

発生学講義 担当:宮田  
平成26年1月16日

# 泌尿器を中心として

いろいろ話の飛び火あり.

生殖器すぐ隣に.

中胚葉,ふたたび.

生殖細胞(動く)

上皮-間充織 相互作用  
復習および新登場.

Superfamily  
の一種 と受容体.

管.

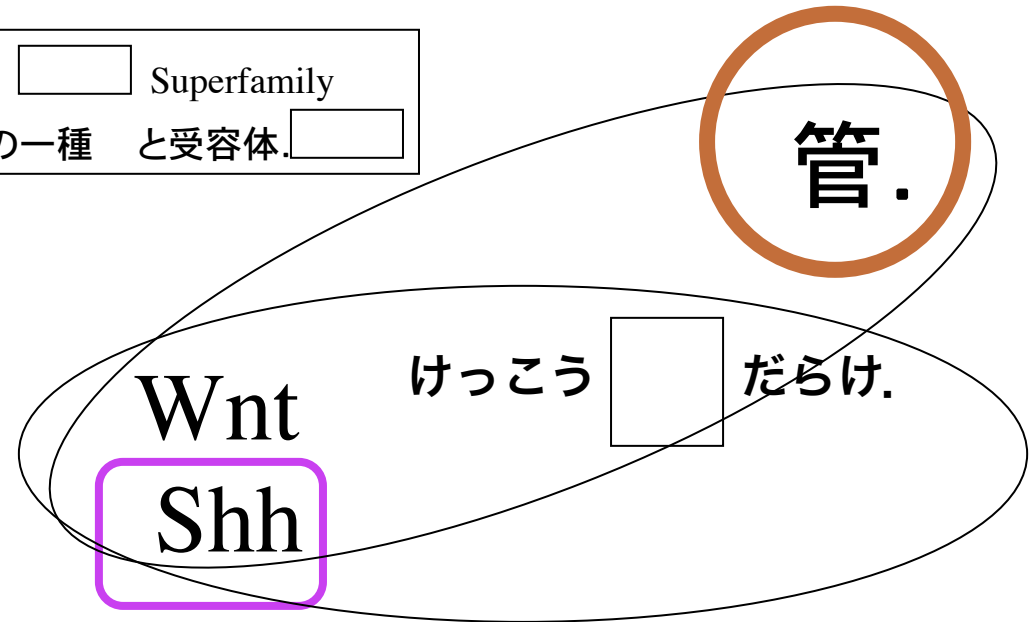
EMTとMET

Wnt

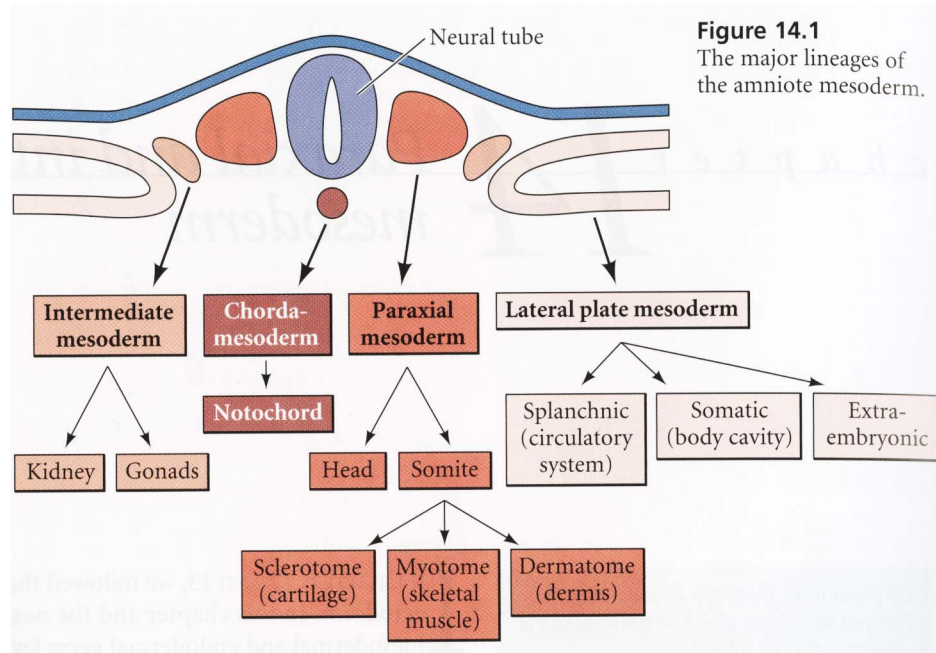
けっこう

だらけ.

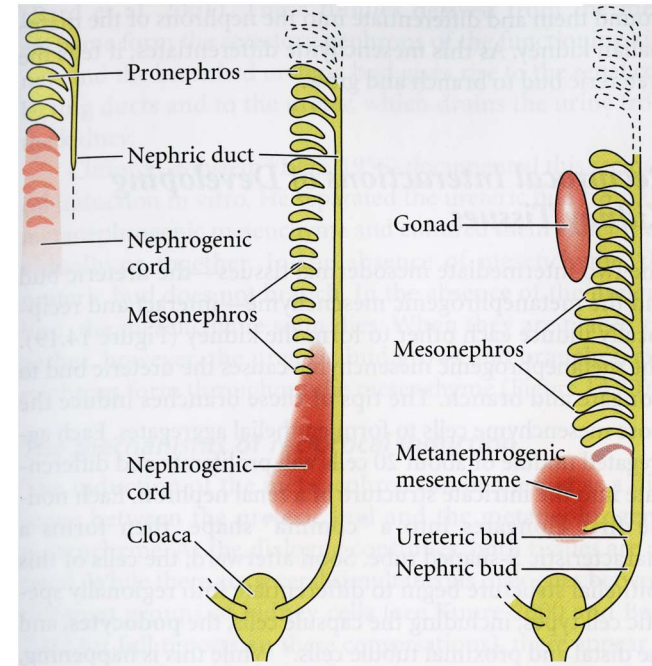
Shh







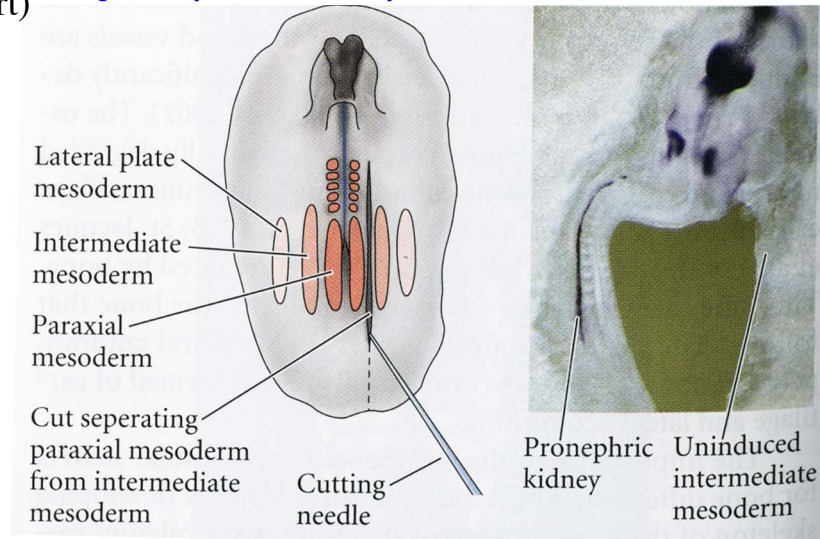
(Developmental Biology, 8<sup>th</sup> edition, Scott F. Gilbert)



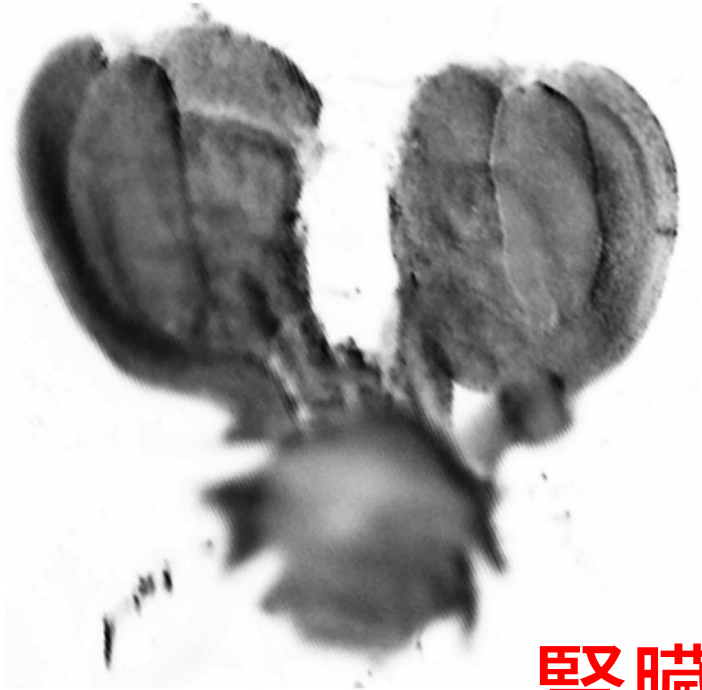
**Surgical separation of the paraaxial mesoderm**



**Placement of Noggin-secreting cells into a prospective region of chick lateral plate mesoderm.**



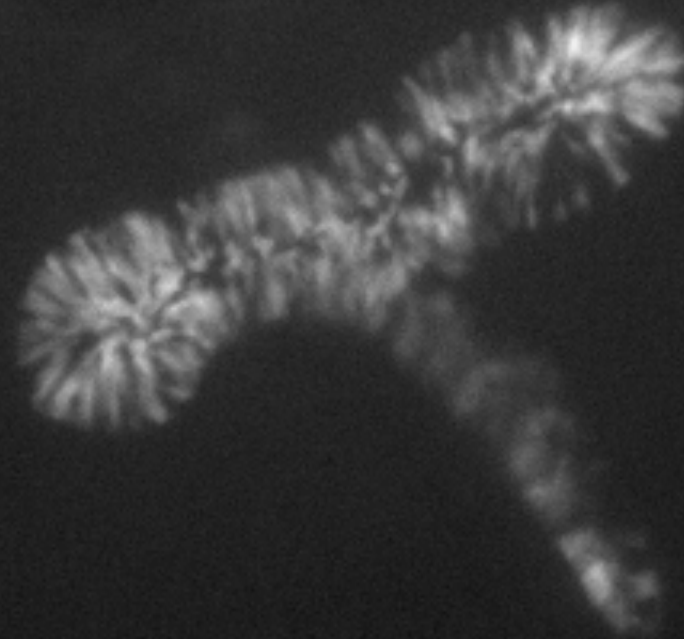
# マウス胎仔の泌尿生殖器



腎臓はどれか？

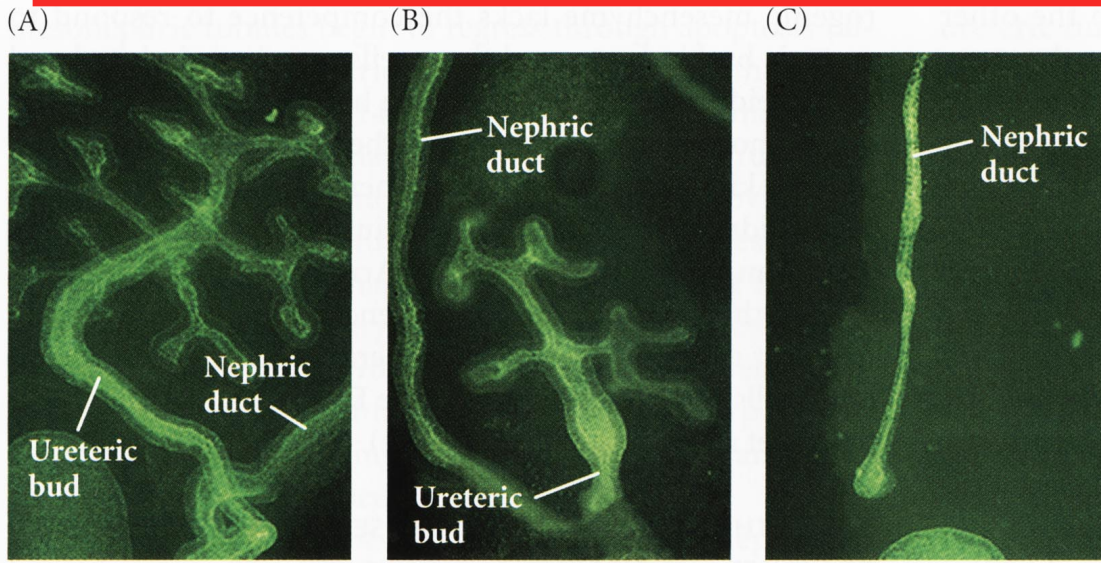


000'00"



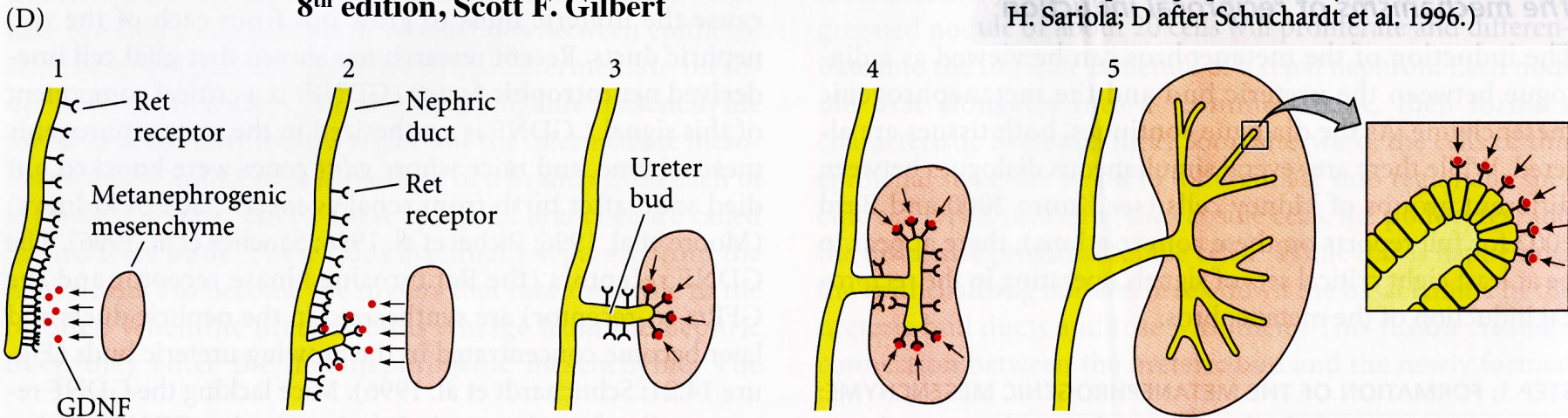
**Shakya, Watanabe, Costantini (2005) Dev Cell 8, 65-74**

# 間充織から,腎管上皮への働きかけ



**Figure 14.21**  
Ureteric bud growth is dependent on GDNF and its receptors. (A) The ureteric bud from a 11.5-day wild-type mouse embryonic kidney cultured for 72 hours has a characteristic branching pattern. (B) In embryonic mice heterozygous for a mutation of the gene encoding GDNF, the size of the ureteric bud and the number and length of its branches are reduced. (C) In mouse embryos missing both copies of the *gdnf* gene, the ureteric bud does not form. (Scale bars = 100 μm.) (D) The receptors for GDNF are concentrated in the posterior portion of the nephric duct. GDNF secreted by the metanephrogenic mesenchyme stimulates the growth of the ureteric bud from this duct. At later stages, the GDNF receptor is found exclusively at the tips of the ureteric buds. (A–C from Pichel et al. 1996, photographs courtesy of J. G. Pichel and H. Sariola; D after Schuchardt et al. 1996.)

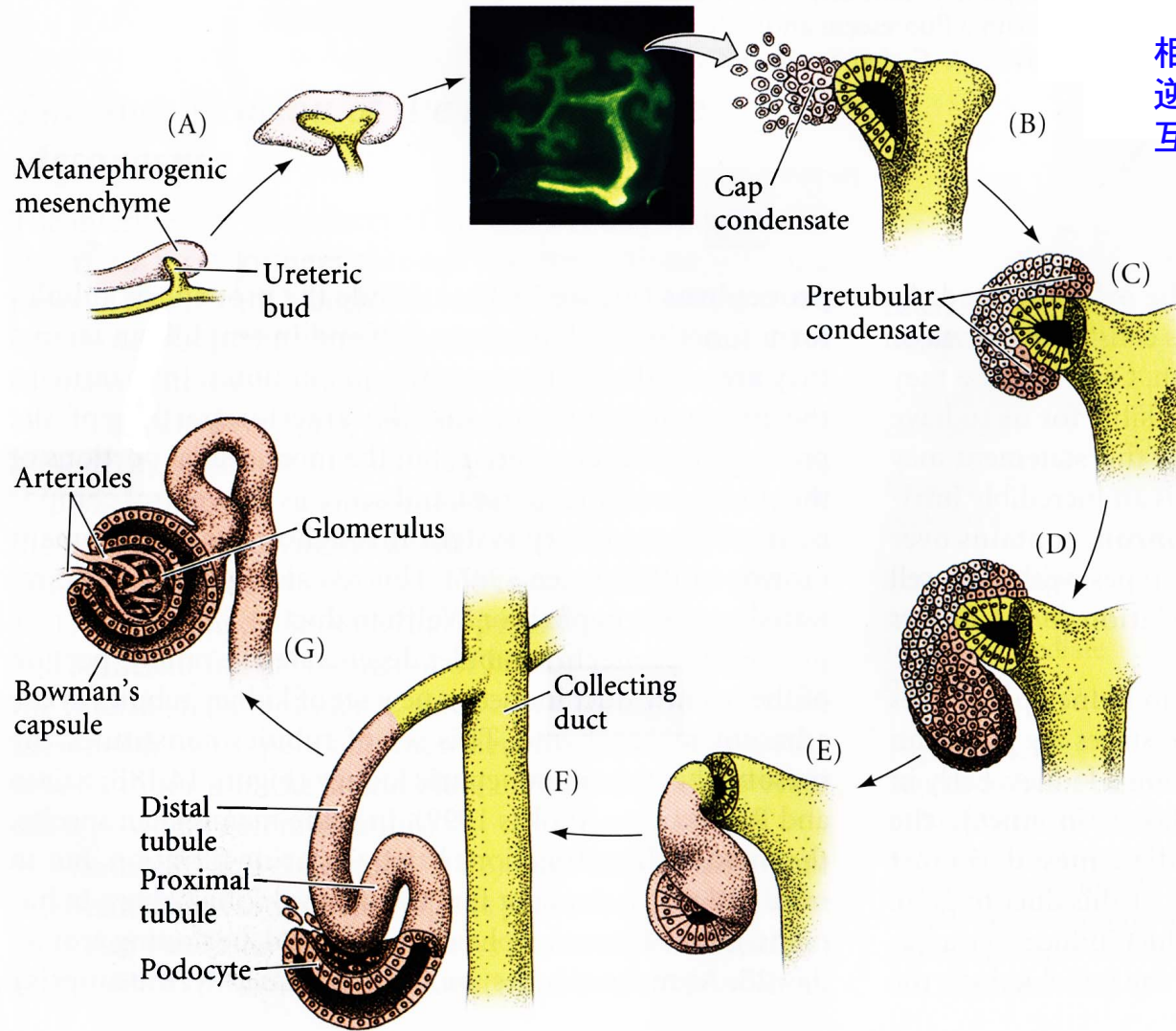
Developmental Biology  
 8<sup>th</sup> edition, Scott F. Gilbert



「GDNF --> Ret」再び。前はいつ,何の話で,でてきたかしら?



Developmental Biology  
8th edition, Scott F. Gilbert



相互の,相互扶助的な  
逆方向の,交換的な,  
互惠的な

Reciprocal induction in the development of the mammalian kidney. (A) As the ureteric bud enters the metanephrogenic mesenchyme, the mesenchyme induces the bud to branch. (B–G) At the tips of the branches, the epithelium induces the mesenchyme to aggregate and cavitate to form the renal tubules and glomeruli (where the blood from the arteriole is filtered). When the mesenchyme has condensed into an epithelium, it digests the basal lamina of the ureteric bud cells that induced it and connects to the ureteric bud epithelium. A portion of the aggregated mesenchyme (the pretubular condensate) becomes the nephron (renal tubules and Bowman's capsule), while the ureteric bud becomes the collecting duct for the urine. (After Saxén 1987 and Sariola 2002.)

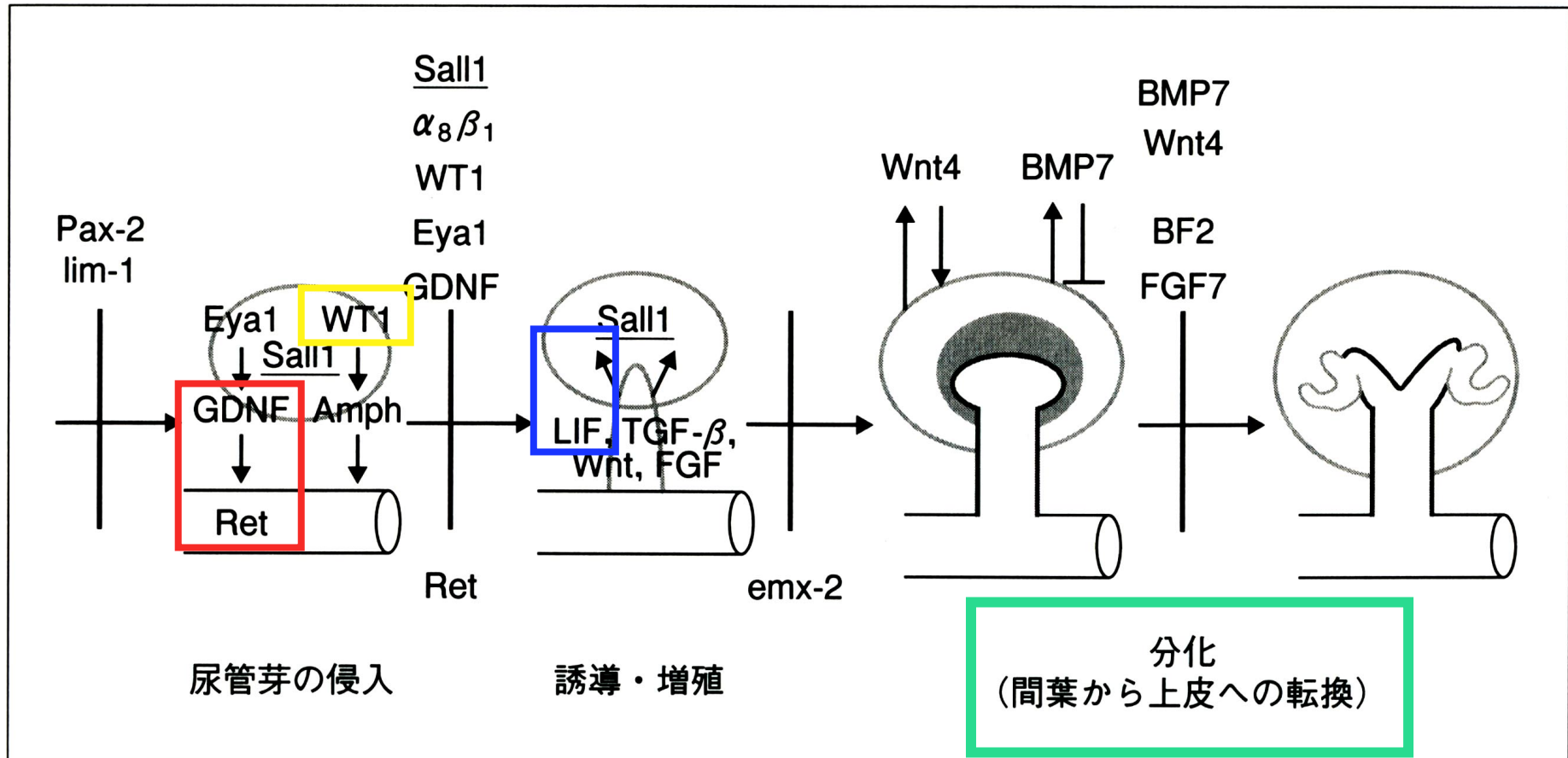
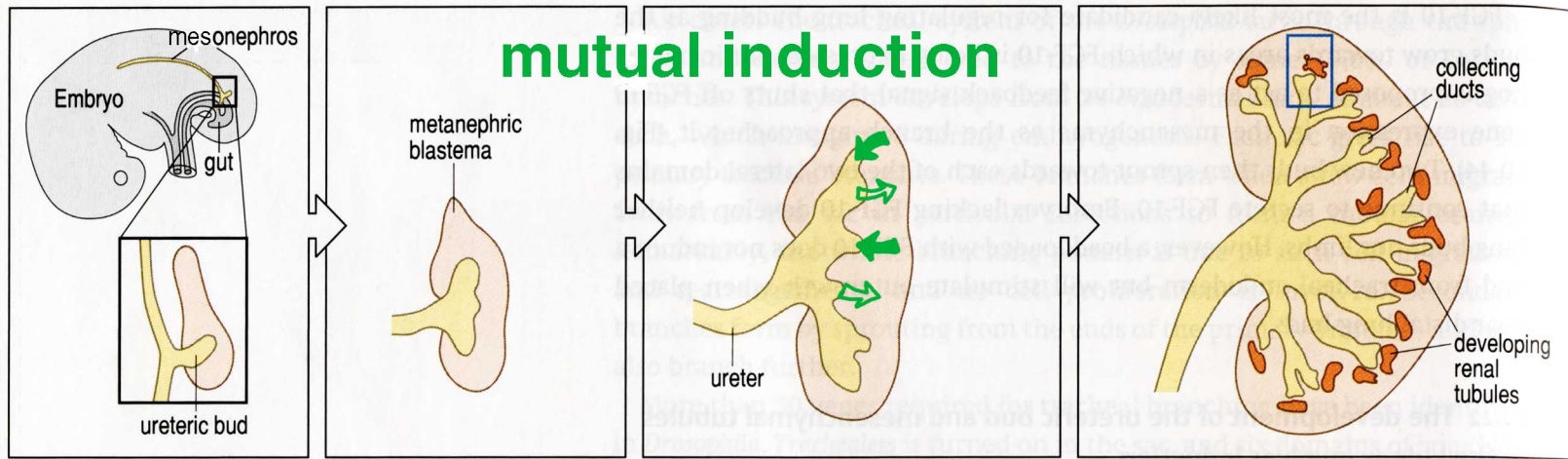


図 3 腎発生の分子メカニズム

縦線は各遺伝子のノックアウトによって発生の障害される時期を示す。

西中村 隆一 博士(東大 医科学研究所 ---> 現在は熊本大学)  
 医学のあゆみ 199, 929-934, 2001

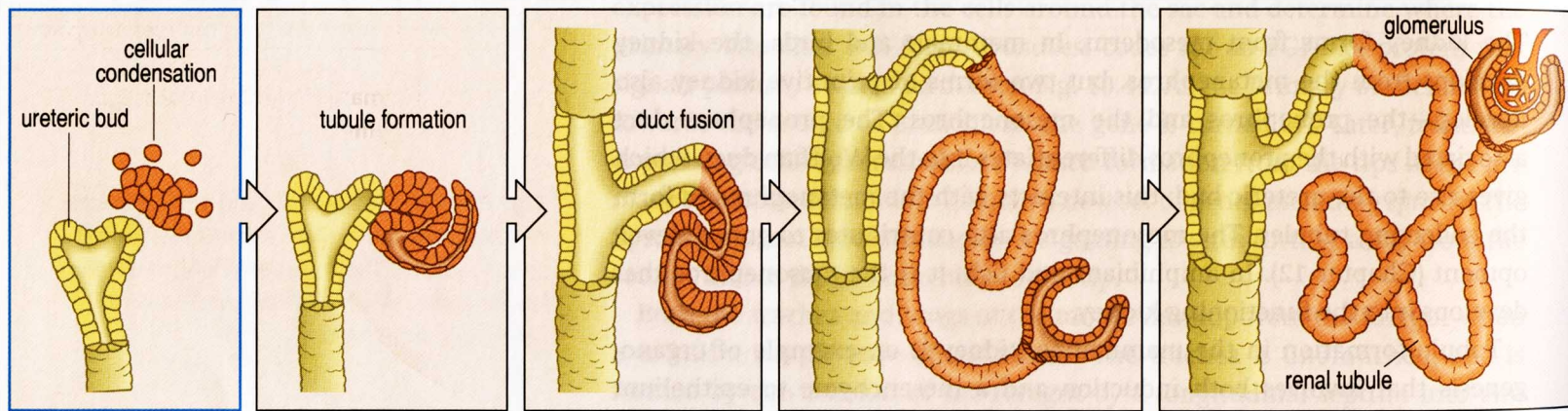




Developmental Biology  
8<sup>th</sup> edition, Scott F. Gilbert

Wt-1 (zinc-finger transcription factor) expression in the blastema is necessary for ureteric bud growth. (\*mutation --> Wilms tumor)

Ret (receptor) <----- GDNF (glial-derived neurotrophic factor)



**MET** mesenchymal-epithelial transition (↔ **EMT**)

道路(滑走路)の「延伸」  
「管仲間」になってくださいな。

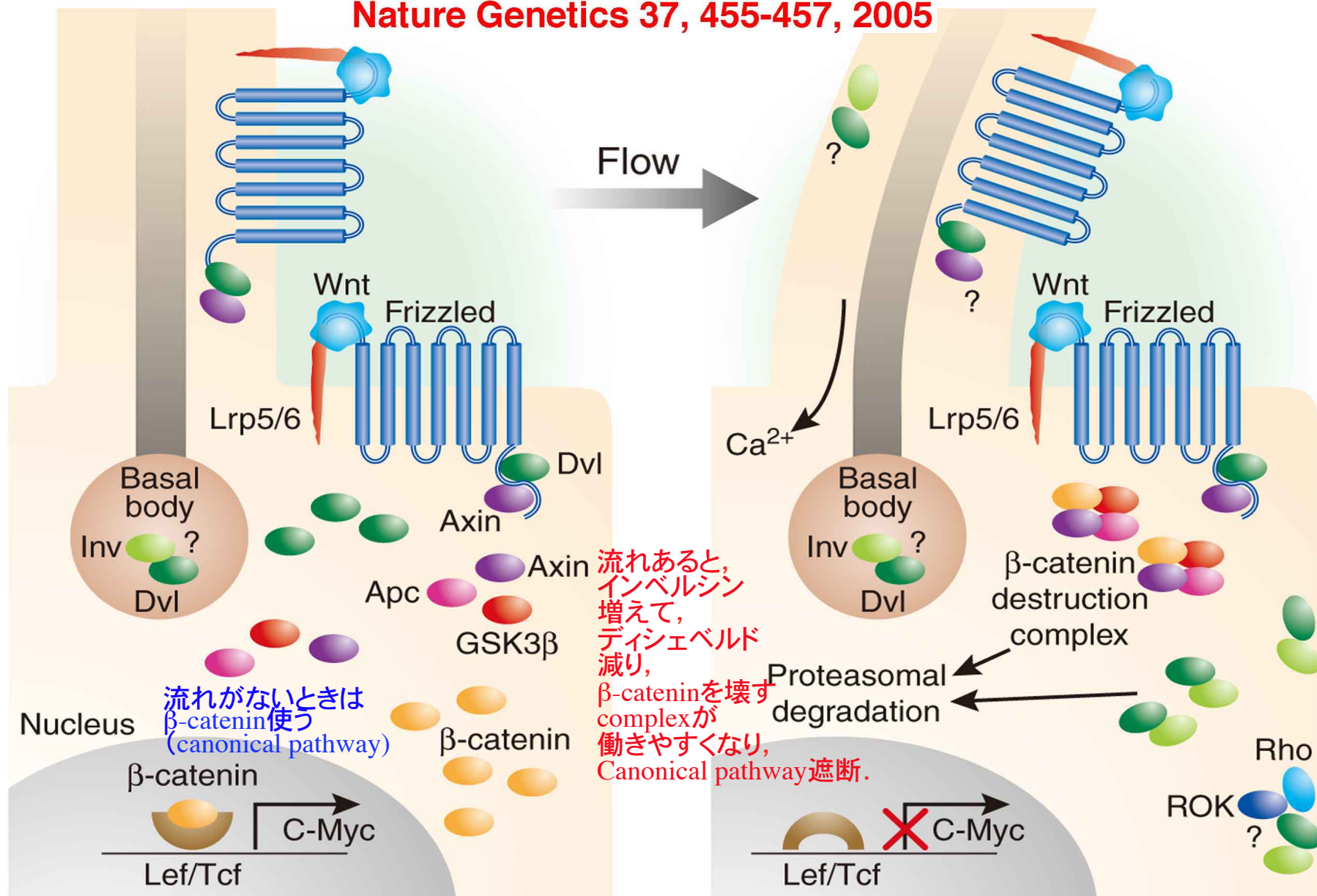
Inversinインベルシン を持たぬマウス (inv/inv) では、  
腎臓形成異常 (tubeの代わりにcystだらけ) ,  
そして, situs inversusをきたす. 一見関係なさそな  
左右軸形成 と 腎発生は,  で結びつく.

腎臓発生初期ではWntシグナルが  
Metanephric mesenchyme形成に必須だが,  
後期にWnt- $\beta$ -catenin pathwayが  
働きすぎると,管出来損なってcyst(嚢胞)に.

Inversinは,Wntシグナリングのcanonicalカノニカル  
(b-catenin依存的) pathwayから,non-canonical pathway  
への切り替えに貢献すると報じられている.

Nature Genetics 37, 455-457, 2005

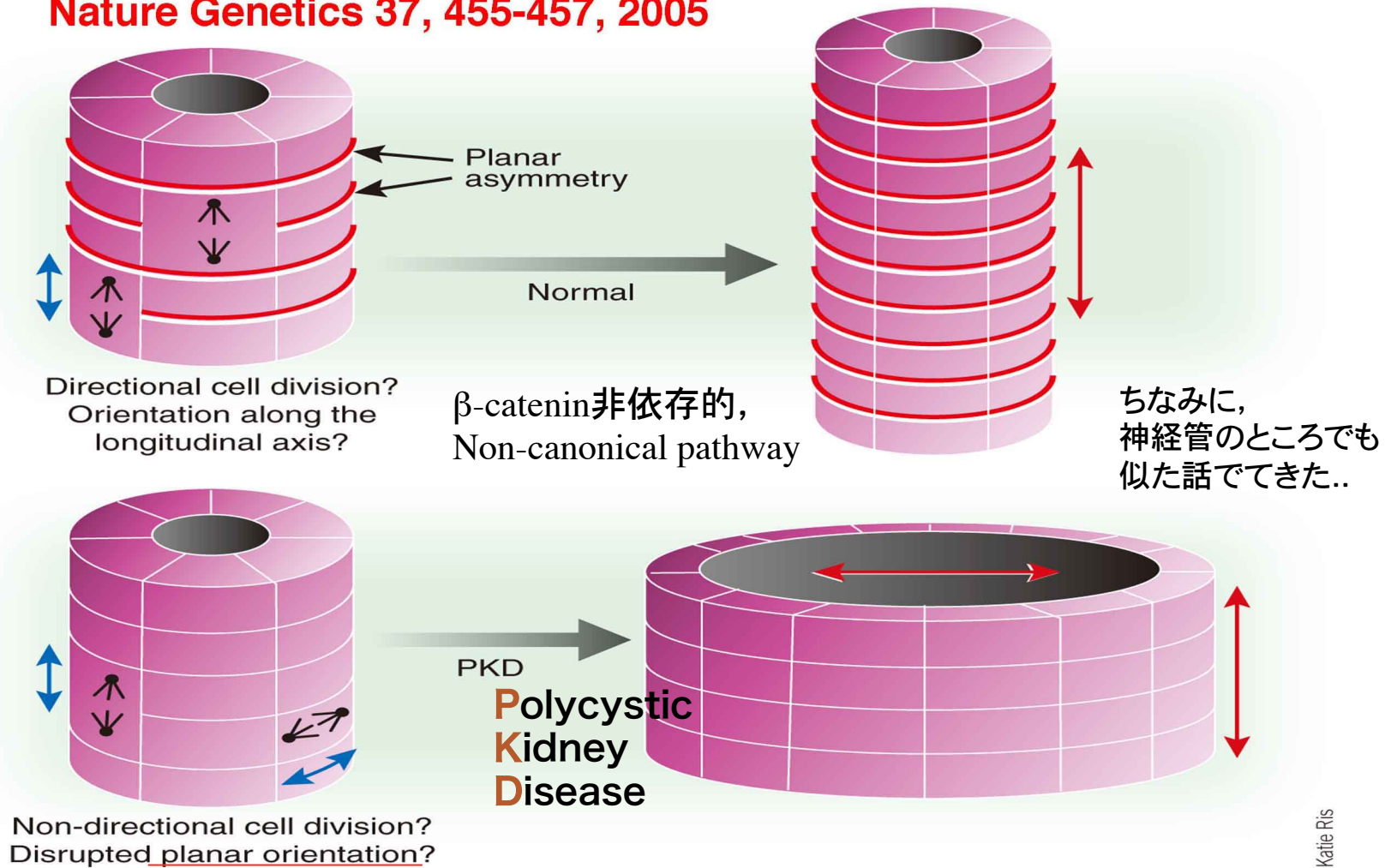
Katie Ris



**Figure 1** Flow-based model of Wnt regulation in the kidney. In the model proposed by Simons *et al.*, Wnt

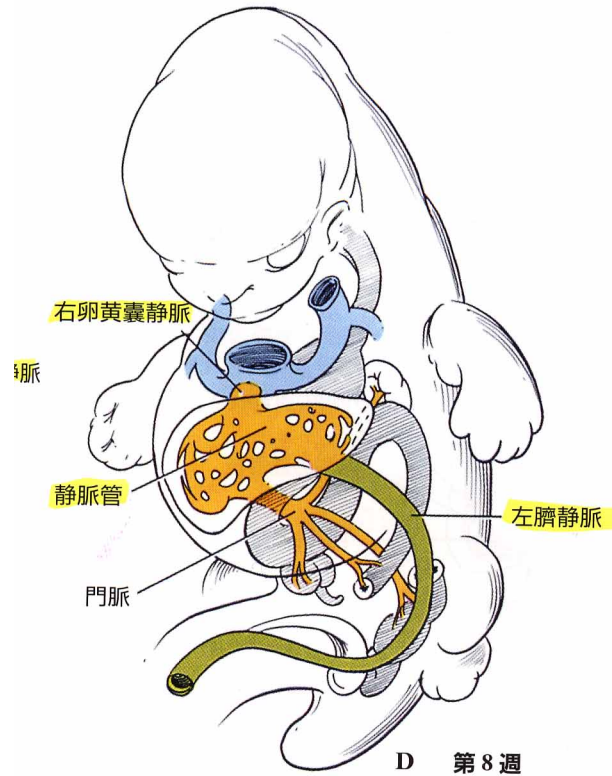
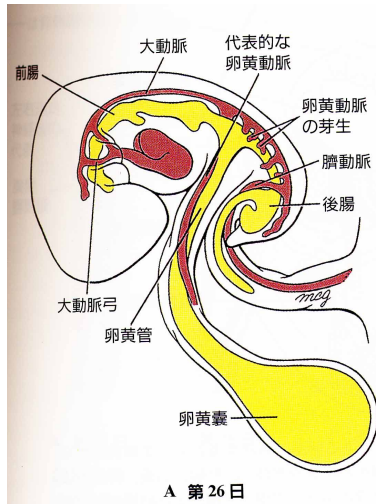


Nature Genetics 37, 455-457, 2005



**Figure 2** Noncanonical Wnt signaling and tubular morphogenesis. Proper apical-basolateral polarity is essential for normal solute and water transport, and tubular epithelial cells must also be correctly oriented with respect to the longitudinal axis of the tubule. This is especially true during renal development when newly formed tubules undergo progressive lengthening. The default structure that would result from disruption of this planar orientation is predicted to be a dilated tubule or cyst. Noncanonical Wnt signaling regulates a number of processes that could help to orient cells properly along the longitudinal axis. Tubular flow could be one of the signals that provides information about cellular orientation.

# ラーセン教科書



## Umbilical Vein From the Placenta

----> Ligamentum  
Teres Hepetis

「おへそ」 佐々木美子  
こどものうた童謡と唱歌  
(を思い出して. . 歌詞少し不確か)

おっへっそ~の中には  
なにがある?(ピッピ)

おっへっそ~の中には  
(2)でこぼこがある(ドンドン)  
(3)ほそみちがある(ドンドン)

(2)おへそのでこぼこは,  
く~らいく~らいかいだんだ.

(3)おへそのほそみちは,  
な~がいな~がいトンネルだ.