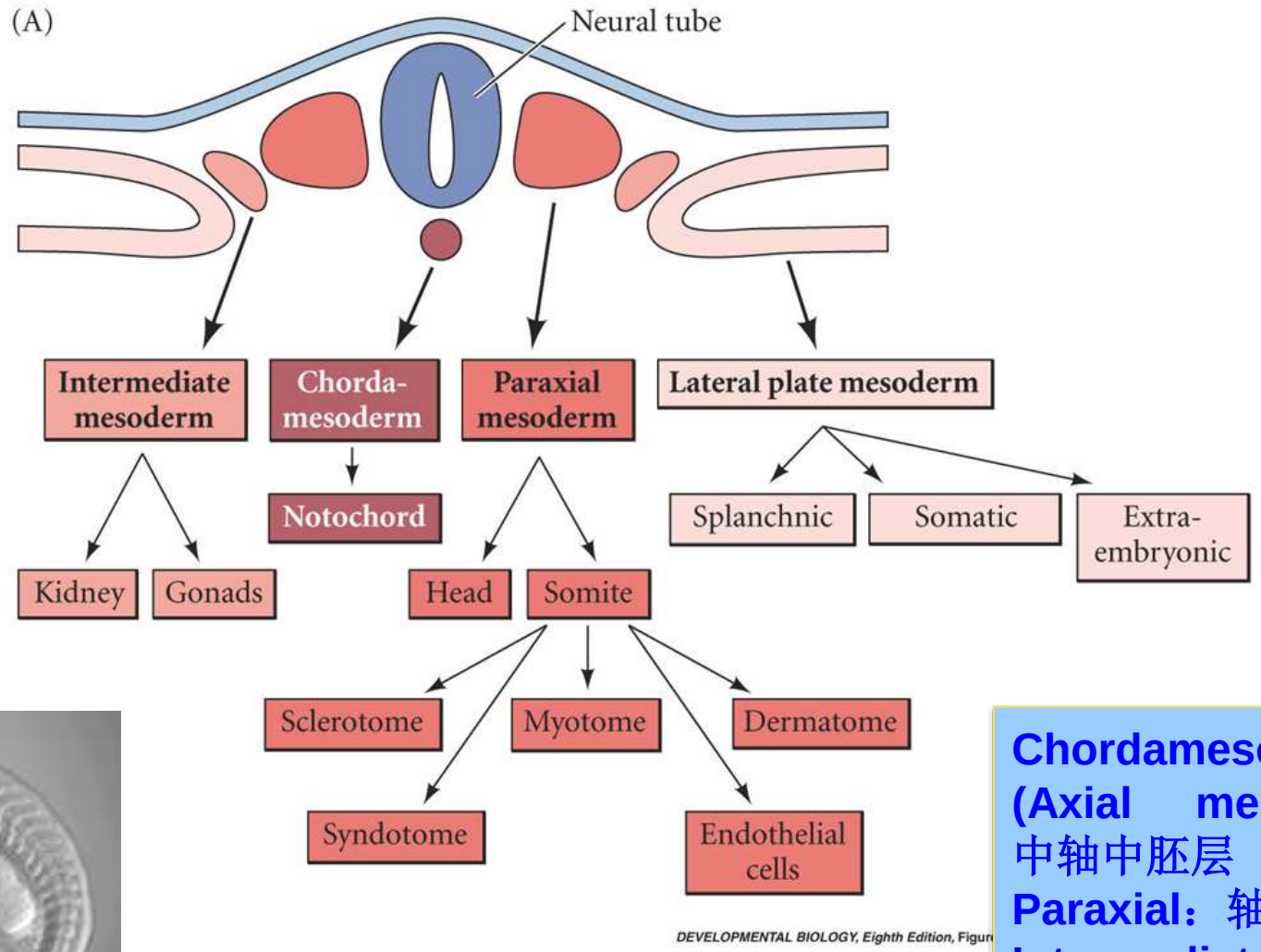
- Mesoderm

  1) paraxial mesoderm （轴旁中胚层）: somite
  2) intermediate （中间）mesoderm : urogenital（泌尿生殖） system
  3) lateral plate （侧板）mesoderm: heart, blood vessels, blood cells

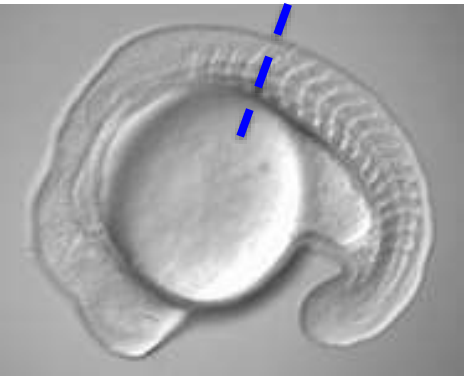
- Endoderm

  gut

Mesoderm derivatives (I)

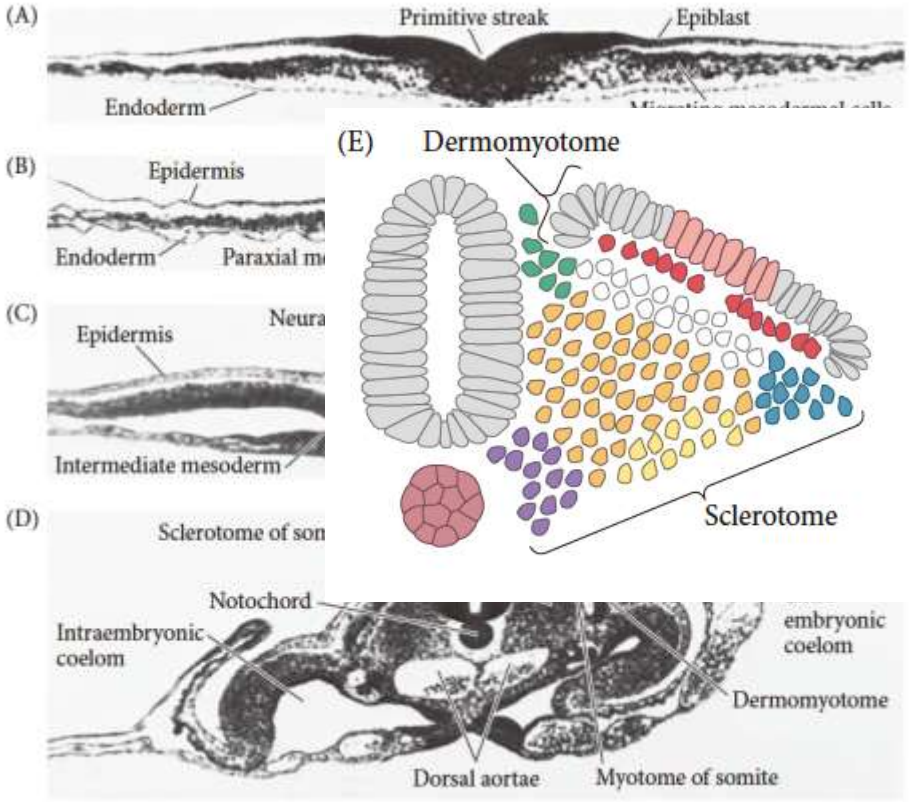


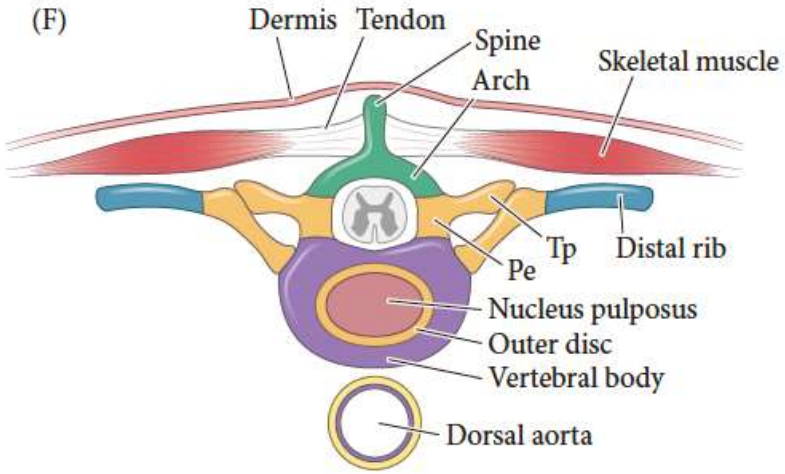
DEVELOPMENTAL BIOLOGY, Eighth Edition, Figur



Chordamesoderm (Axial mesoderm): 中轴中胚层
Paraxial：轴旁
Intermediate: 中间
Lateral plate: 侧板

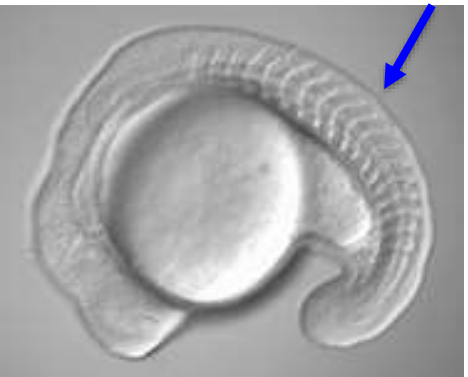
Gastrulation and neurulation in the chick embryo



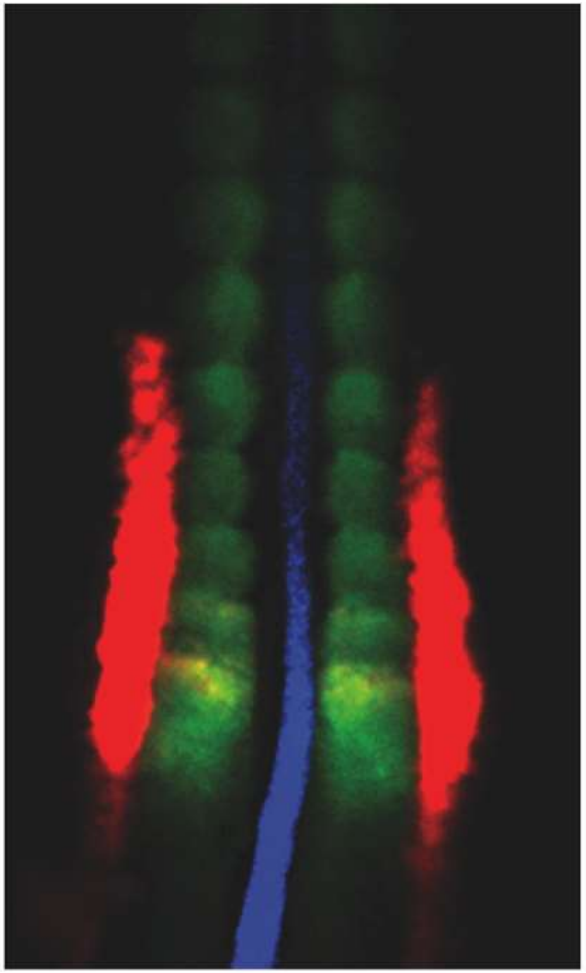


- Arthrotome: vertebral joints (Pe, Tp), proximal rib, outer disc
- Dorsomedial sclerotome: spine, arch
- Ventrolateral sclerotome: distal rib
- Ventromedial sclerotome: vertebral body
- Notochord: inner disc/nucleus pulposus
- Ventral posterior sclerotome: endothe precursor: outer dorsal aorta
- Syndetome: tendons
- Myotome
- Dermatome: dermis

Mesoderm derivatives in chick embryo (II)



(B)

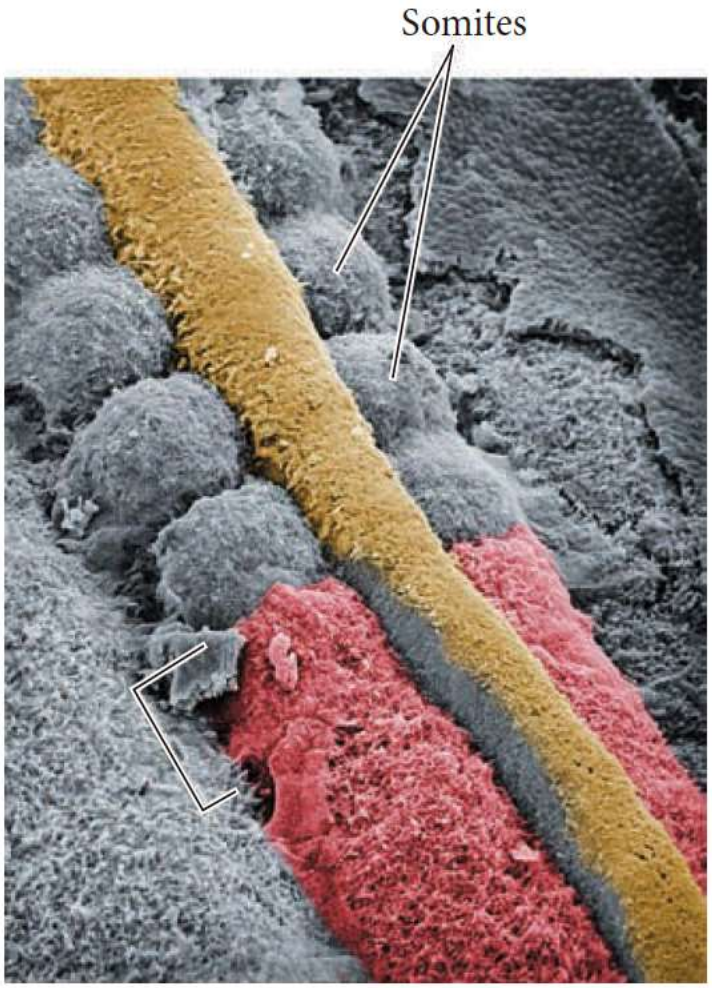


***chordin*: notochord（脊索）**

***paraxis*: somite（体节，轴旁中胚层）**

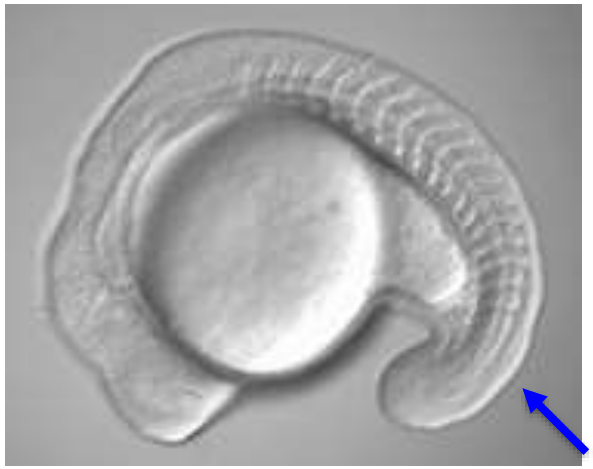
***pax2*: intermediate mesoderm（中间中胚层）**

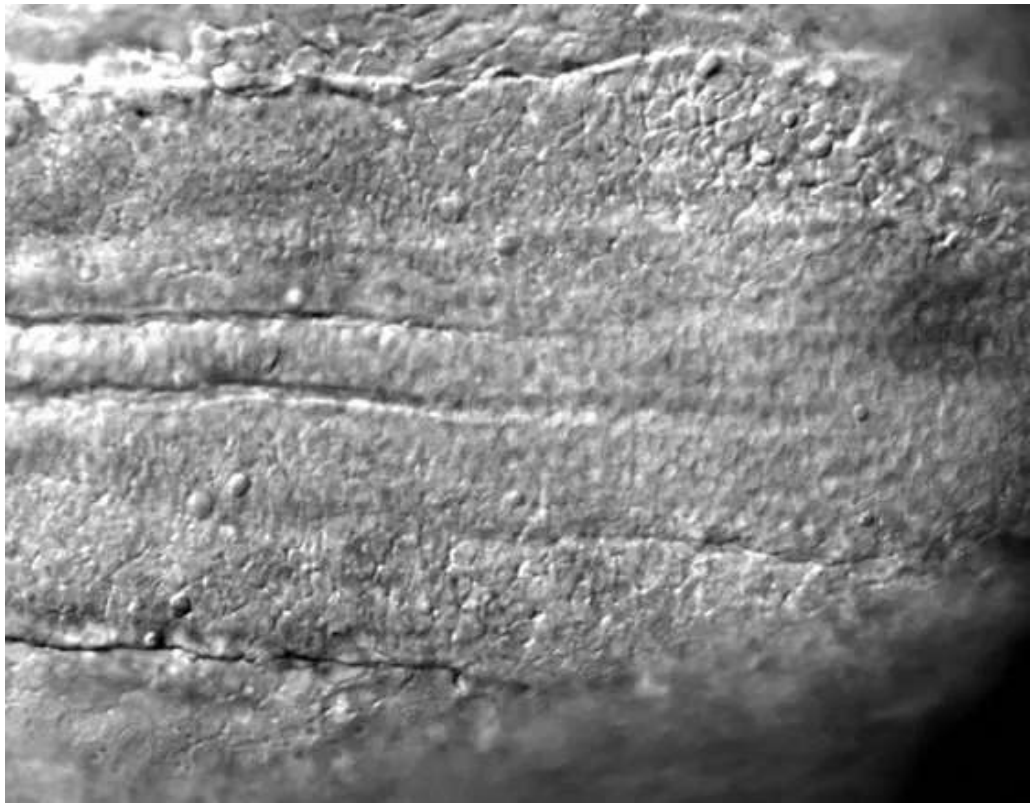
Somite in chick embryo



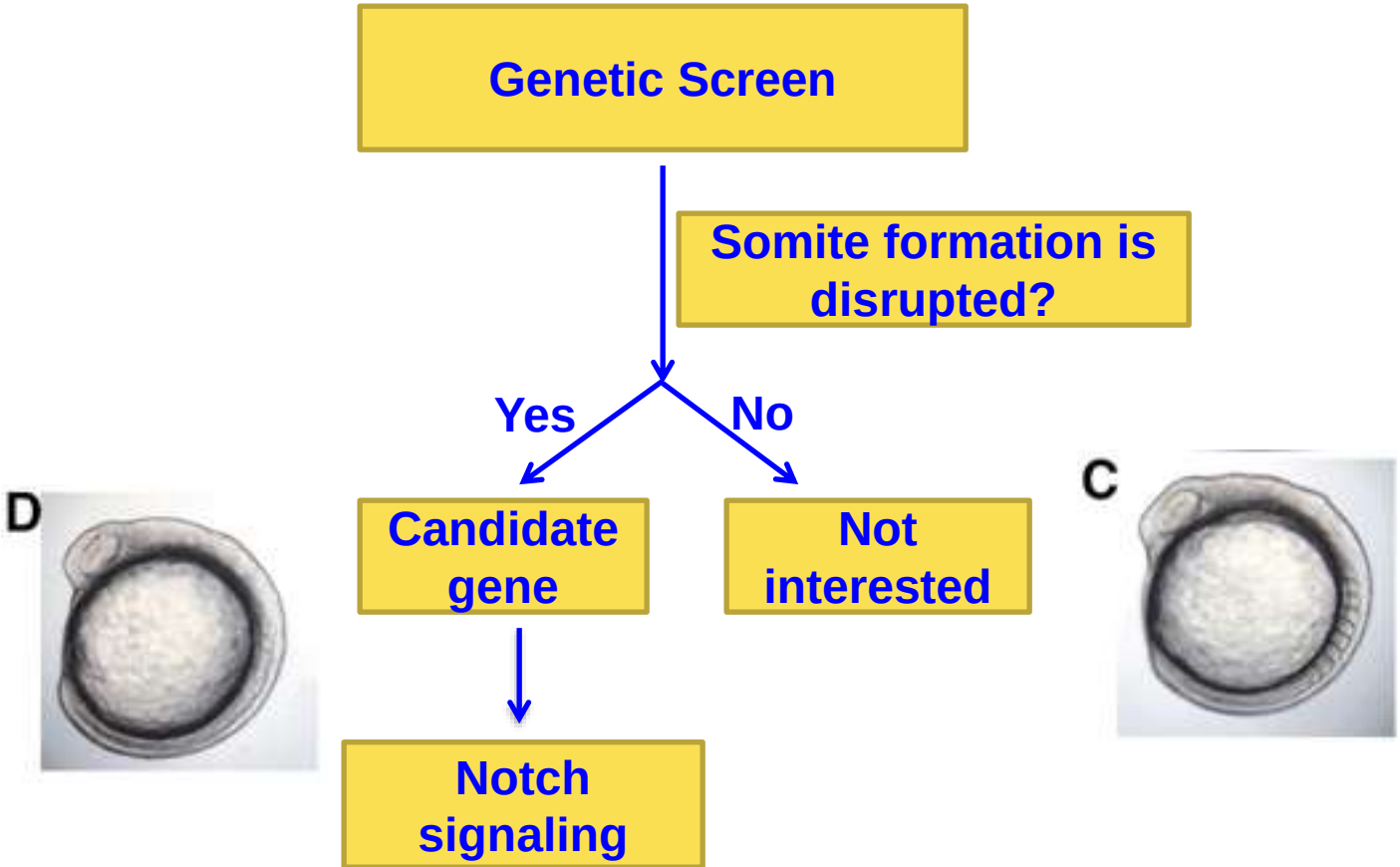
Somite
Presomitic Mesoderm (PSM)
Neural Crest cells

Somitogenesis (体节发生) in zebrafish embryo

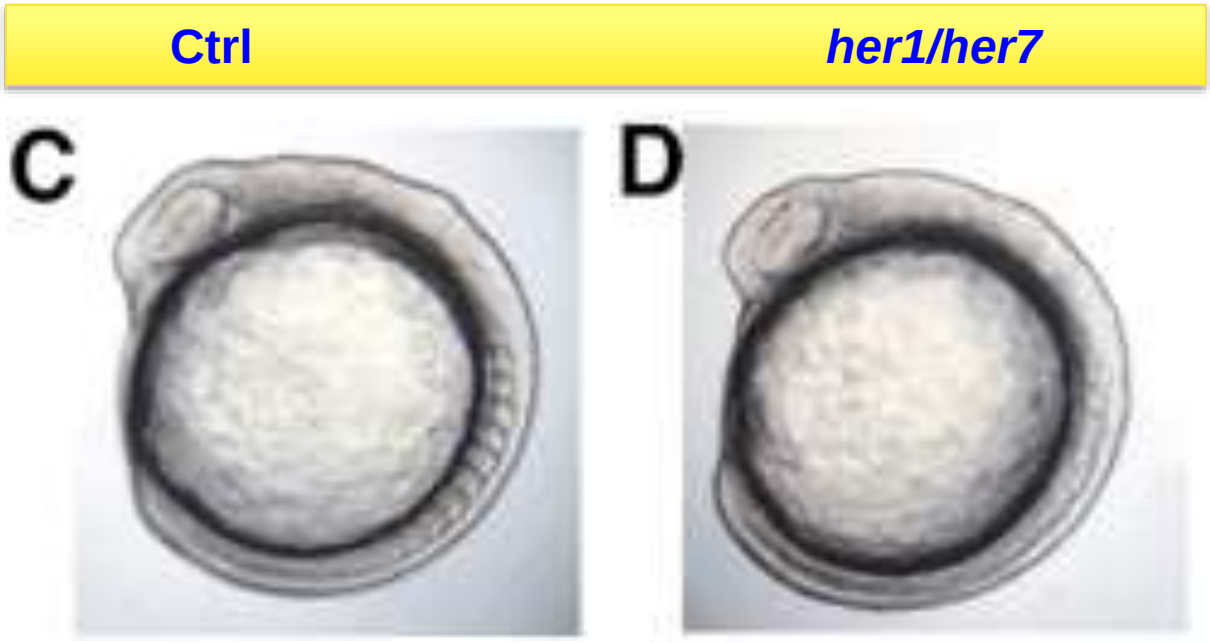




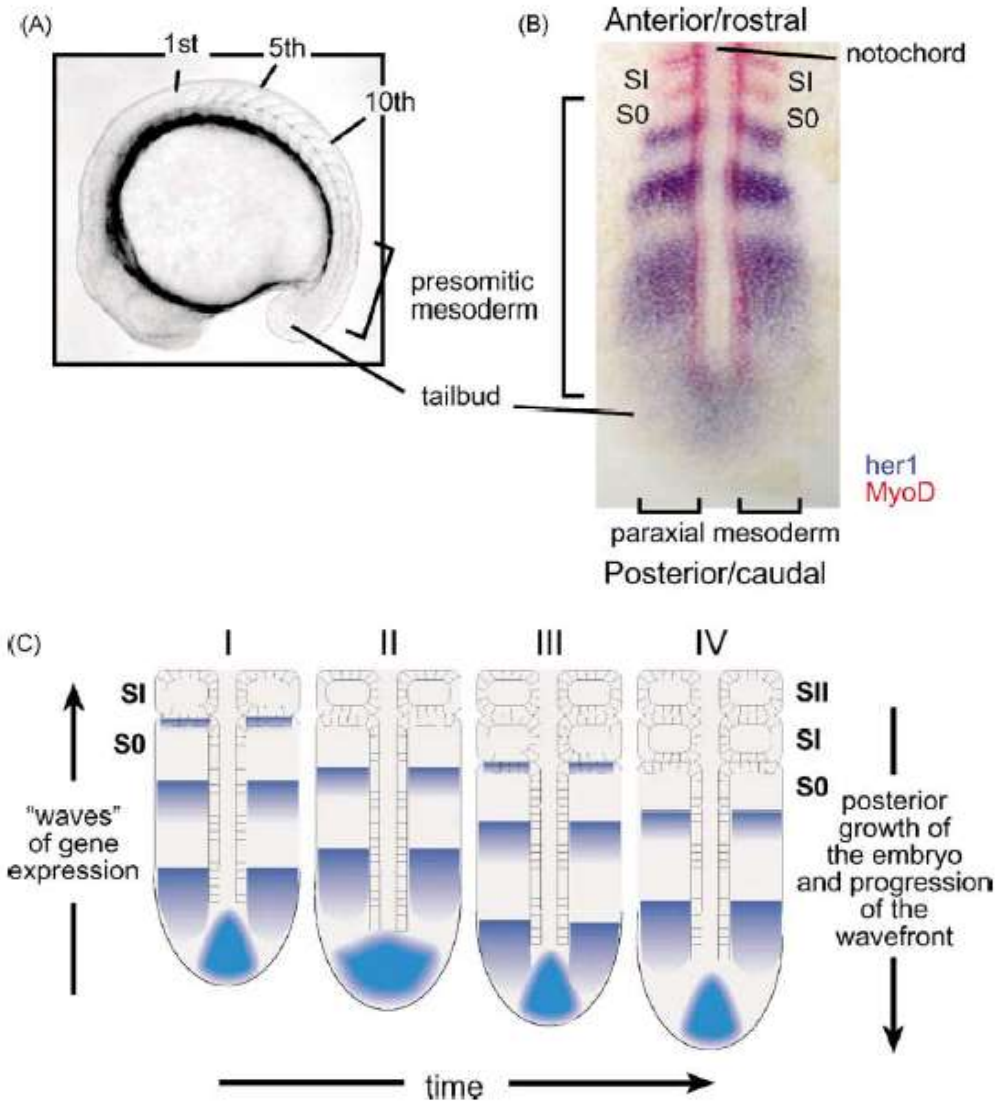
- What's the mechanism of somitogenesis?



Somitogenesis is disrupted in *her1/her7* double mutant



"Oscillation"（震荡）pattern of Somitogenesis in zebrafish embryo



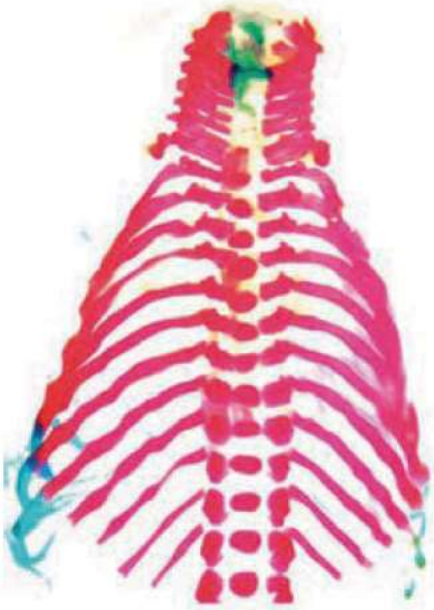
Presomitic mesoderm/ plate:
前体节中胚层/板

Holley et al, 2002

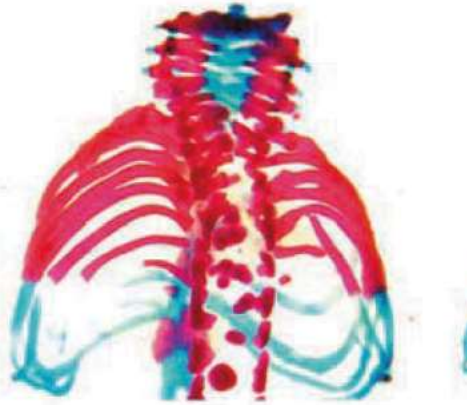
Delta-Notch signaling is essential for proper somitogenesis in the mouse and in humans

(A) Mouse

Wild-type



Lfng$^{-/-}$

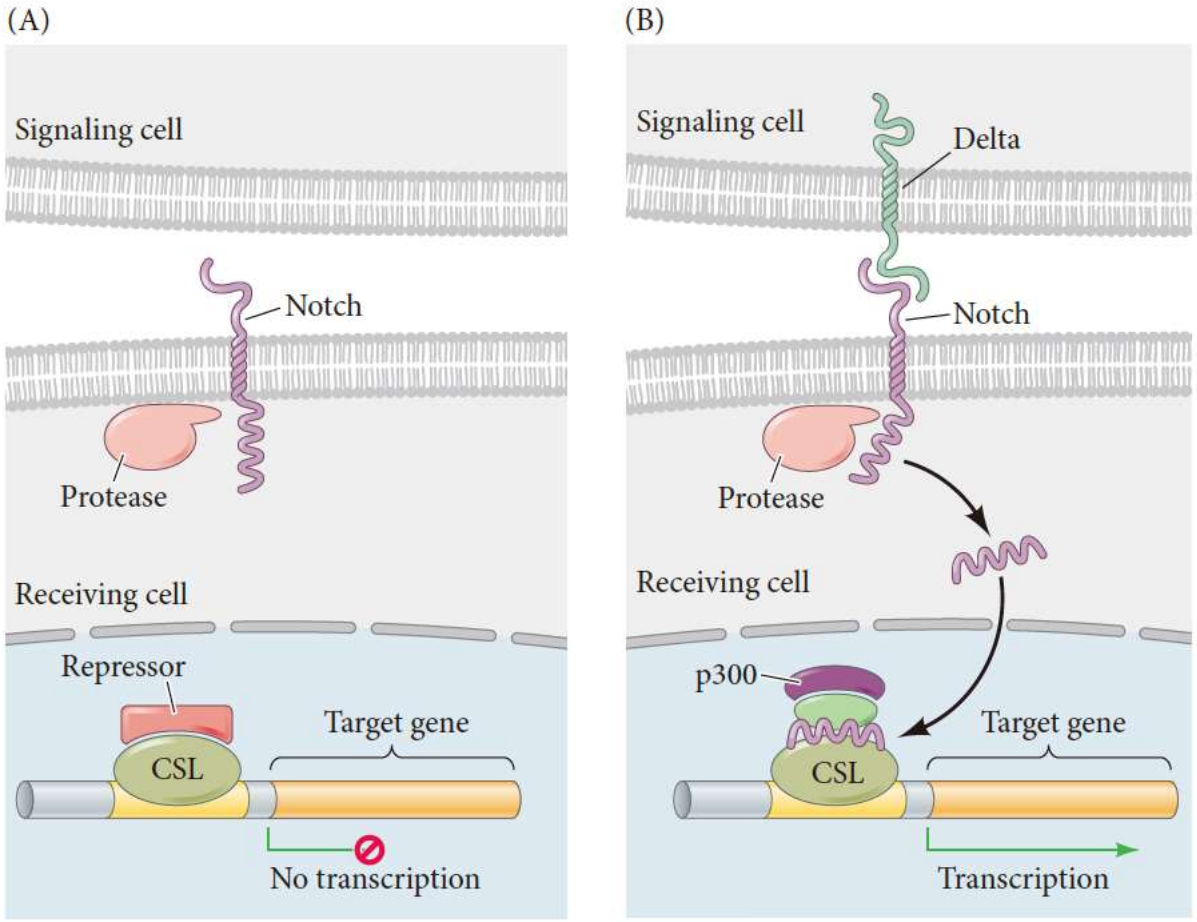


(B) Human

Lfng 564 C-to-A missense mutation (inactive enzyme)

Lfng: Lunatic fringe, the Notch target
Dll3: Distaless3, the Notch binding partner

Notch Signaling



Notch signaling in wikipedia

ia.org/wiki/Notch_signaling_pathway

Ensembl | UCSC genome | ZFIN | MGI | Xenbase | GeneCards | GTR | GUDMAP | HHMI | Wikipedia | 同济信息门户 | 同济 | 搜狗地图 | 其他书签

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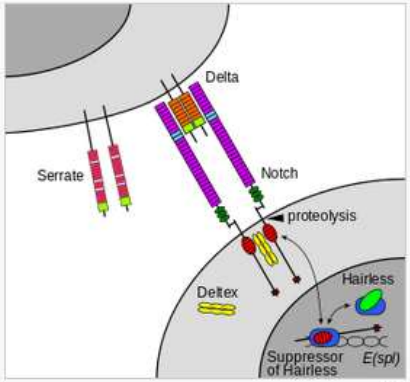
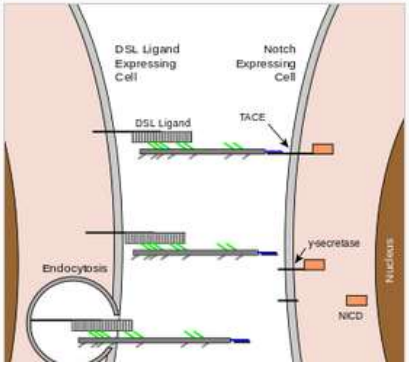


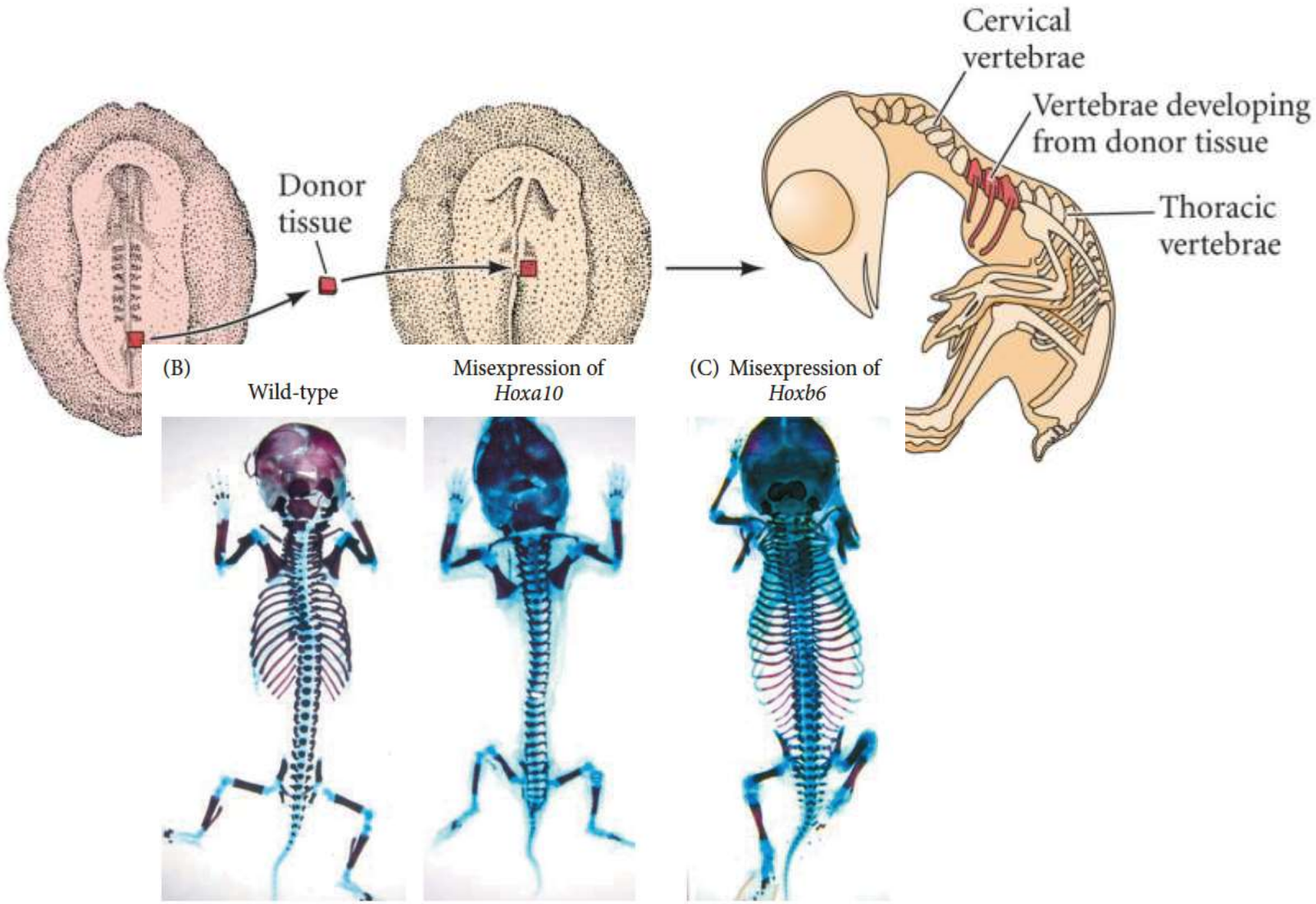
Notch-mediated juxtacrine signal between adjacent cells.



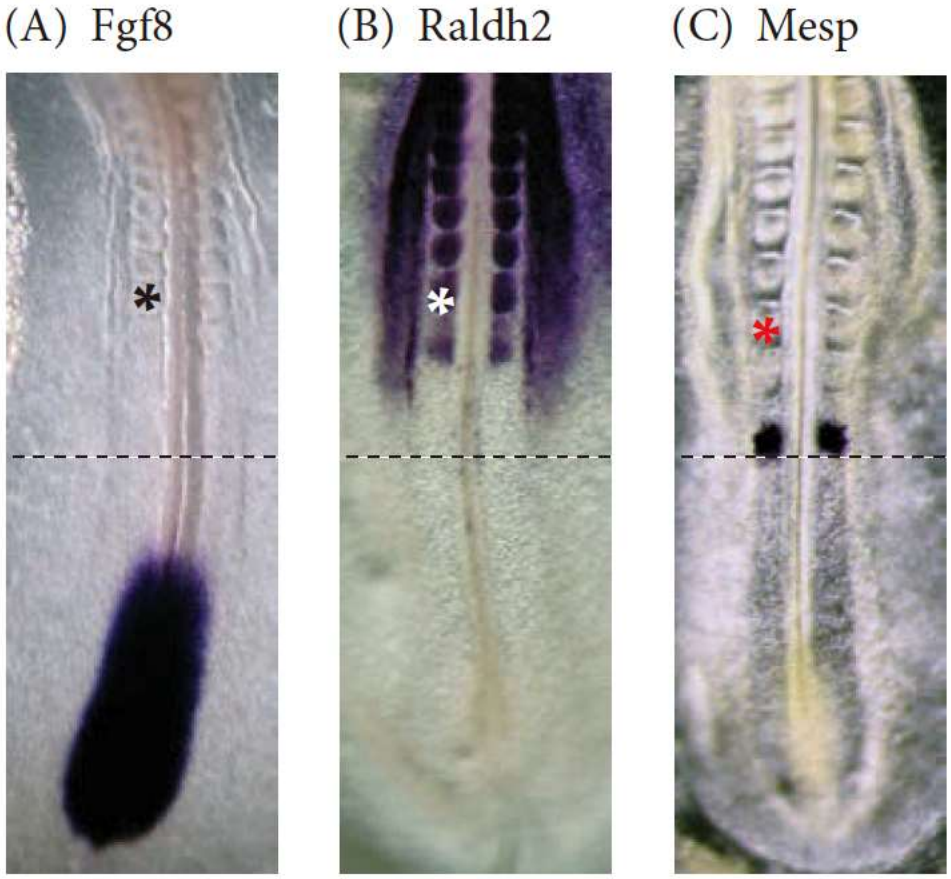
Patterning of somite

- Anterioposteria (AP, 前后) patterning
- Dorsoventral (DV, 背腹) patterning

AP patterning of the somites

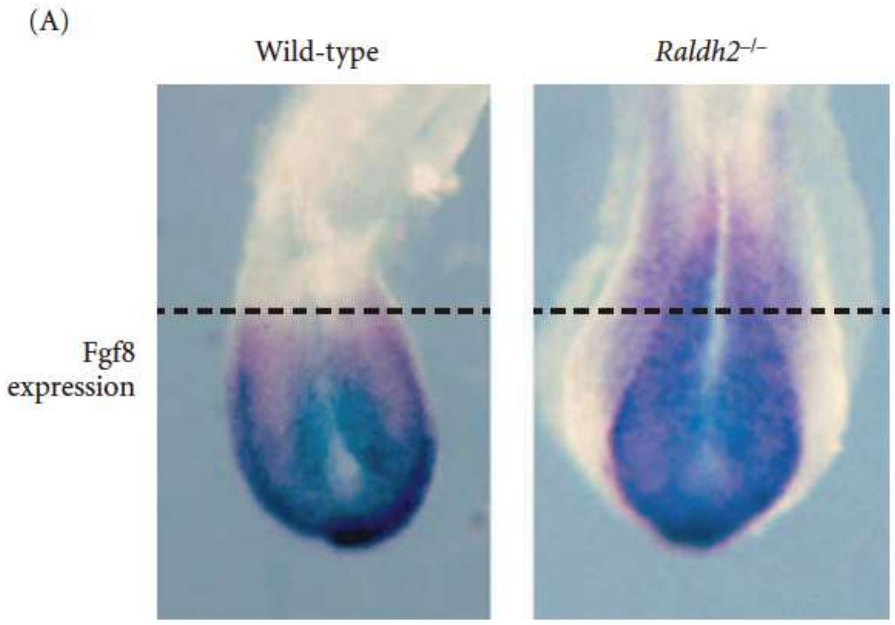


Somites form at the junction of retinoic acid and FGF domains.

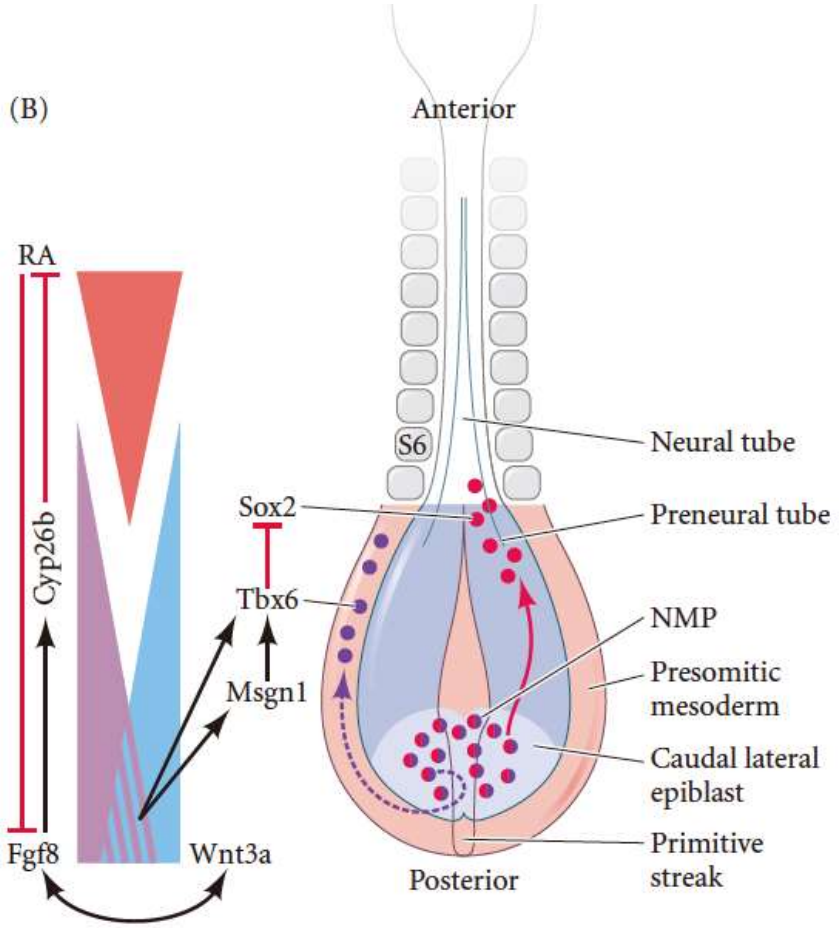


Raldh2
(retinoic acid-synthesizing enzyme)

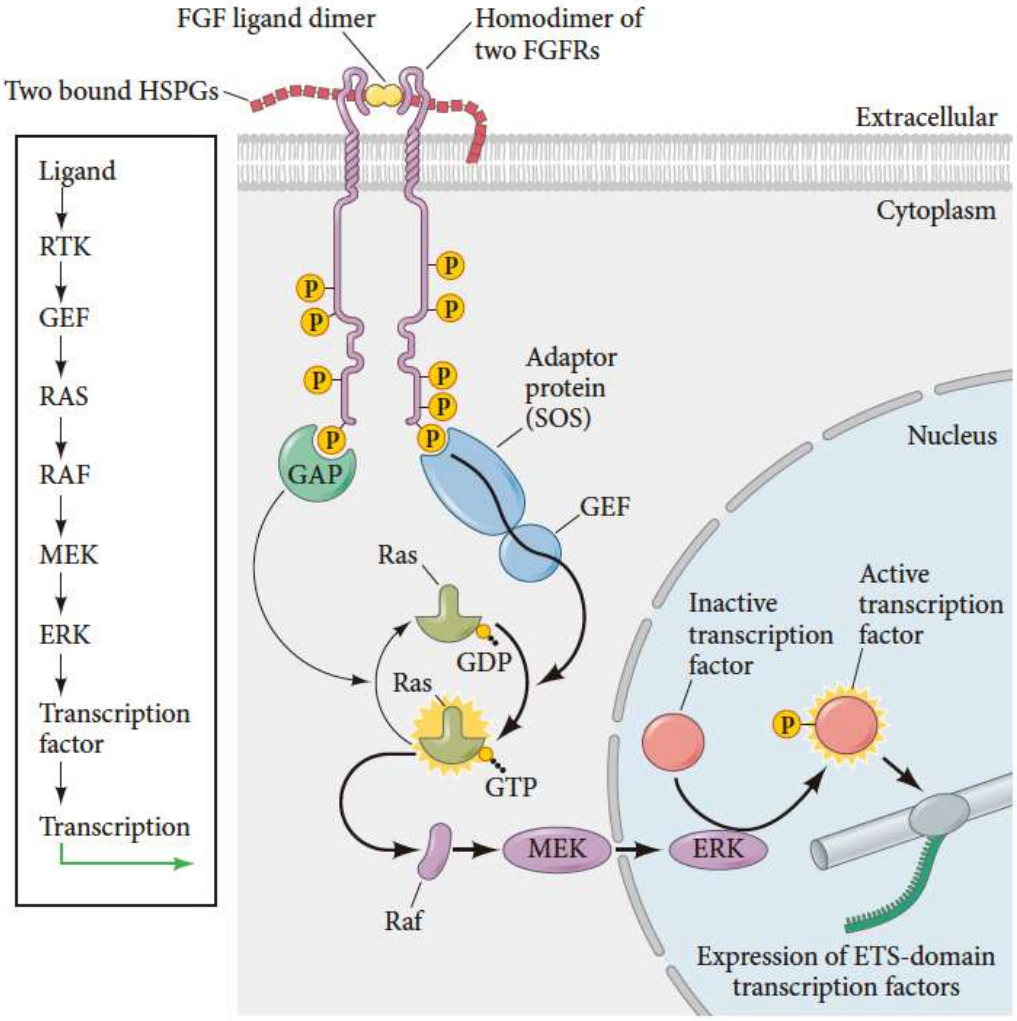
RA and Wnt/Fgf signaling in AP patterning of the somites.



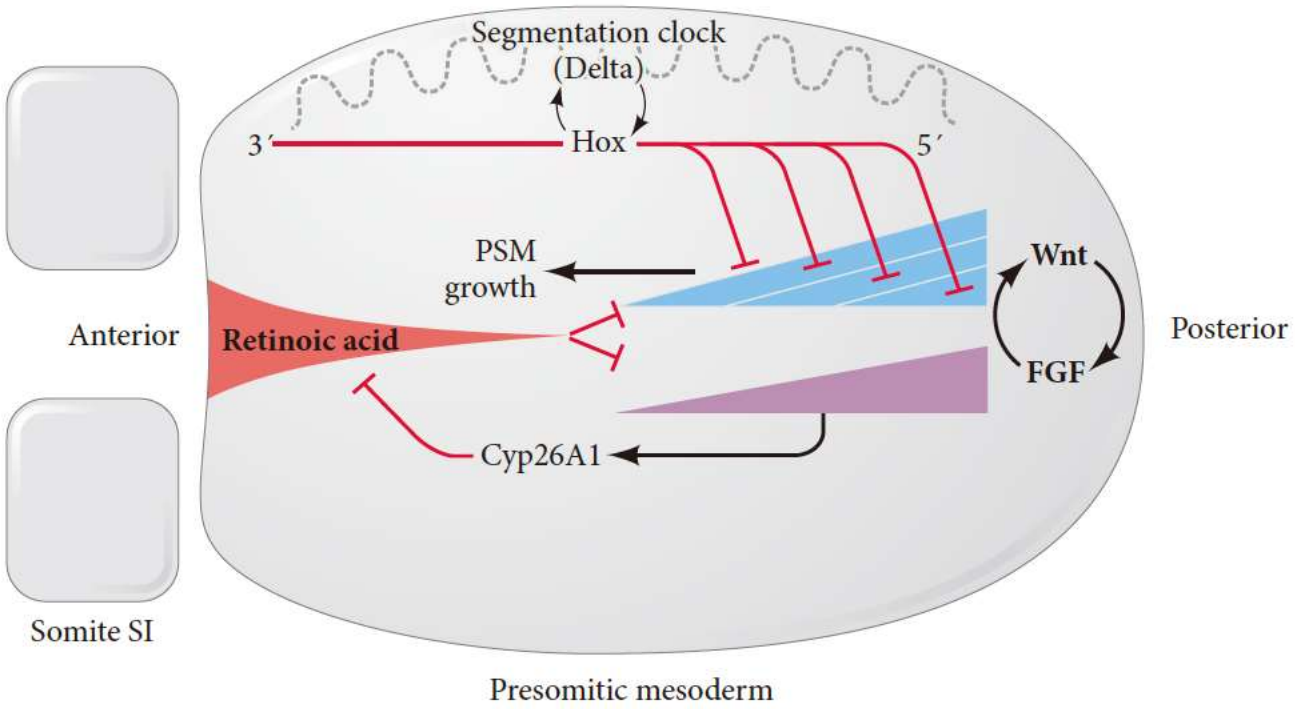
Raldh2 **(Retinoic Acid-synthesizing enzyme)**



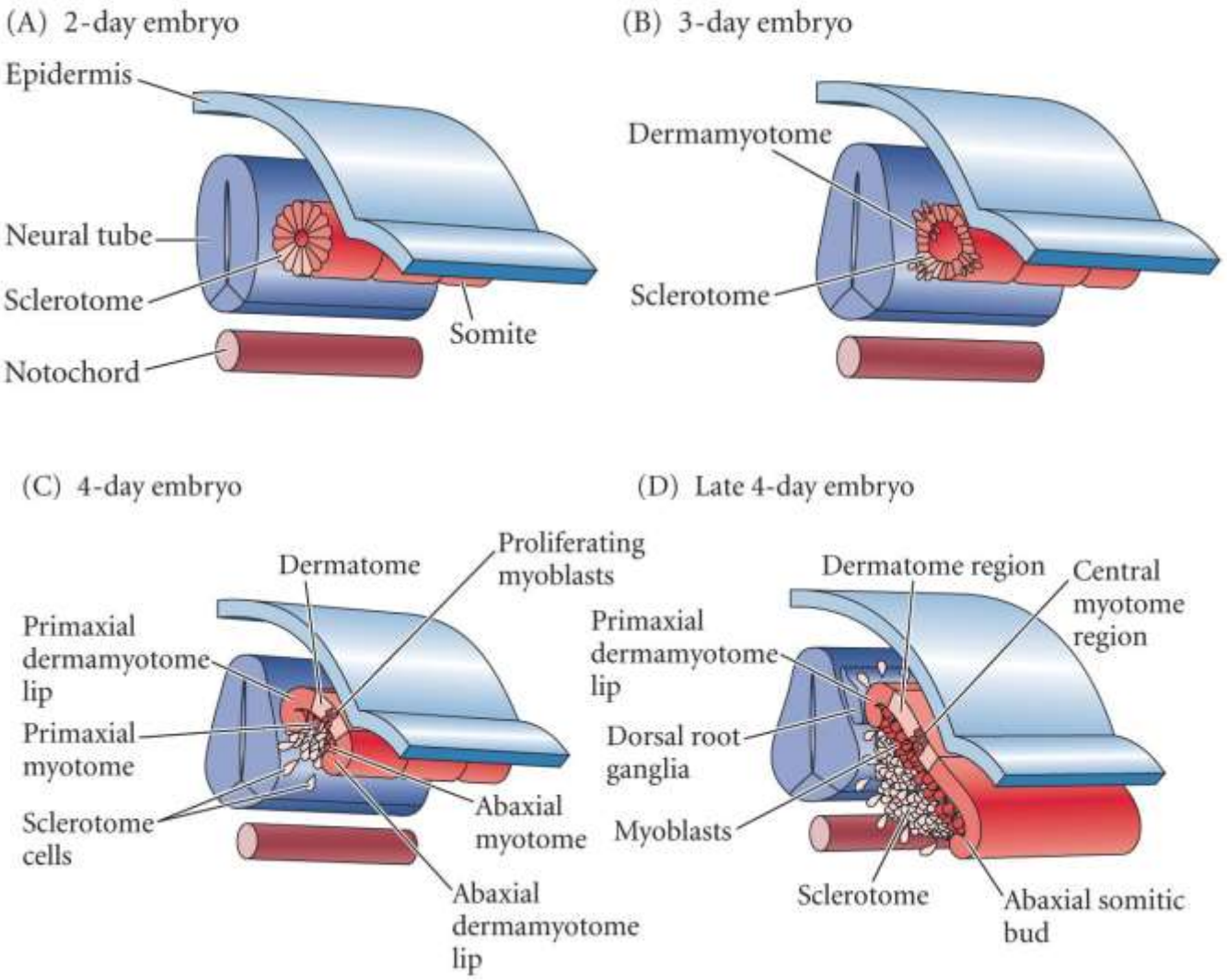
FGF and RTK signaling



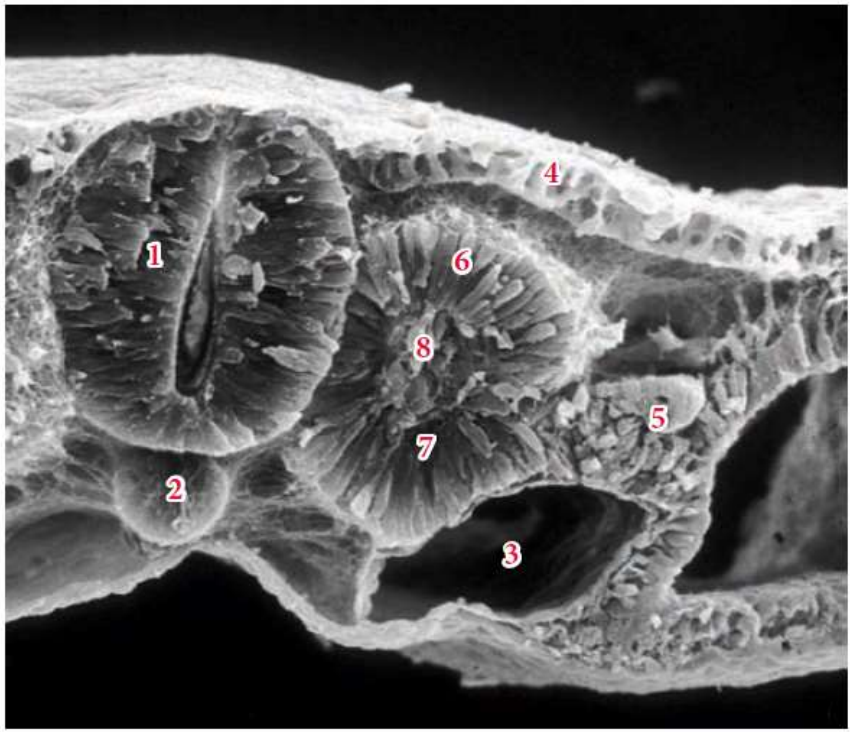
Model of the regulatory mechanisms governing somitogenesis

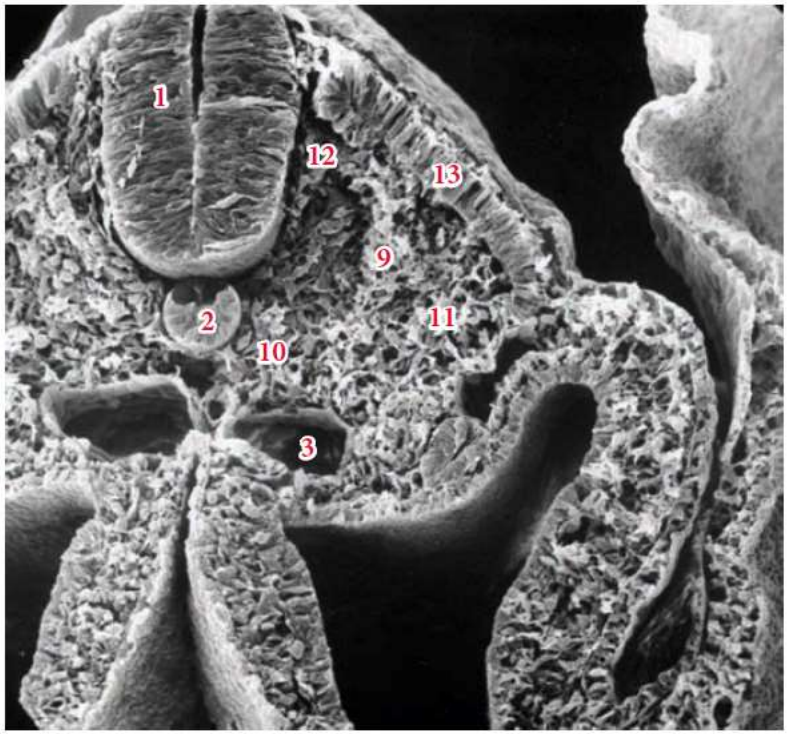


DV patterning of somite



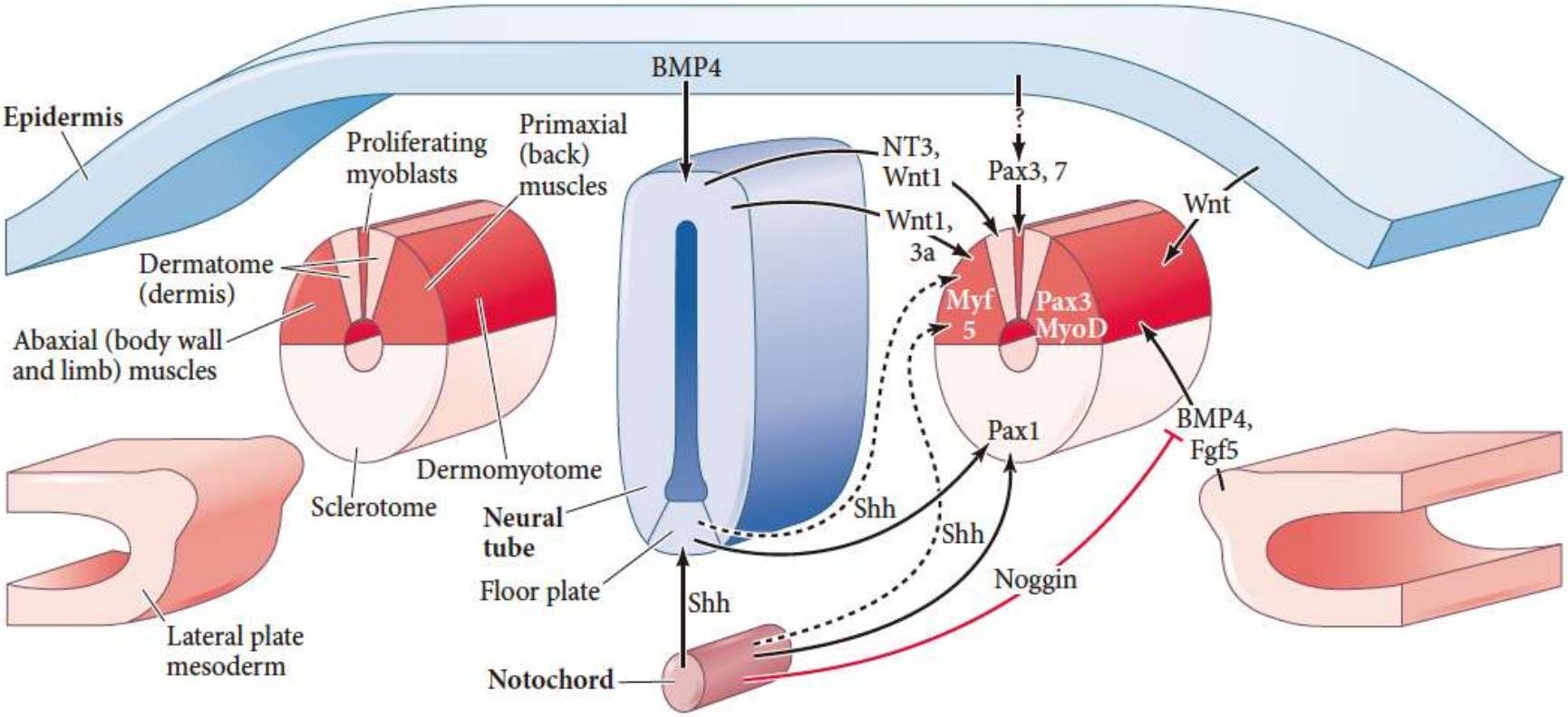
Transverse section through the trunk of a chick embryo on days 2–4





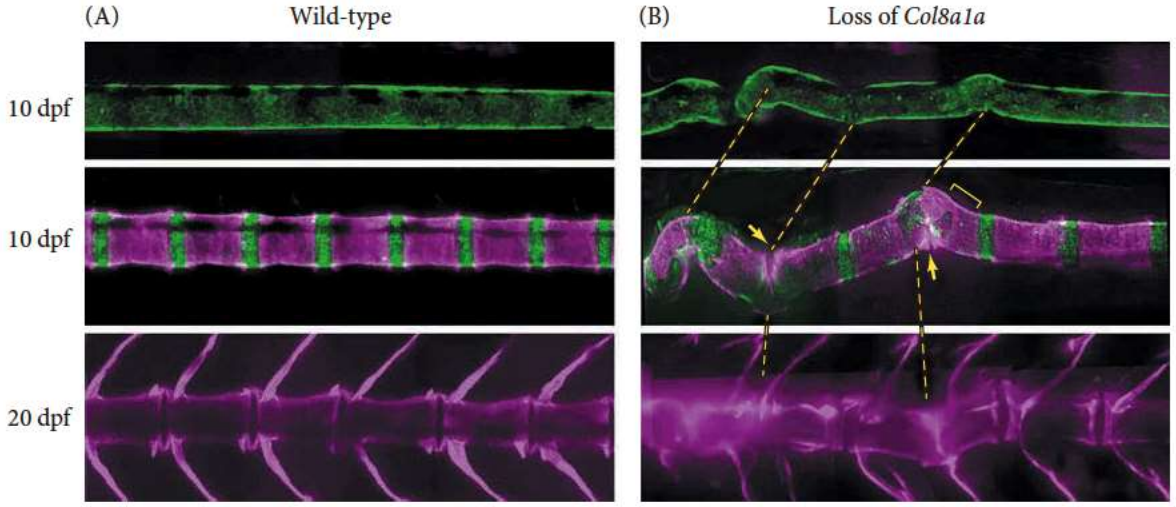
1, neural tube; 2, notochord; 3, dorsal aorta; 4, surface ectoderm; 5, intermediate mesoderm; 6, dorsal half of somite; 7, ventral half of somite; 8, somitocoel/arthrotome; 9, central sclerotome; 10, ventral sclerotome; 11, lateral sclerotome; 12, dorsal sclerotome; 13, dermomyotome

Model of major postulated interactions in the patterning of the somite

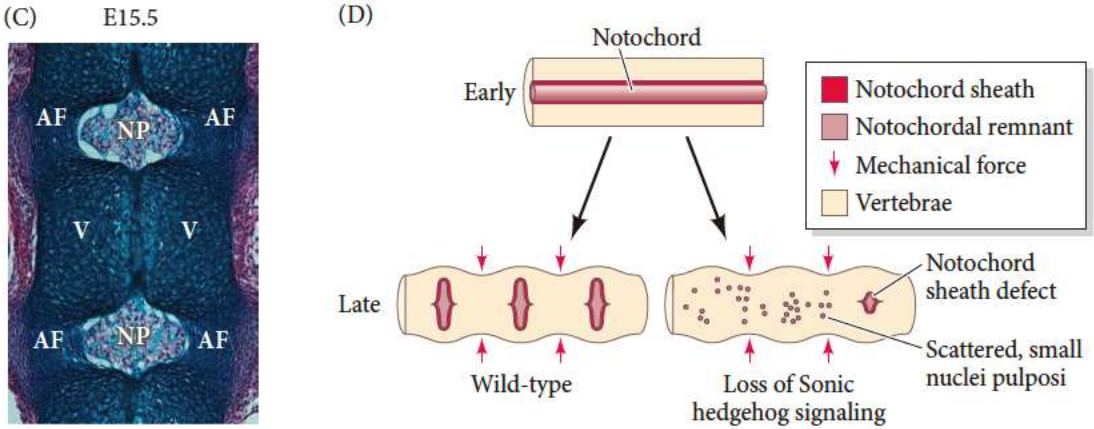


Development of the spinal column and intervertebral discs

Zebrafish embryo



Mouse embryo



Osteogenesis (骨的发生)

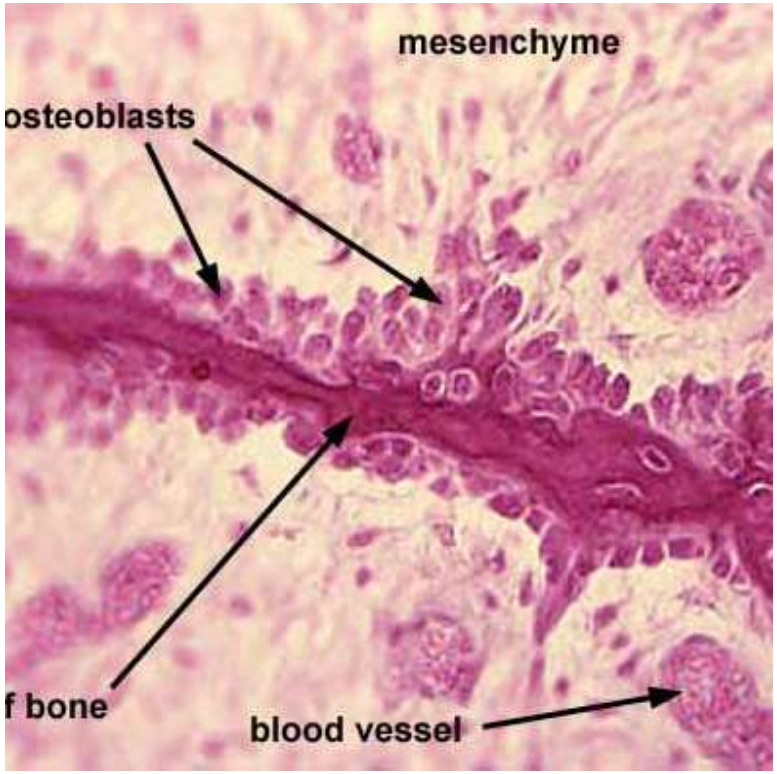
Three cell origins (生骨细胞的来源)：

1. Somite (体节)：→ axial skeleton (背部骨骼, 肋骨)
2. Lateral plate (侧板中胚层)：→limb (肢体) skeleton
3. Neural crest cells (神经嵴细胞)：craniofacial bones and cartilage (颅面骨和软骨)

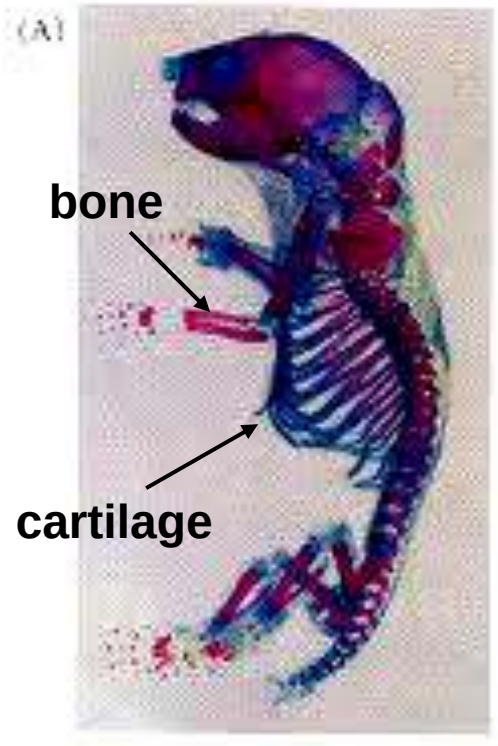
Two major modes of osteogenesis：

1. intramembrane ossification (膜内成骨): mesenchymal cells (间质细胞)→ bone
2. endochondral ossification (软骨内成骨): mesenchymal cells → cartilage (软骨) →bone

Intramembranous (膜内) vs Chondrondral (软骨) Ossification



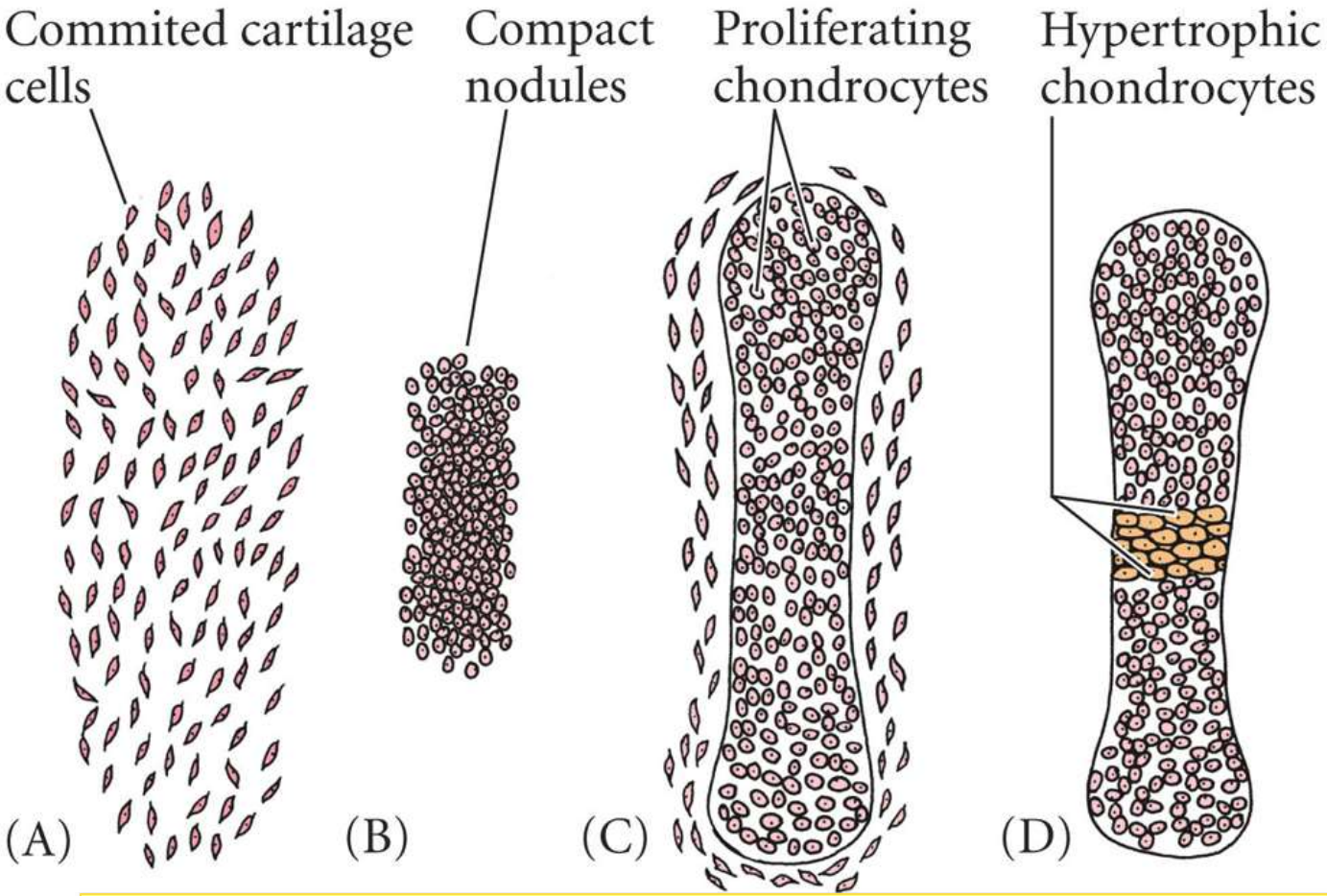
WT



Cbfa1$^{-/-}$

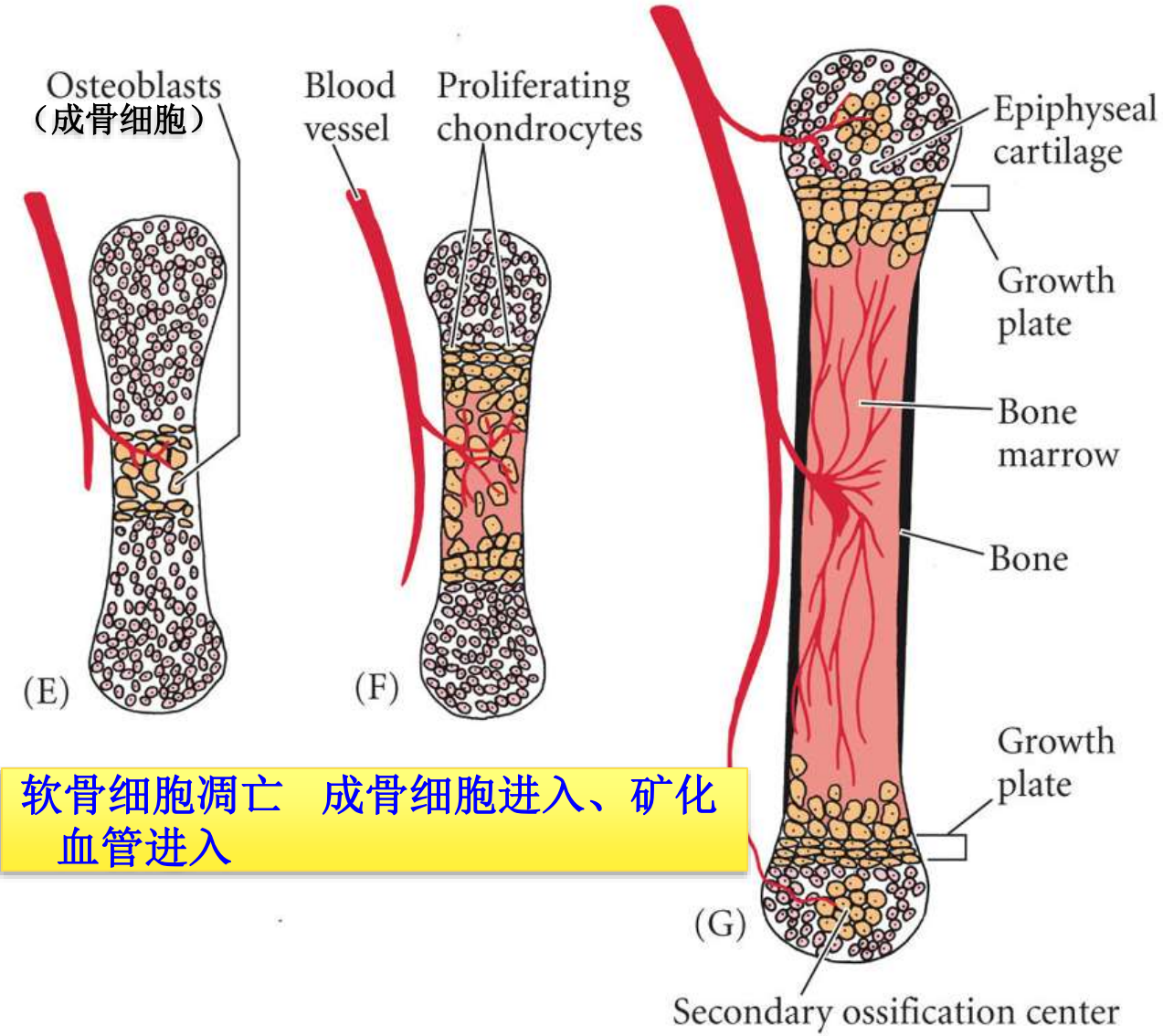
***Cbfa1*: is required for process of cartilage (软骨) → bone**

Endochondral Ossification (I)



软骨细胞　　致密结　　软骨细胞增殖　　软骨细胞肥大

Endochondral Ossification (II)



软骨细胞凋亡　成骨细胞进入、矿化
血管进入

BMP promote bone formation

Figure 2. Skeleton of a 40-year-old man who died from pneumonia secondary to fibrodysplasia ossificans progressiva. Plates and ribbonsof ectopic bone can be seen throughout the body. It has been found that overexpression of BMP4 in lymphocytes may be responsible for such diseases.

Bone Morphogenetic Protein (BMP)

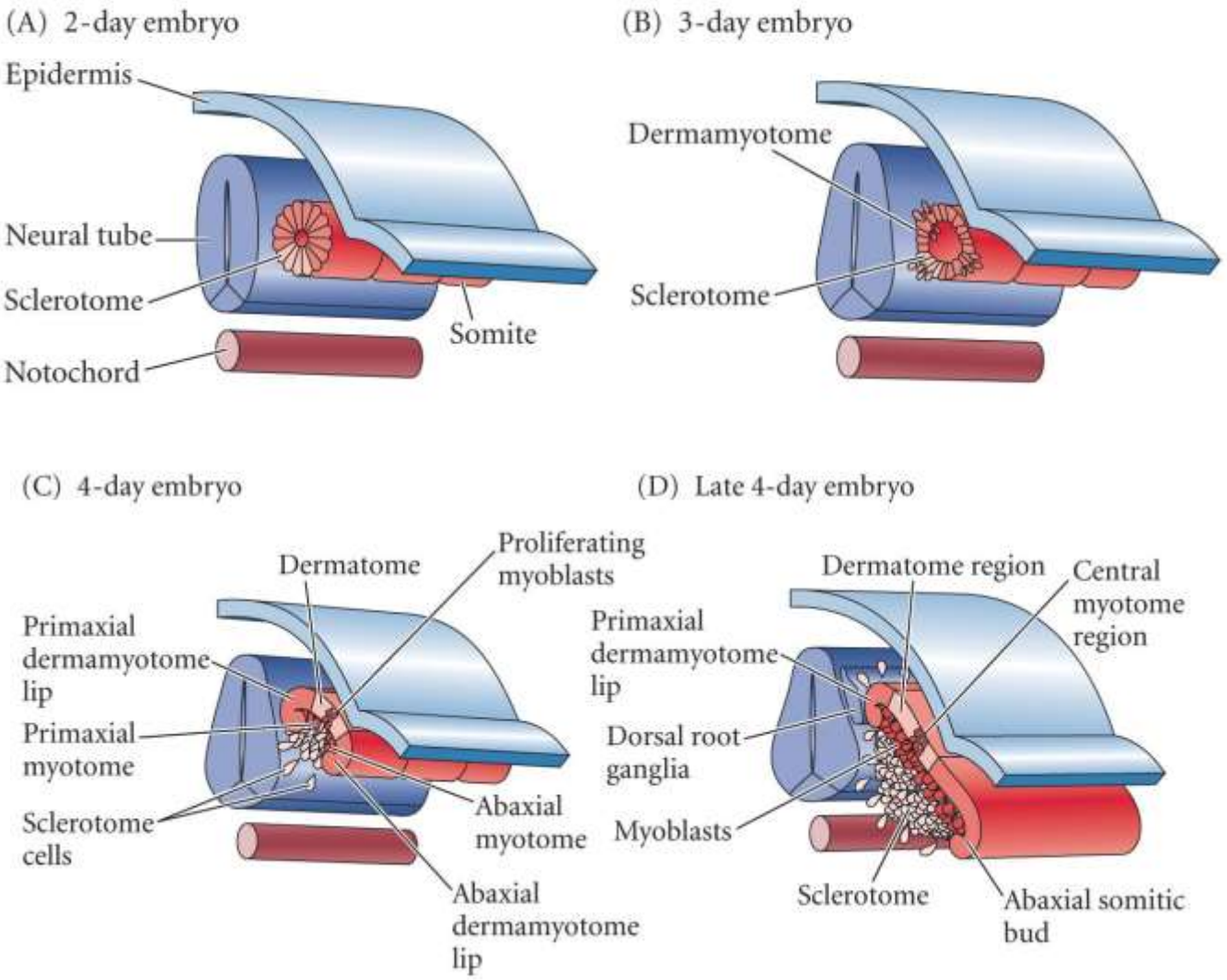
- From the time of Hippocrates (
，古希腊的名医) it has been kn
bone has considerable potentia
regeneration and repair.

- Senn, a surgeon at Rush Medi
in Chicago, described the utility of bone implants in the treatment of osteomyelitis (骨髓炎骨) and certain bone deformities.

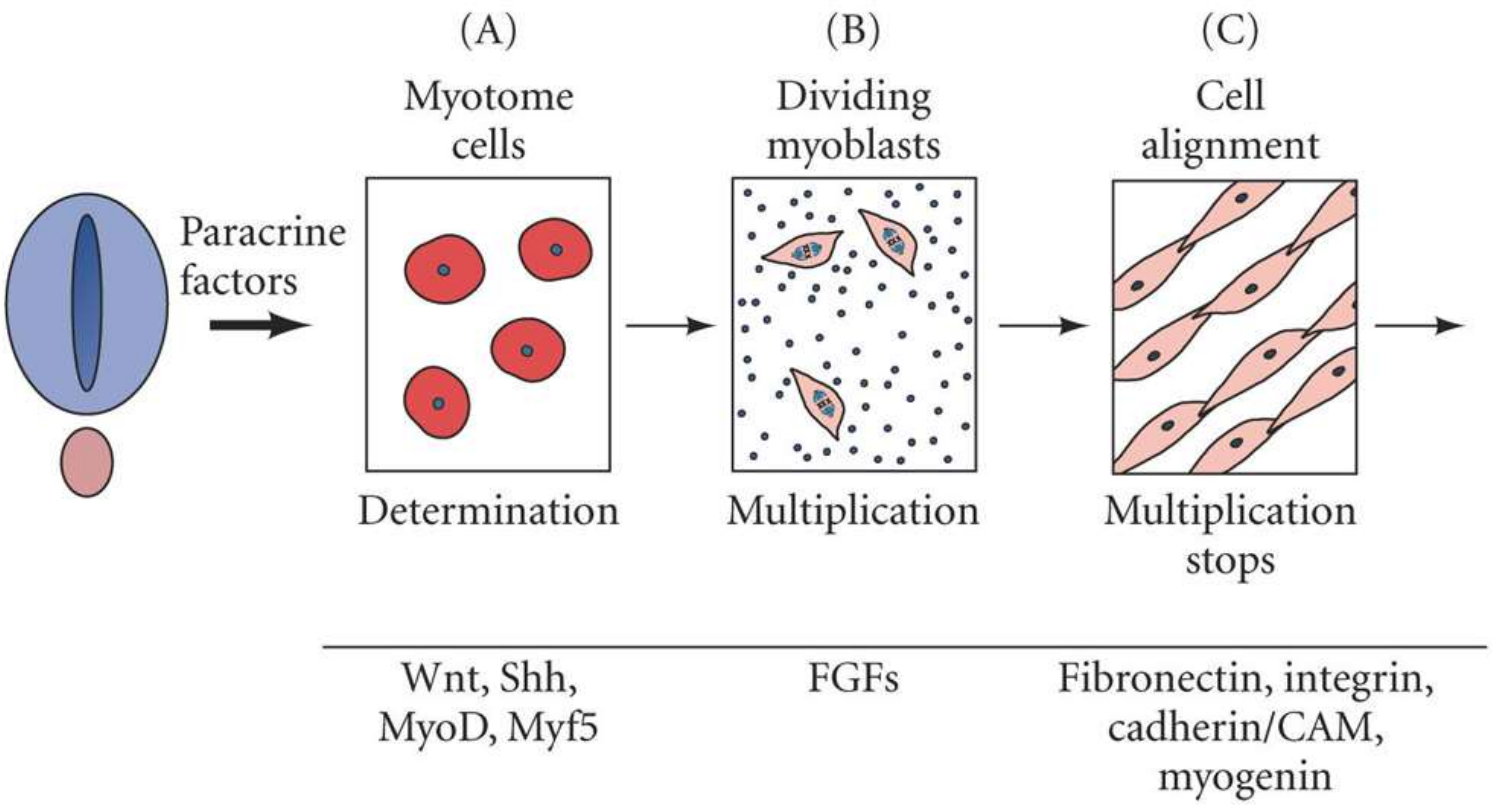
Bone Morphogenetic Protein (BMP)

- Marshall Urist (1914-2001) made the key discovery that demineralized (去除矿物质) segments of bone induced new bone formation when implanted in muscle pouches in rabbits. Marshall Urist proposed the name “Bone Morphogenetic Protein”.

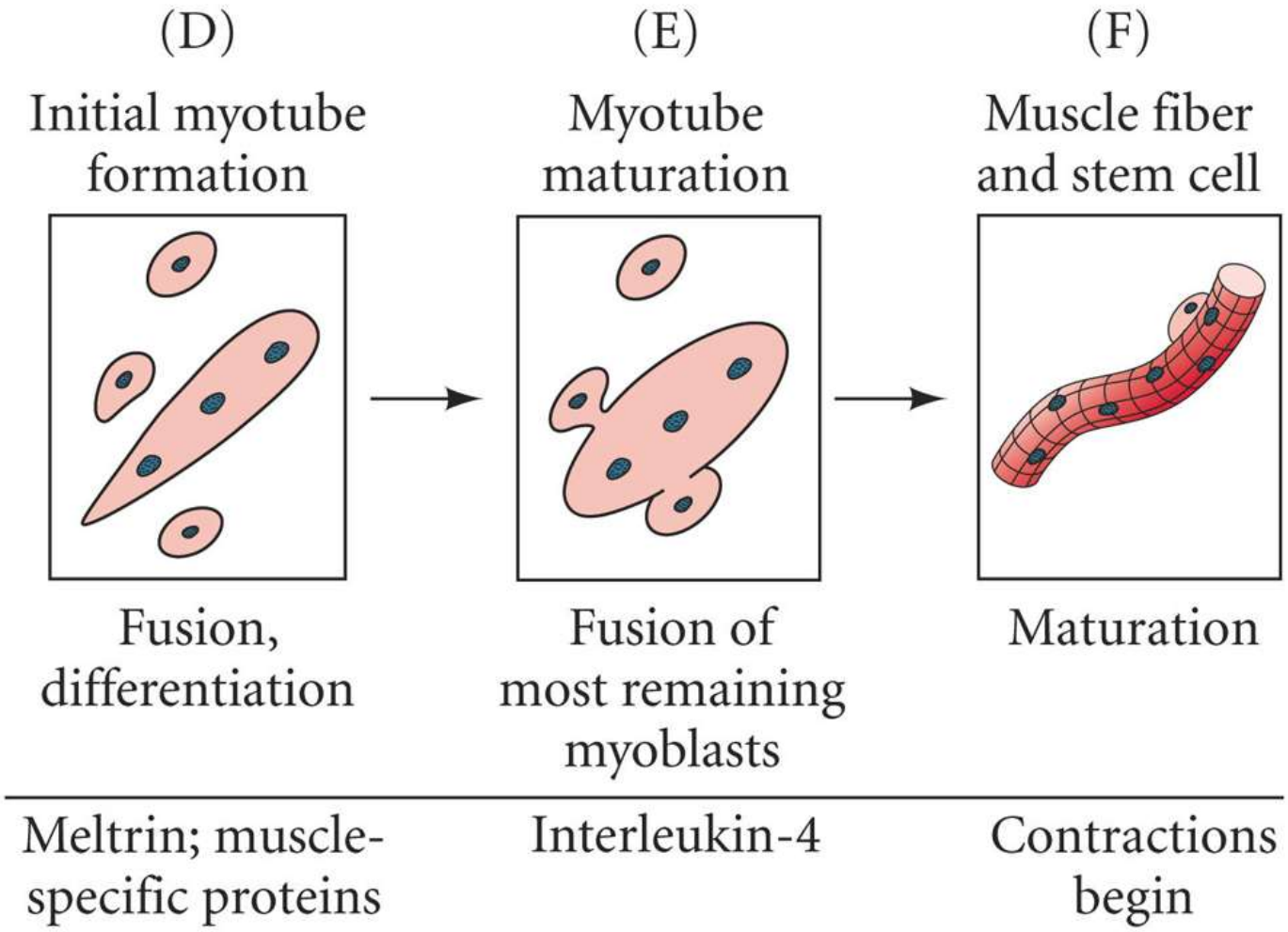
DV patterning of somite



Muscle differenciation (I)



Muscle differenciation (II)



Summary (III)

- Key word:

  paraxial mesoderm, somite, Notch, oscillation pattern

- Event and mechanism

  somitogenesis, osteogenesis，AP patterning of the somite, DV patterning of the somite

outline

- Ectoderm

  1) neural tube formation and differentiation

  2) neural crest cells

  3) eye development

- Mesoderm

  1) paraxial mesoderm: somite

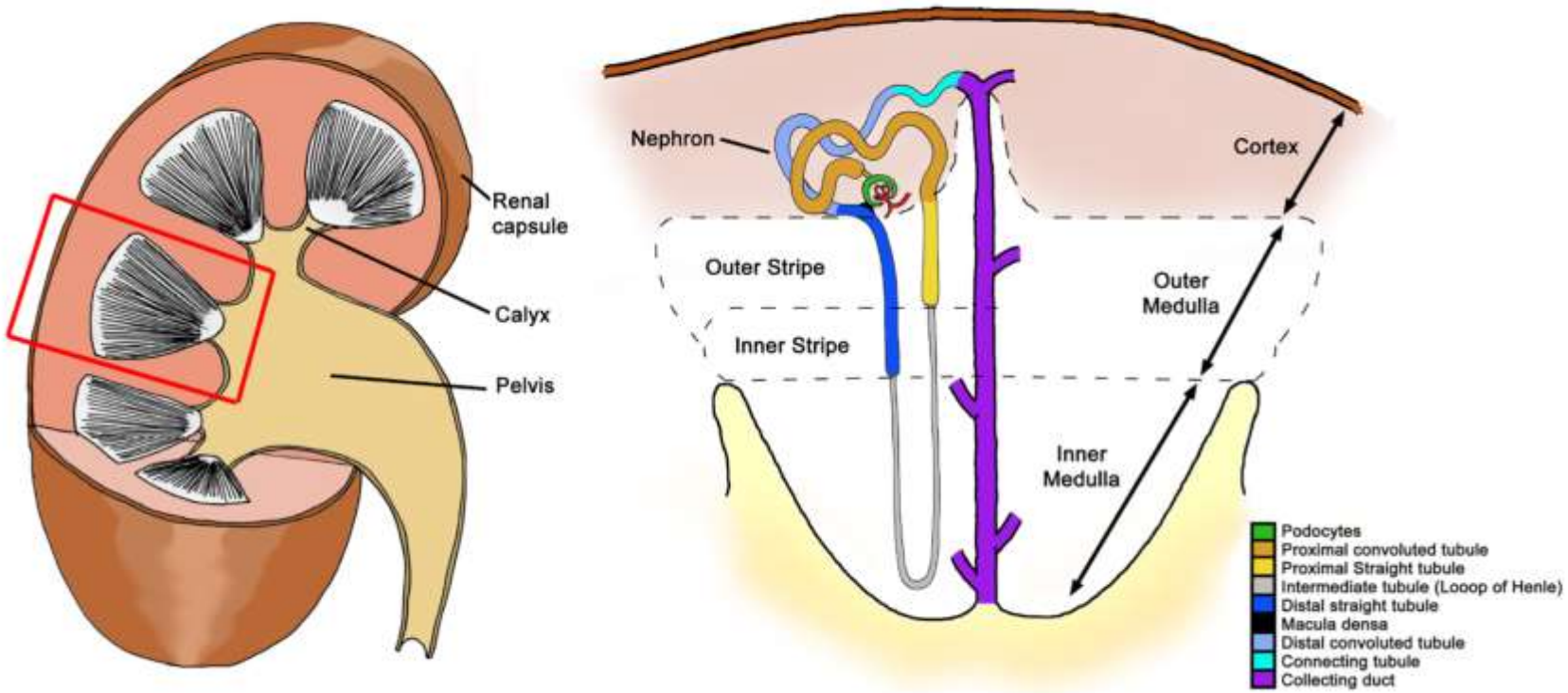
  2) intermediate (中间) mesoderm: urogenital (泌尿生殖) system

  3) lateral plate mesoderm: heart, blood vessels, blood cells

- Endoderm

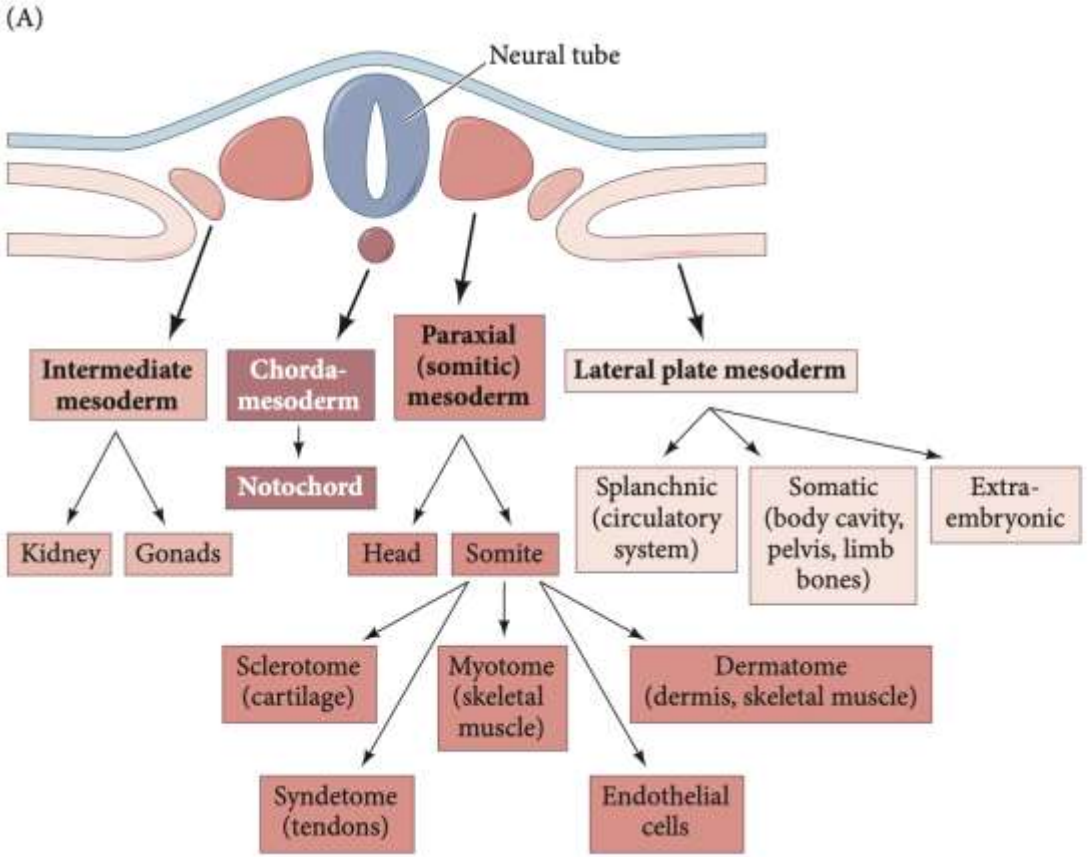
  gut & lung

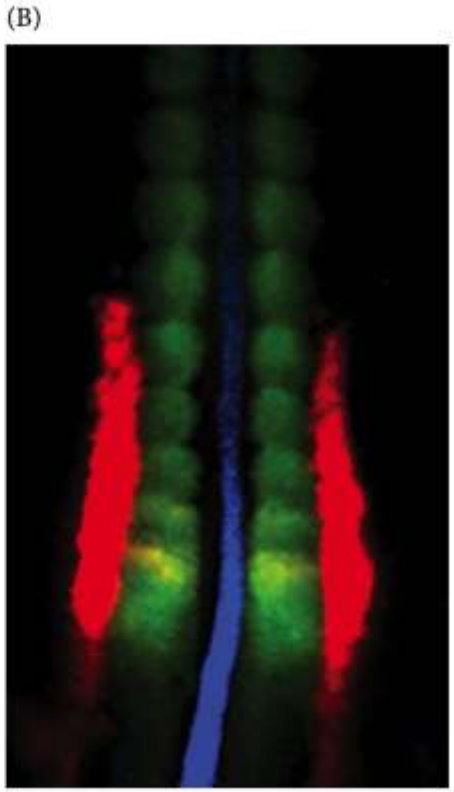
Structure of the mammalian kidney



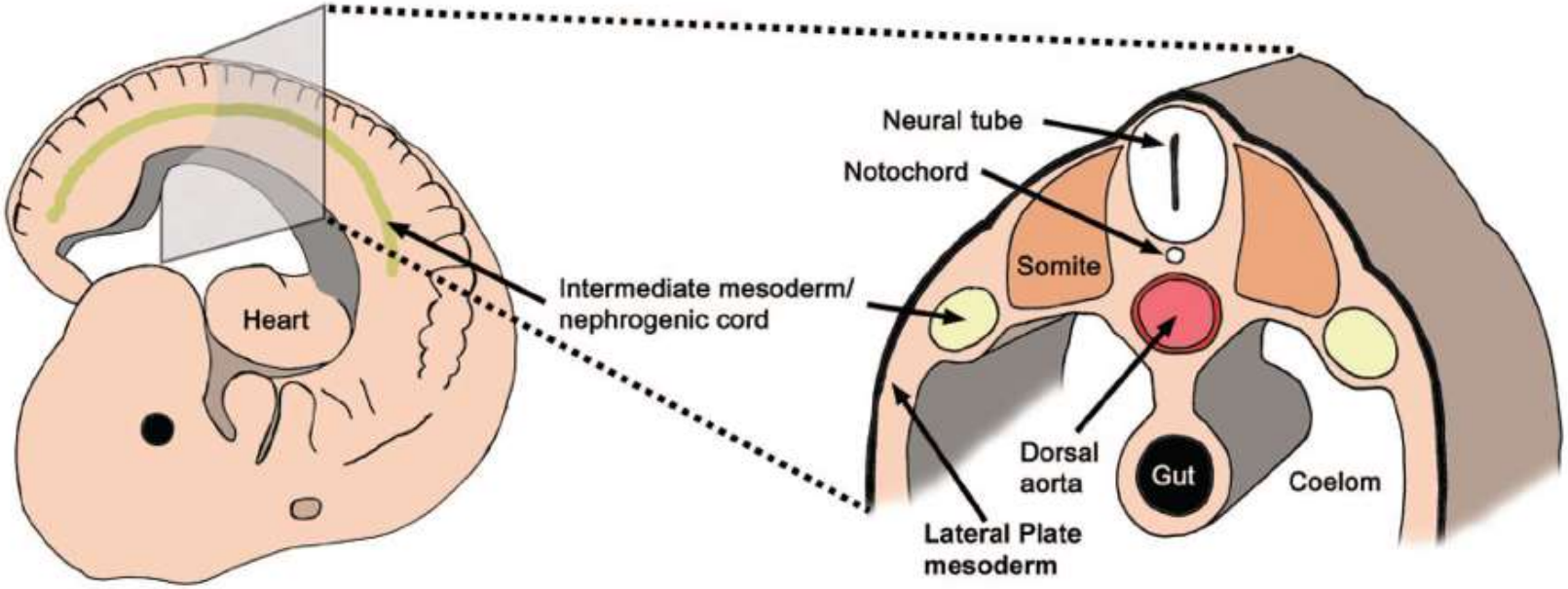
Davidson, 2009, *StemBook*

Intermediate mesoderm differentiates into kidney



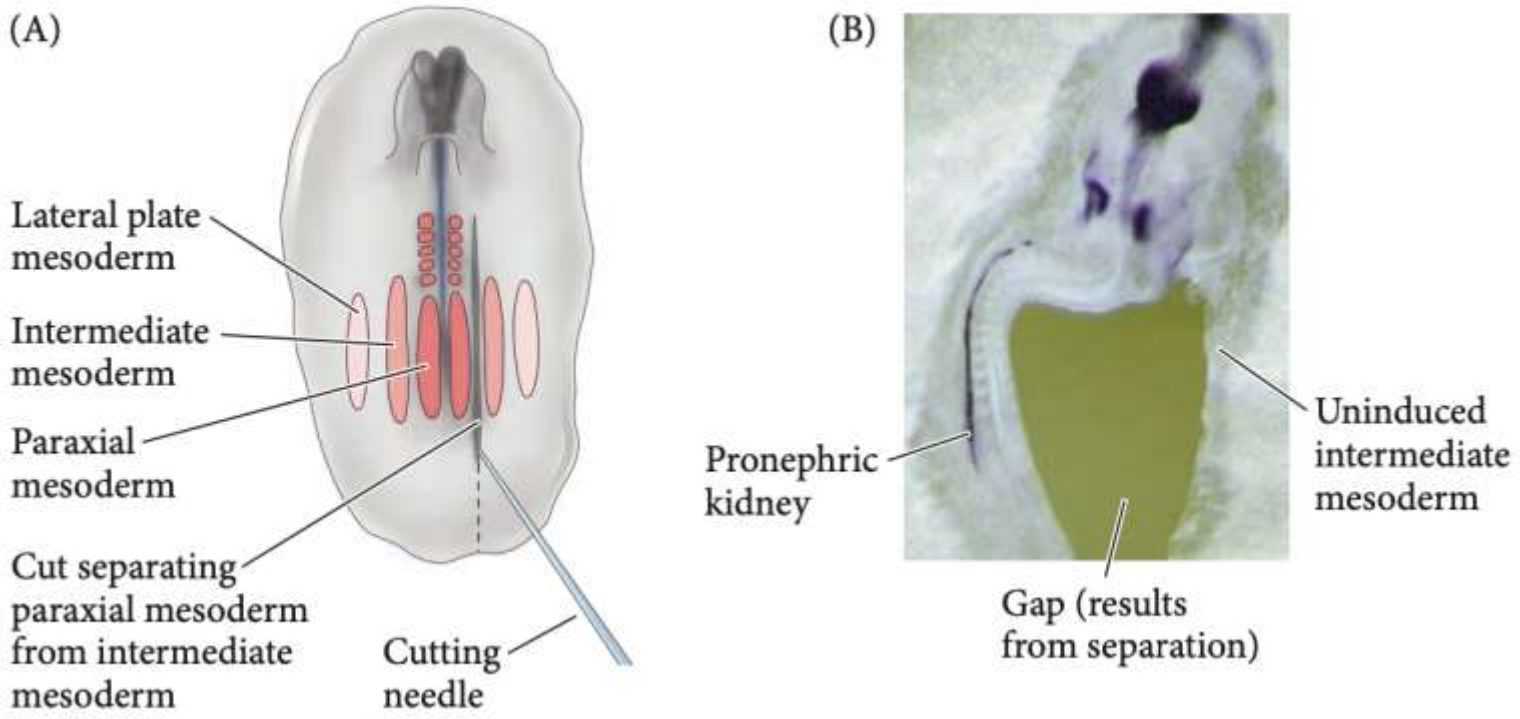


Intermediate mesoderm differentiates into kidney

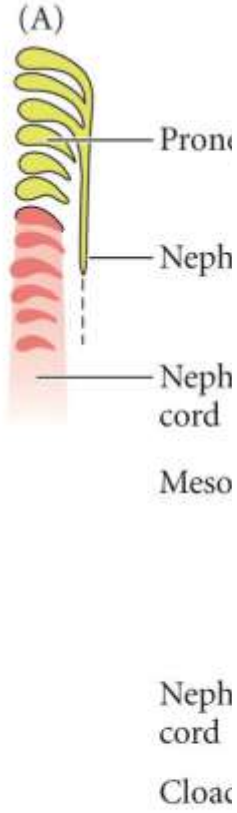


Davidson, 2009, *StemBook*

Intermediate mesoderm is induced into kidney by paraxial mesoderm



General scheme of development in the vertebrate kidney

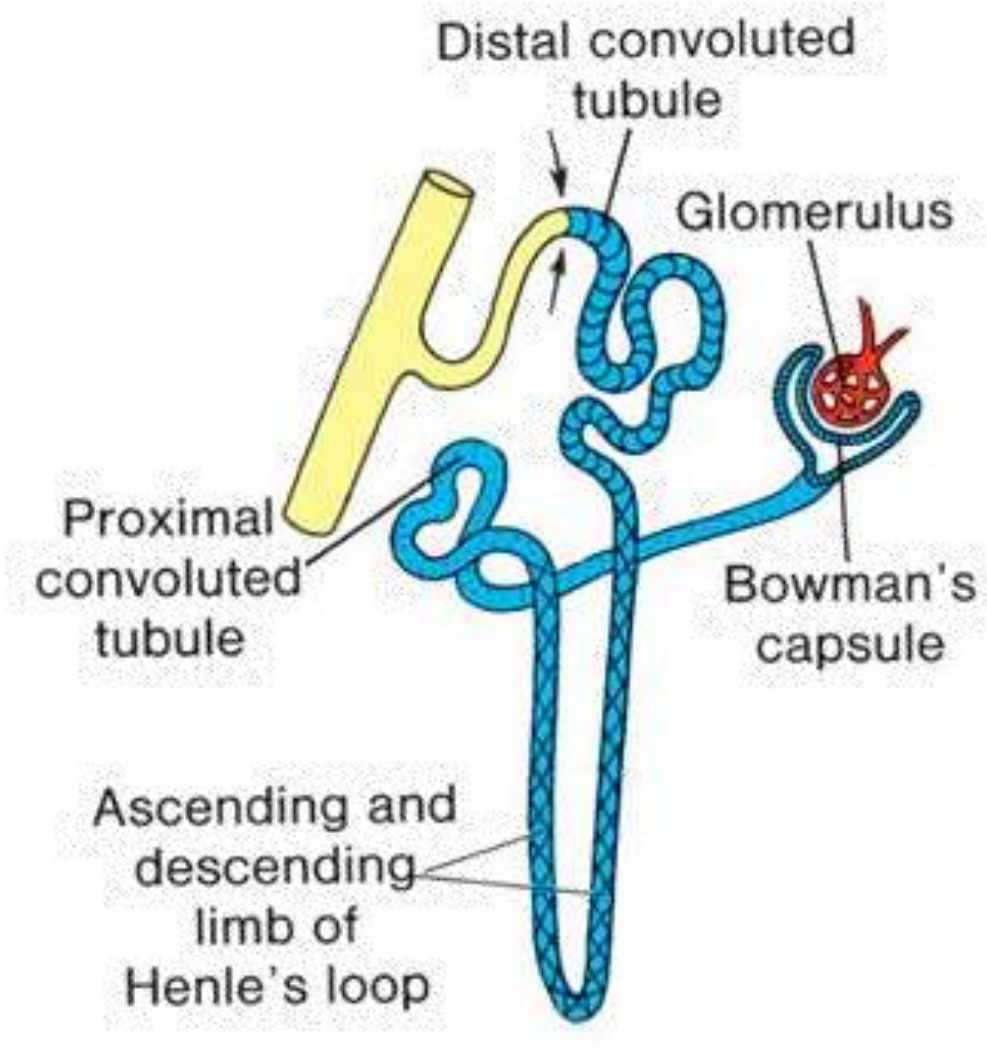


Pronephros: 前肾；mesonephros: 中肾；metanephros: 后肾

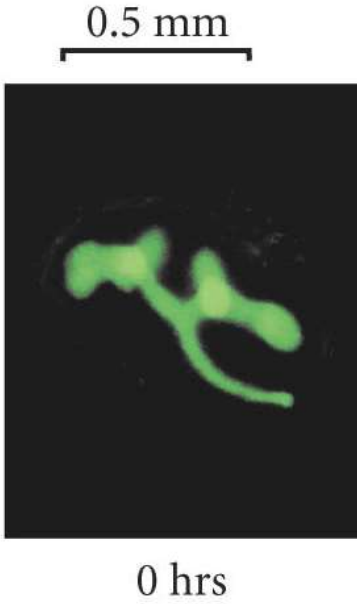
Development of the Metanephros

Two Systems:

- **Collecting System**
- **Excretory System (Nephron)**

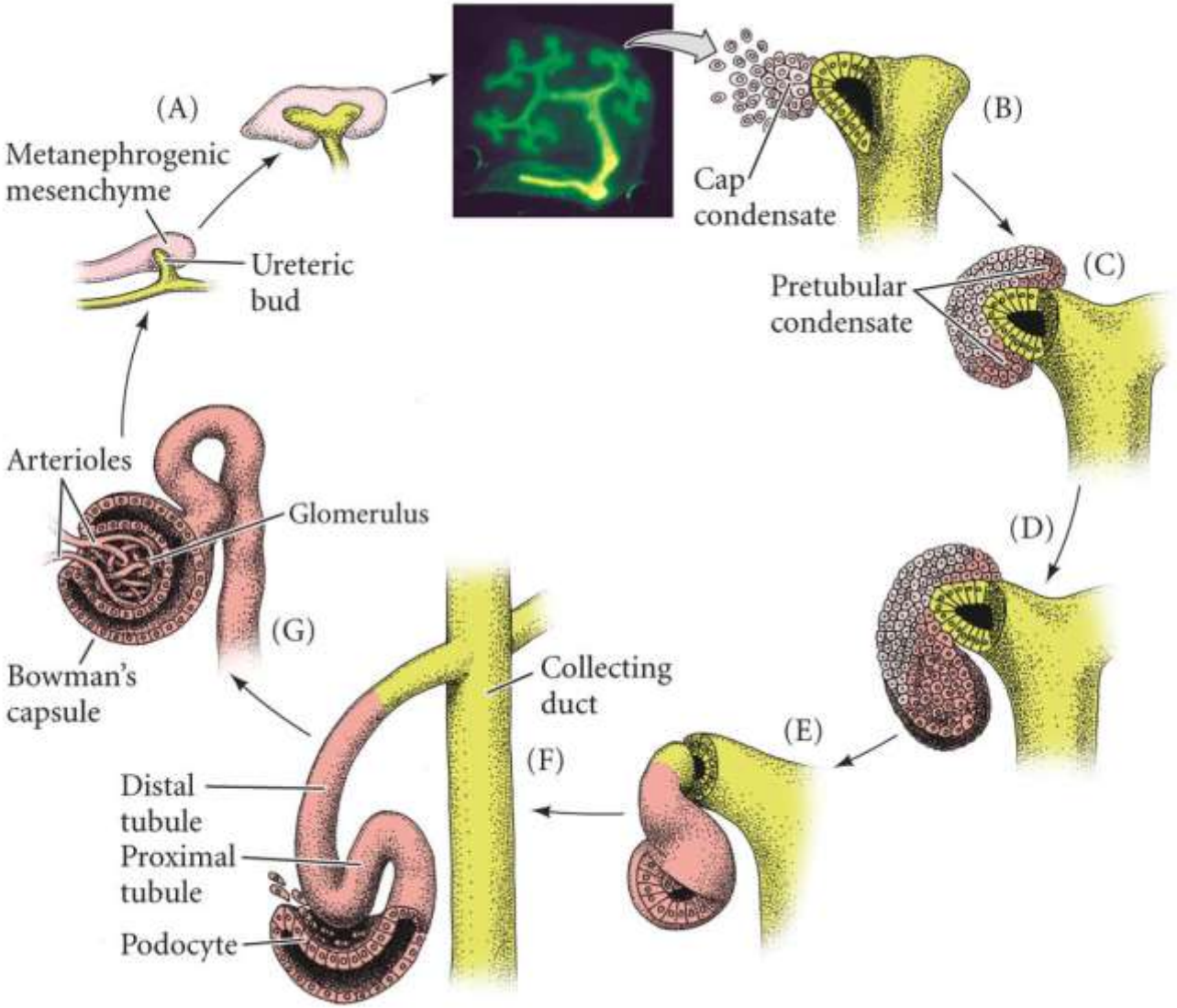


Kidney induction in vitro

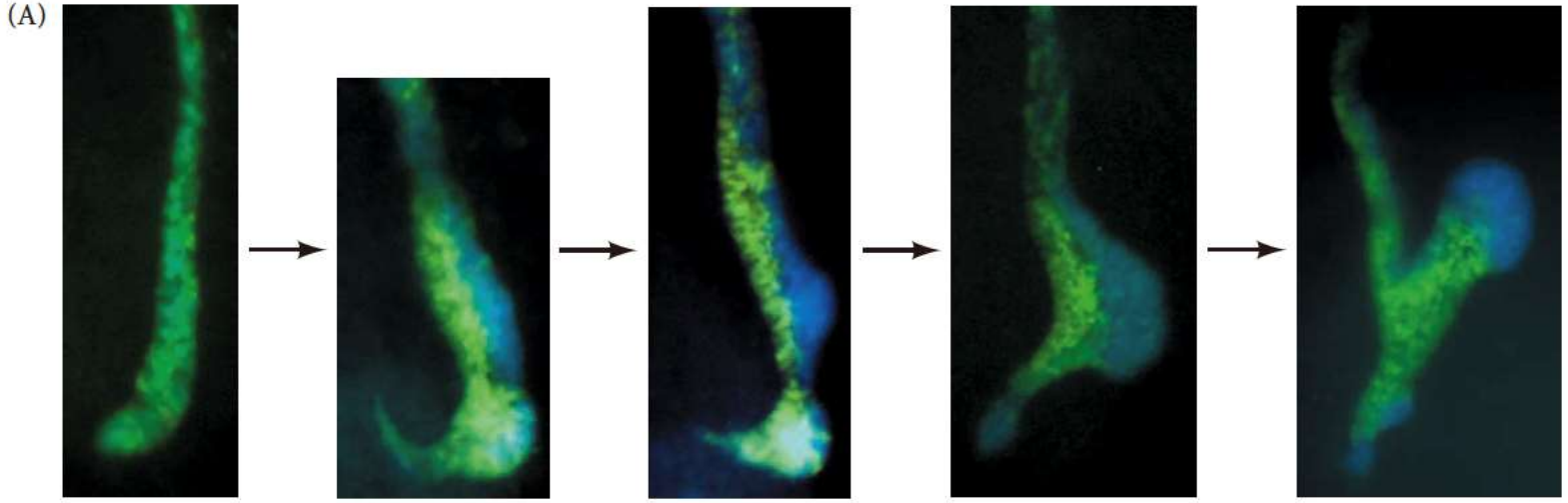


Hoxb7:GFP
Kidney rudiment from 11.5-day mouse embryo

Reciprocal induction in the development of mammalian kidney

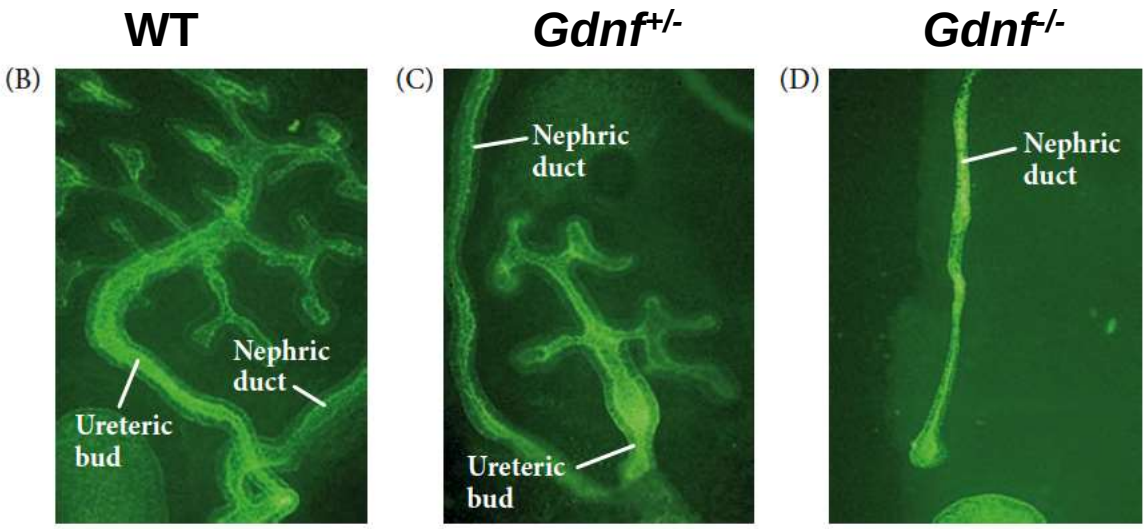


Ureteric bud growth is dependent on GDNF and its receptors

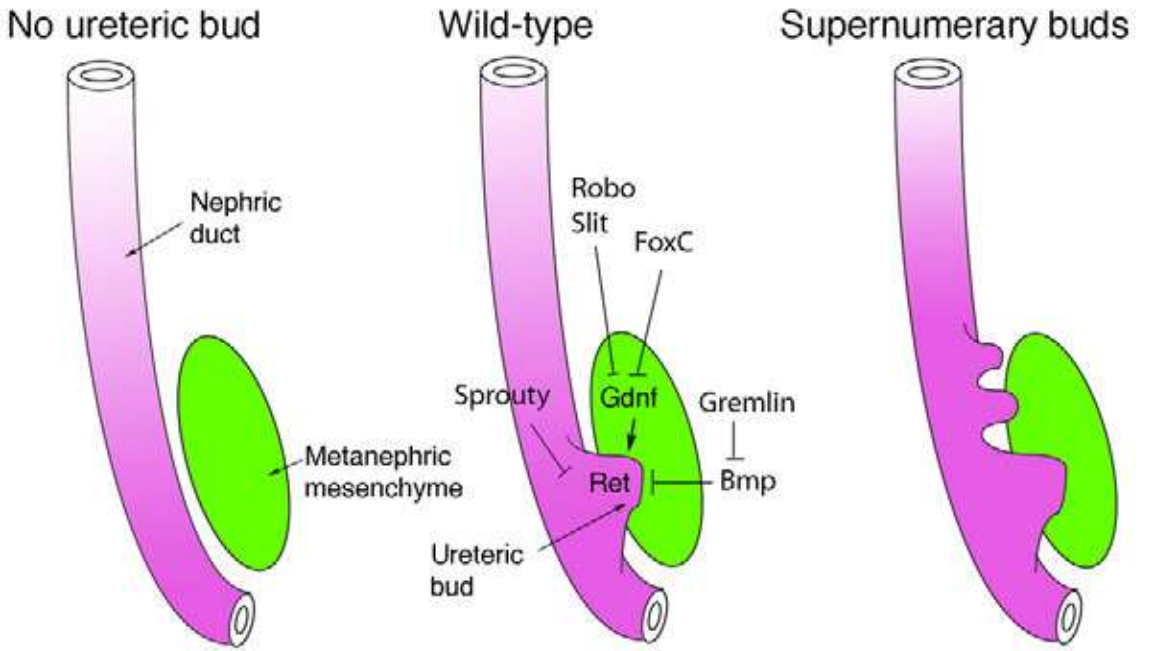


Ret-deficient cells

Ret-expressing cells



Genes involved in ureteric bud growth



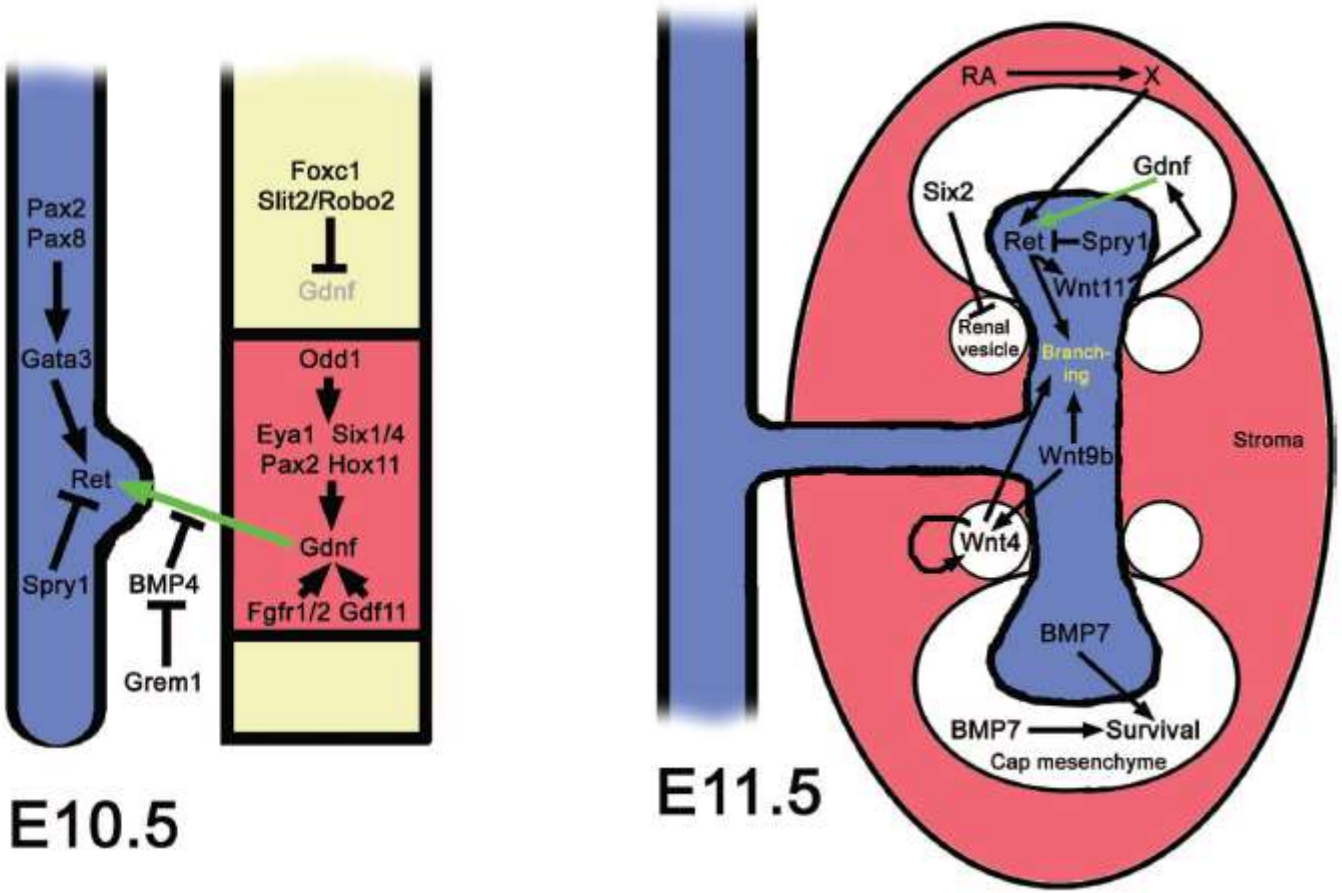
Caused by mutations in:

Gdnf
Ret
Gfra1
Grem1
Pax2
Eya1
Six1
Hox11 paralogues

Caused by mutations in:

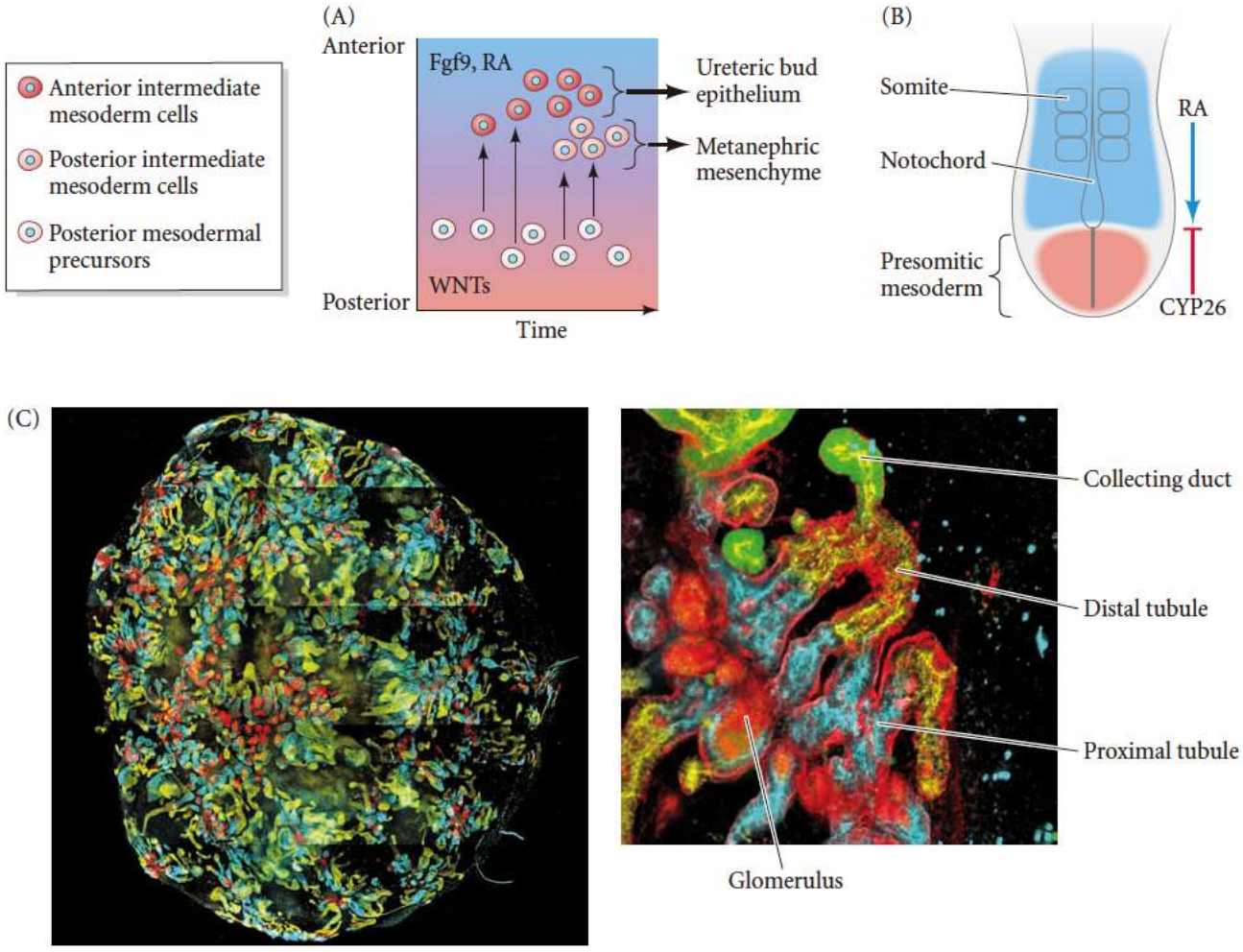
Spry1
Bmp4
Robo2
Slit2
Foxc1/c2

Key molecular pathways involved in early metanephric kidney development



Davidson, 2009, *StemBook*

Creating organoids of mouse kidneys from induced pluripotent stem cells



Summary (IV)

- Key word

  kidney, pronephros, mesonephros, metanephros，GDNF/Ret

- Event and mechanism

  kidney induction,

outline

- Ectoderm

  1) neural tube formation and differentiation

  2) neural crest cells

  3) eye development

- Mesoderm

  1) paraxial mesoderm: somite

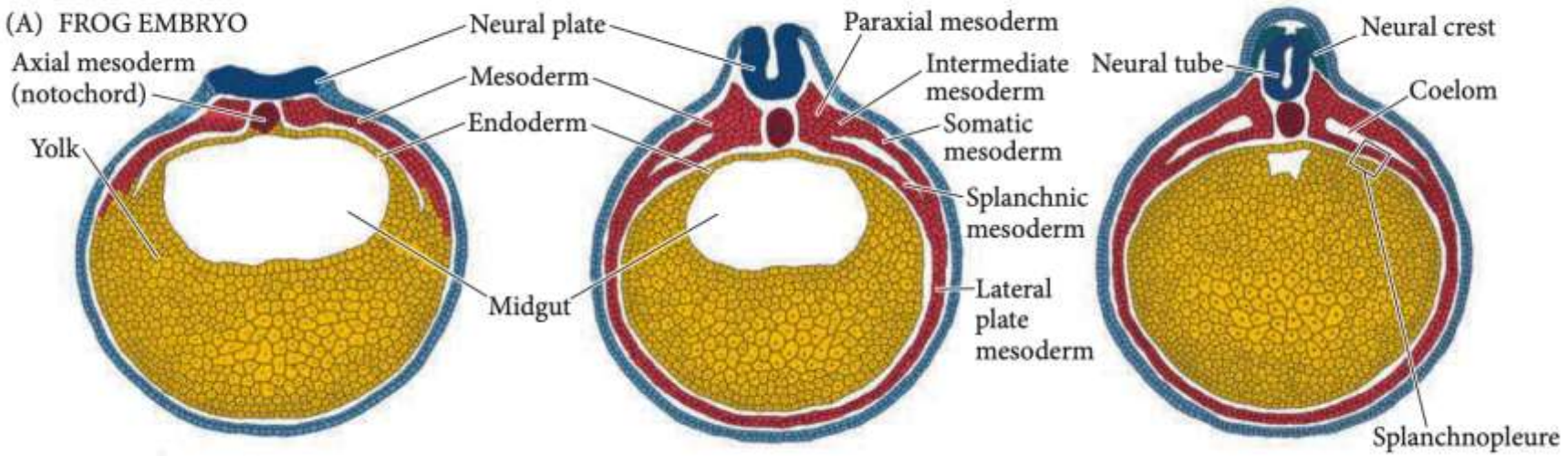
  2) intermediate mesoderm: kidney

  3) lateral plate mesoderm: heart, blood vessels, blood cells

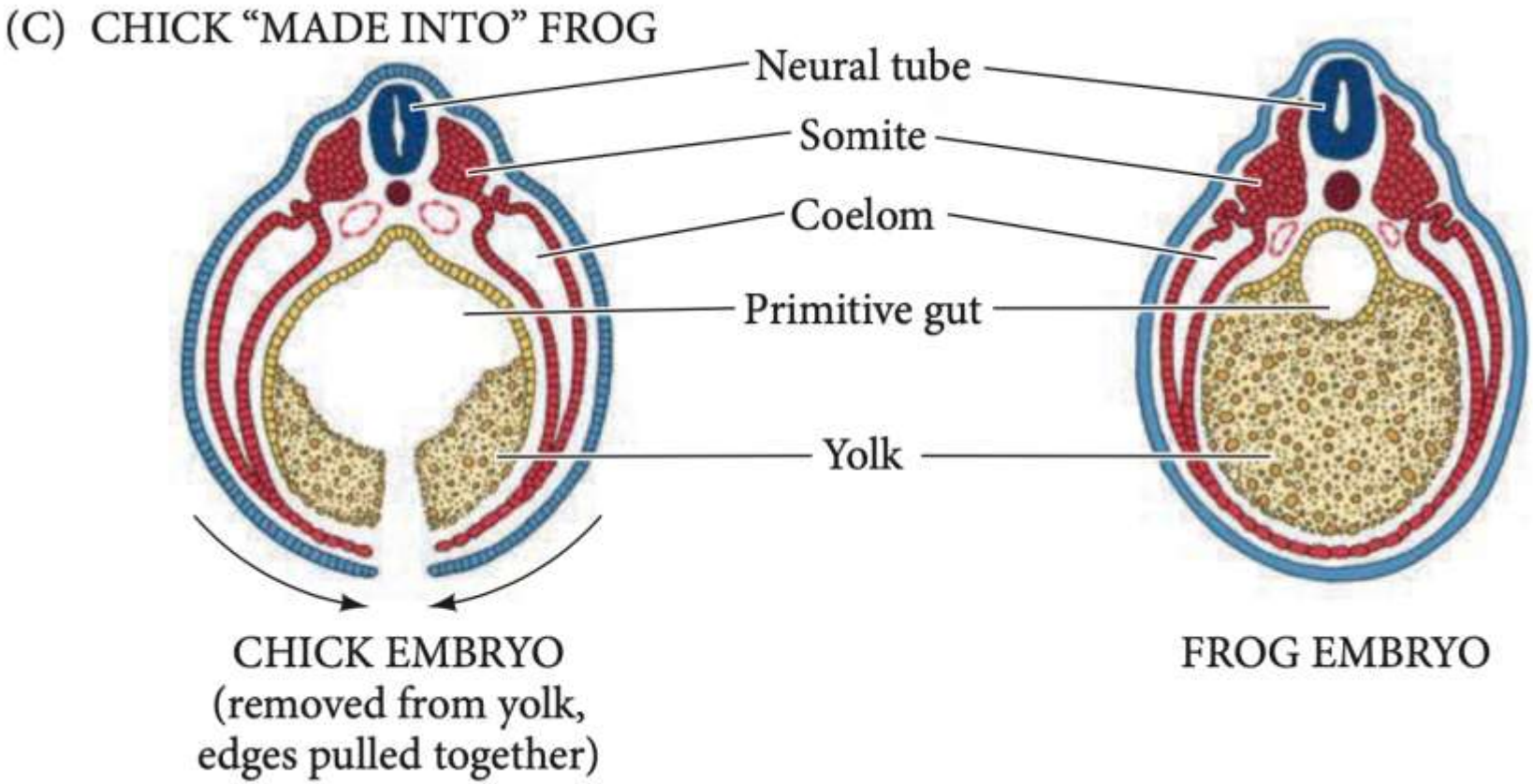
- Endoderm

  gut & lung

Mesodermal development in frog embryos



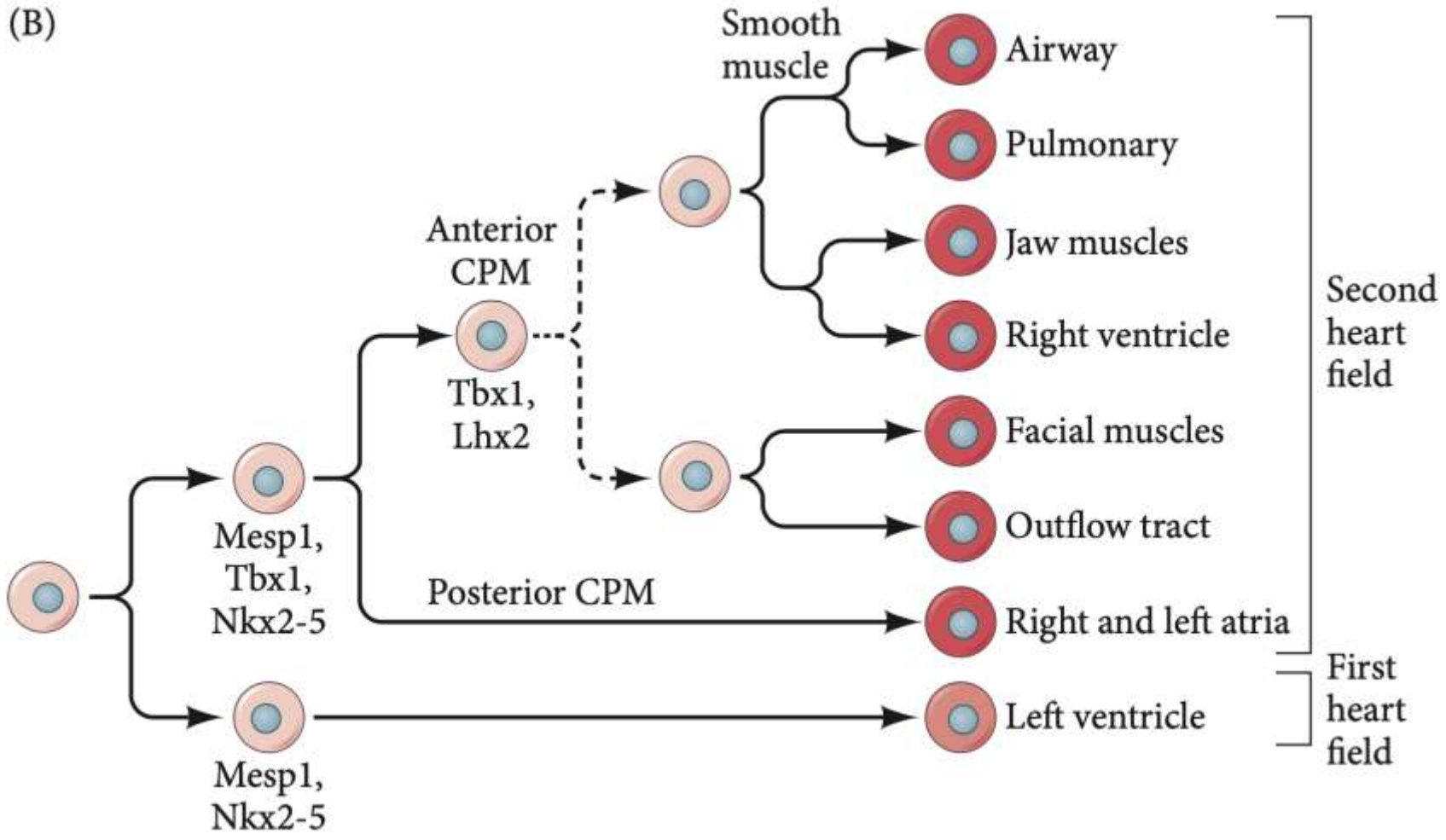
Mesodermal development in chick embryos



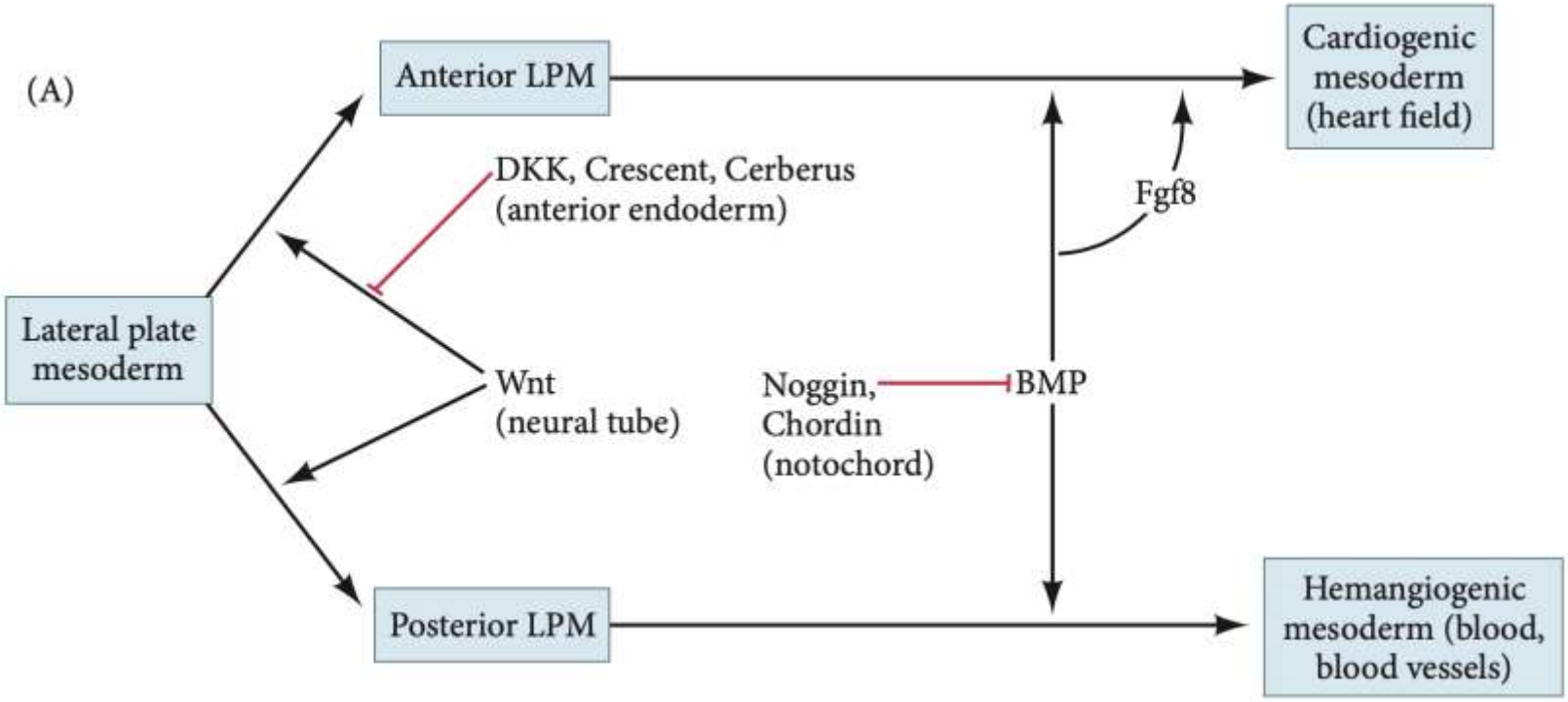
Heart formation

- Specification of heart tissures—heart primordia (心原基的形成)
- Fusion of the heart primordia and initial heartbeats （心原基迁移融合成单一的心管, 心跳启动）
- Looping（环绕）(rightward heart looping) and formation of heart chambers

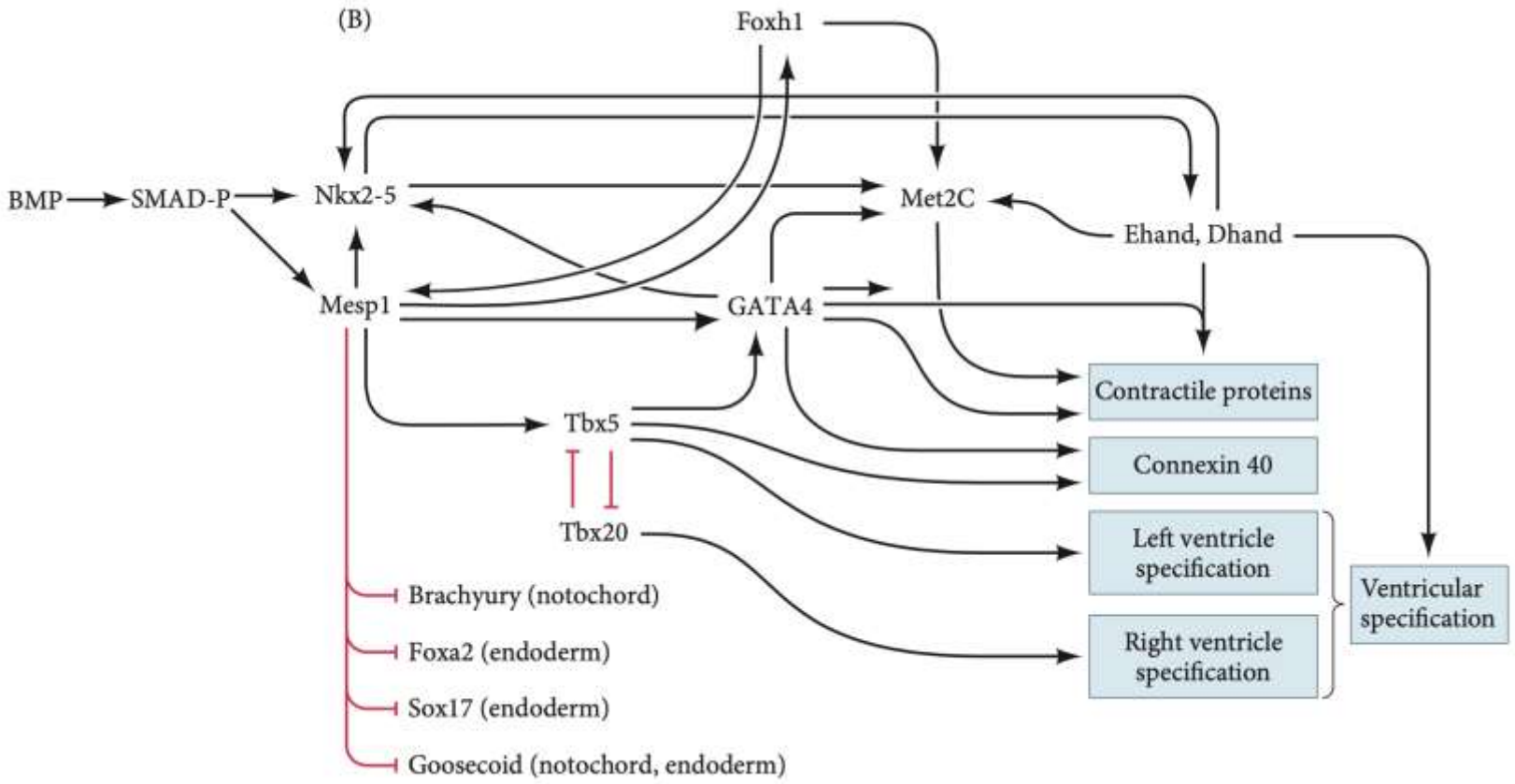
The heart fields in the mouse embryo



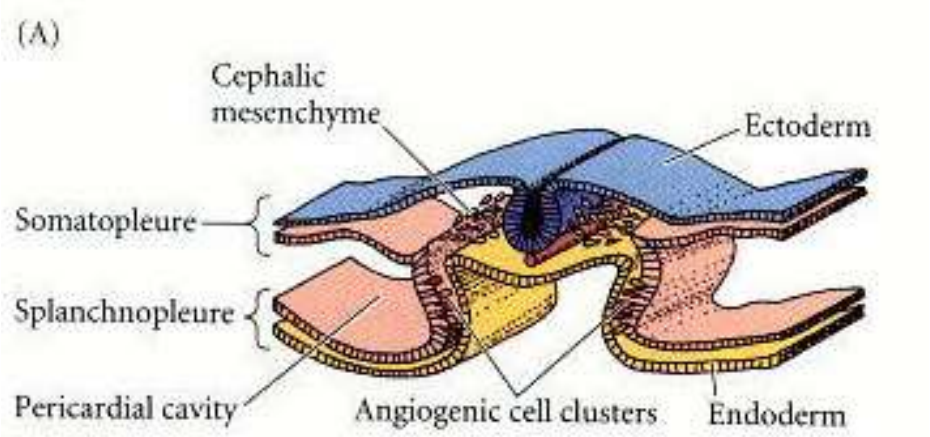
Wnt signals from the neural tube instruct LPM to become precursors of the blood and blood vessels.



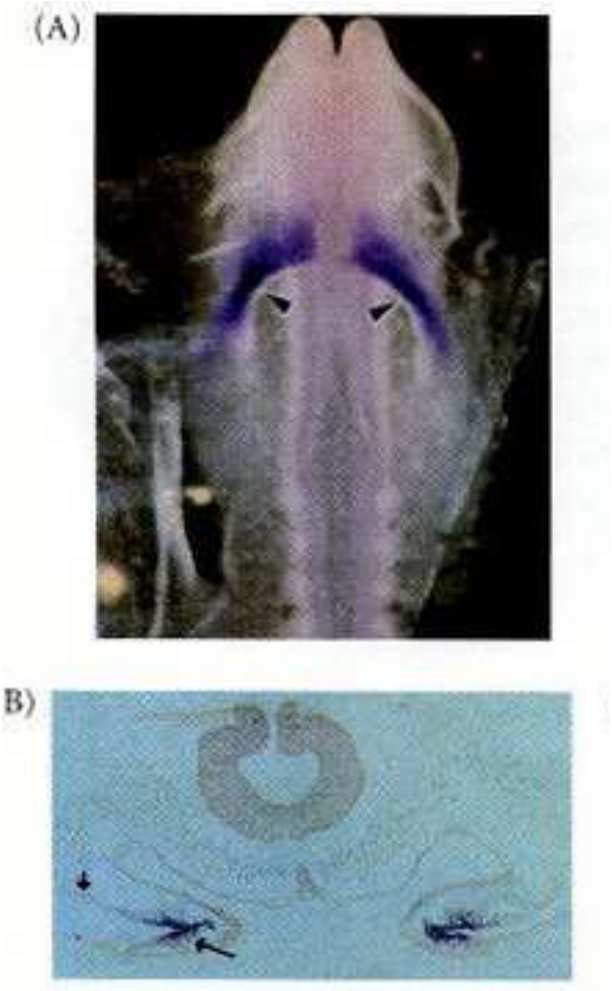
Model gene regulatory network for the vertebrate heart initiated by BMP signals



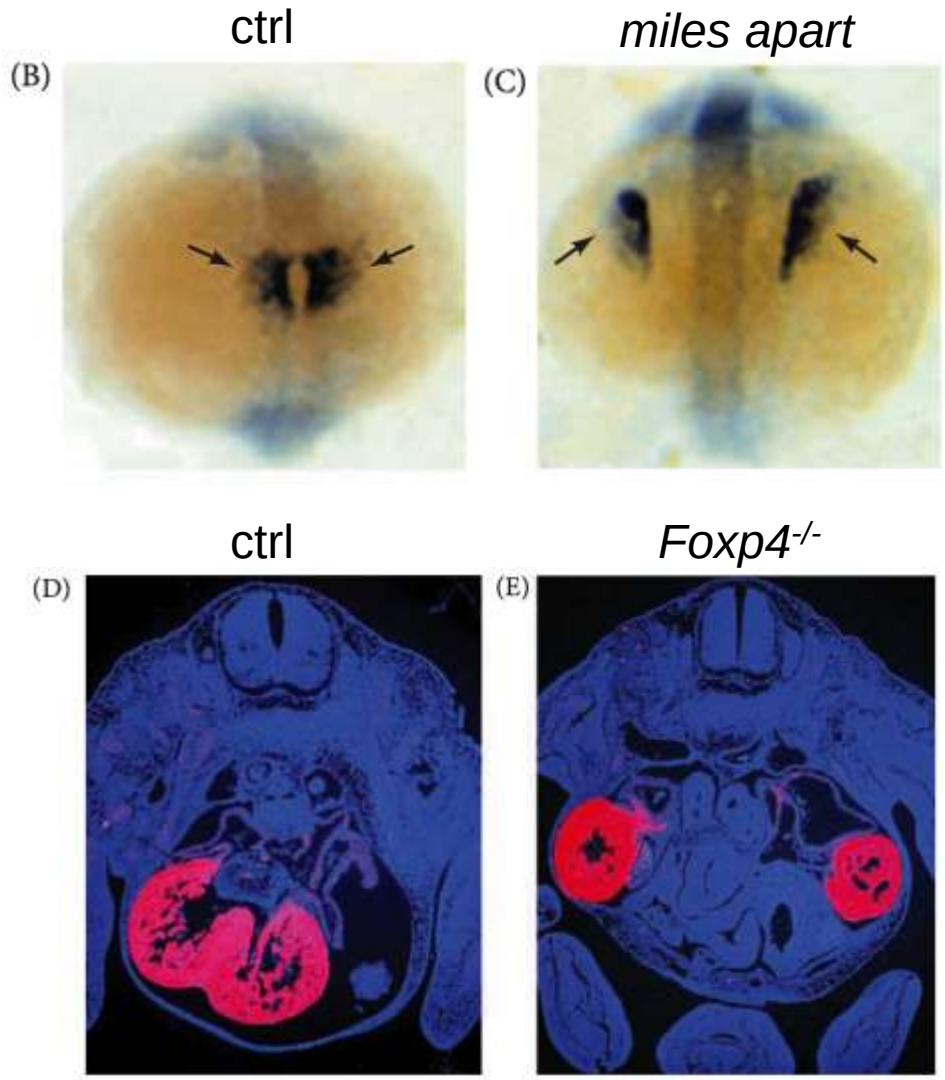
Heart tube formation in chick



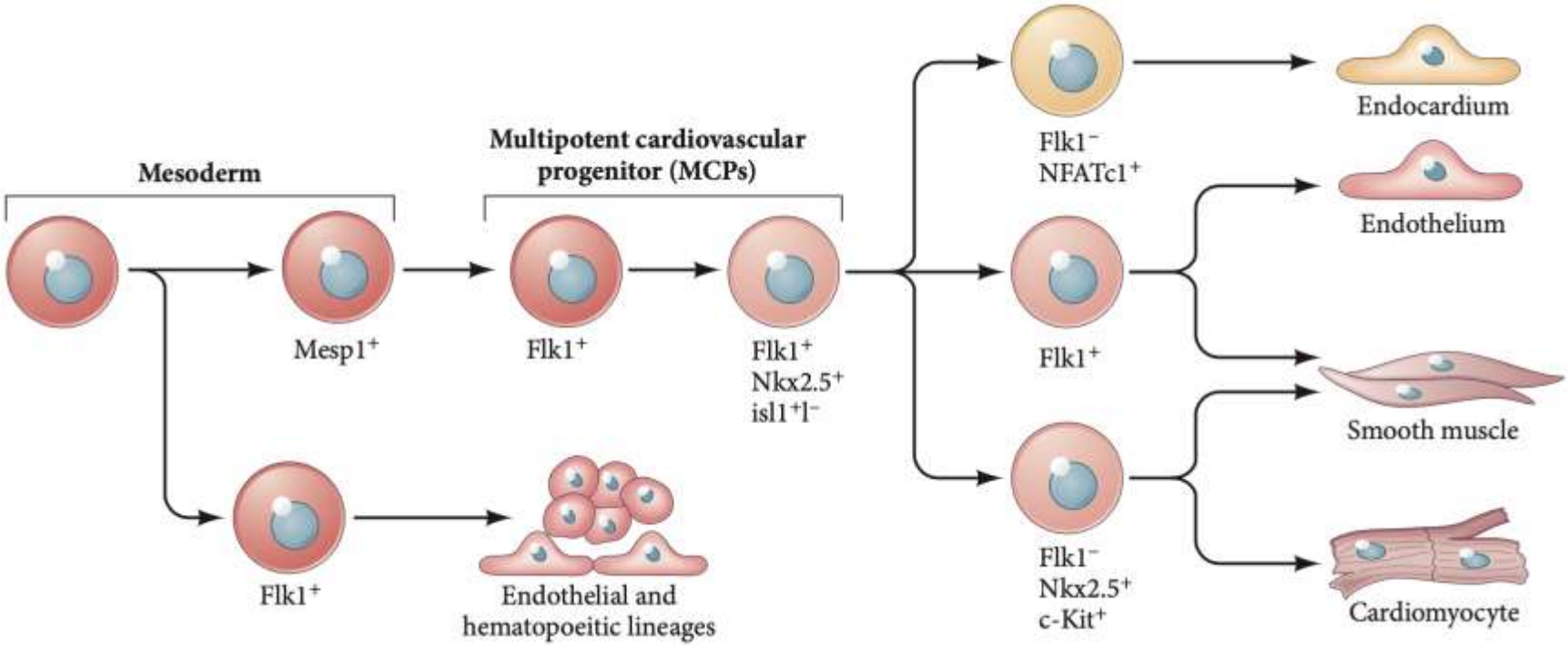
Migration of Heart primordia



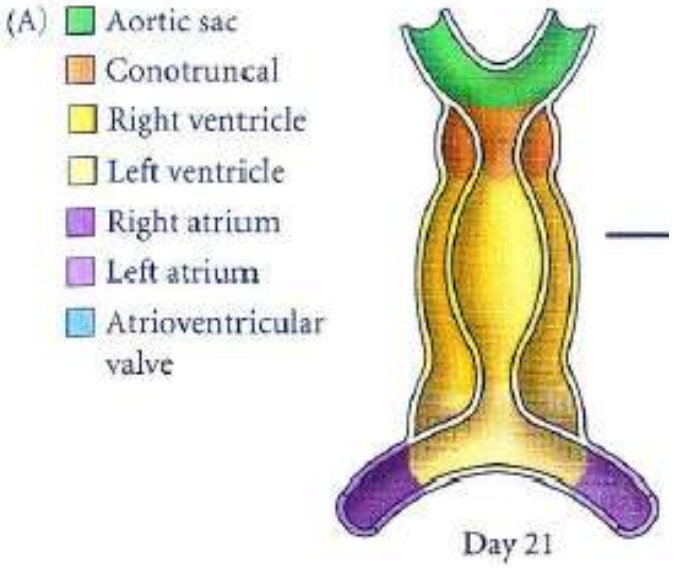
Migration of Heart primordia



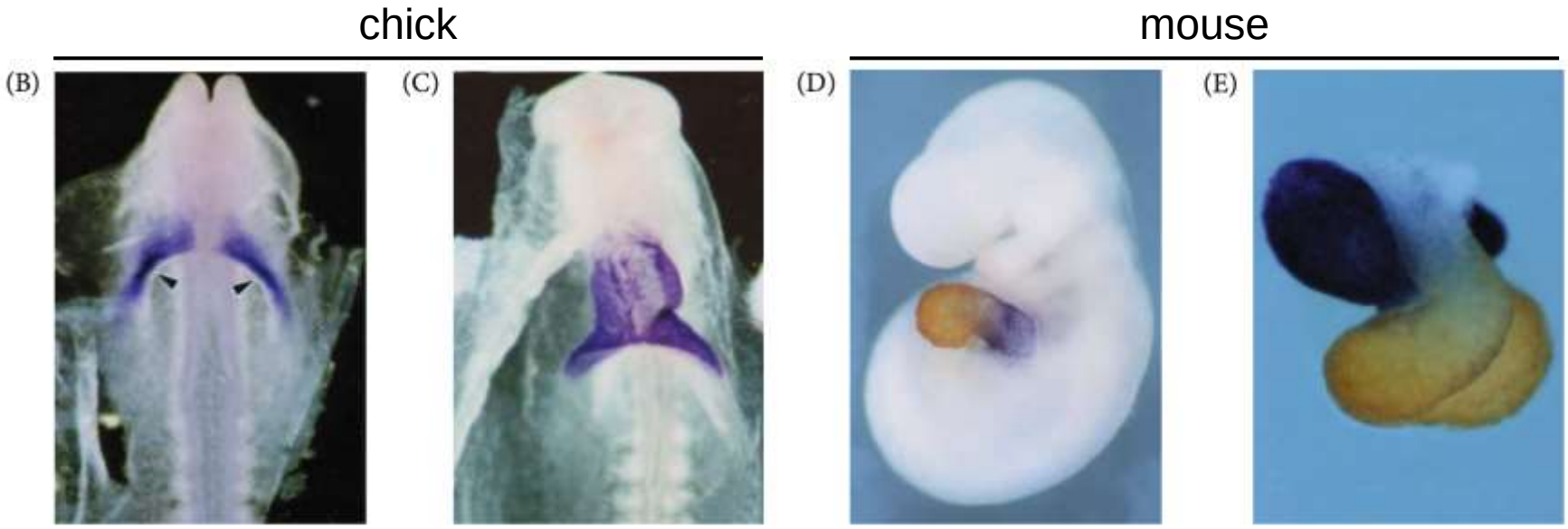
Model for early cardio-vascular lineages



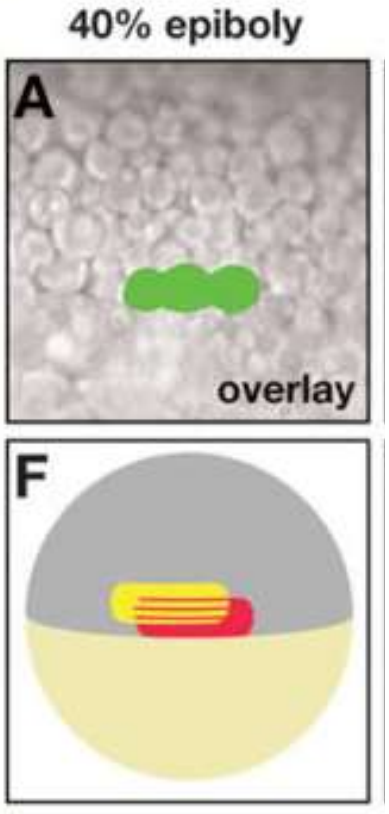
Schematic diagram of cardiac morphogenesis in humans



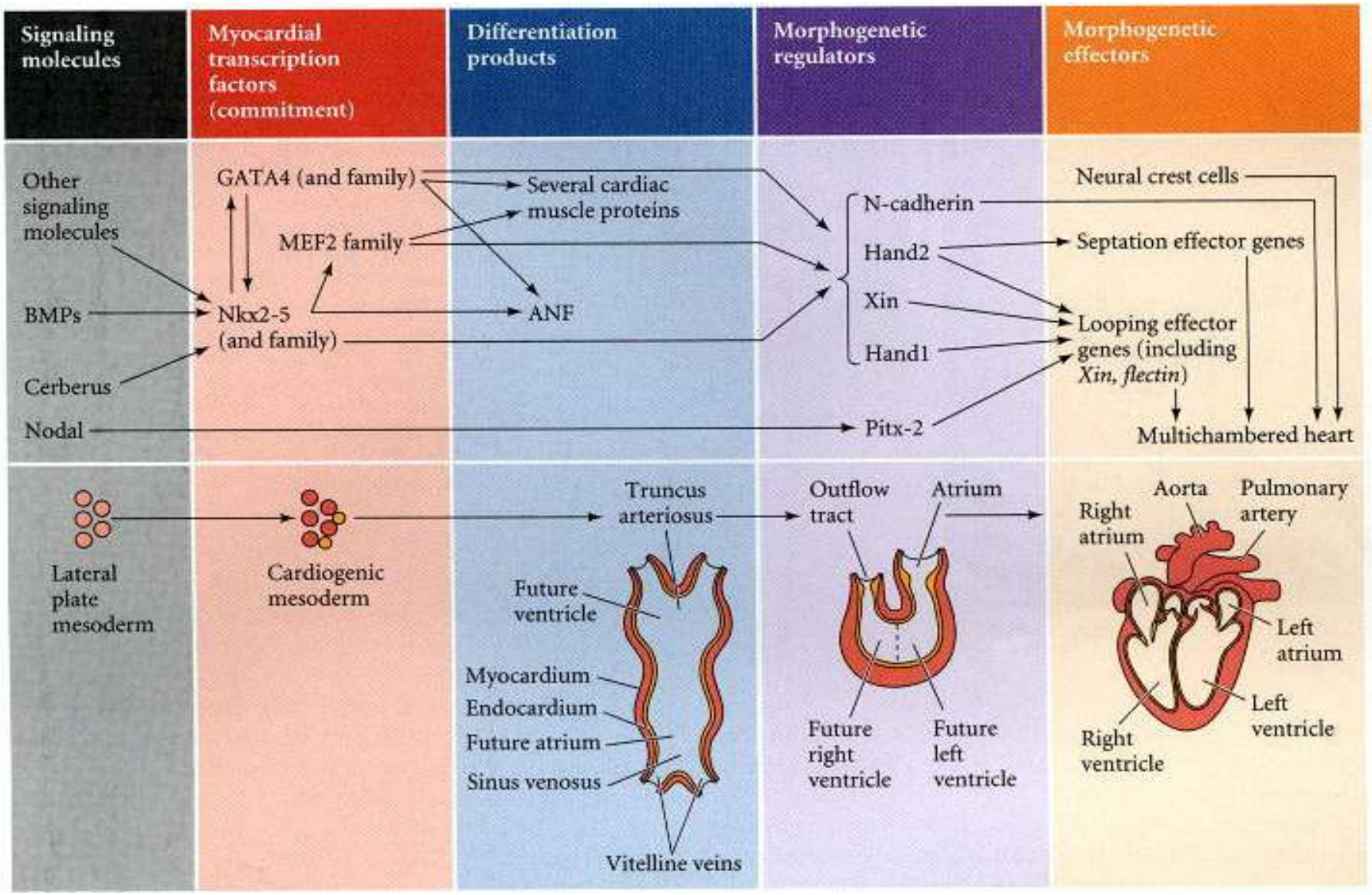
Cardiac looping and chamber formation



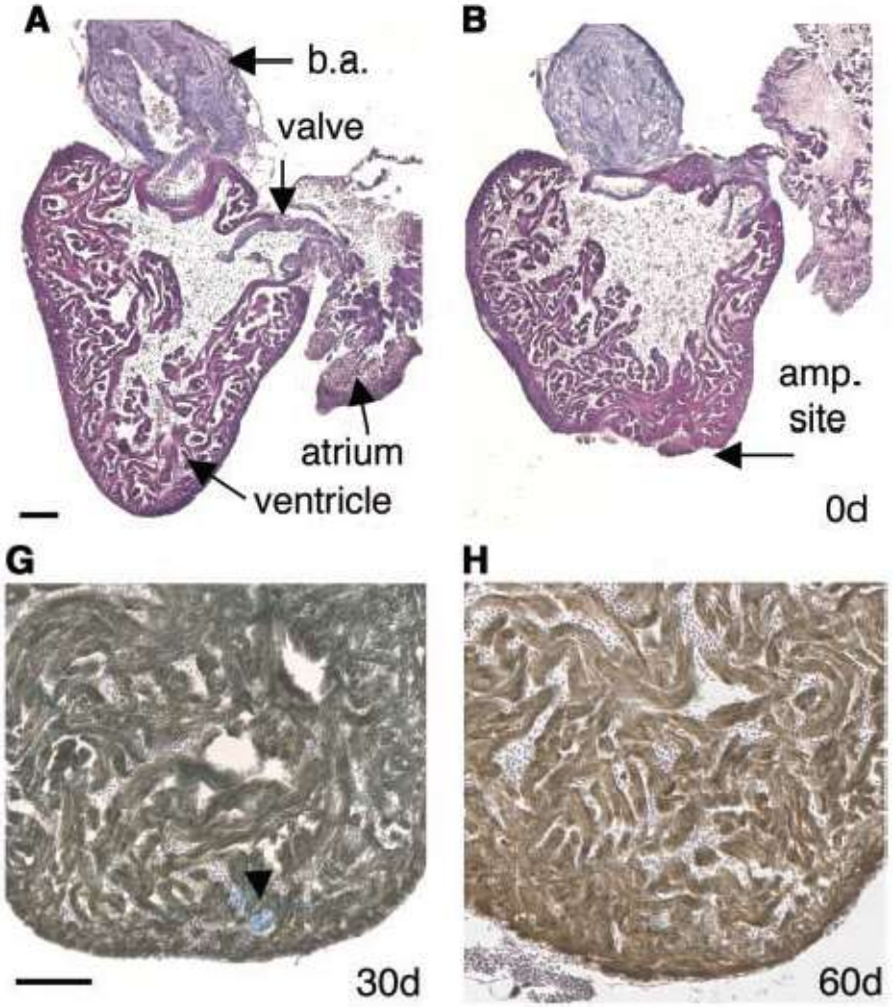
Heart formation in zebrafish

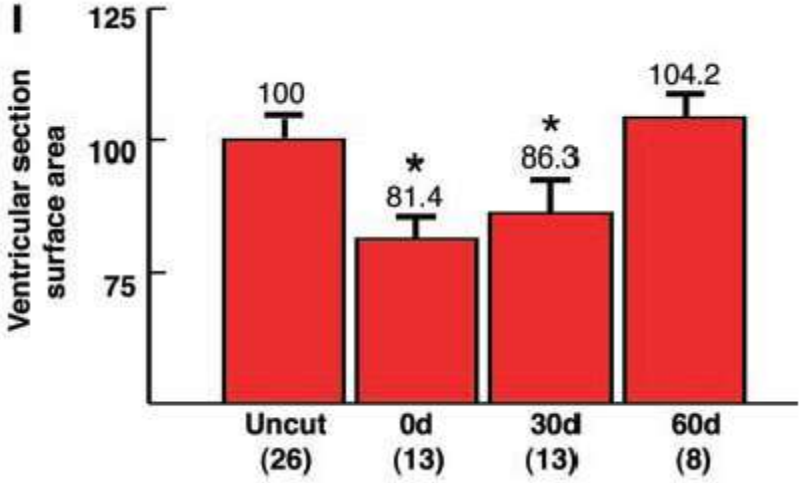


Cascade of heart development



Heart Regeneration





Poss, *et al.*, 2002 Science

Origin of regenerated cardiac cell: progenitor vs dedifferentiation?

Cell

nature Vol 464|25 March 2010|doi:10.1038/nature08899

LETTERS

Zebrafish heart regeneration occurs by cardiomyocyte dedifferentiation and proliferation

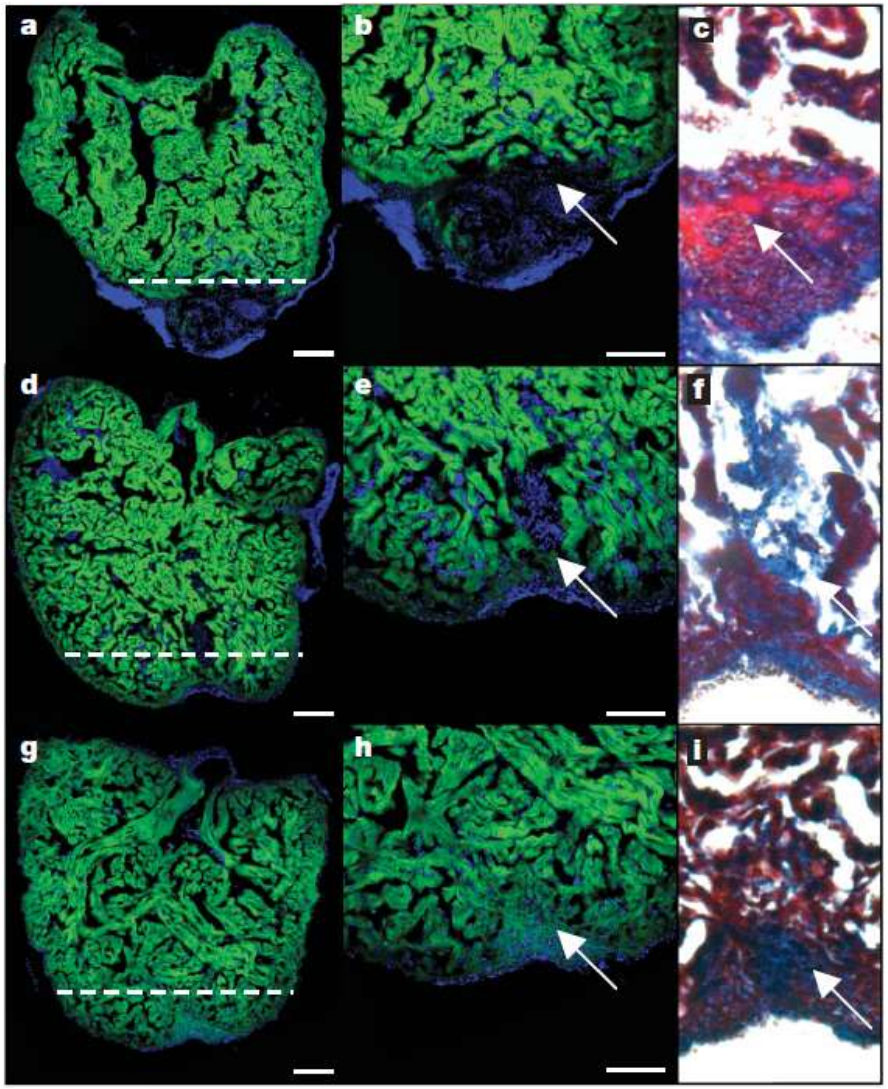
Chris Jopling[1], Eduard Sleep[1,2]†, Marina Raya[1]†, Mercè Martí[1], Angel Raya[1,2,3]† & Juan Carlos Izpisúa Belmonte[1,2,4]

Regenerated cardiomyocytes are derived from differentiated cardiomyocytes

7 dpa

14 dpa

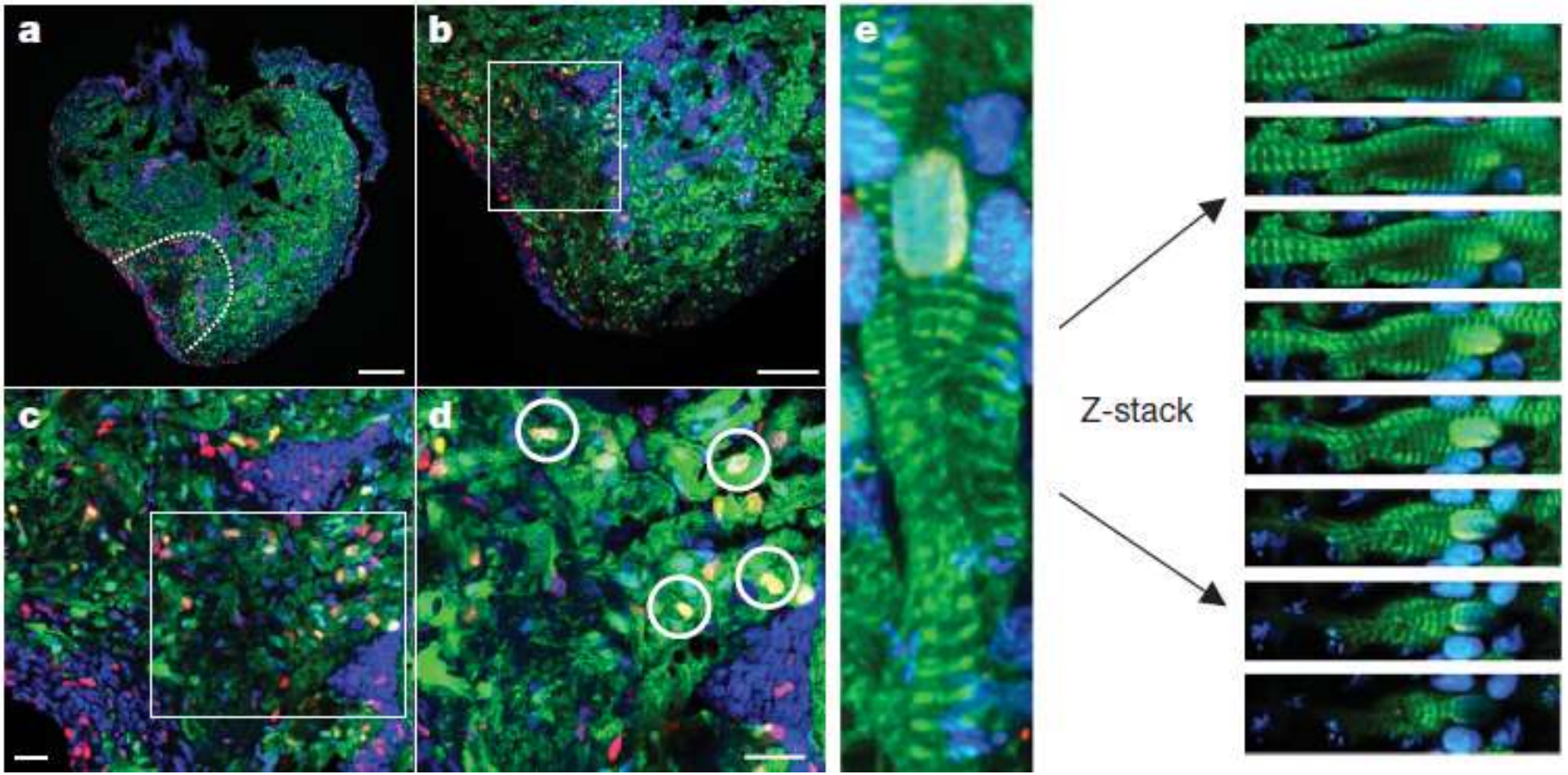
30 dpa



tg-cmlc2a-Cre-Ert2; tg-cmlc2a-LnL–GFP

Jopling, *et al.*, 2010 Nature

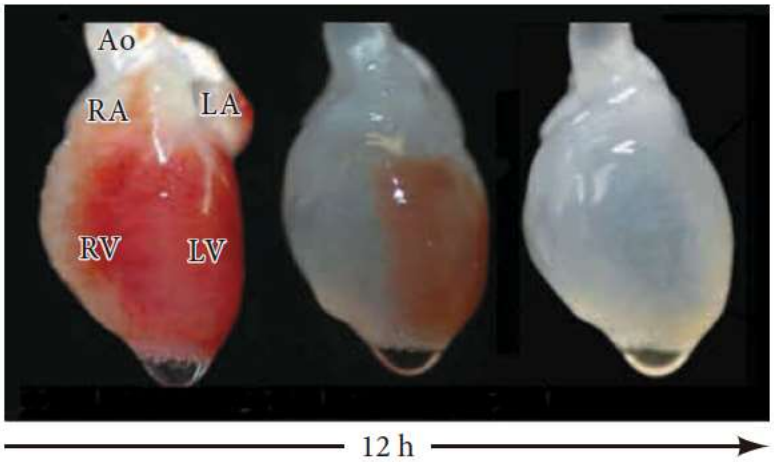
Differentiated cardiomyocytes re-enter the cell cycle



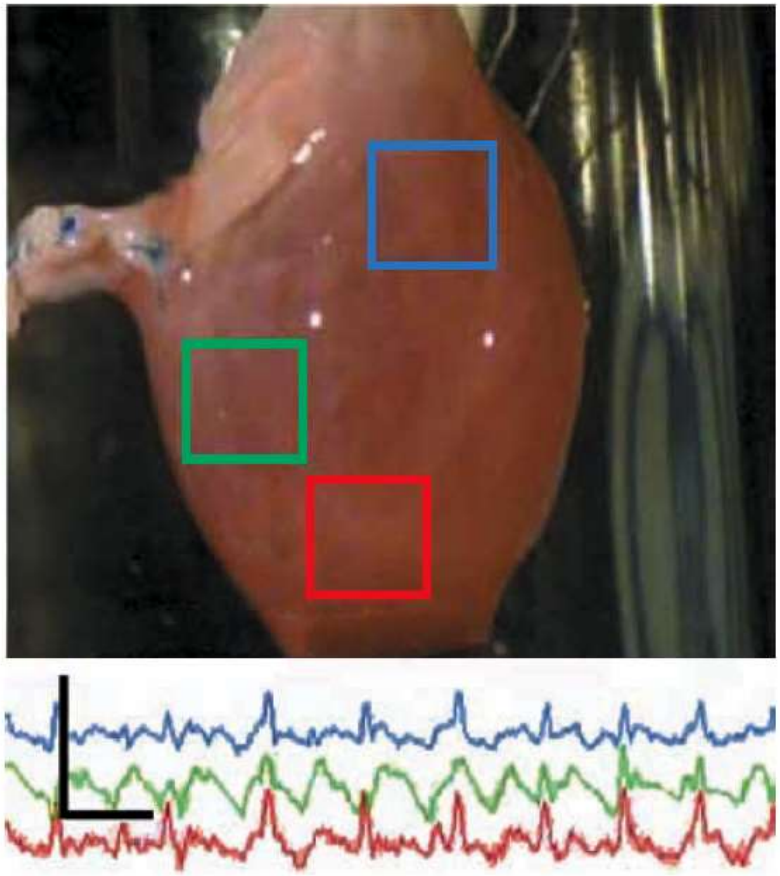
Jopling, *et al.*, 2010 Nature

Reconstructing a decellularized rat heart

(A) Decellularization



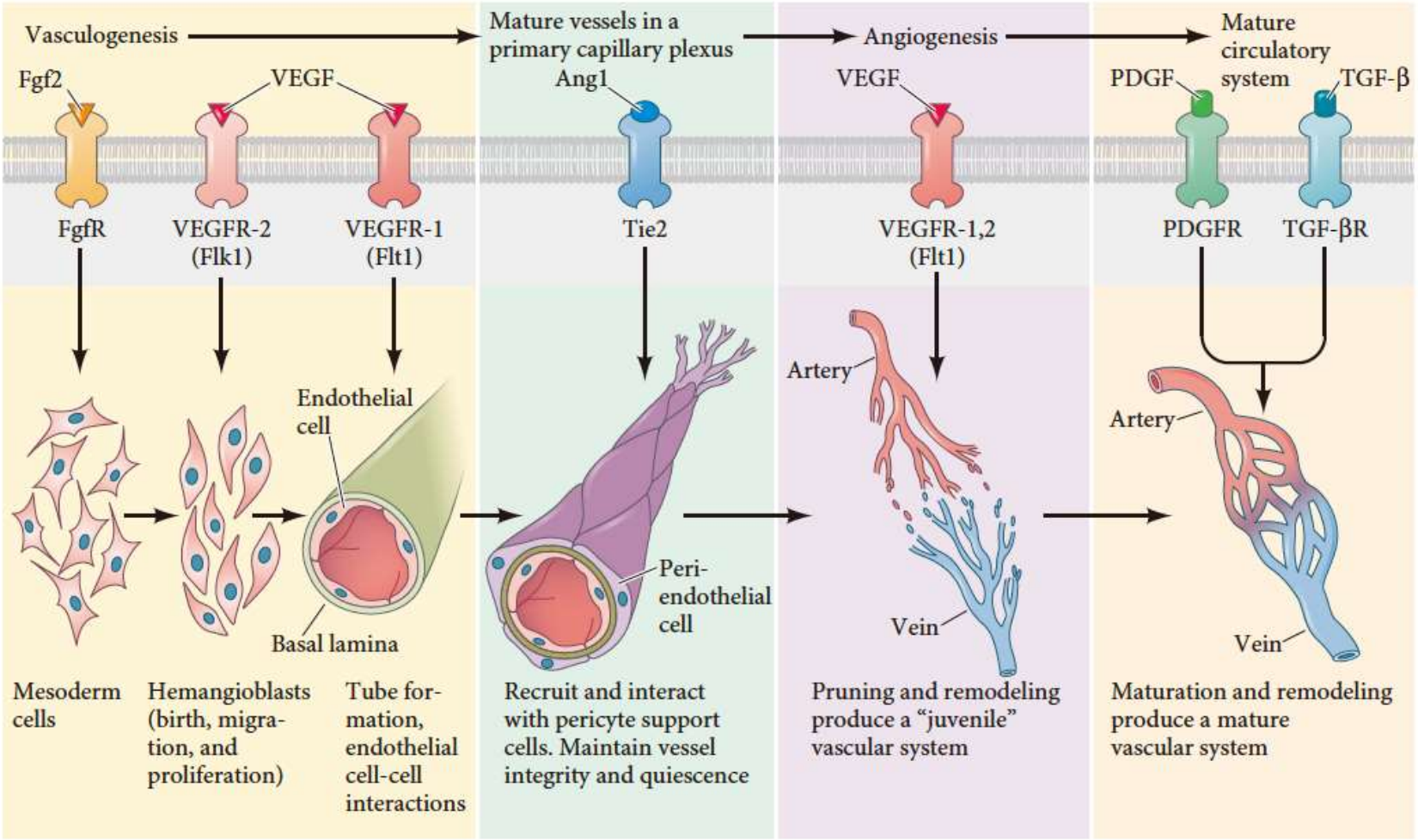
(B) Recellularized beating heart



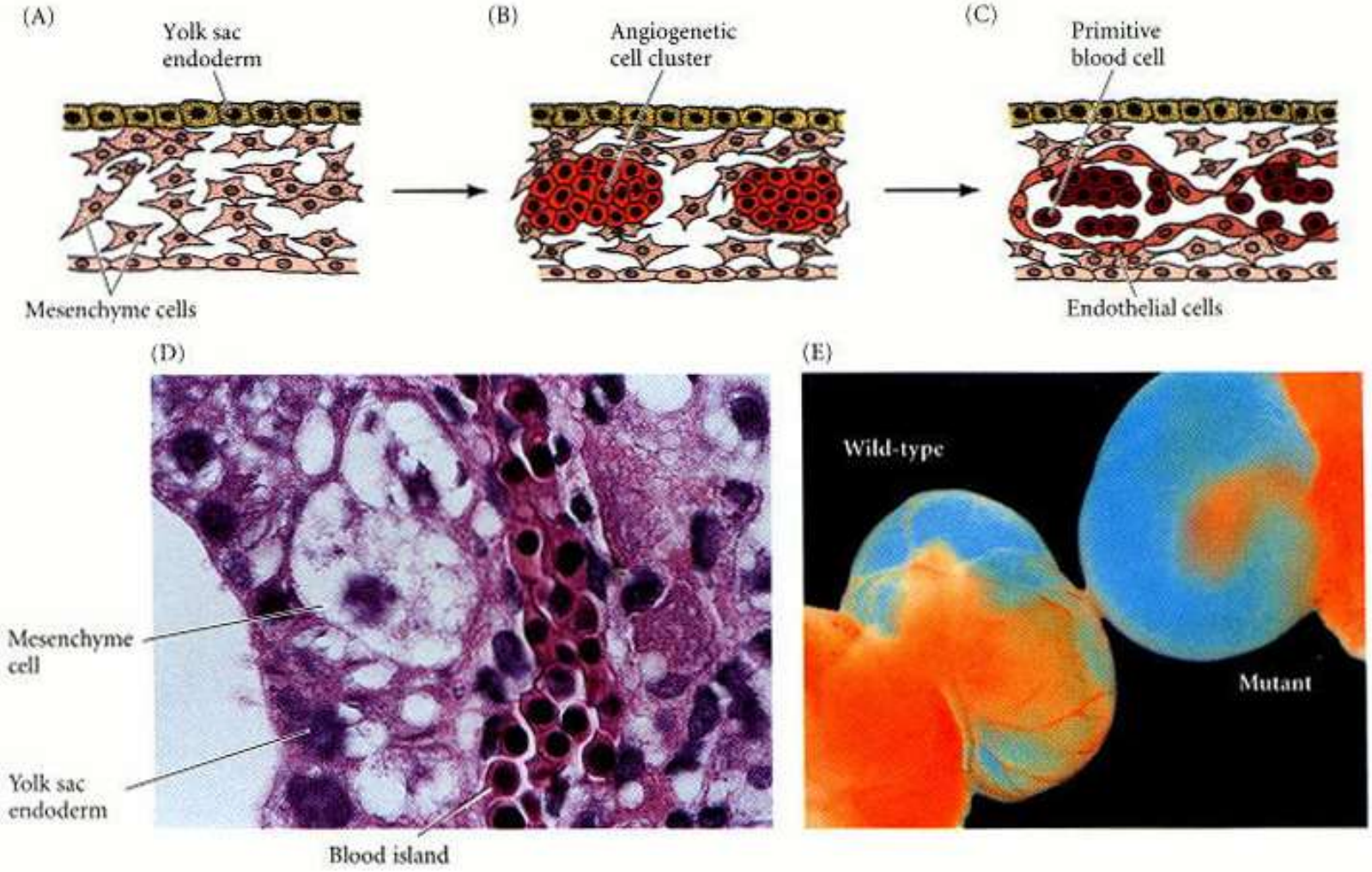
Hemangioblast (血管、血液前体细胞)

De Val & Black, 2009

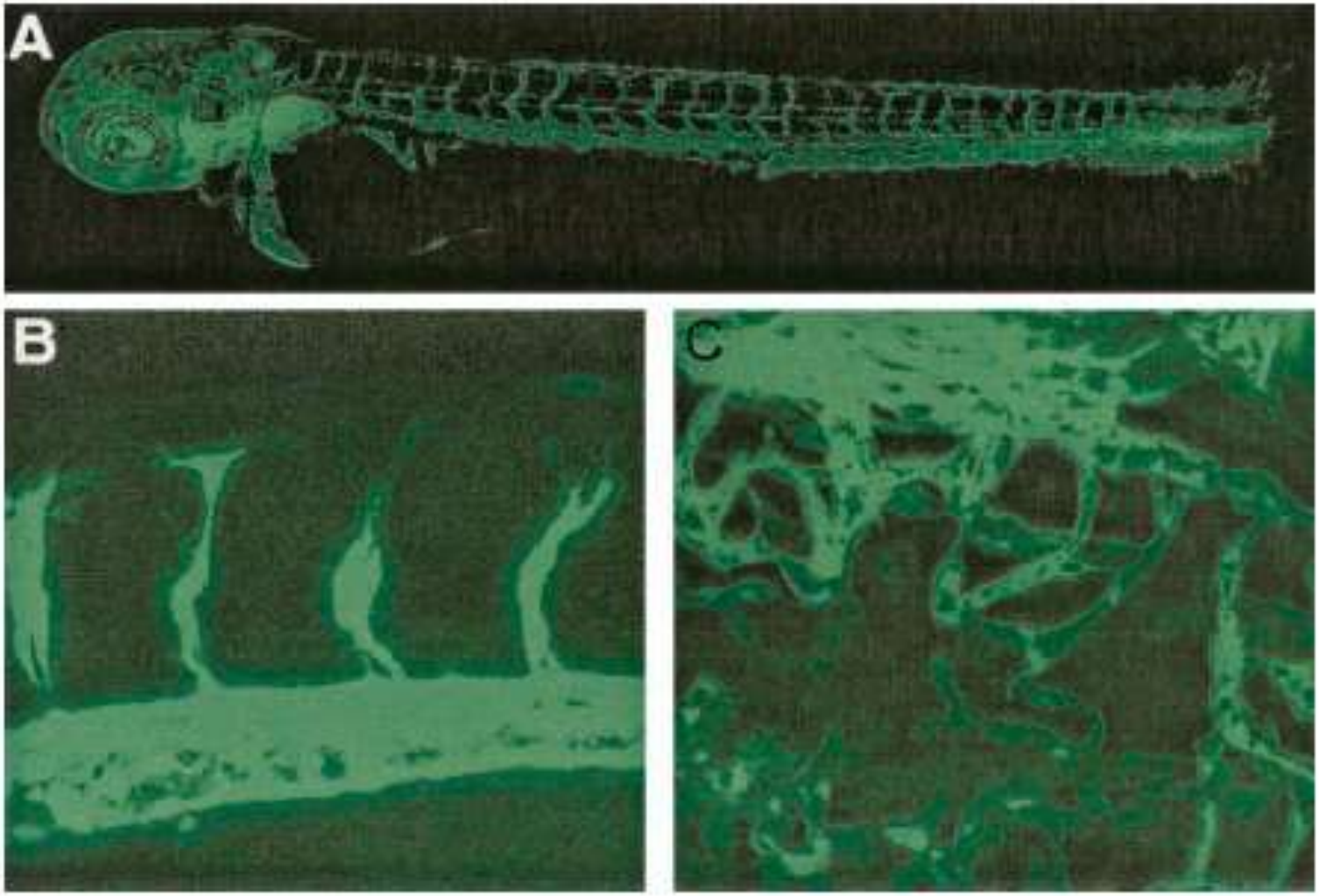
Blood vessel (血管) formation: Vasculogenesis and angiogenesis



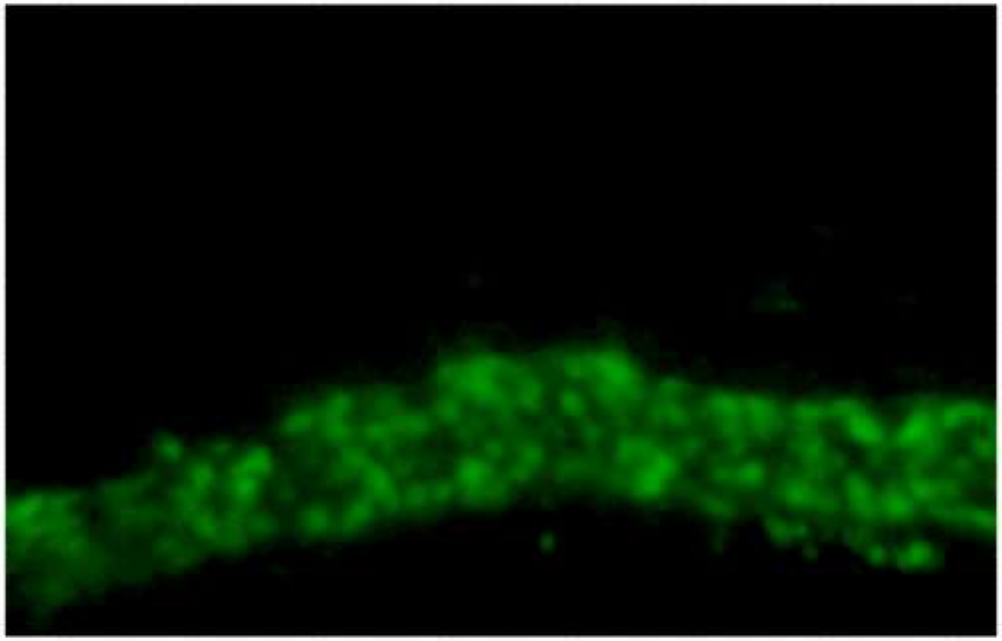
Vasculogenesis （初级血管形成）



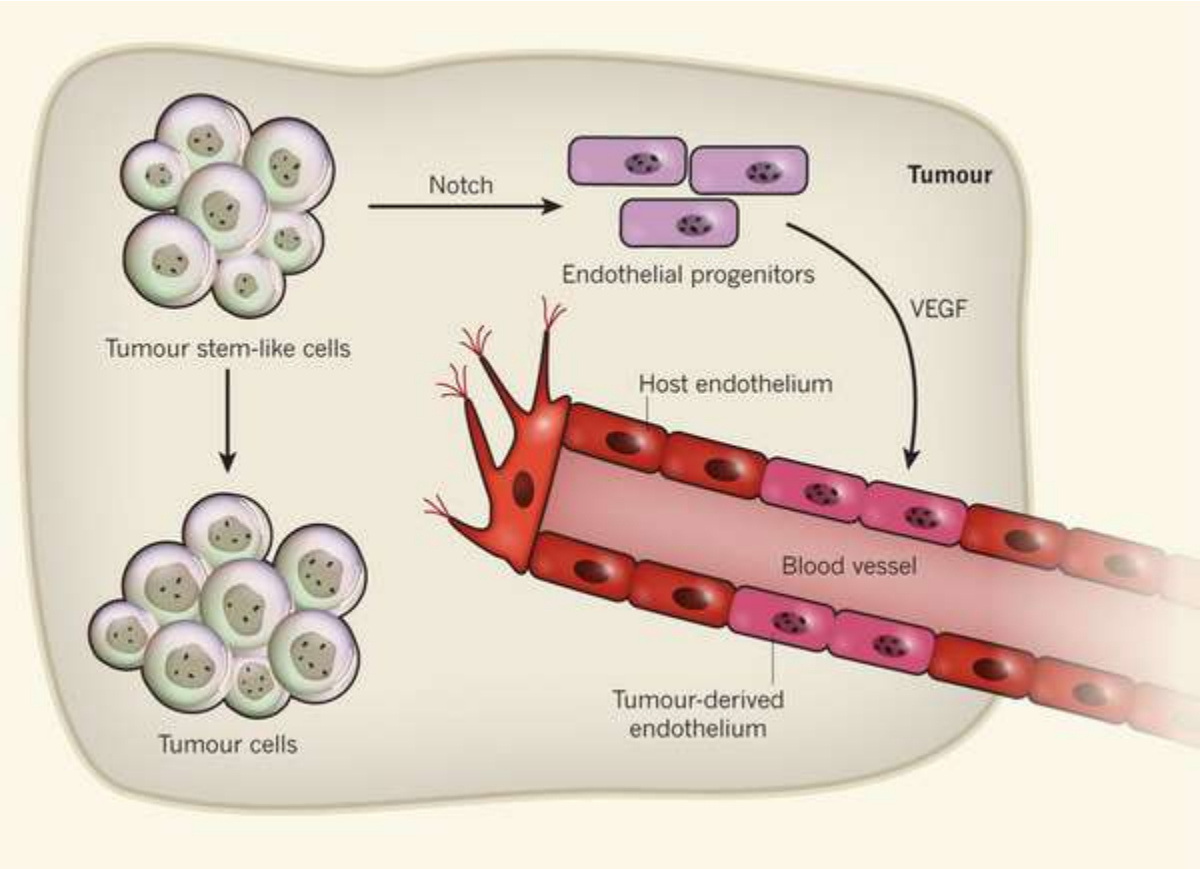
Blood vesscle (血管) in zebrafish (Fli:EGFP)



Angiogenesis （次级血管形成）in zebrafish



Angiogenesis and cancer



Blood vessel (血管) specification in zebrafish embryo

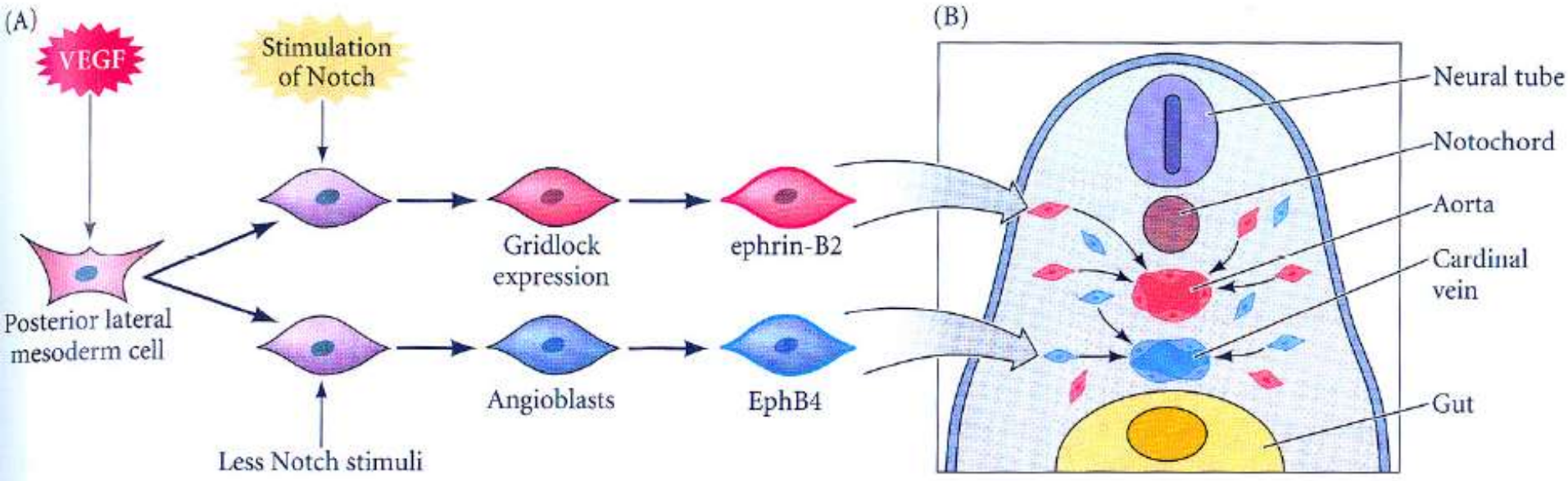


Figure 15.17
Blood vessel specification in the zebrafish embryo. (A) Angioblasts experiencing activation of Notch upregulate the Gridlock transcription factor. These cells express ephrin-B2 and become aorta cells. Those angioblasts experiencing significantly less Notch activation do not express Gridlock, and they become EphB4-expressing cells of the cardinal vein. (B) Once committed to forming veins or arteries, the cells migrate toward the midline of the embryo and contribute to forming the aorta or cardinal vein.

Notch signaling in wikipedia

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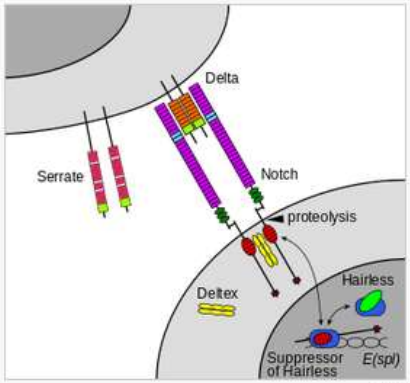
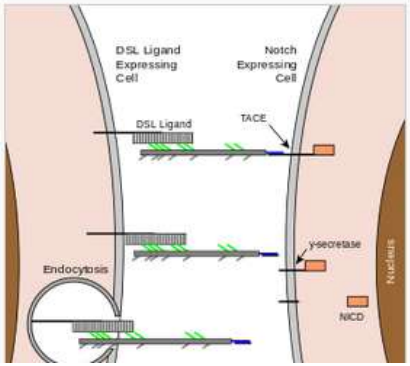


Notch-mediated juxtacrine signal between adjacent cells.



Blood cell formation

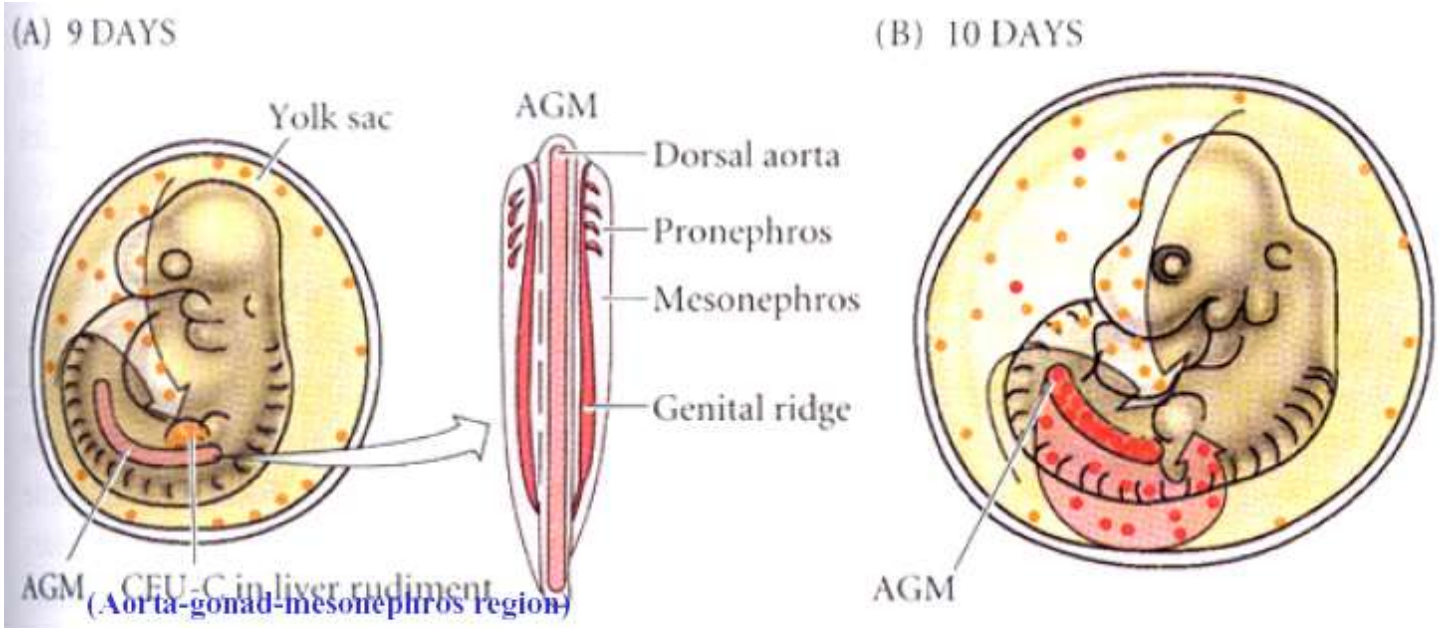
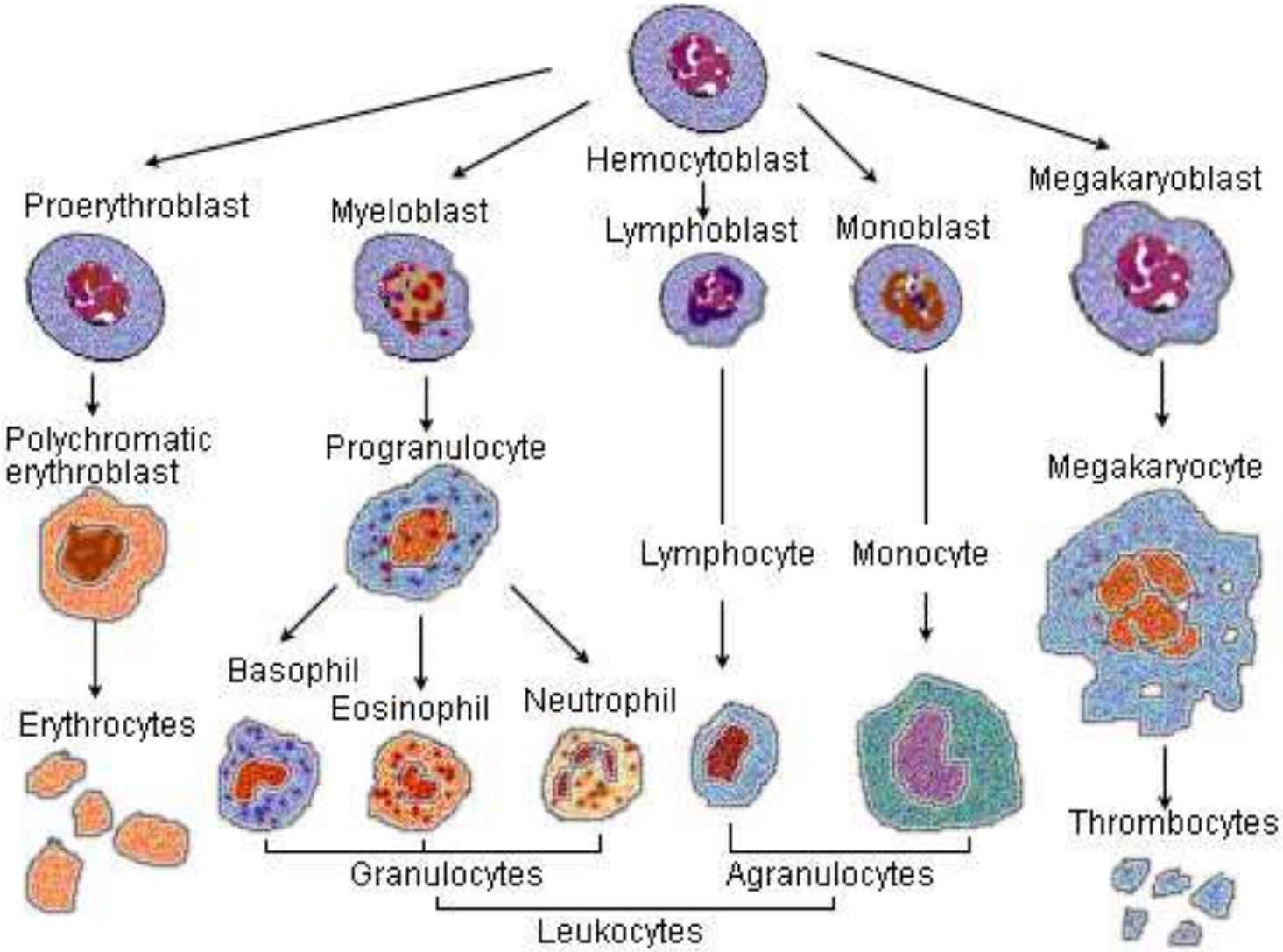


Figure 15.24
Colonization of the mouse liver by two waves of hematopoietic stem cells. The two main sources of hematopoietic progenitor cells are the yolk sac and the AGM region. (A) At day 9, the yolk sac contributes an early line of CFU-C cells that probably does not last long after birth, and which makes a population of predominantly red blood cells. This cell population is thought to be the major source of the first wave of hematopoiesis in the liver. (B) At day 10, the AGM-derived cells provide CFU-S cells and pluripotential hematopoietic stem cells. These constitute the major cells of the second wave. (After Dzierzak and Medvinsky 1995.)

哺乳动物造血器官：胚胎卵黄囊→胎儿**AGM**→成年个体骨髓和脾脏。

鱼类造血器官：胚胎**ICM**→成年肾脏。

Blood cell lineage



summary

- Key word:

  heart field, heart tube, looping, Vasculogenesis, Angiogenesis, VEGF,

- Event and mechanism

  heart formation, blood cell formation

outline

- Ectoderm

  1) neural tube formation and differentiation

  2) eye development

- Mesoderm

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  2) intermediate mesoderm: kidney

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- Endoderm

  gut, lung