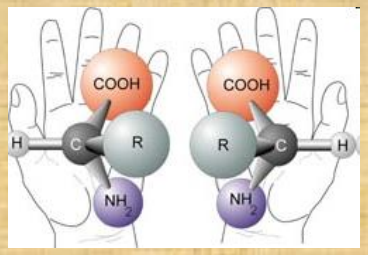
脊椎动物器官左右不对称发育的分子机制

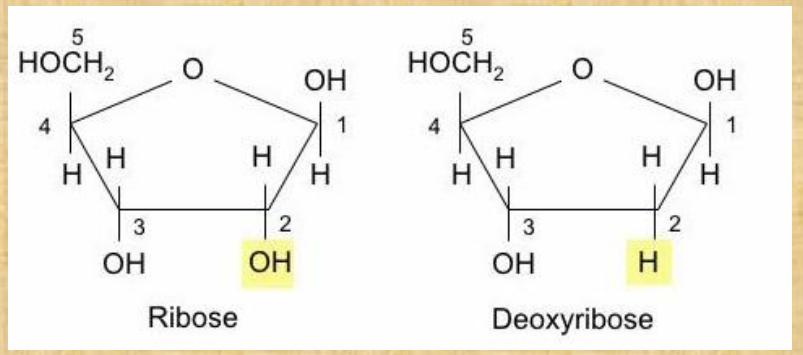
舒晓东

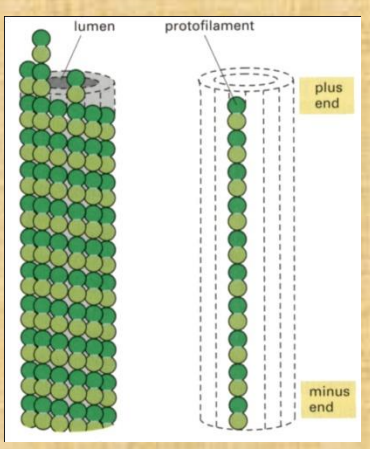
中国科学院广州生物医药与健康研究院

分子水平的手性

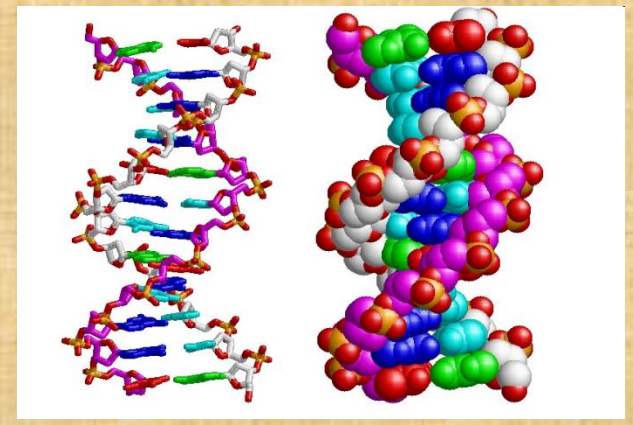


Amino acid





Microtubule



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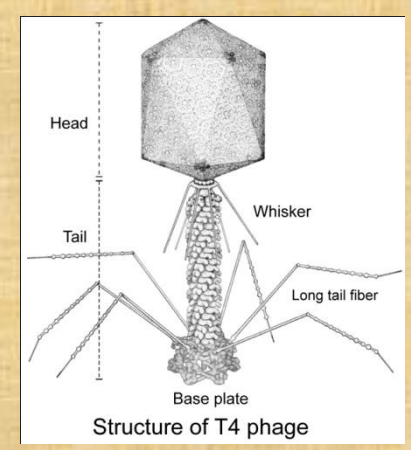


Phage

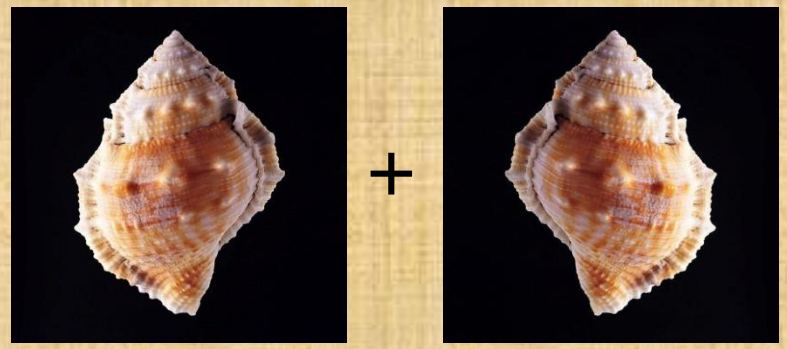
生物个体/器官水平的不对称性



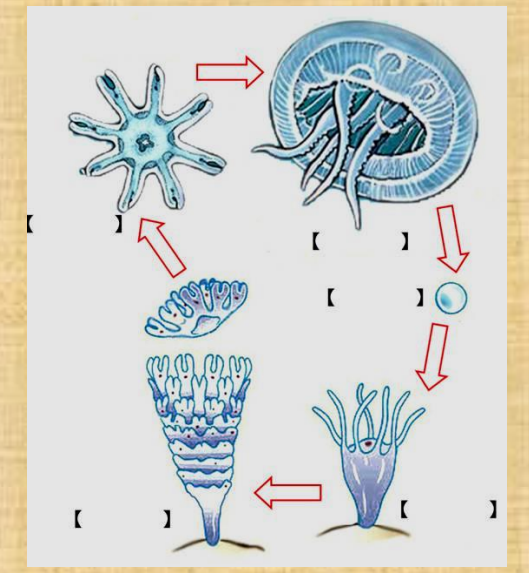


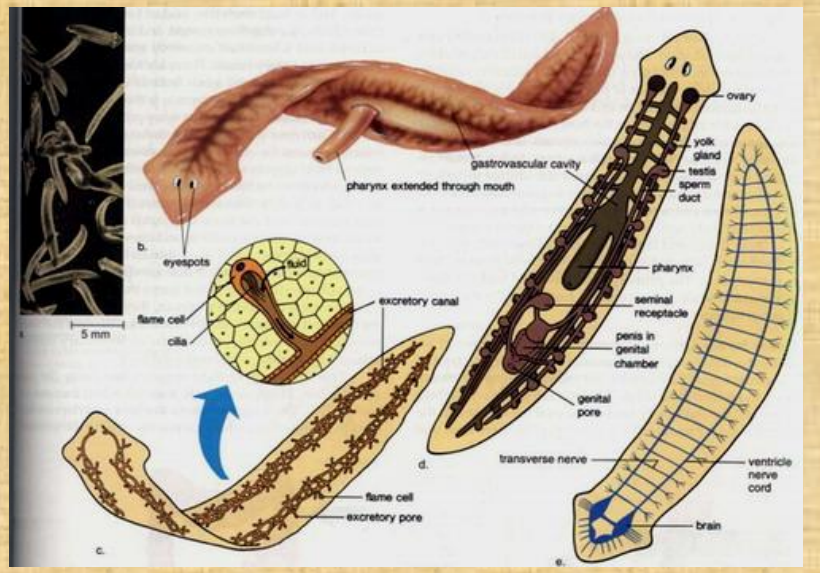

Directionally asymmetric:

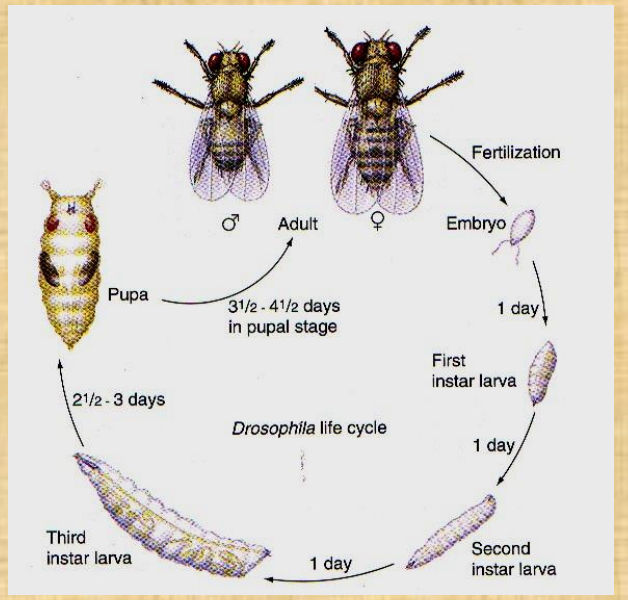
Randomly asymmetric (antisymmetric):

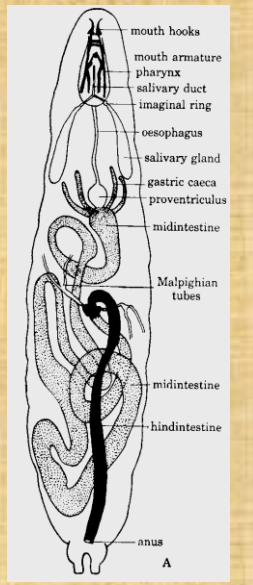


无脊椎动物左右体轴的对称性问题

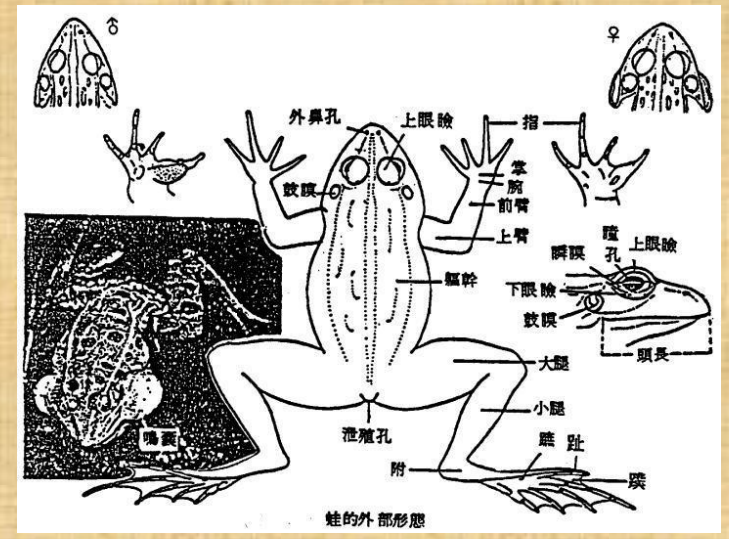




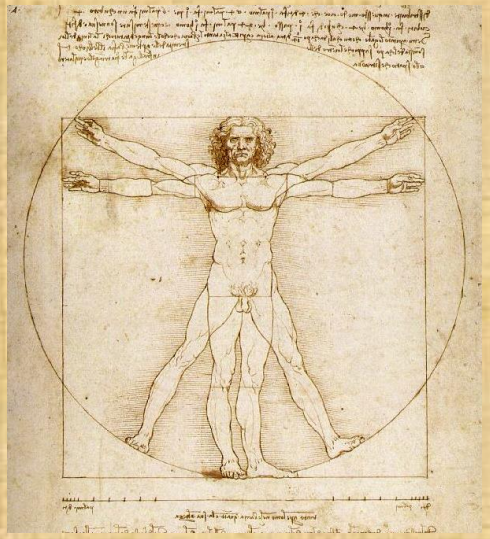


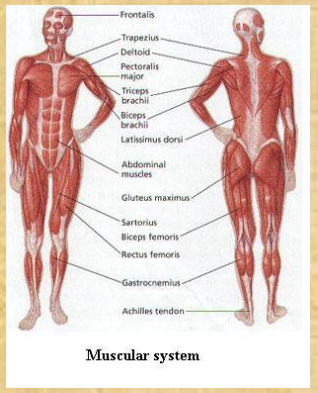


脊椎动物左右体轴的对称性问题

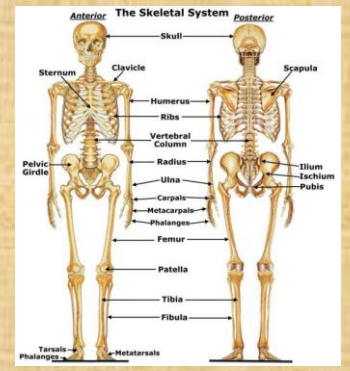


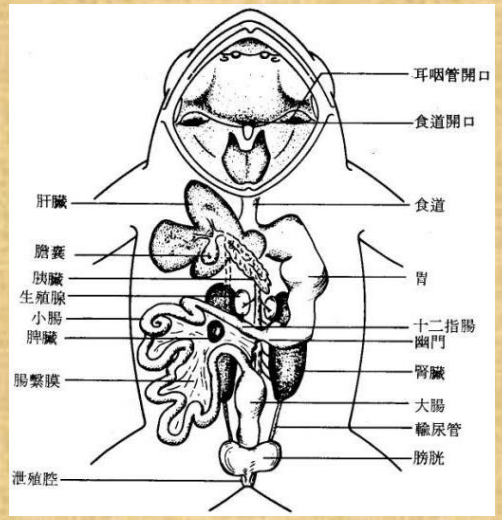
蛙的外部形態

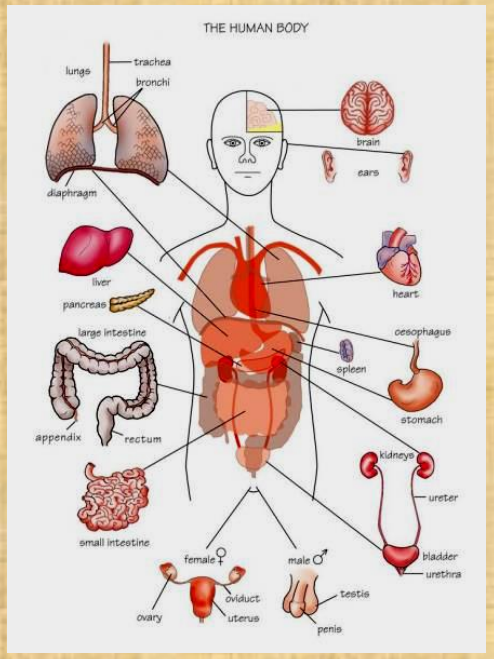


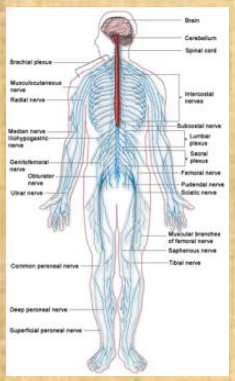


Muscular system









内脏器官左右不对称的几个特征

- 在群体中不是随机分布的，且在代与代之间可稳定遗传；

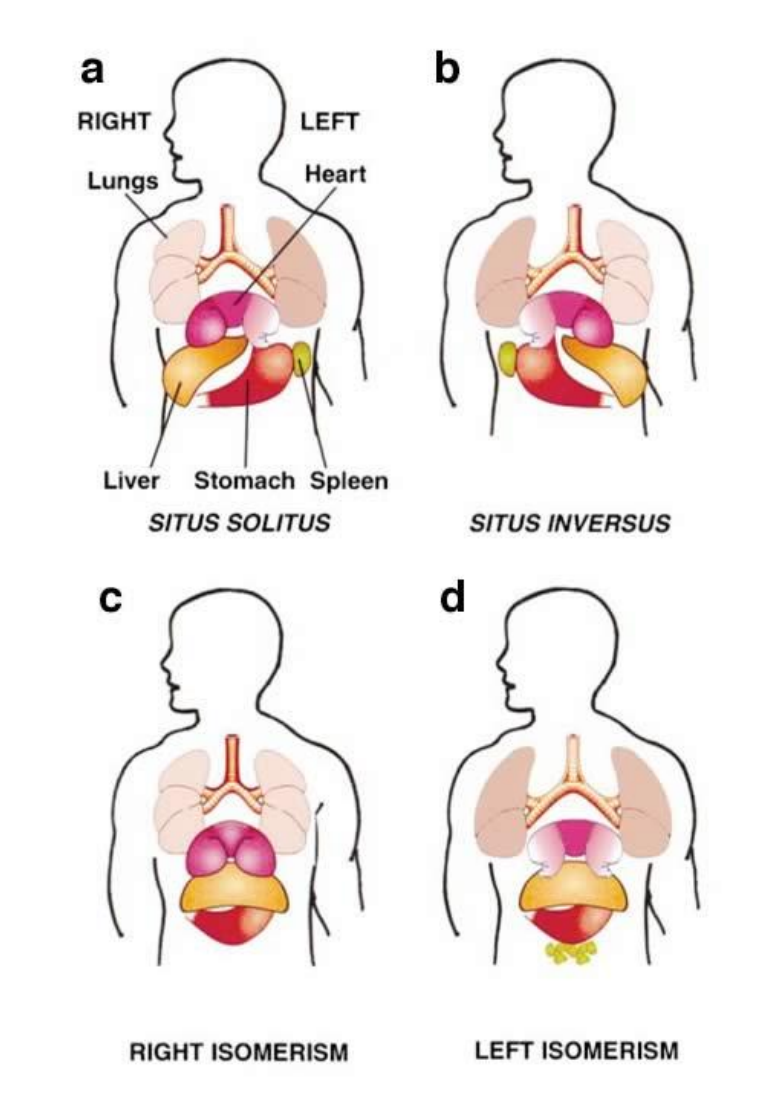
  ---受基因控制？

- 全部器官体位的反转通常不会引起明显的生理缺陷；

  ---左右不对称与进化的关系？

- 器官水平左右不对称的缺陷通常是致病的。

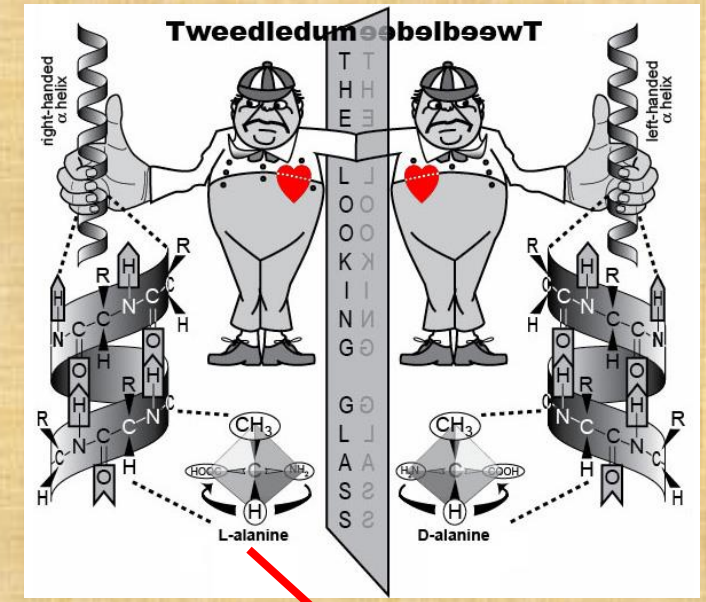
  ---医学问题

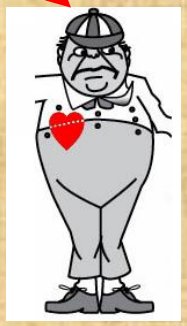


如何进行器官左右不对称的研究？

- 分子的手性与器官作用不对称性的关系：

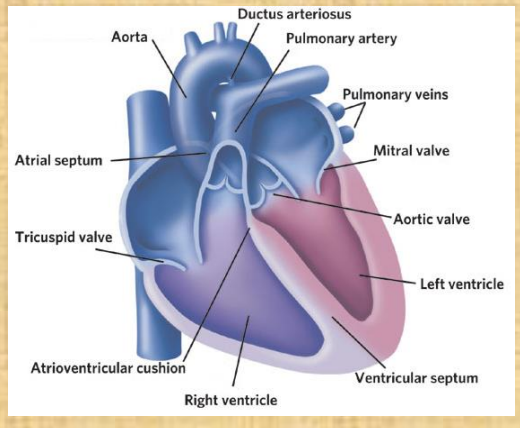
---非决定性的？



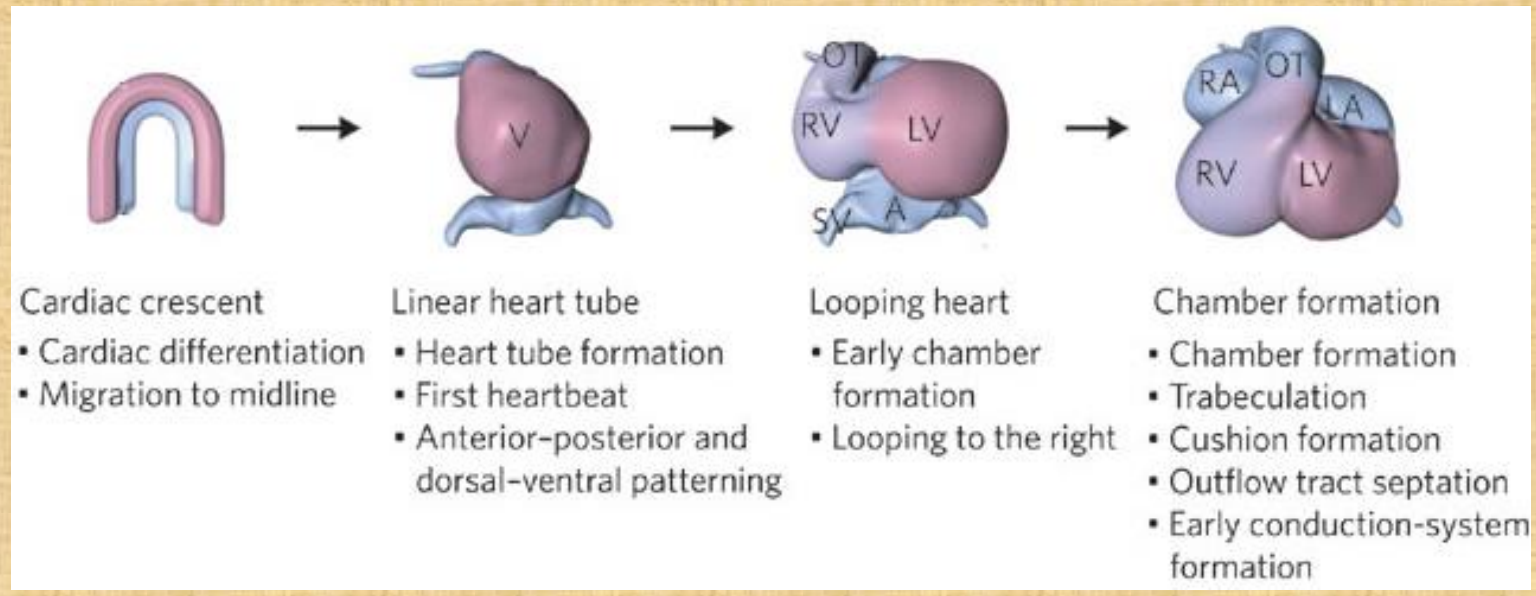


如何进行器官左右不对称的研究？

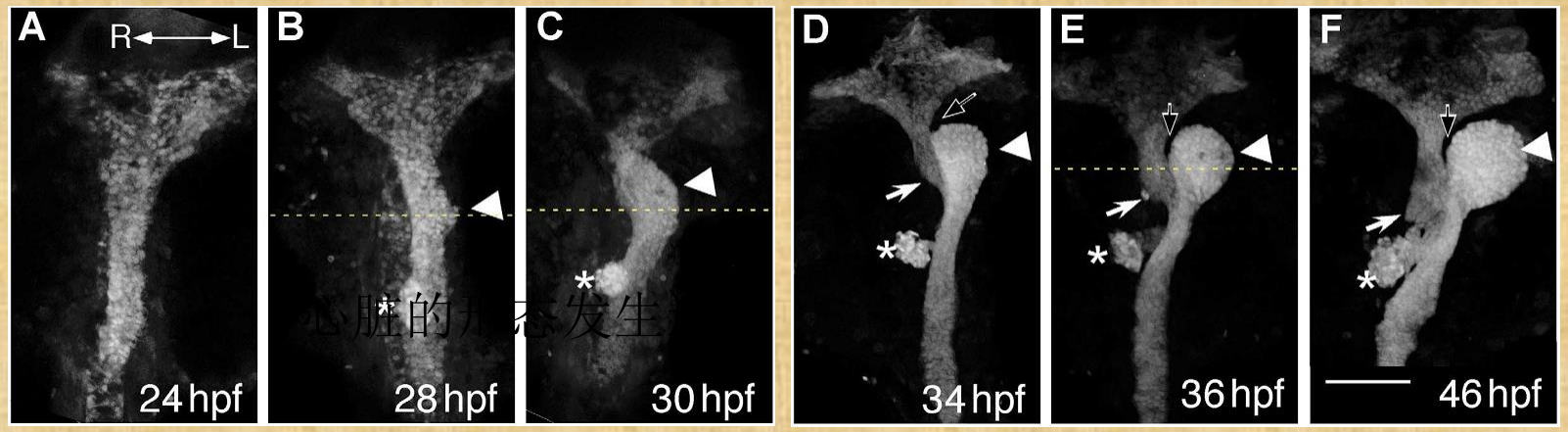
- 从形态发育方面研究特定器官不对称发生的过程：



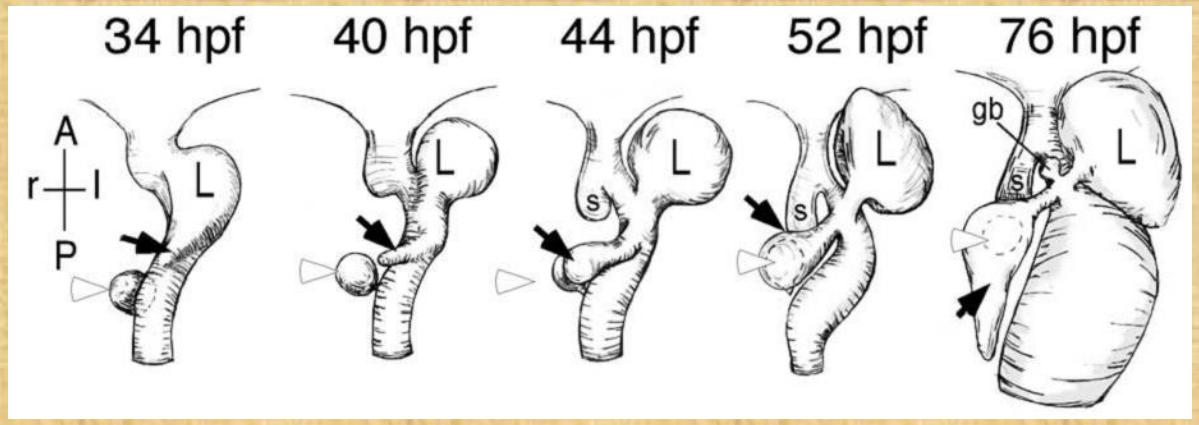
心脏的形态发生过程



内胚层器官（肝脏、胰腺、小肠）的形态发生：



心脏的形态发生



适合：阐明特定器官形态发生的过程；

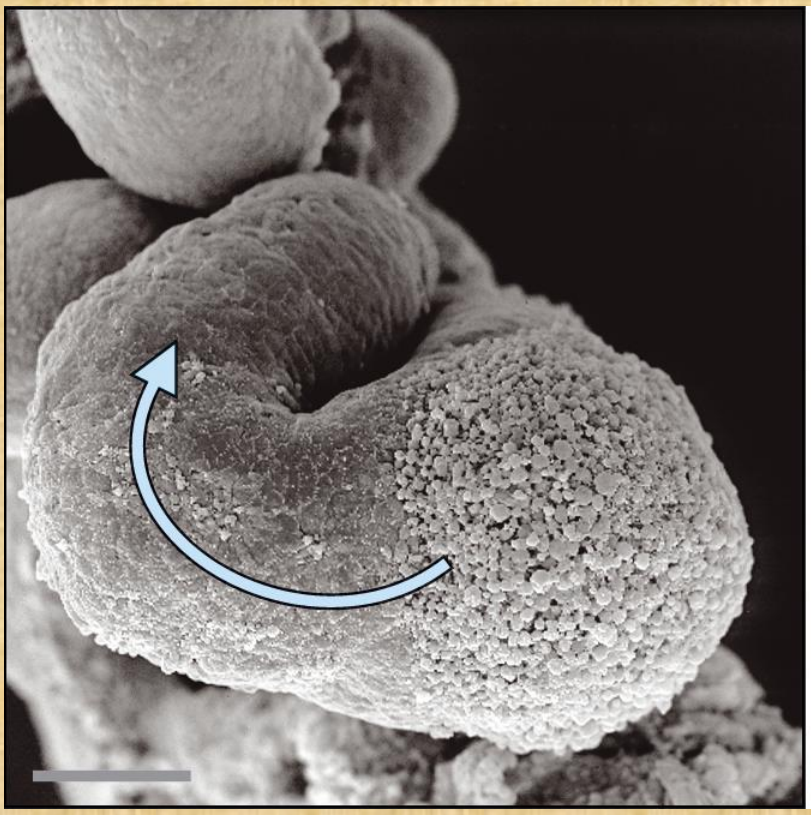
比较不同物种中该过程的保守性。

不适合：阐明该过程的调控机制。

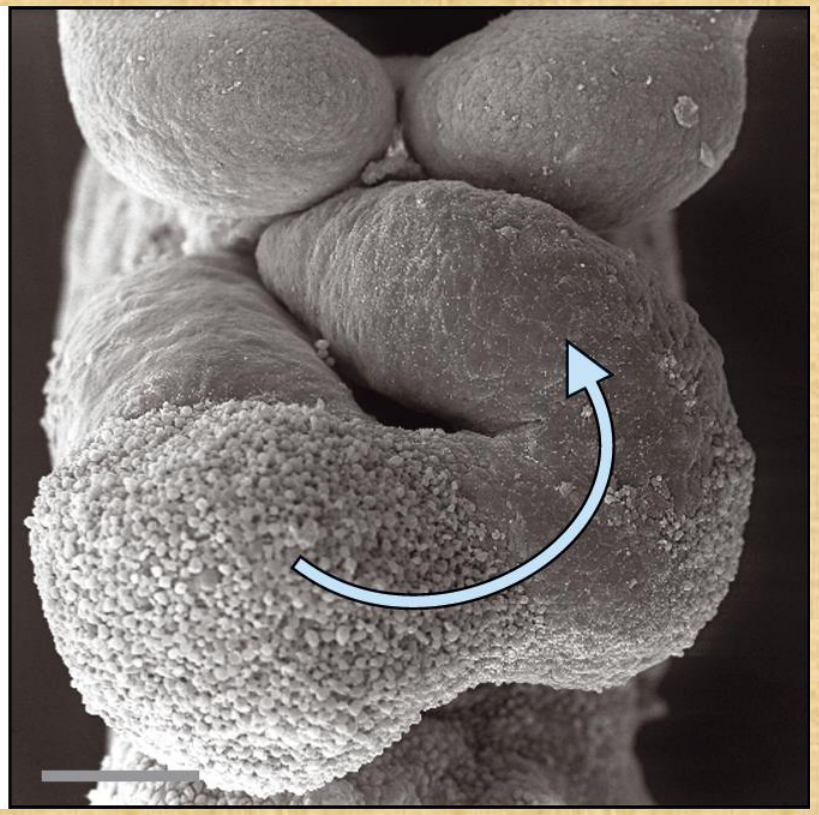
如何进行器官左右不对称的研究？

- 基于发育遗传学的研究：
  - 从具有器官不对称发育缺陷的突变体中鉴定出调控该过程的基因；
  - 鉴定左右不对称表达的基因及其相关的信号传导通路；
  - 研究上述基因在相应器官形成过程中的作用机制；
  - 分析上述信号传导通路在不同物种中的保守性。

Left-right asymmetry of the mouse heart is under genetic control



WT



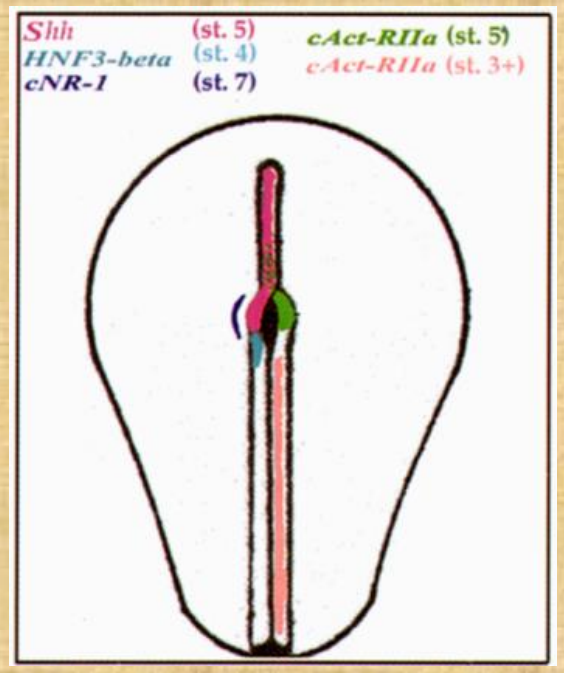
iv

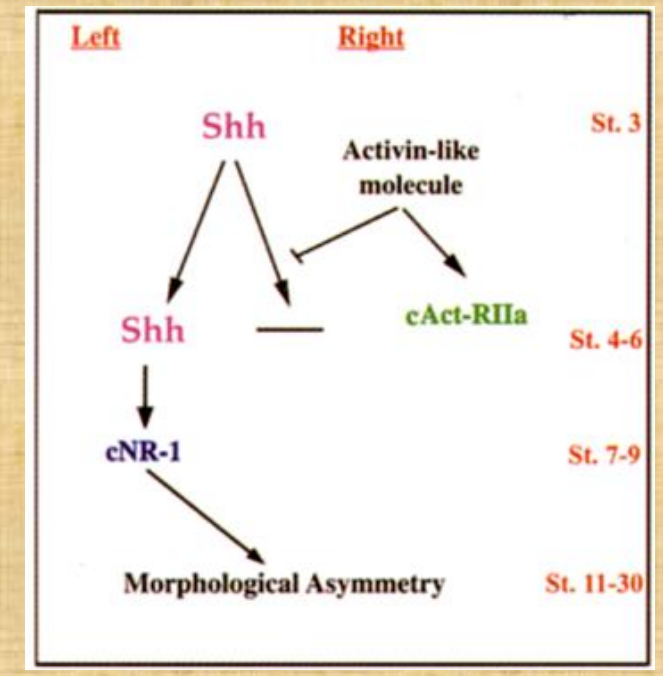
左右不对称基因表达的发现

Cell, Vol. 82, 803–814, September 8, 1995, Copyright © 1995 by Cell Press

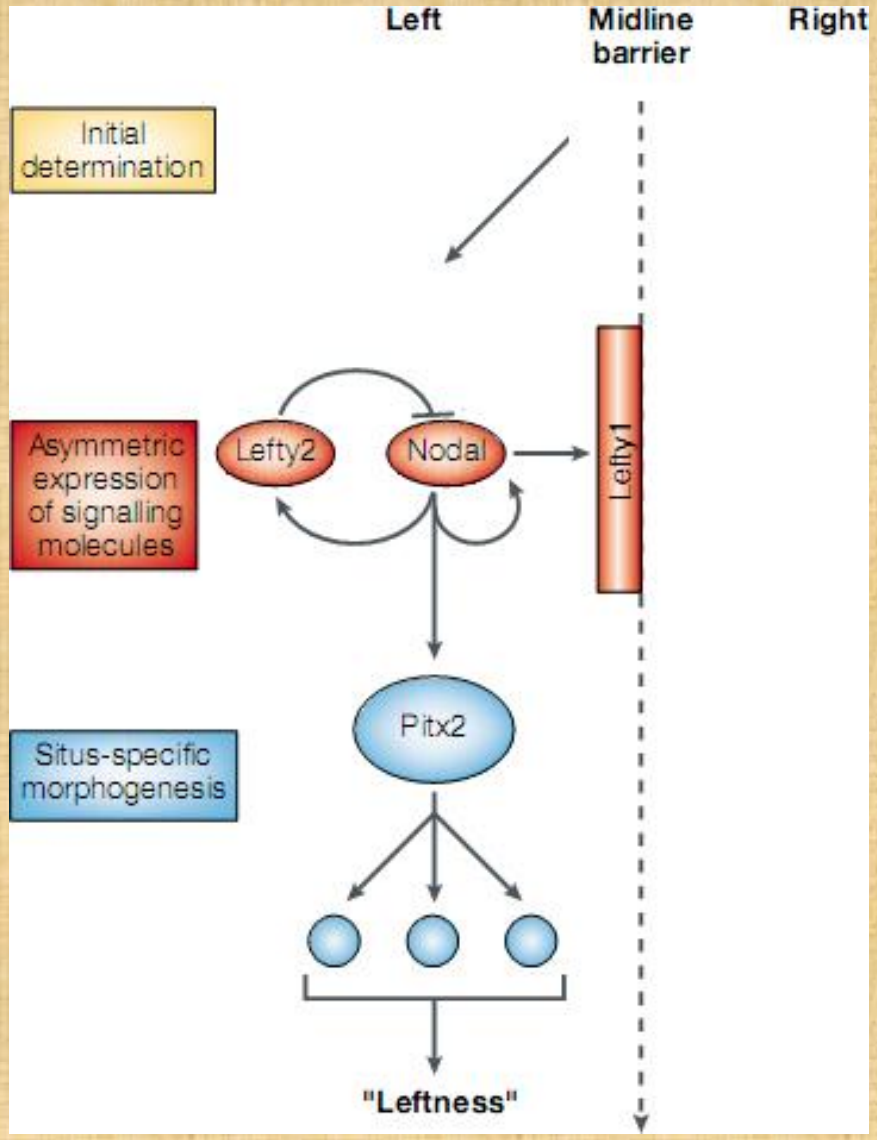
A Molecular Pathway Determining Left-Right Asymmetry in Chick Embryogenesis

Michael Levin,* Randy L. Johnson,*
Claudio D. Stern,† Michael Kuehn,‡
and Cliff Tabin*

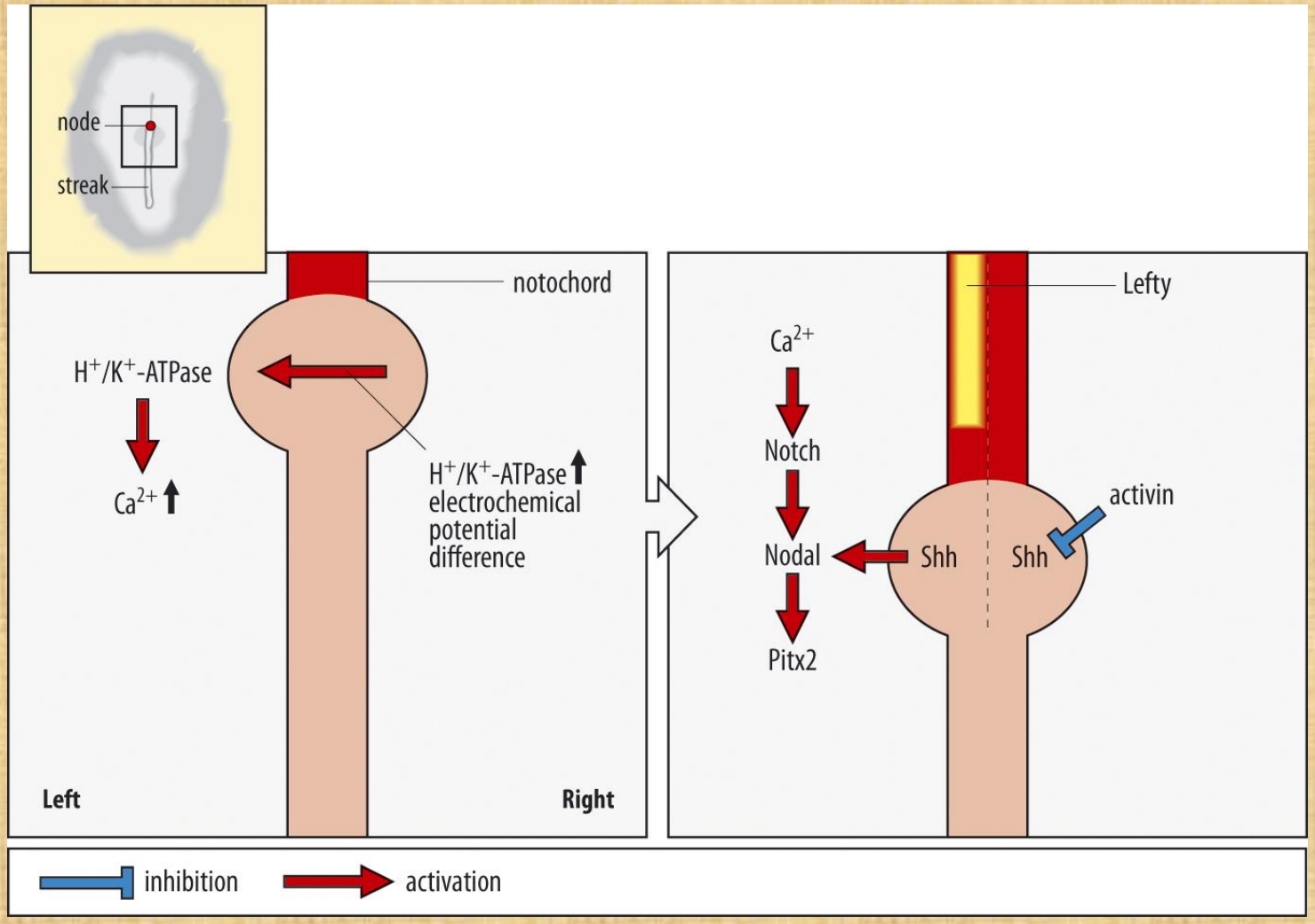




各物种中保守的不对称基因表达模式



Determination of left-right asymmetry in the chick

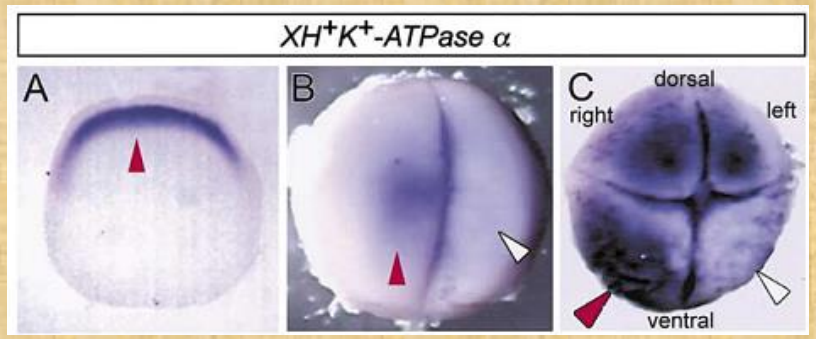


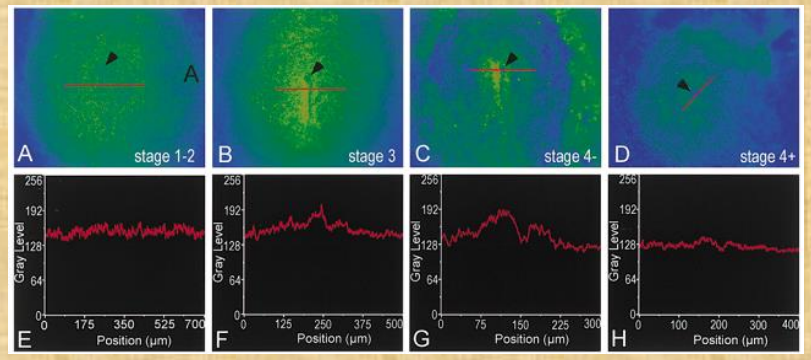
爪蛙胚胎发育中最早的左右不对称事件

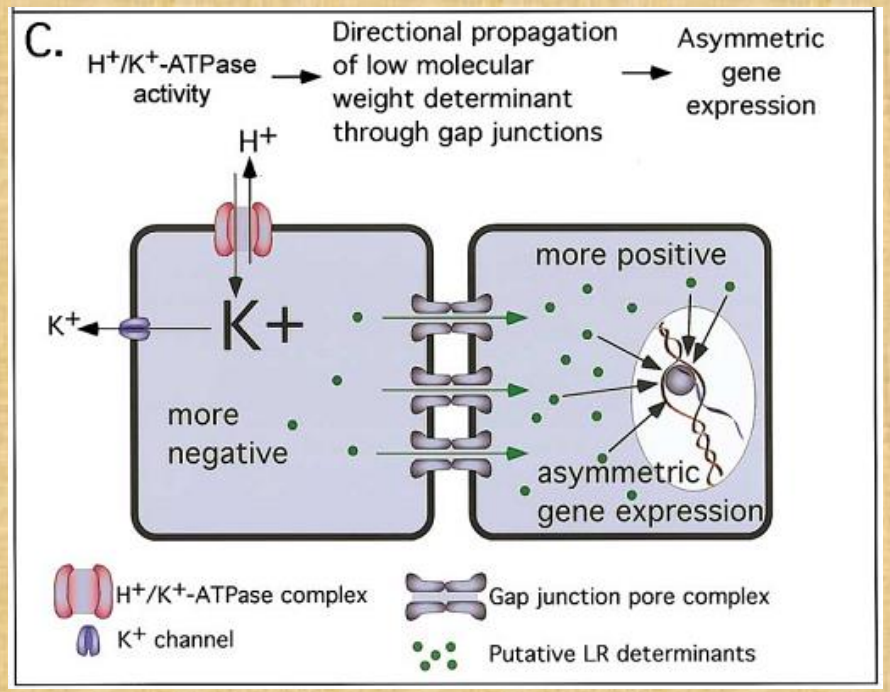
Cell, Vol. 111, 77–89, October 4, 2002, Copyright ©2002 by Cell Press

Asymmetries in H^+/K^+-ATPase and Cell Membrane Potentials Comprise a Very Early Step in Left-Right Patterning

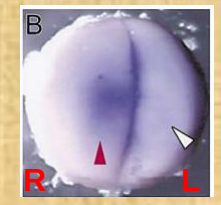
Michael Levin,[1,2] Thorleif Thorlin,[3,4]
Kenneth R. Robinson,[4] Taisaku Nogi,[2]
and Mark Mercola[1,5,6]



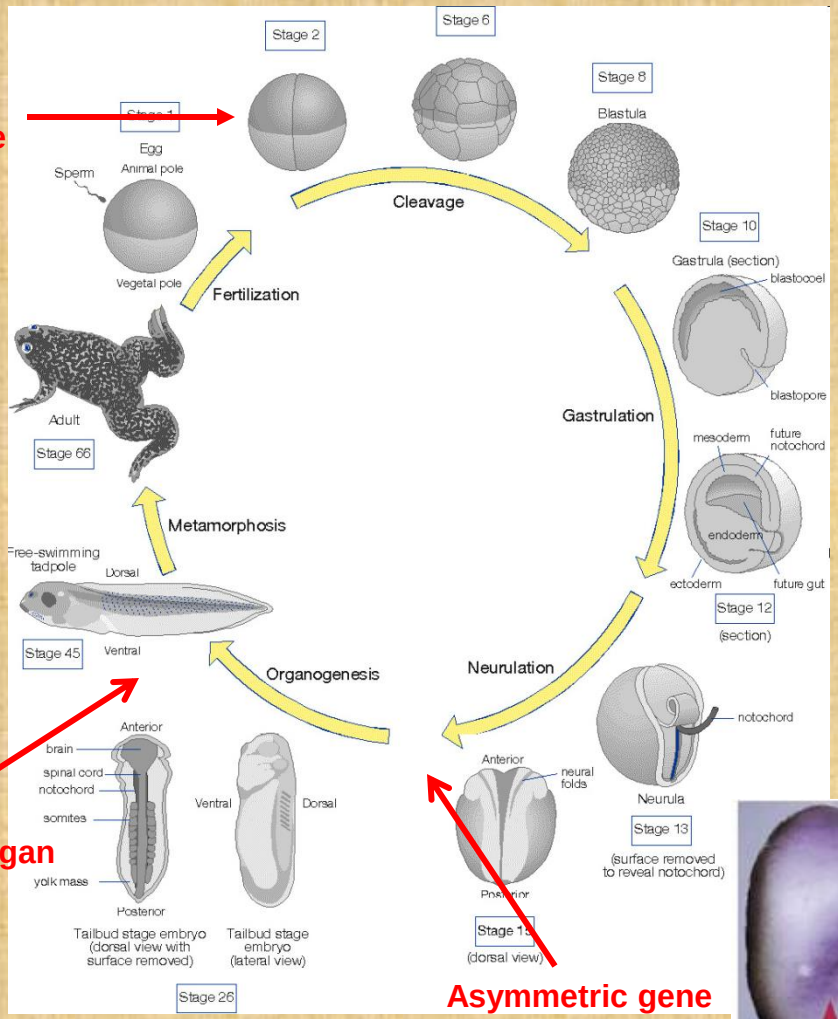




爪蛙胚胎左右不对称发育的几个关键点

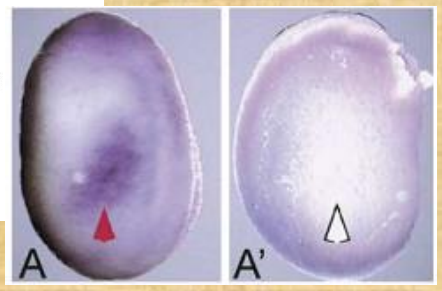


Asymmetric H^+/K^+-ATPase

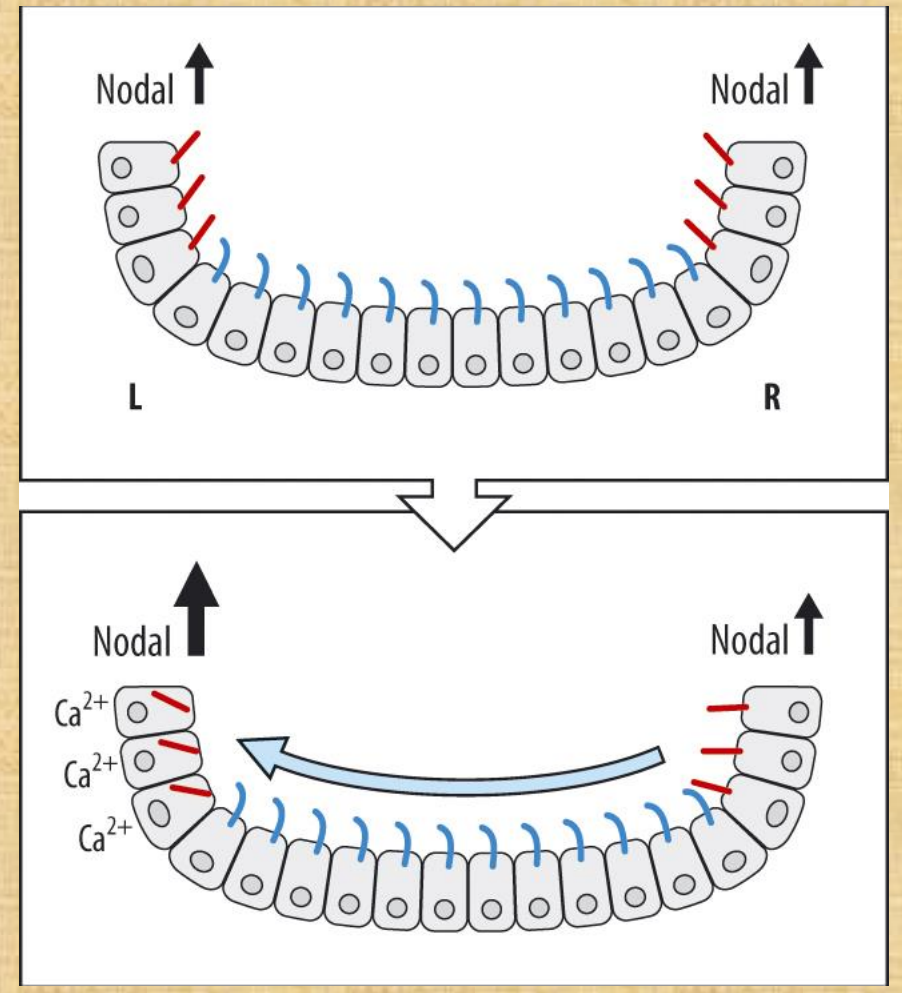


Asymmetric organ formation

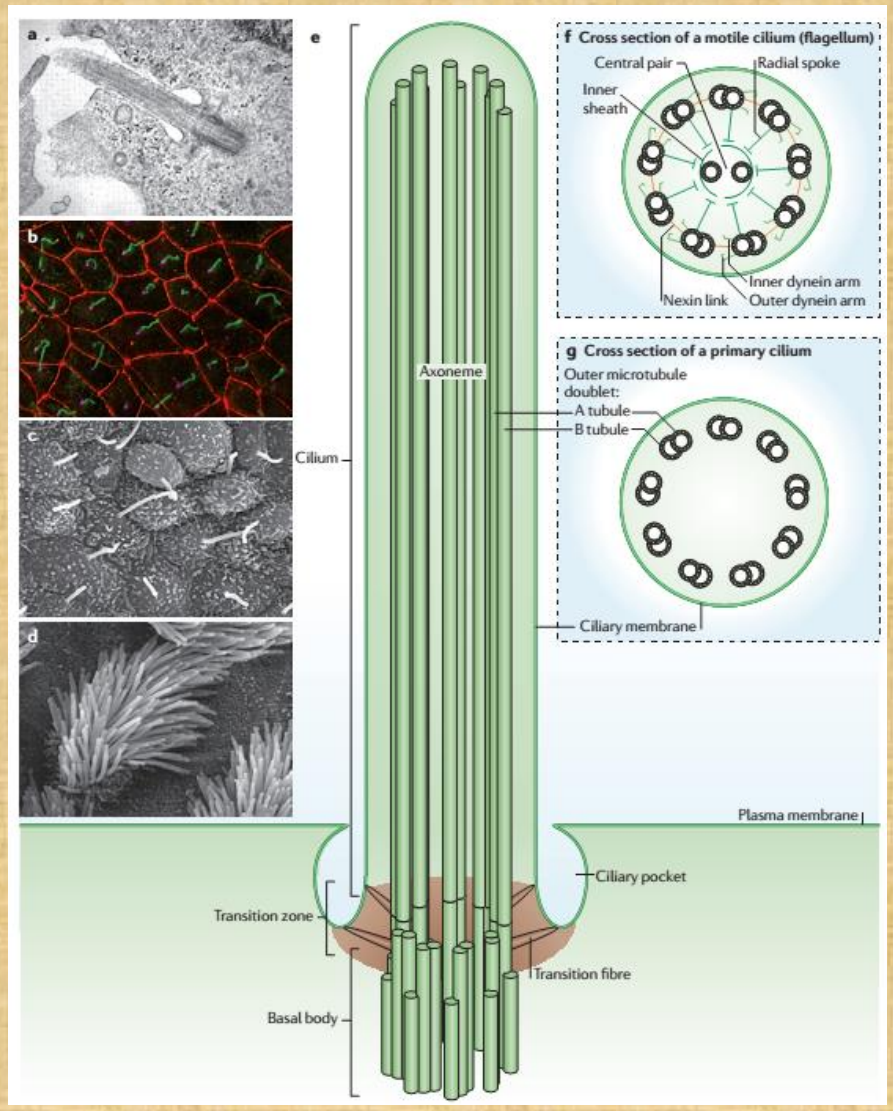
Asymmetric gene expression

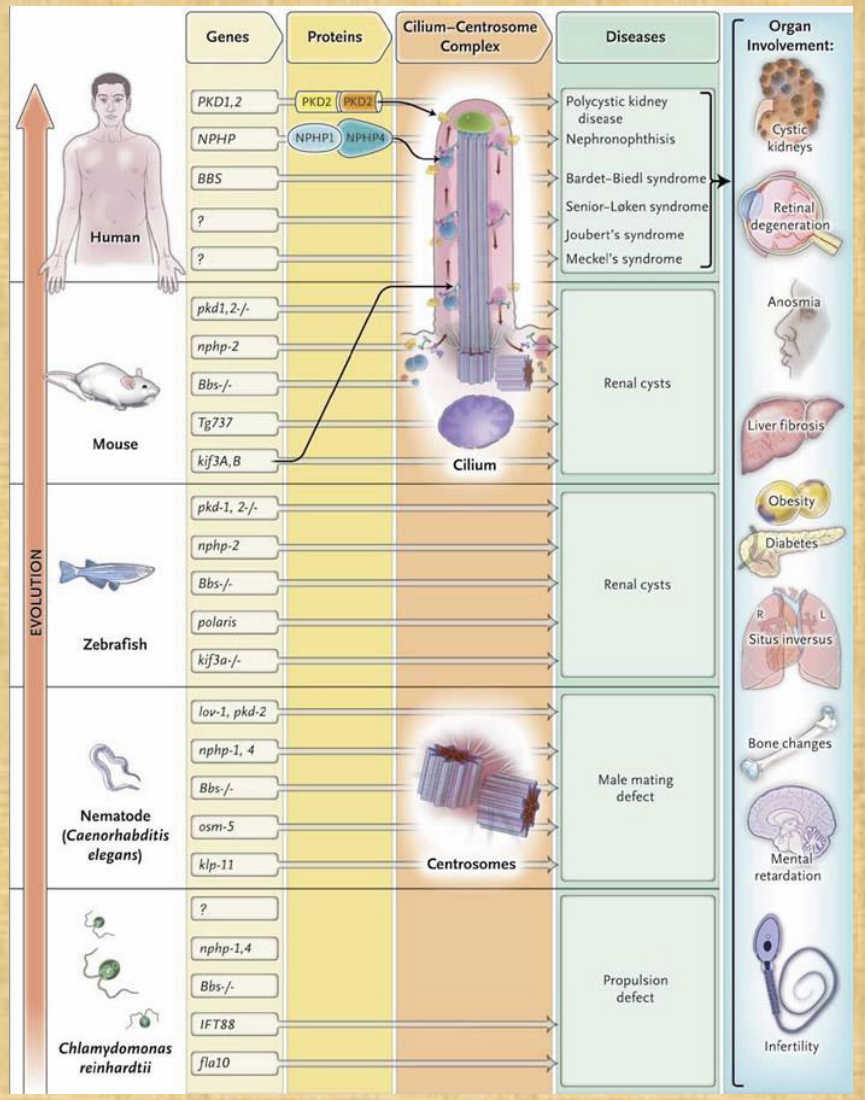


Leftward flow of extracellular fluid generates left-right asymmetry



纤毛的结构及与纤毛相关的人类疾病



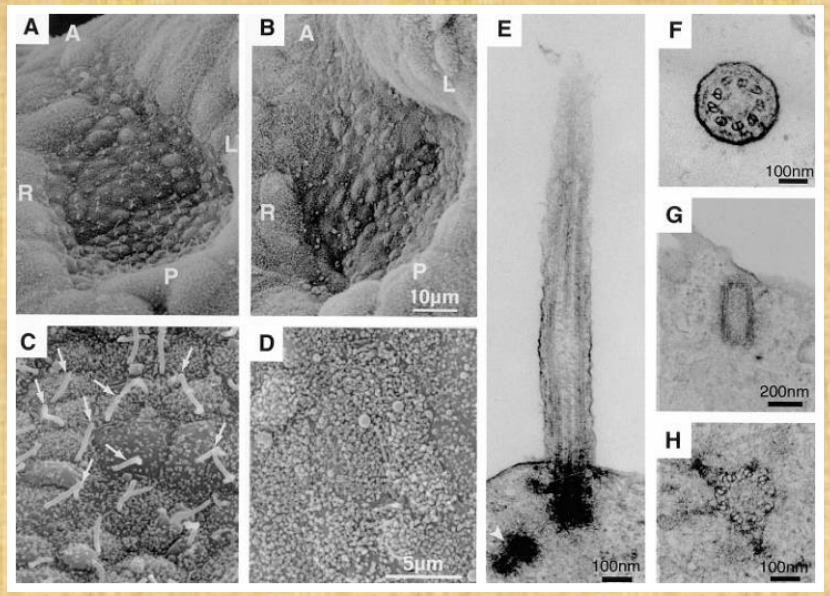


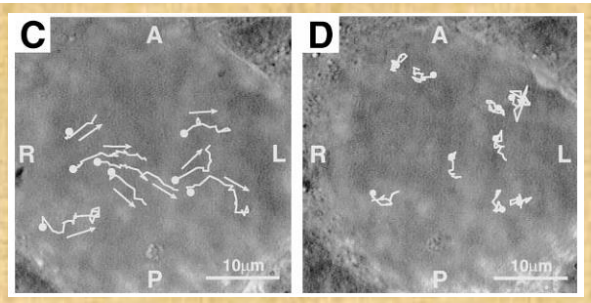
小鼠胚胎发育中左右不对称的发生机制

Cell, Vol. 95, 829–837, December 11, 1998, Copyright ©1998 by Cell Press

Randomization of Left–Right Asymmetry due to Loss of Nodal Cilia Generating Leftward Flow of Extraembryonic Fluid in Mice Lacking KIF3B Motor Protein

Shigenori Nonaka, Yosuke Tanaka,
Yasushi Okada, Sen Takeda,
Akihiro Harada, Yoshimitsu Kanai,
Mizuho Kido, and Nobutaka Hirokawa*

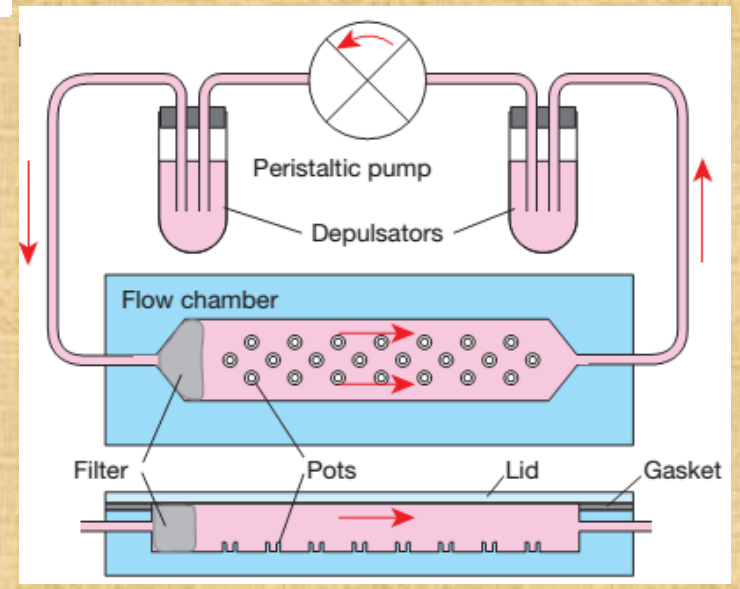


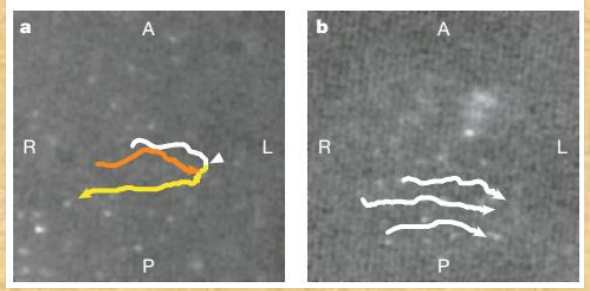


NATURE | VOL 418 | 4 JULY 2002 | www.nature.com/nature

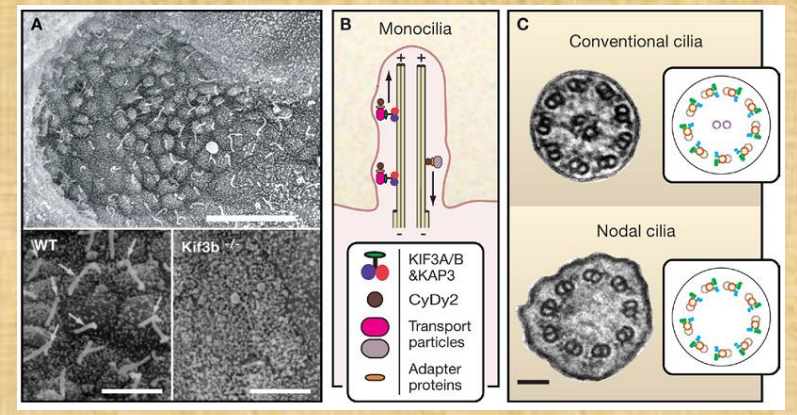
Determination of left–right patterning of the mouse embryo by artificial nodal flow

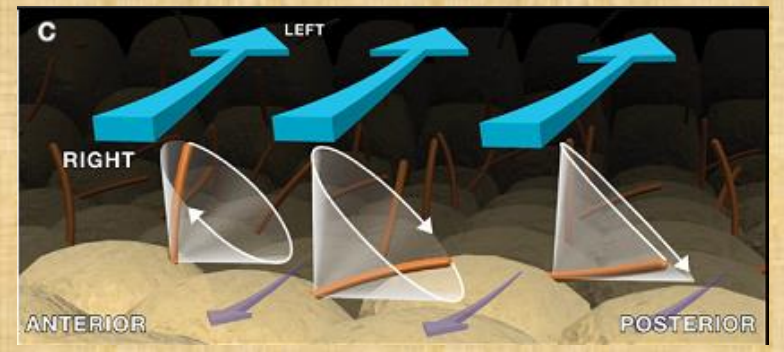
Shigenori Nonaka, Hidetaka Shiratori, Yukio Saijoh & Hiroshi Hamada





小鼠左右不对称器官发育的模型





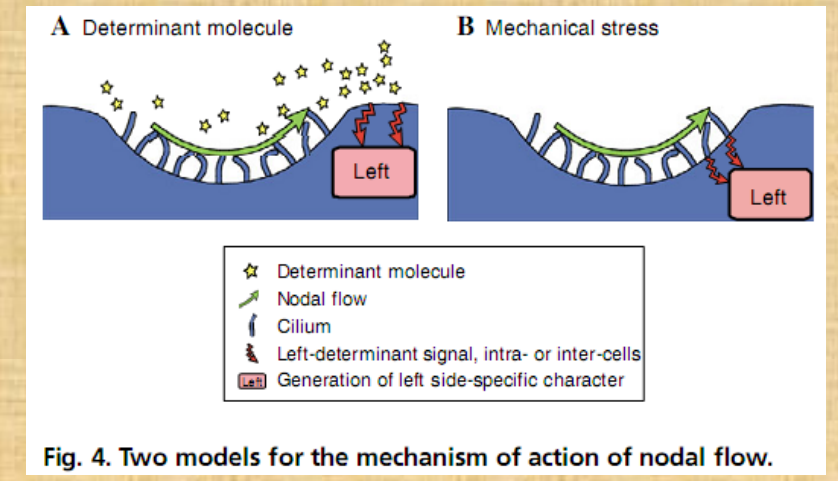
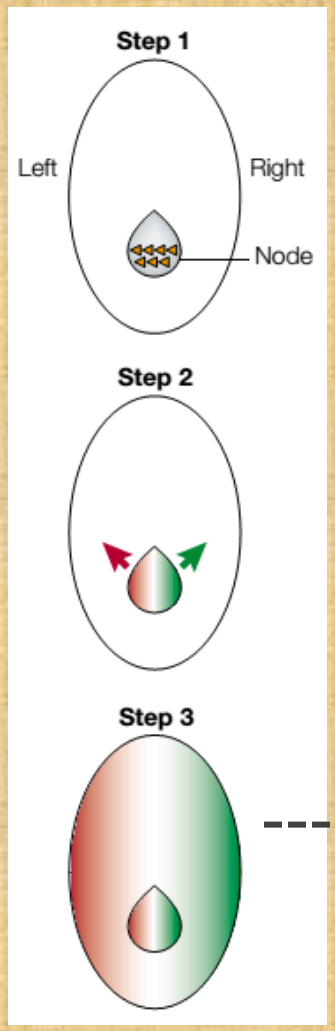
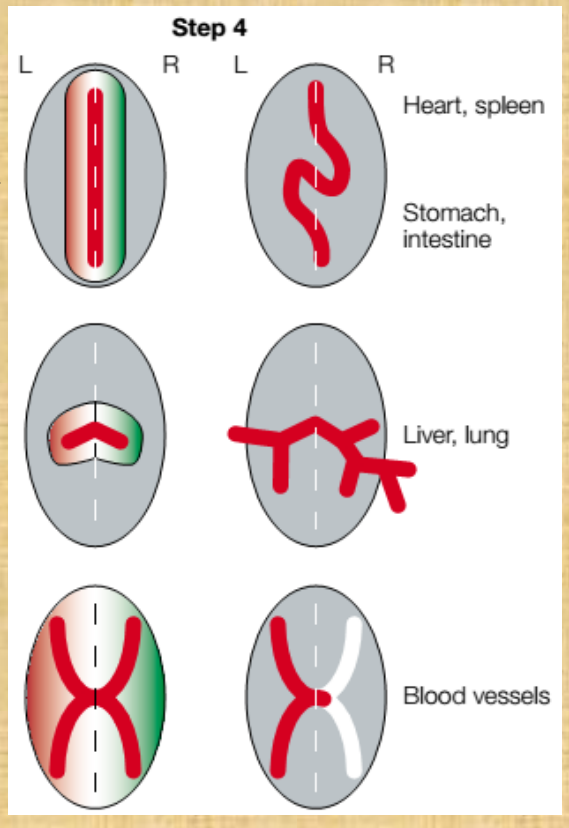
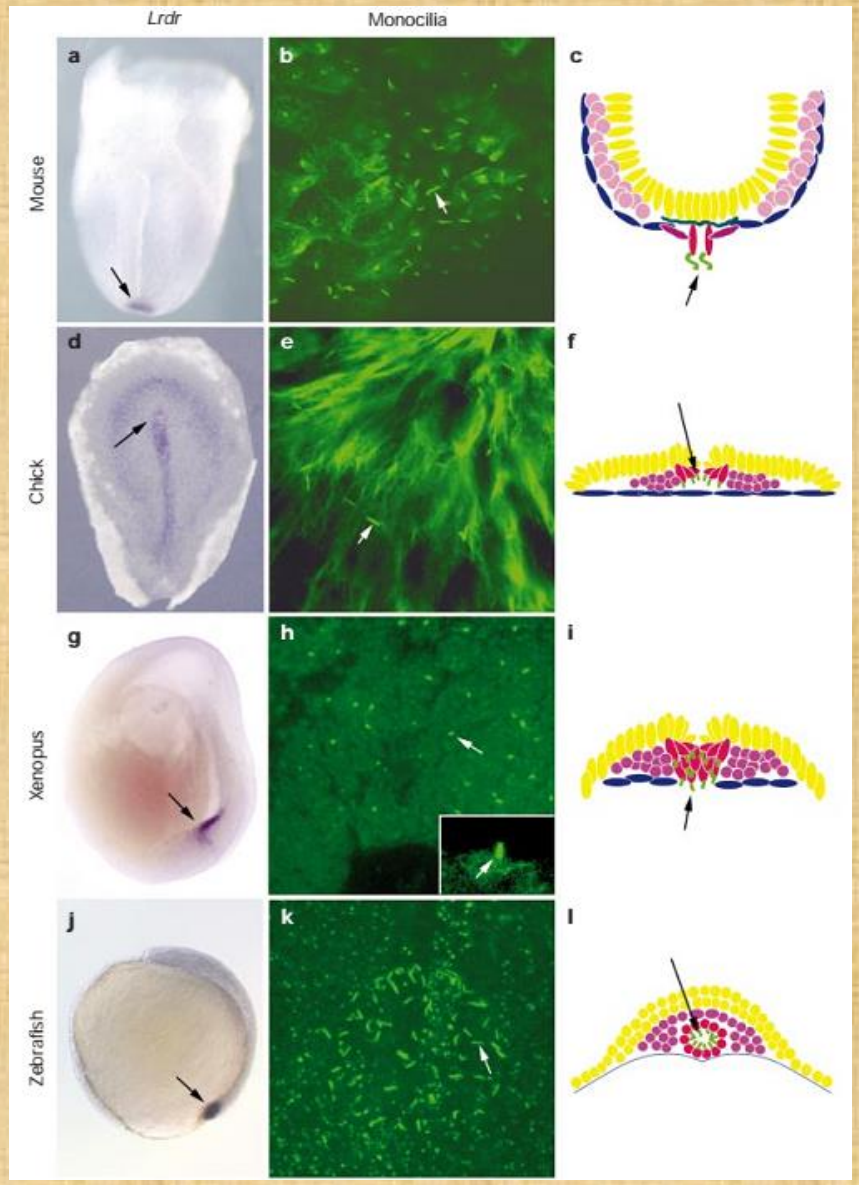


Fig. 4. Two models for the mechanism of action of nodal flow.





纤毛在各种脊椎动物Node中的分布



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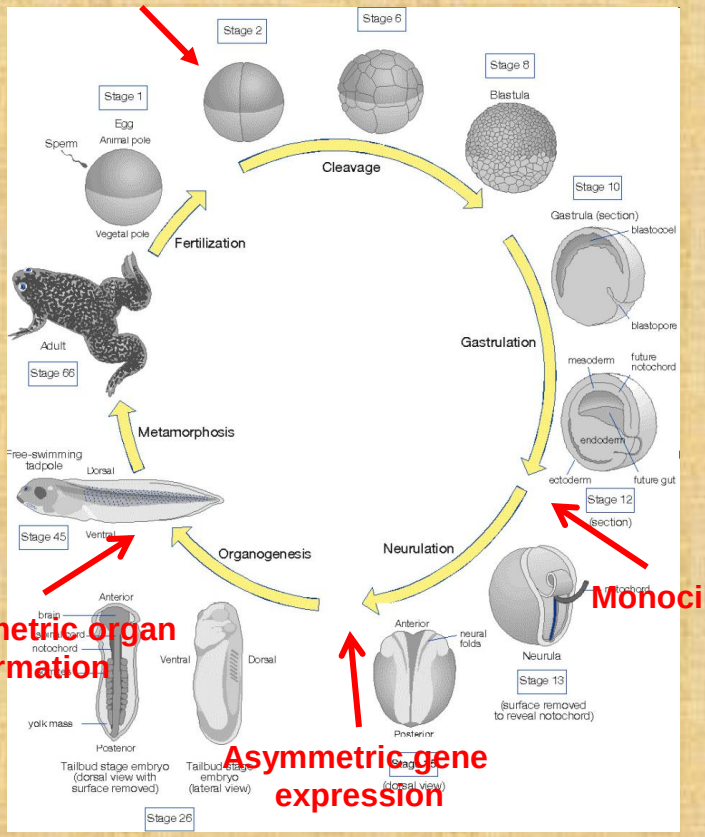
Asymmetric H^+/K^+-ATPase

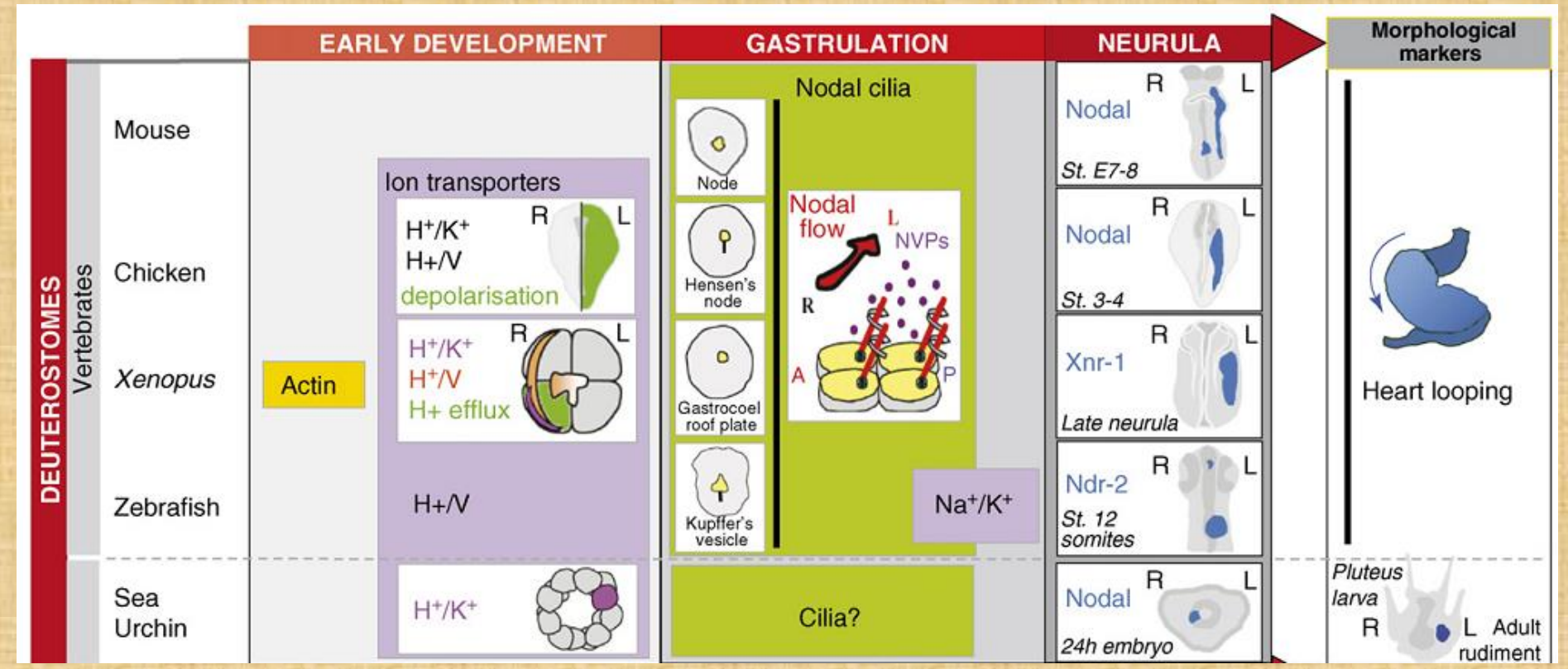


Asymmetric organ formation

Monocilia

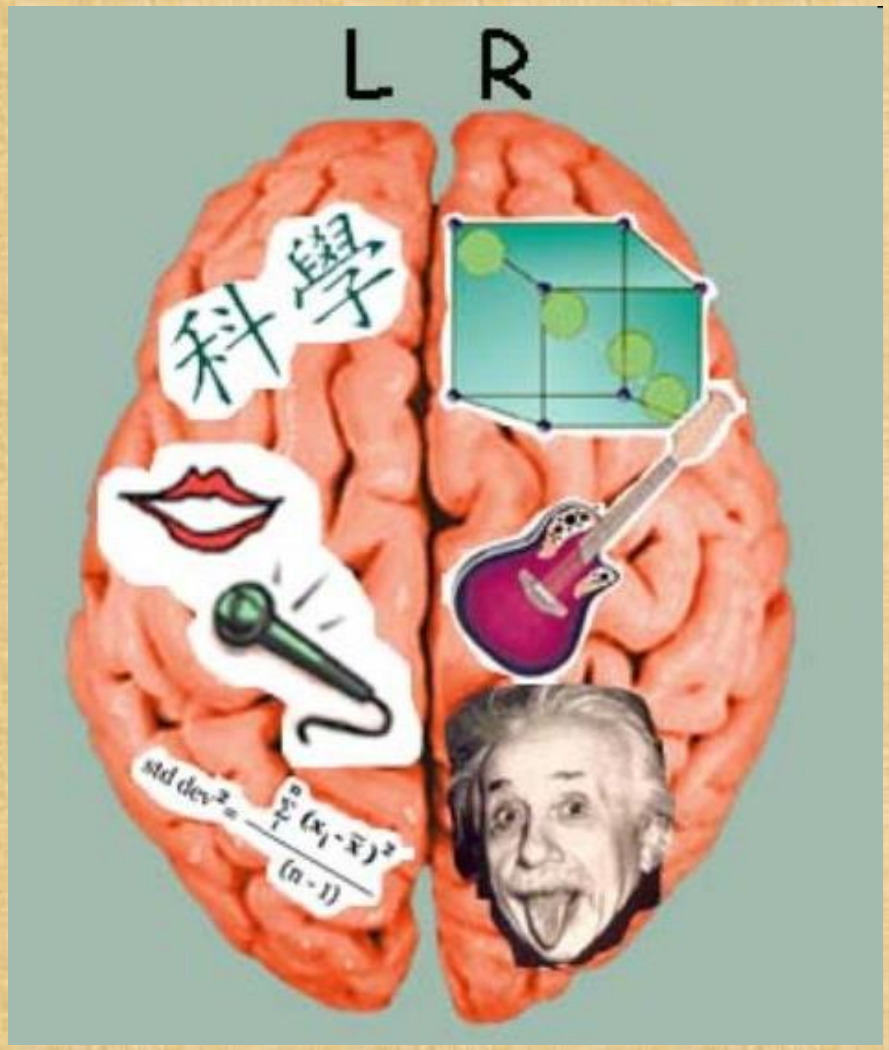
Asymmetric gene expression

脊椎动物作用不对称器官发育的比较

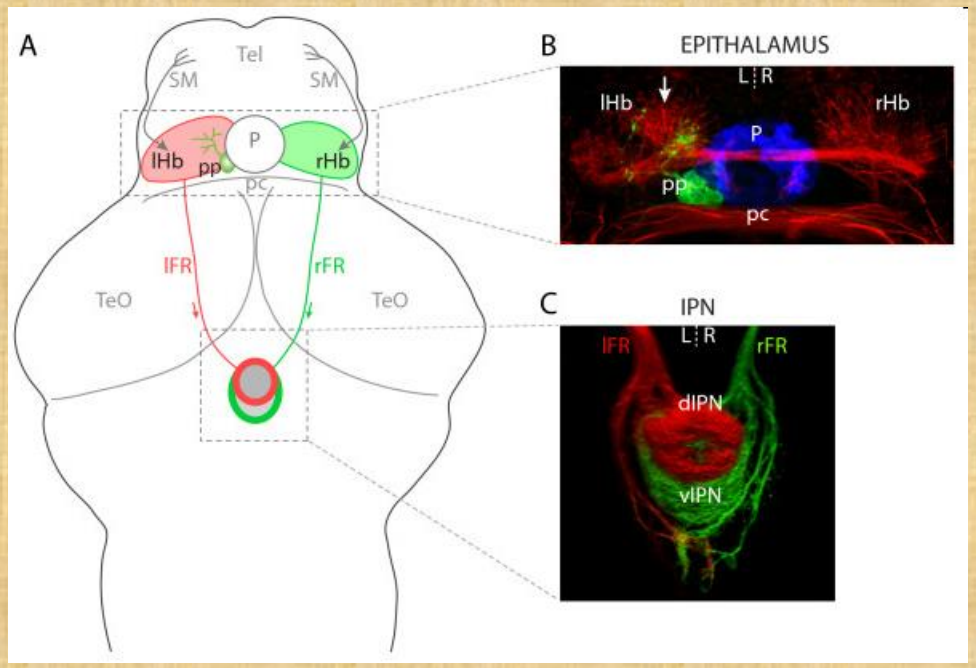


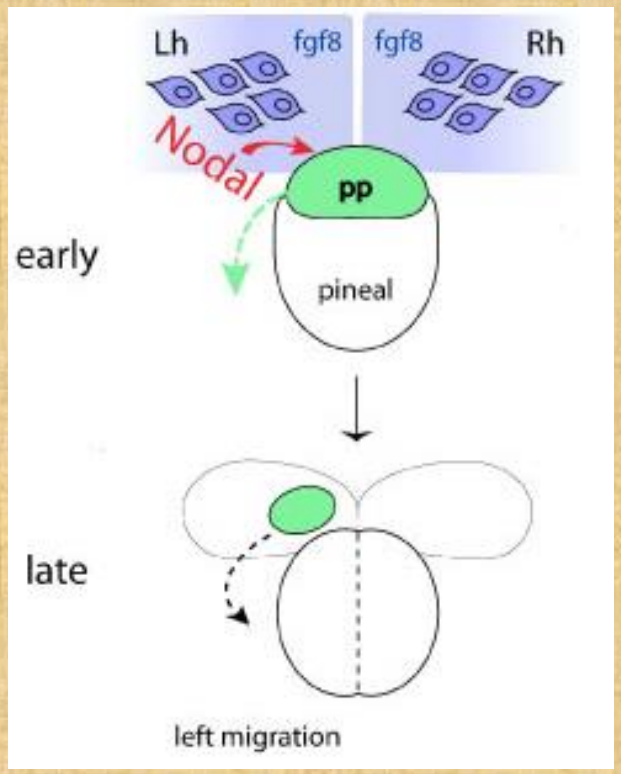
Current Opinion in Genetics & Development 2007, **17**:1–8

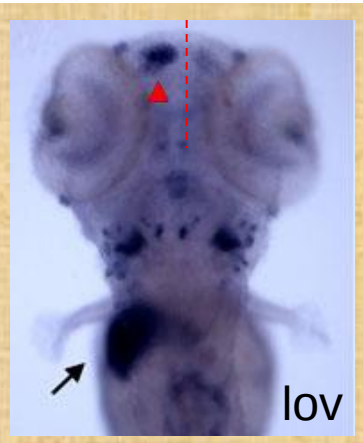
神经系统结构/功能的不对称性



斑马鱼神经系统具有左右不对称的结构







Hb: habenula

pp: parapineal

IPN: interpeduncular nucleus

斑马鱼中与左右不对称相关的行为实验

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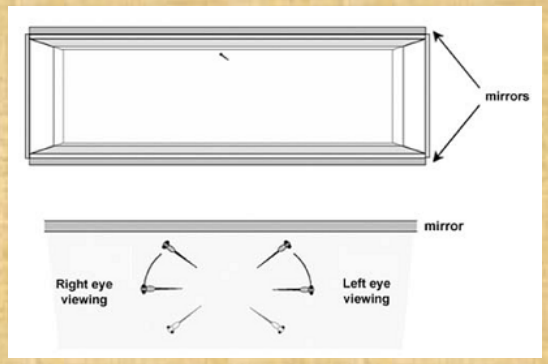
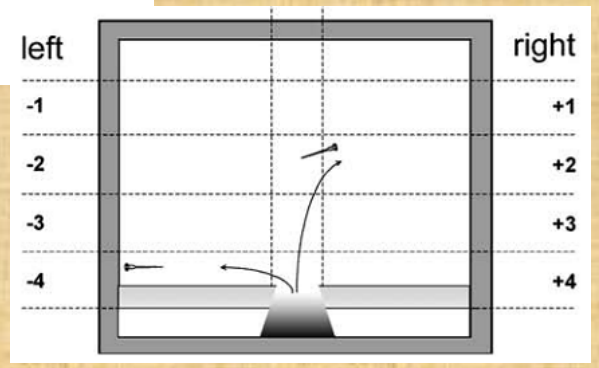
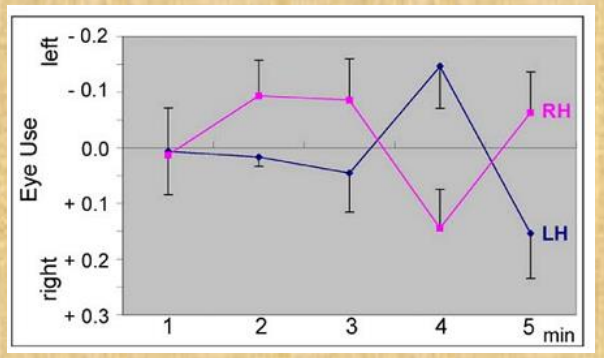
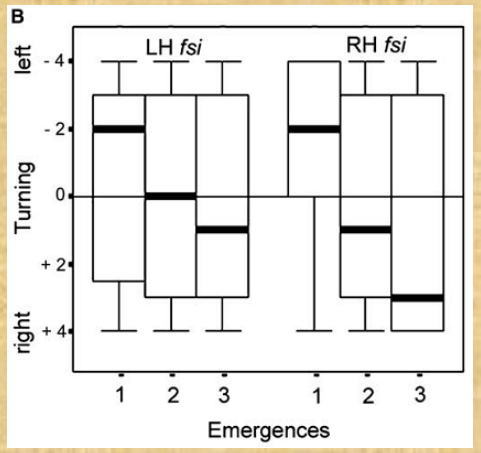
fsi Zebrafish Show Concordant Reversal of Laterality of Viscera, Neuroanatomy, and a Subset of Behavioral Responses

K. Anukampa Barth,[1] Adam Miklosi,[2]
Jenny Watkins,[3] Isaac H. Bianco,[1]
Stephen W. Wilson,[1,*] and Richard J. Andrew[3,*]







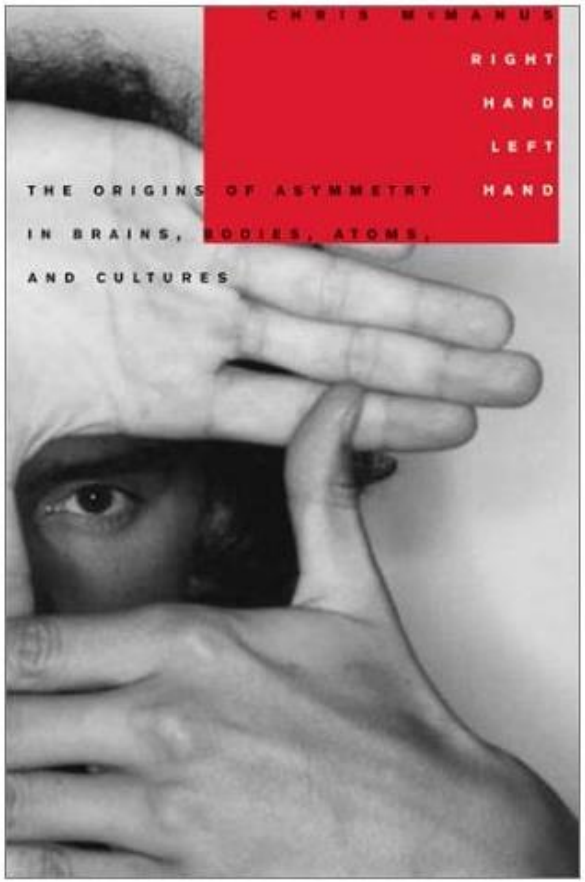


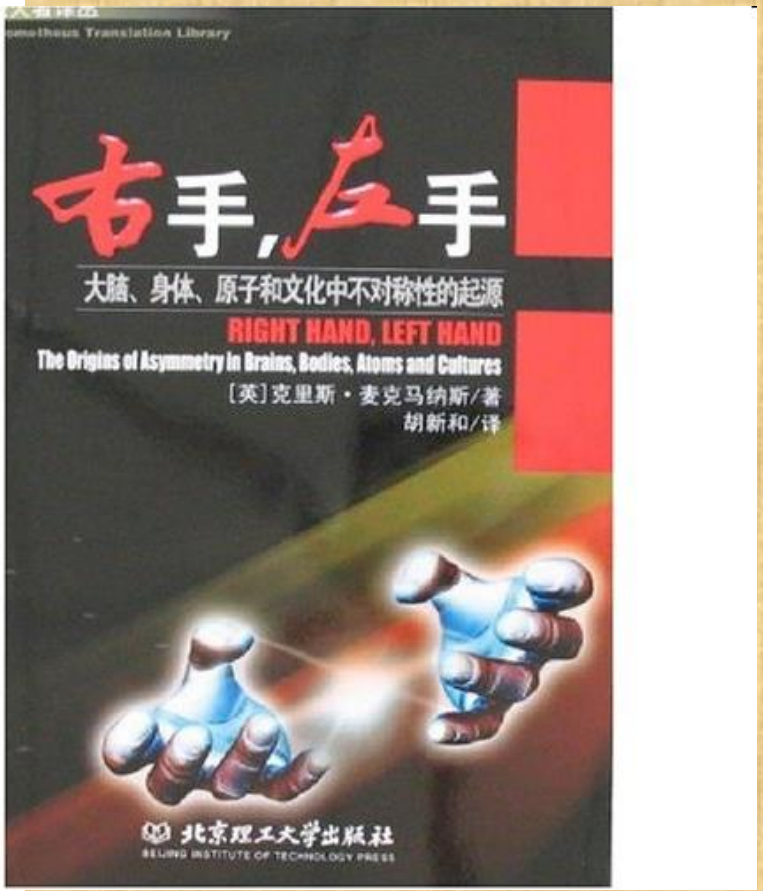
Mirror viewing test
(Reversed in RH)

Swimway test
(Normal in RH)

小　结

- 打破体轴左右对称性的最初事件：H^+/K^+-ATPase vs.nodal flow?
- 与左右不对称相关的保守信号传导途径：nodal/lefty/pitx2
- 器官左右不对称性与分子手性的关系：相关性vs.决定性？
- 行为方面的不对称性vs.脑/内脏器官结构的不对称性？
- 左右不对称与进化：偶然性vs.必然性？





《右手,左手:大脑、身体、原子和文化中不对称性的起源》覆盖了广泛的论题，来自物理学、生物学、化学、神经科学和心理学等各个学科领域的读者，从各自的 视角，都会发现它在某些方面是引人入胜的。作者在概括和整合来自不同学科的丰富成果以论证左和右的本质问题上做出了了不起的工作。《右手,左手:大脑、身 体、原子和文化中不对称性的起源》是严密的科学论证与迷人的游戏和窍门的绝妙结合，以及各种轶事奇闻的宝库，充满了乐趣，令人愉悦，科学界和公众读者定能 雅俗共赏，爱不释手。

徽宗建龙德宫成……殿前植荔枝，既结实，喜动天颜。偶孔雀在其下，亟召画院众史令图之。各极其思，华彩烂然，但孔雀欲升藤墩，先举右脚。上曰：“未也。”众史愕然莫测。后数日，再呼问之，不知所对。则降旨：**“孔雀升高，必先举左。”**众史骇服。

---（《画继》）