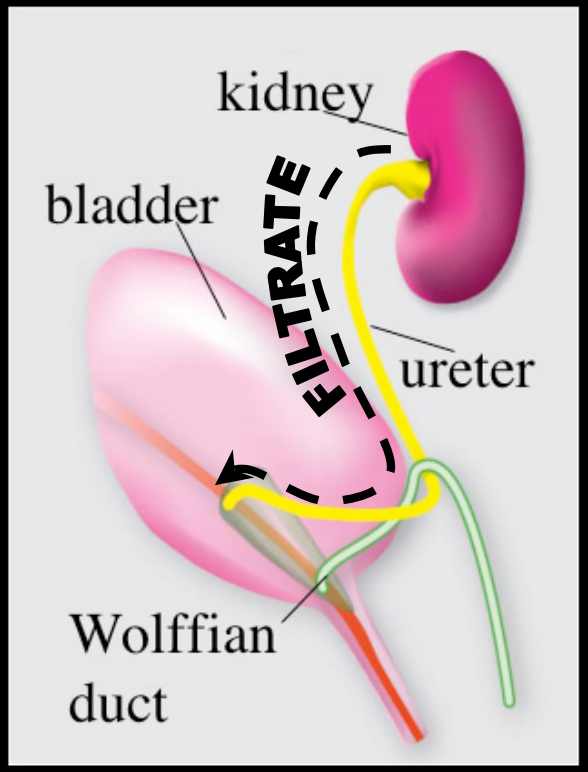


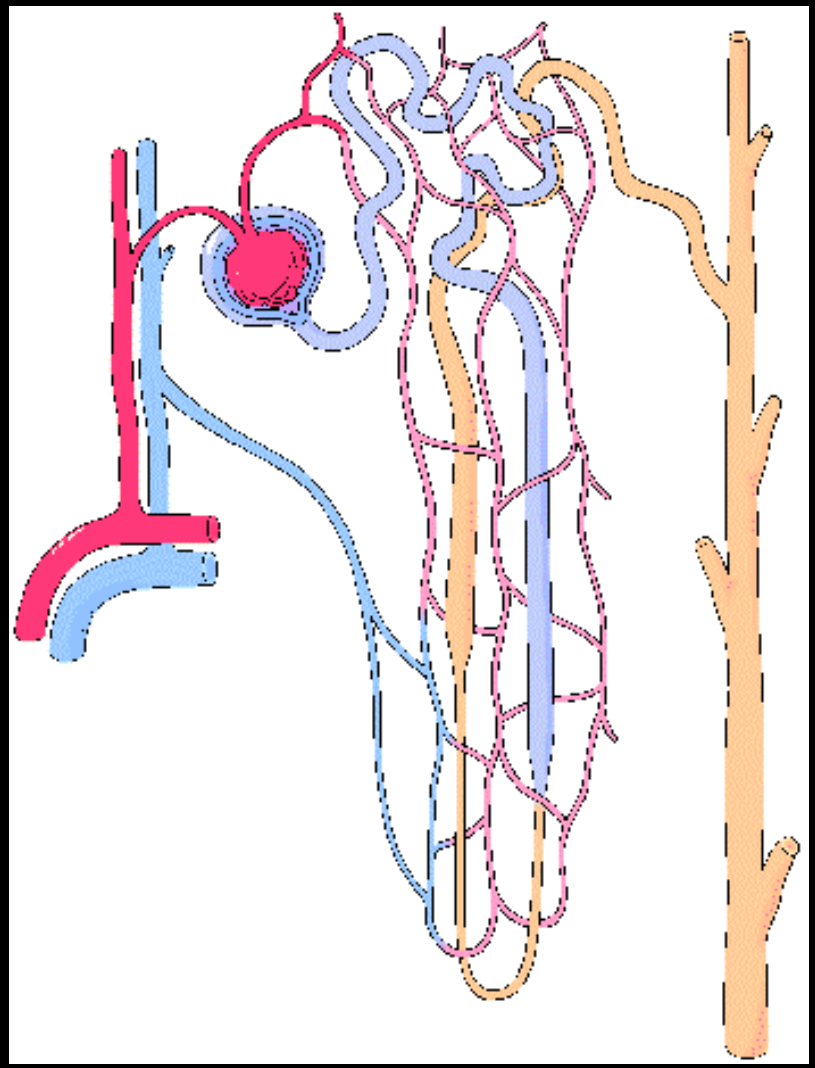
nephrons in the kidney generate urine that is propelled
to the ureters and then to the bladder for storage and excretion

The Urinary outflow tract:

- monitors and regulates extra-cellular fluids
- excretes harmful substances in urine, including nitrogenous wastes (urea)
- returns useful substances to bloodstream
- maintain balance of water, electrolytes (salts), acids, and pH in the body fluids

Formation of Urine:

- blood filtered to the glomerulus
- capillary walls thin
- blood pressure higher inside capillaries than in Bowman's capsule



Formation of Urine

nitrogen-containing waste products of protein metabolism, urea and creatinine, pass on through tubules to be excreted in urine

urine from all collecting ducts empties into renal pelvis

urine moves down ureters to bladder

empties via urethra

Formation of Urine

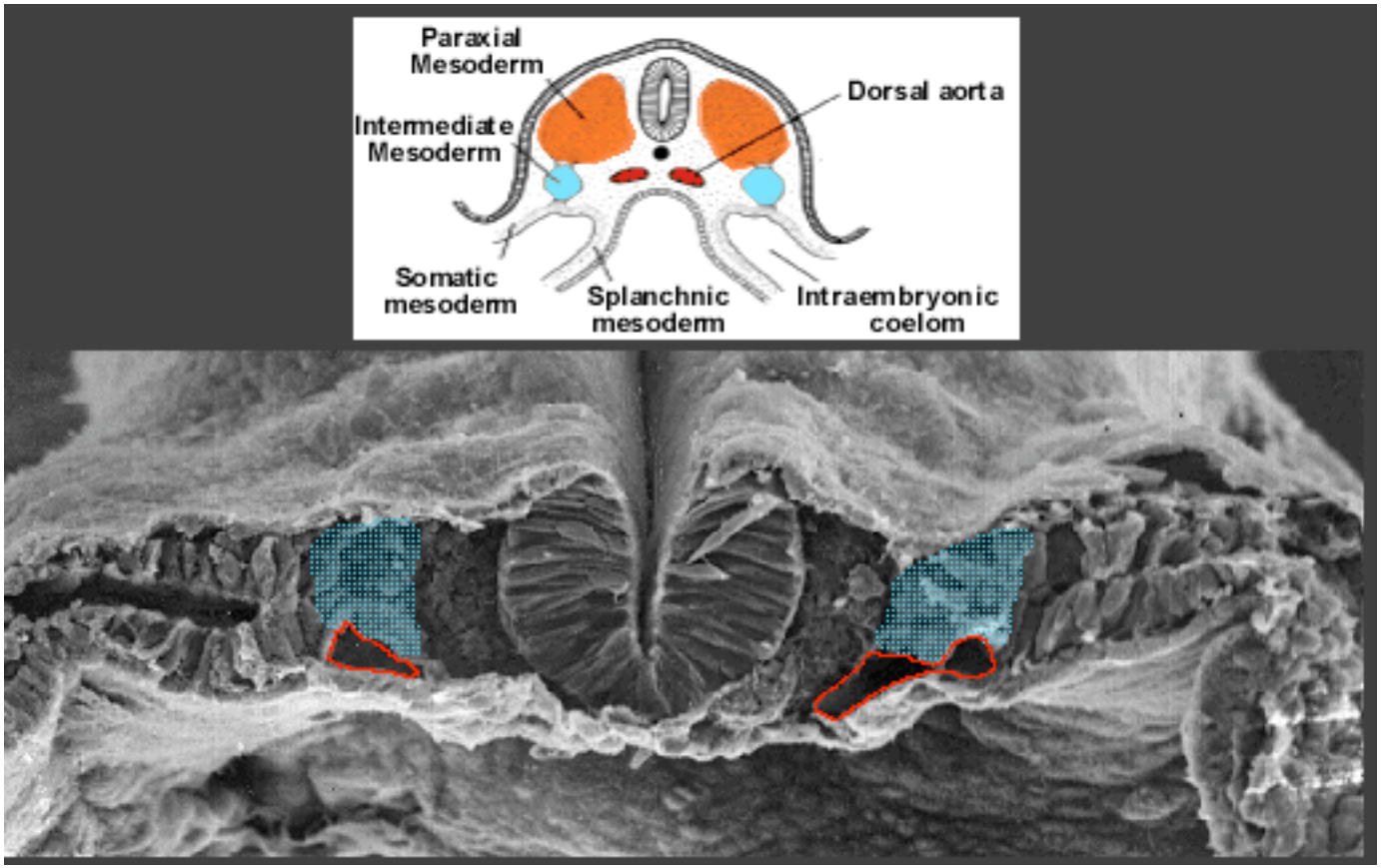
in healthy nephron, neither protein nor RBCs filter into capsule

in proximal tubule, most of nutrients and large amount of water reabsorbed back to capillaries

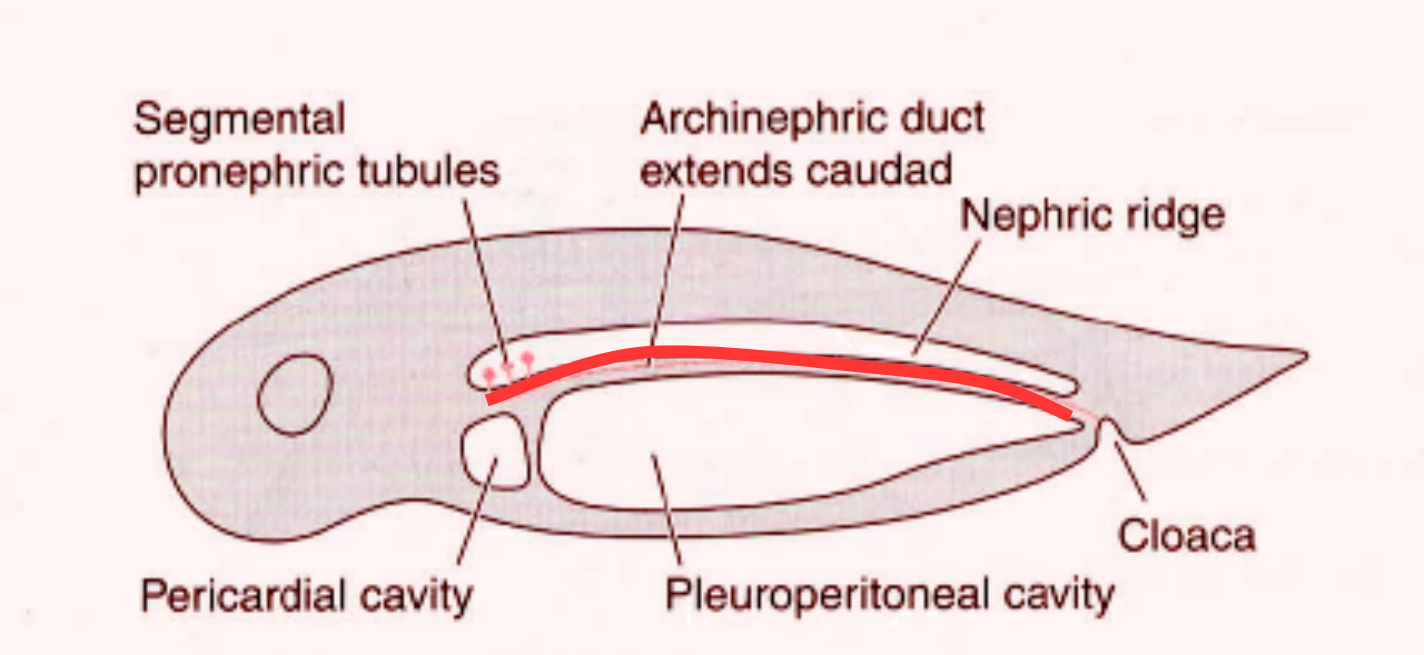
salts selectively reabsorbed according to body's needs

water reabsorbed with salts

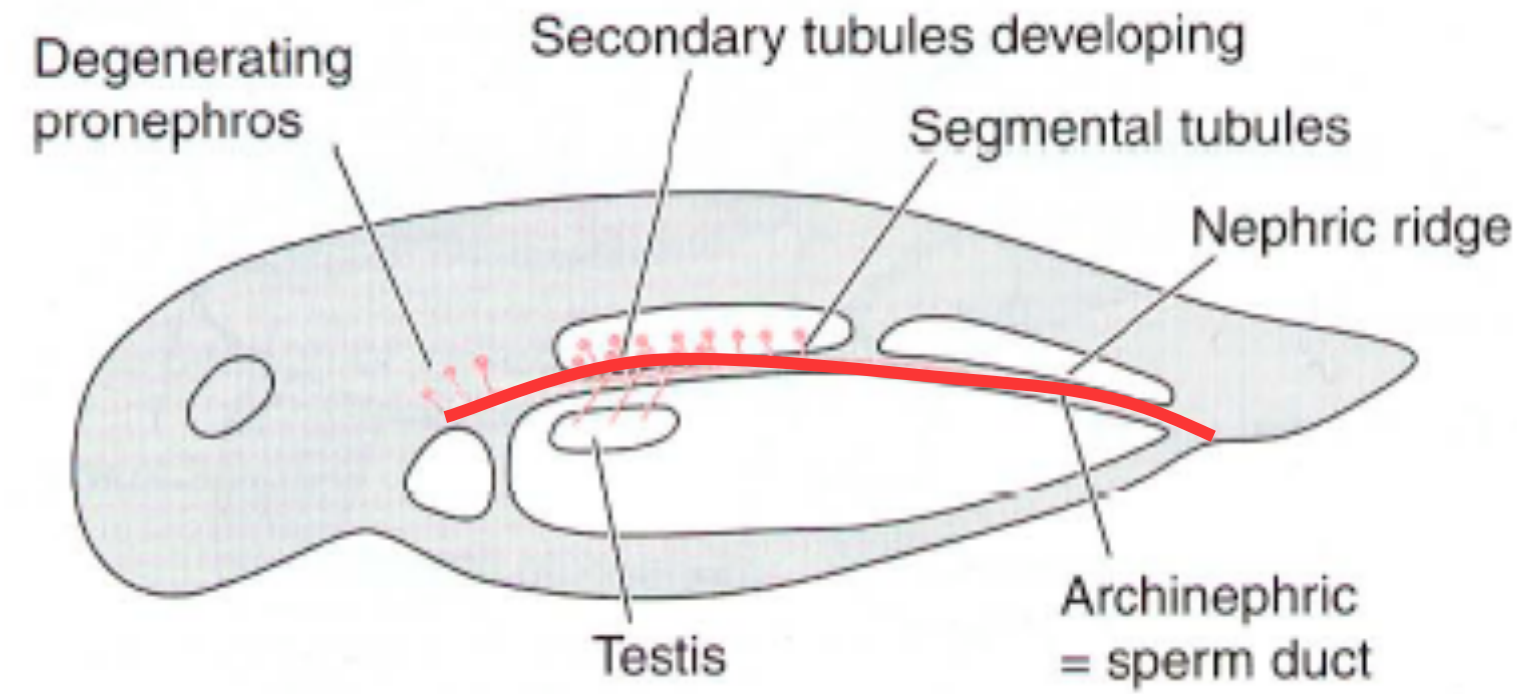
The urogenital system derives predominantly from intermediate mesoderm



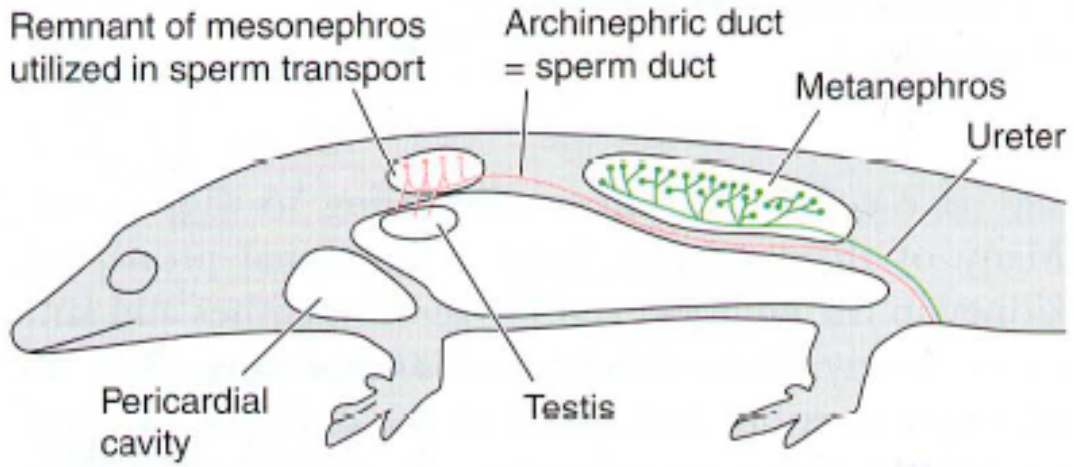
During development, 3 successive kidneys form:



pronephros in an early embryo



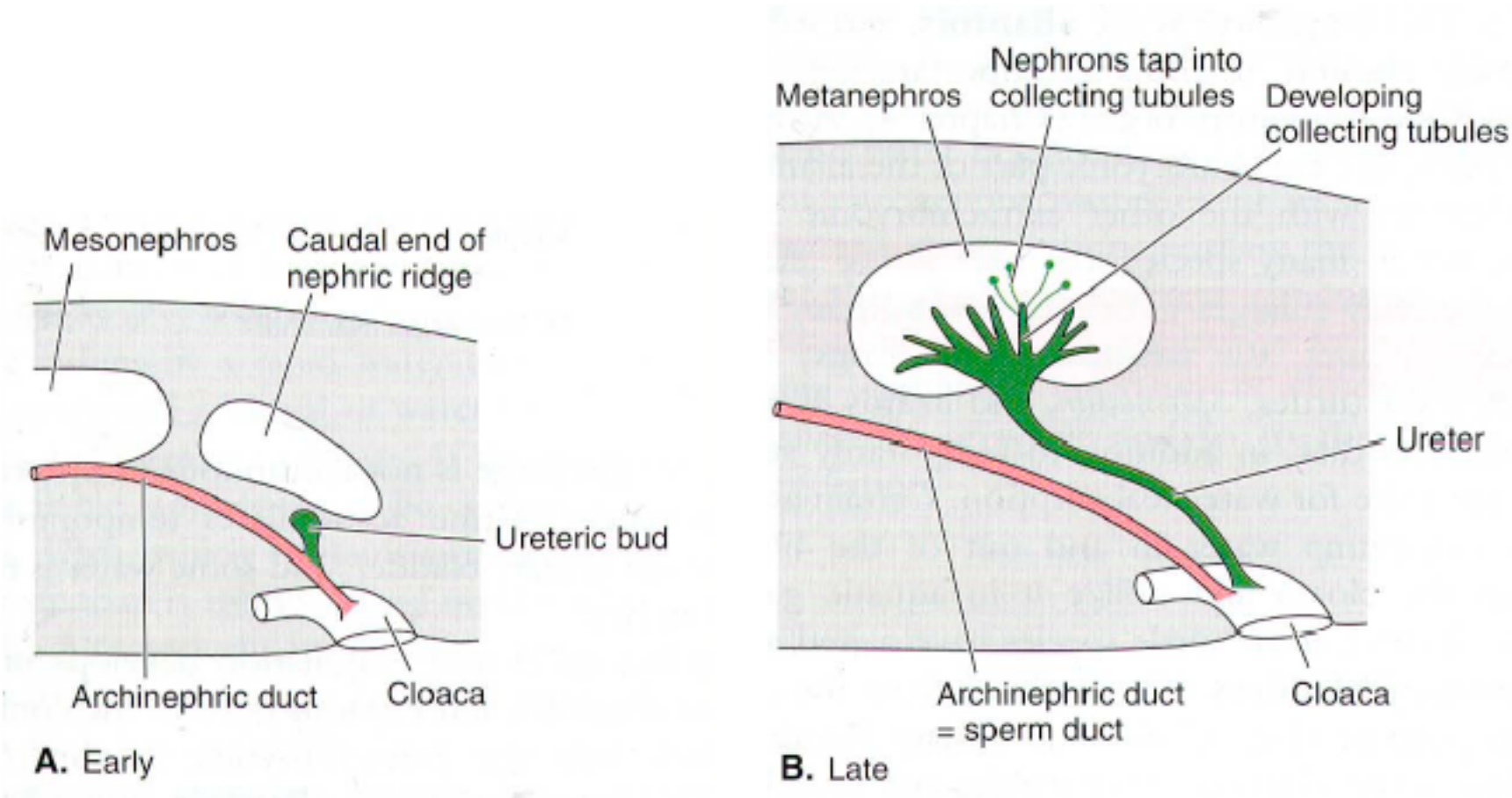
Mesonephros in intermediate embryo



C. Metanephros in late embryo and adult

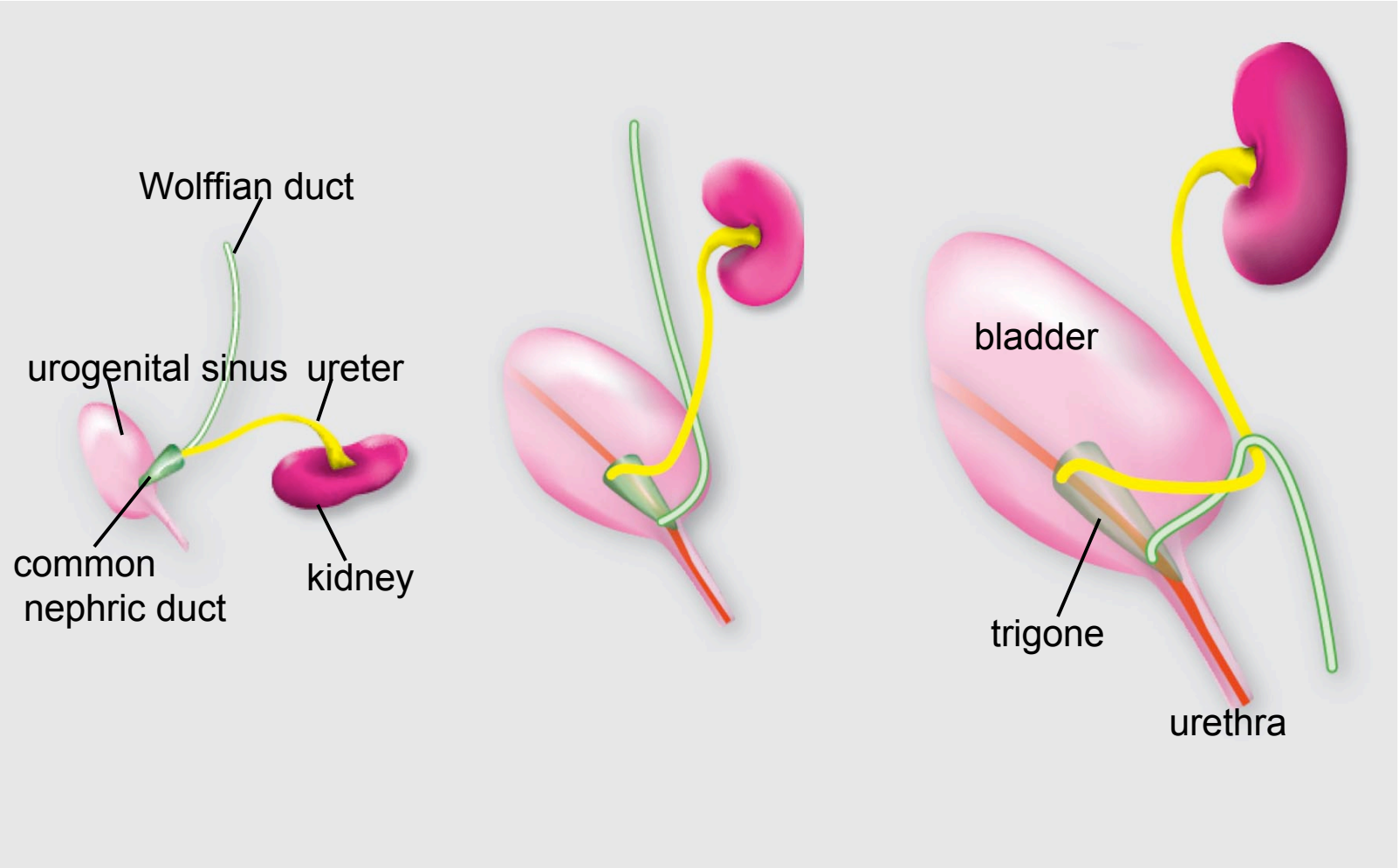
A **metanephros** is always drained exclusively by one duct, the ureter.

In birds in reptiles the ureter separates from the nephric duct and enters the cloaca. In mammals, the ureter separates from the nephric duct and enters the bladder

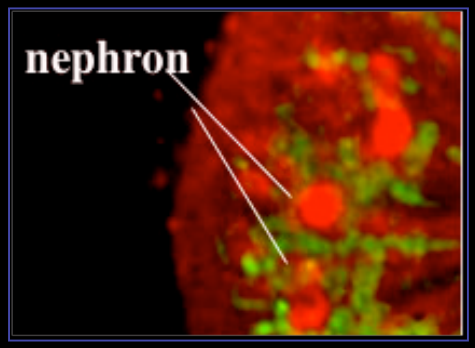


renal development begins when the ureteric bud invades kidney mesenchyme (**the metanephric blastema)**

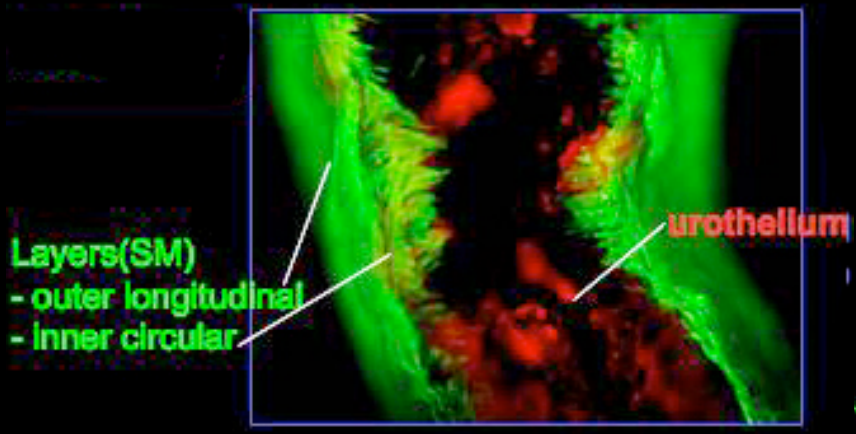
As the embryo grows, the **ureters lengthen**, and the **kidneys rotate** and **ascend** along the dorsal body wall



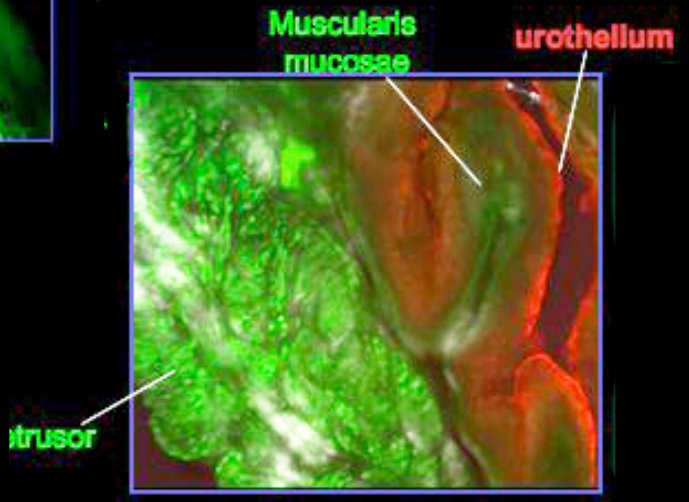
the different compartments of the urinary outflow tract are lined with distinct cell types that perform diverse functions



the kidney



the ureters



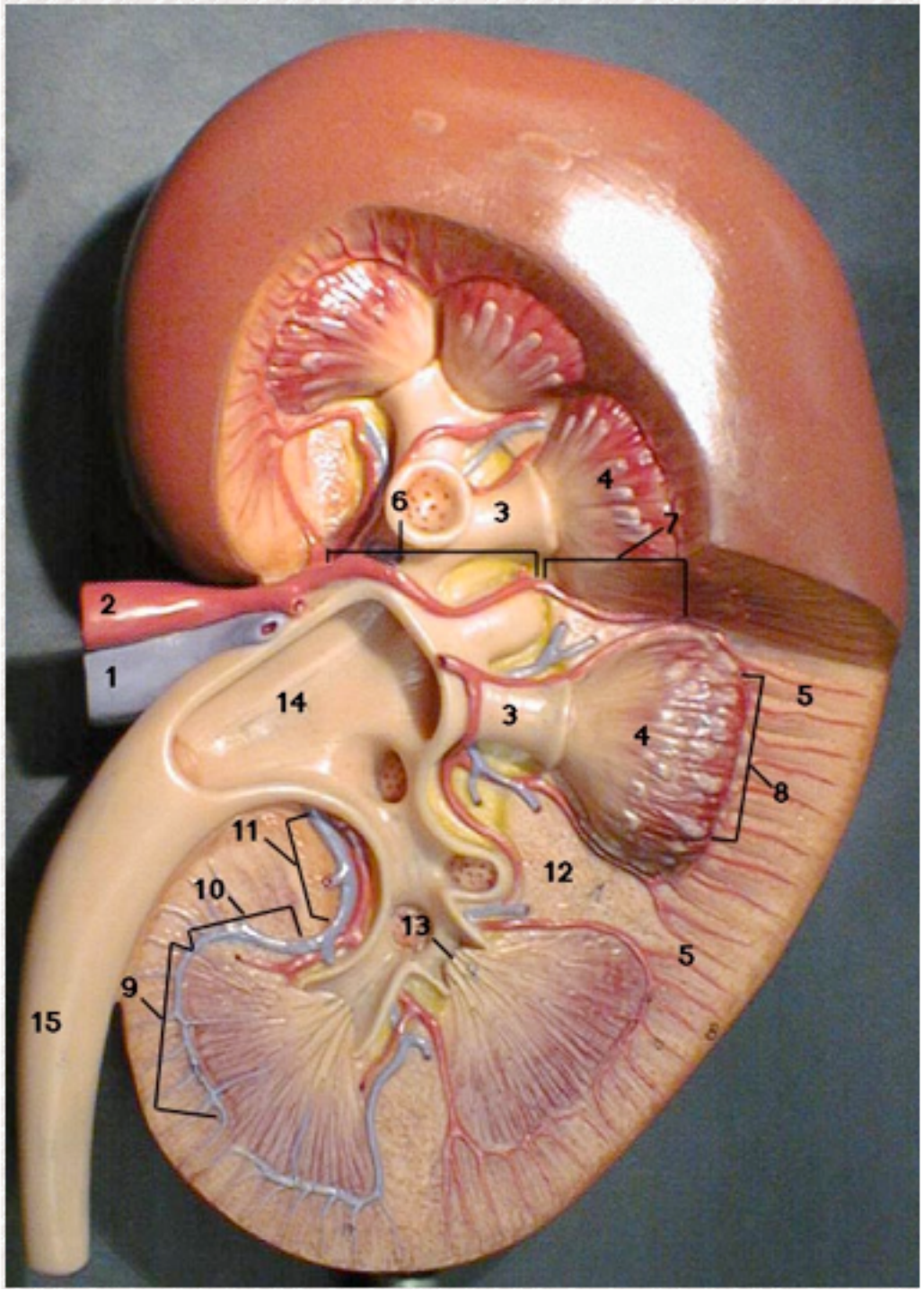
the bladder

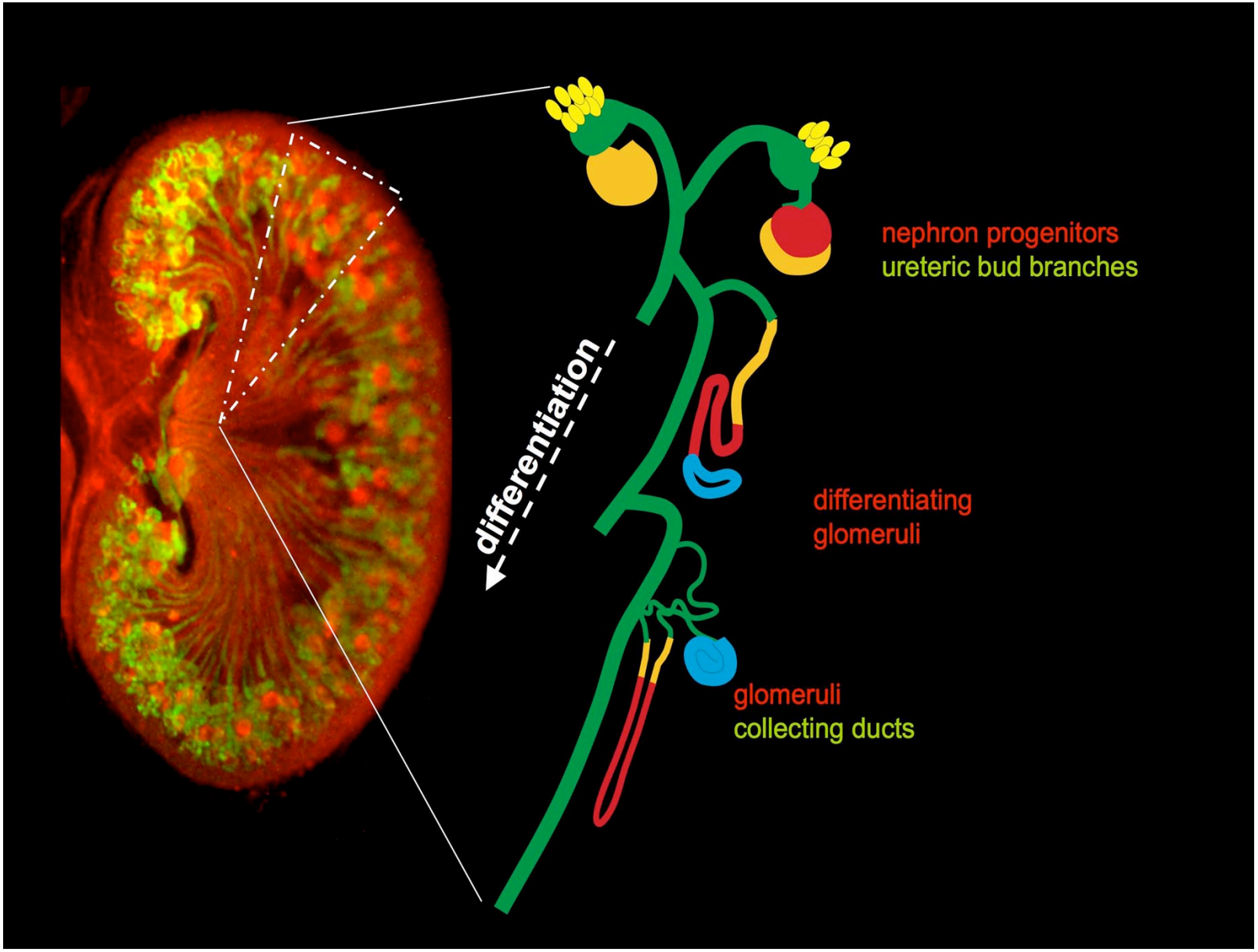
How are the diverse cell types in the kidney, ureter and bladder formed?

making a kidney

Model Kidney

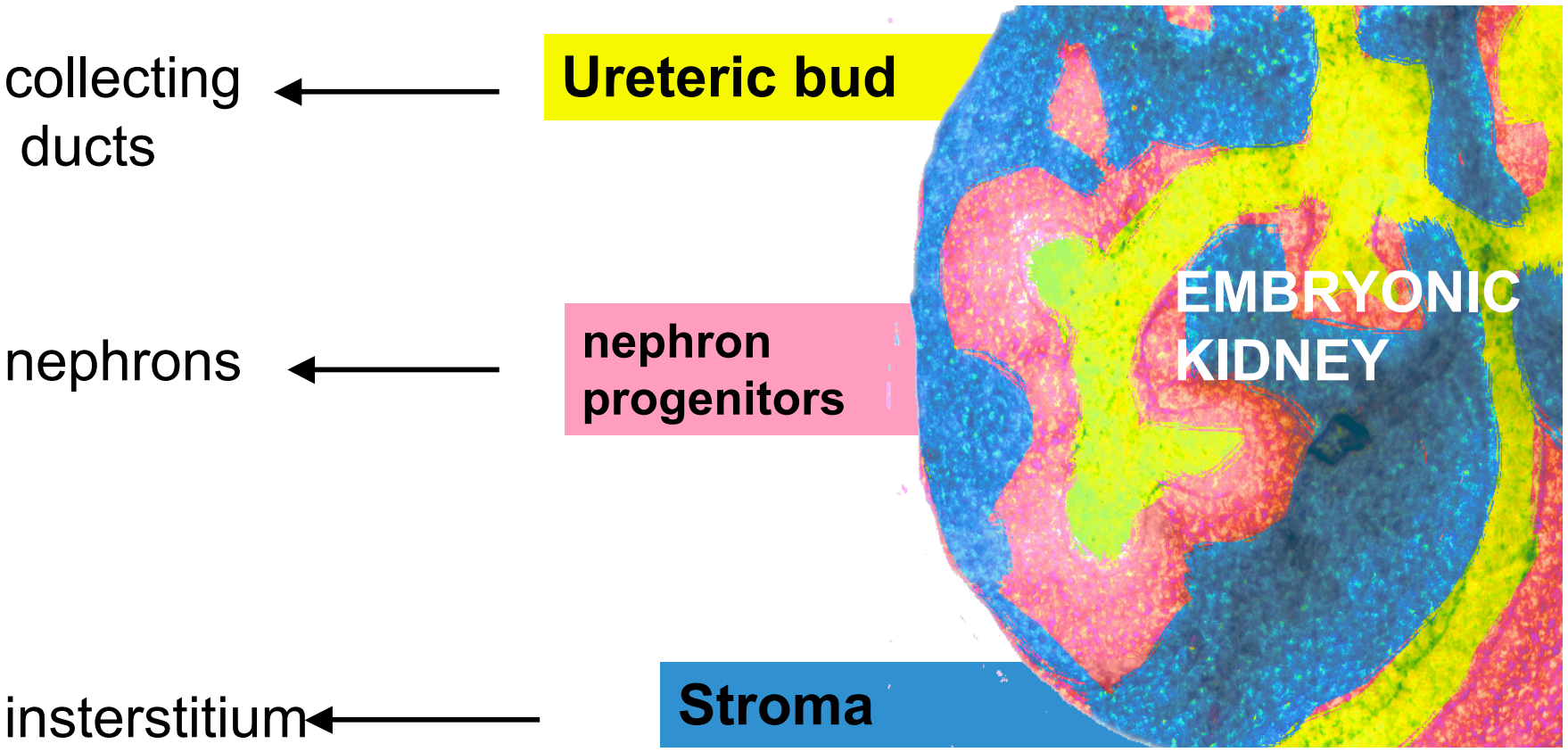
1. Renal Vein
2. Renal Artery
3. Renal Calyx
4. Medullary Pyramid
5. Renal Cortex
6. Segmental Artery
7. Interlobar Artery
8. Arcuate Artery
9. Arcuate Vein
10. Interlobar Vein
11. Segmental Vein
12. Renal Column
13. Renal Papillae
14. Renal Pelvis
15. Ureter



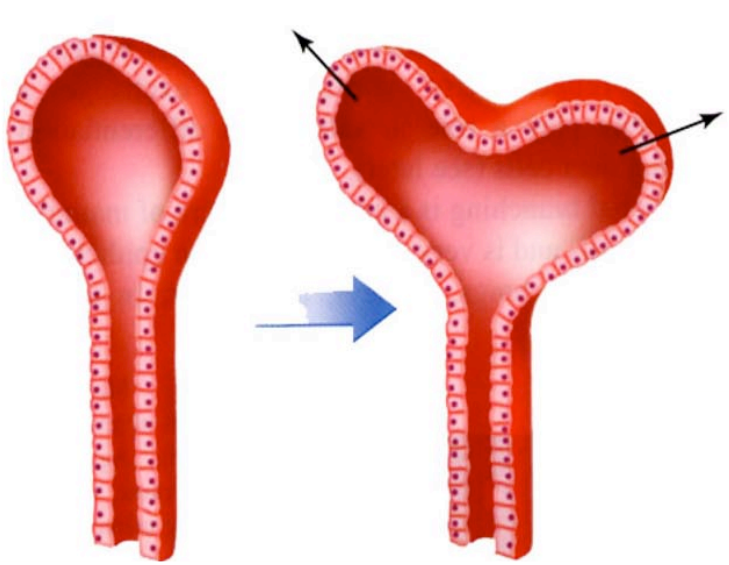


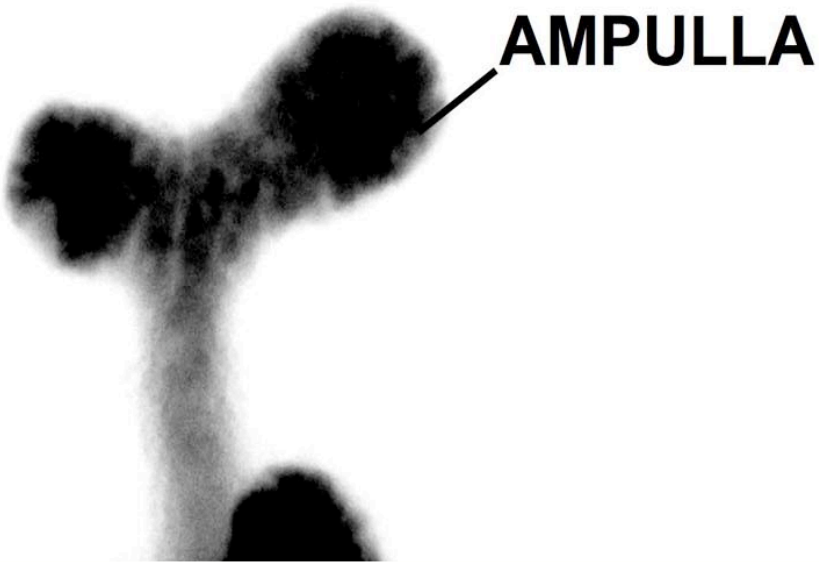
the kidney is radially patterned

The kidney forms via interactions between 3 main cell types

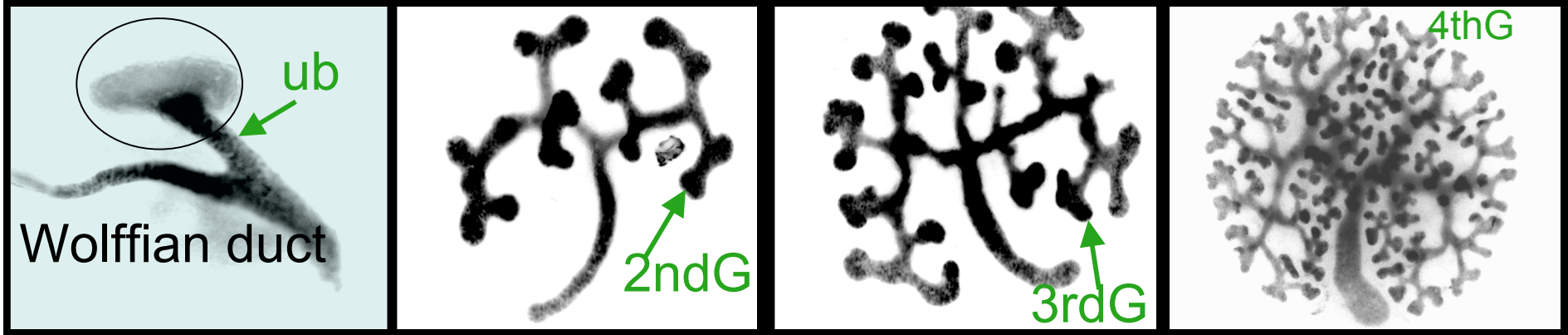


local proliferation at ureteric bud tips forms an ampulla

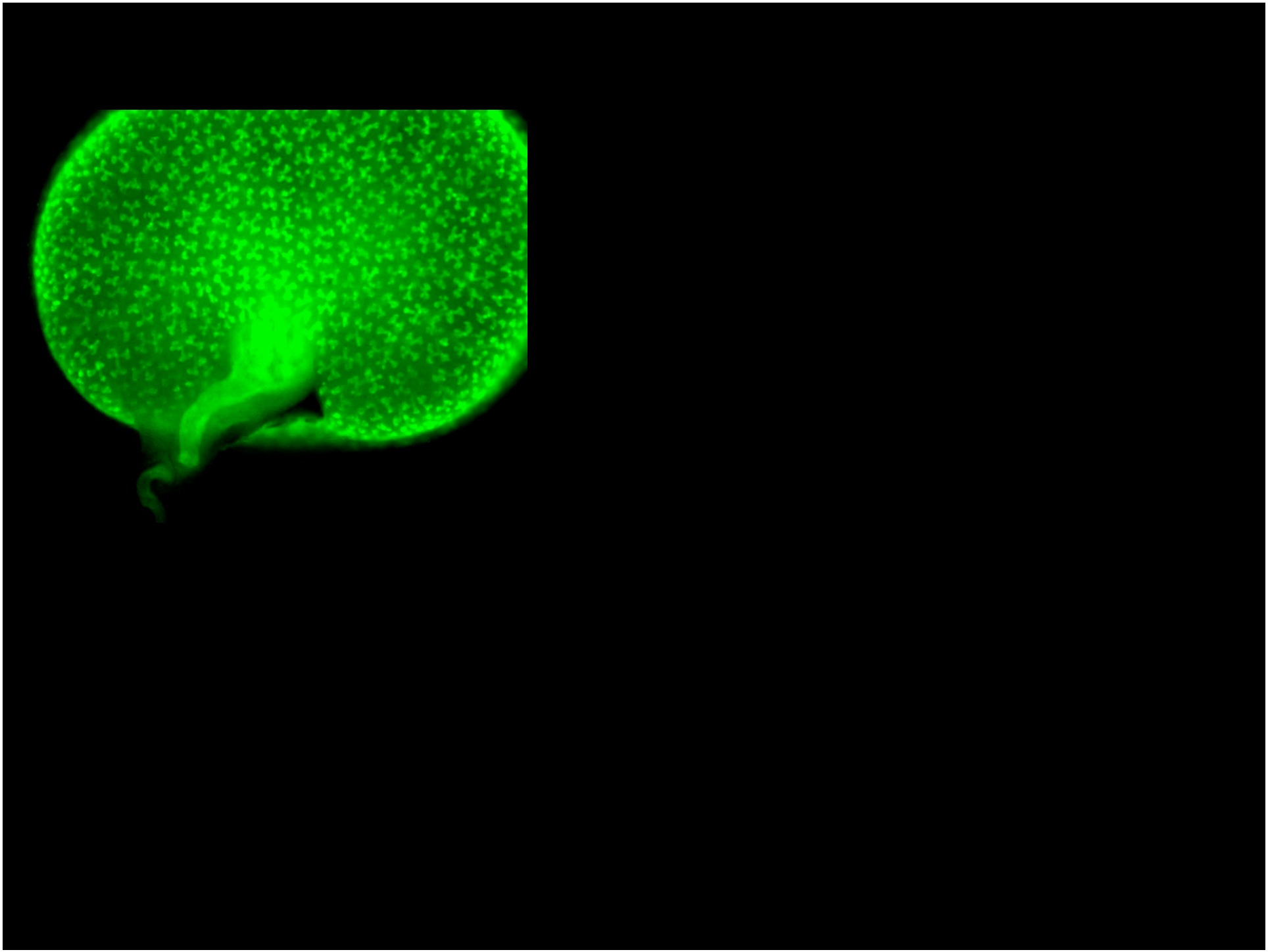




The ampulla splits to form two new tips

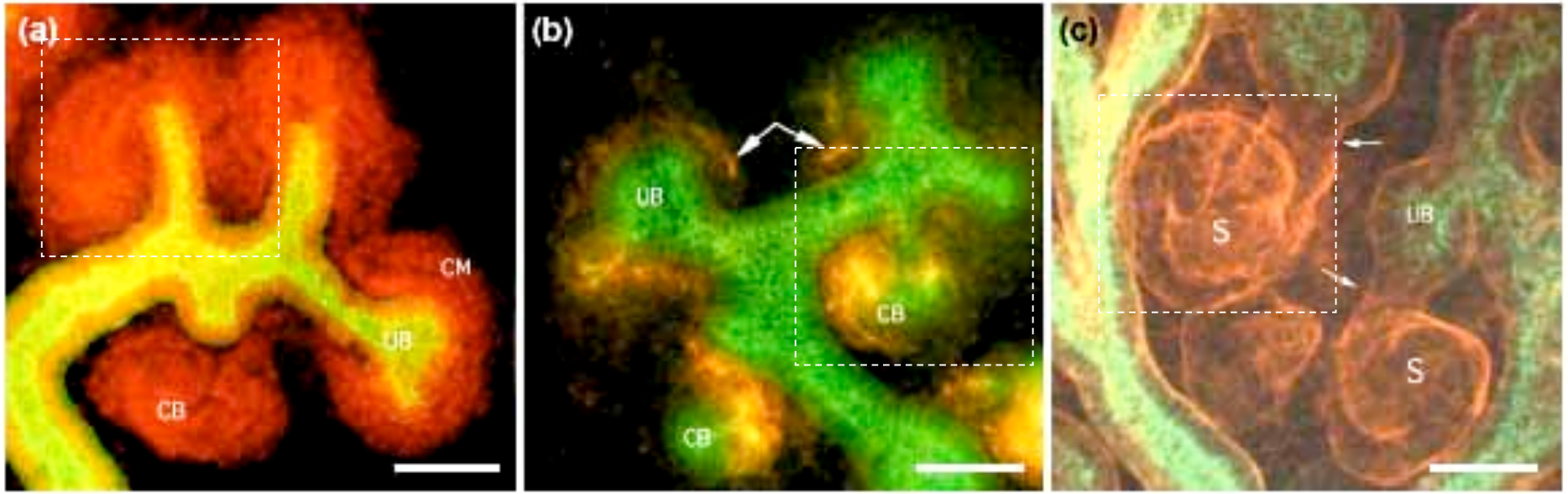


The collecting duct system grows by **dichotomous branching**



HRONS FORM EXCLUSIVELY AT **URETERIC BUD TIPS** IN RESPONSE TO LO
SIGNALS

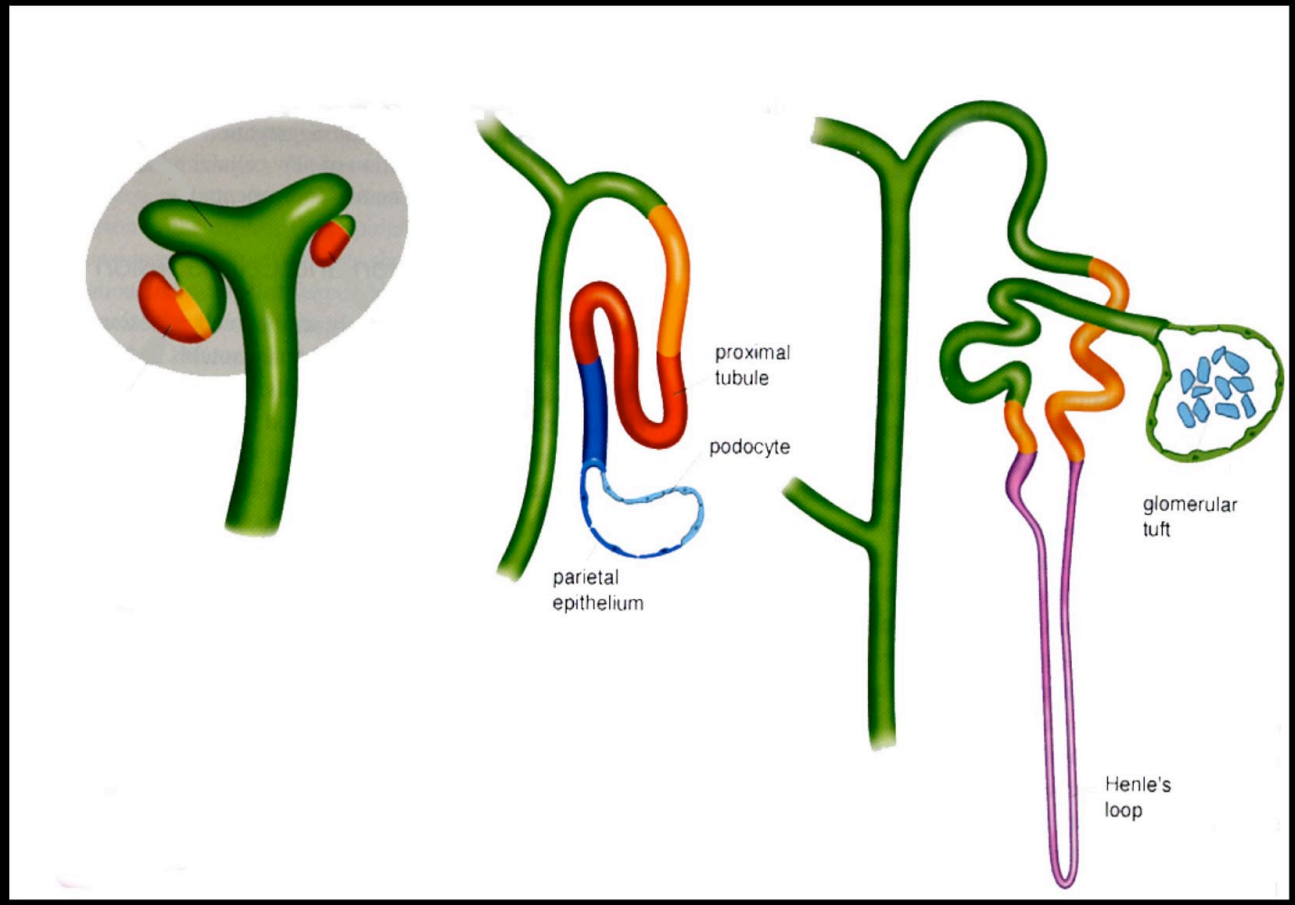
Nephron
progenitors condense at ub tips, **aggregate**



TRENDS in Cell Biology

and **trans-differentiate** into epithelial cells
that make up **Comma** and **S-shaped bodies**

nephrons differentiate from mesenchymal progenitors



Diverse cell types lining the nephron perform distinct functions

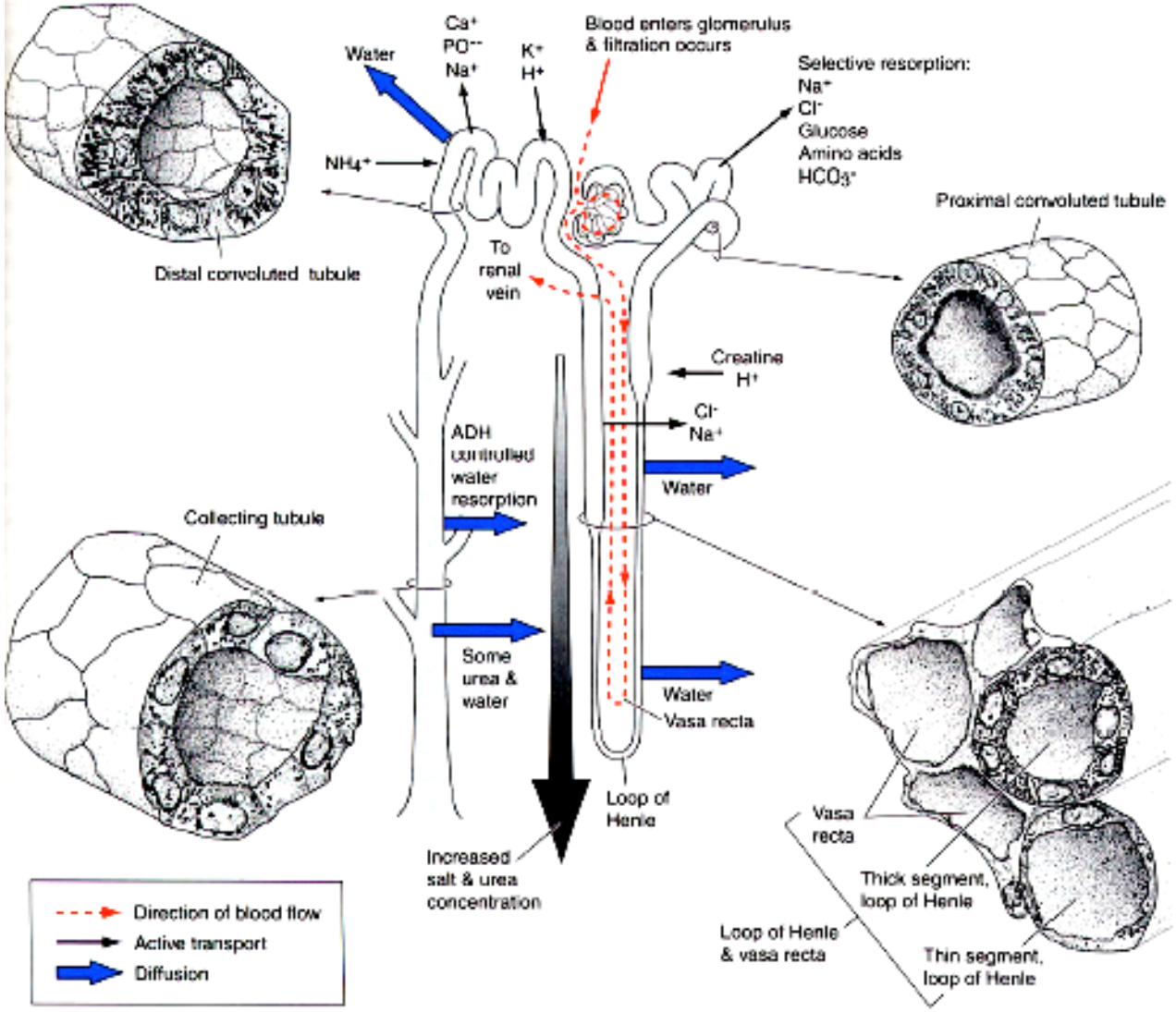
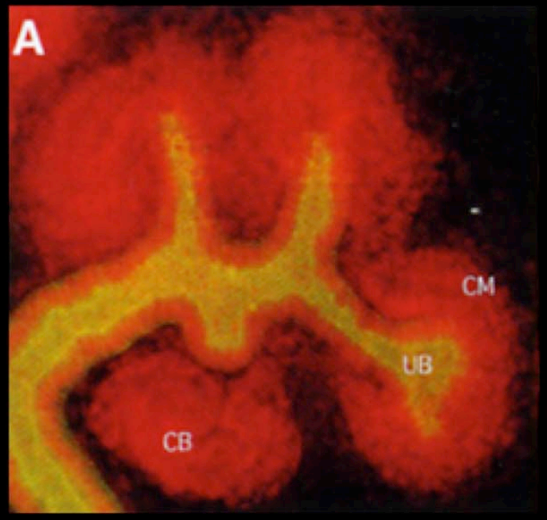
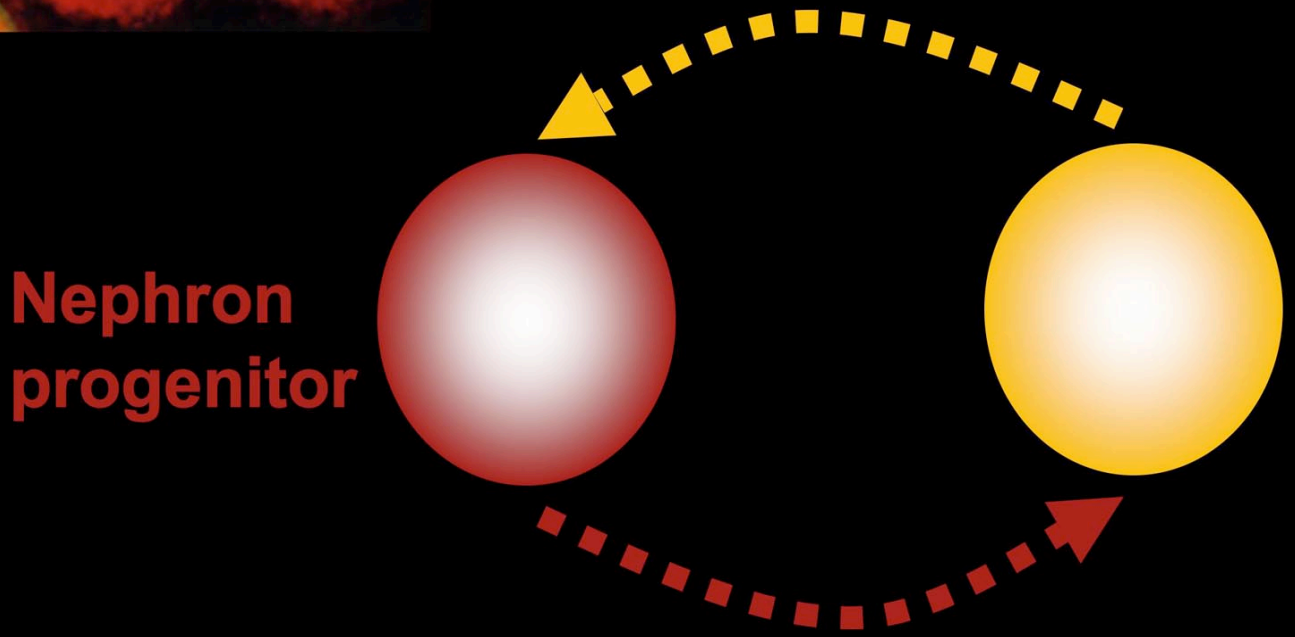


FIGURE 20-14

A mammalian nephron. Dashed red arrows represent blood flow. The regions where materials are exchanged by active transport (*narrow black arrows*) or by passive diffusion (*wide blue arrows*) are shown. The combined result of kidney action is the production of a hypertonic urine. *(Modified from Williams et al.)*

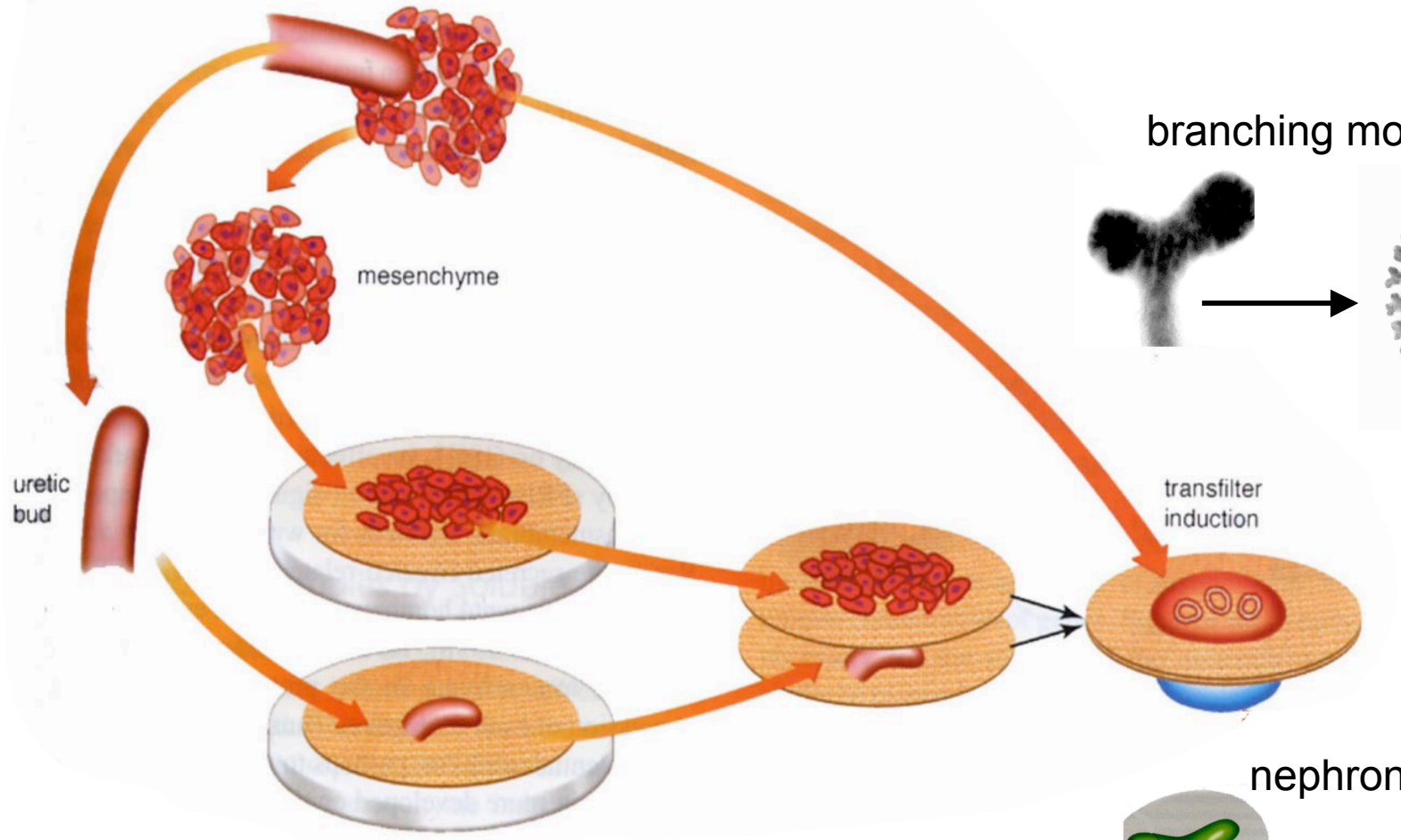
Reciprocal signaling between epithelial and mesenchymal cell types is crucial for organ formation





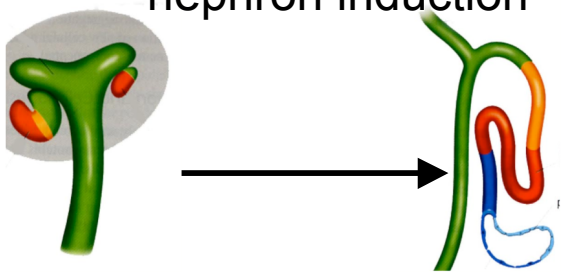
Reciprocal Signaling is required for branching morphogenesis and for nephron differentiation during renal development

co-culture experiments demonstrate reciprocal
signaling between ureteric bud epithelial and nephron progenitors

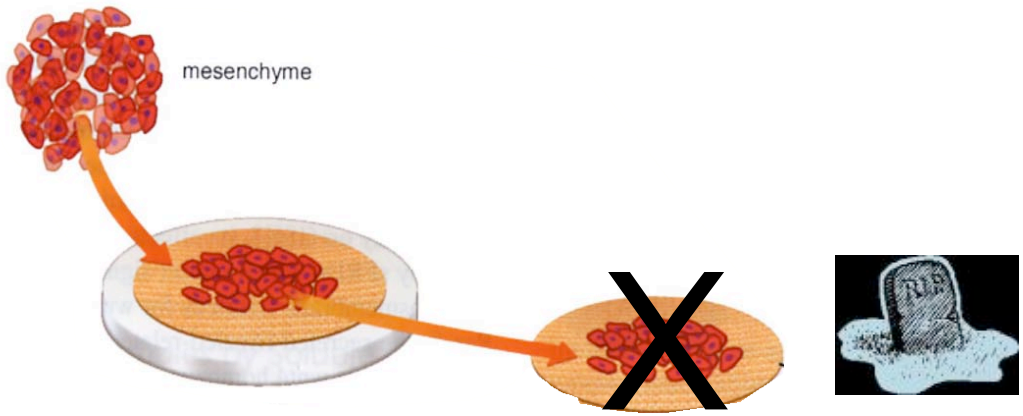


branching morphogenesis

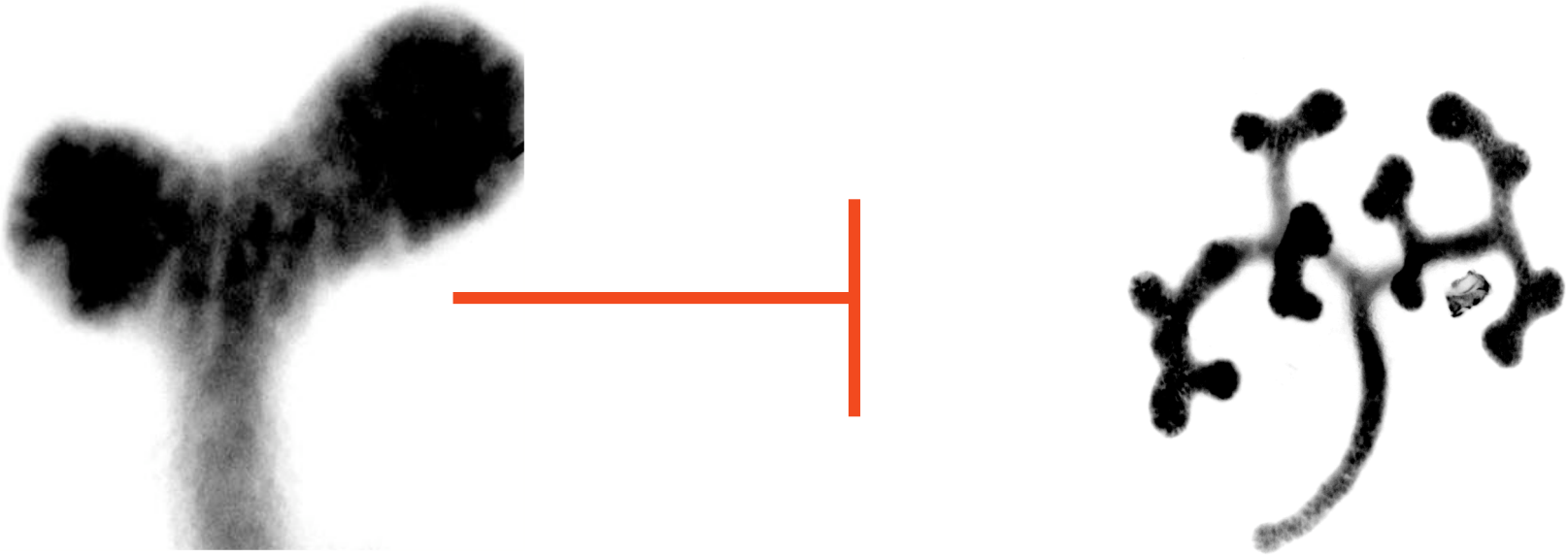
nephron induction



•no ureteric bud, nephron progenitors undergo apoptosis



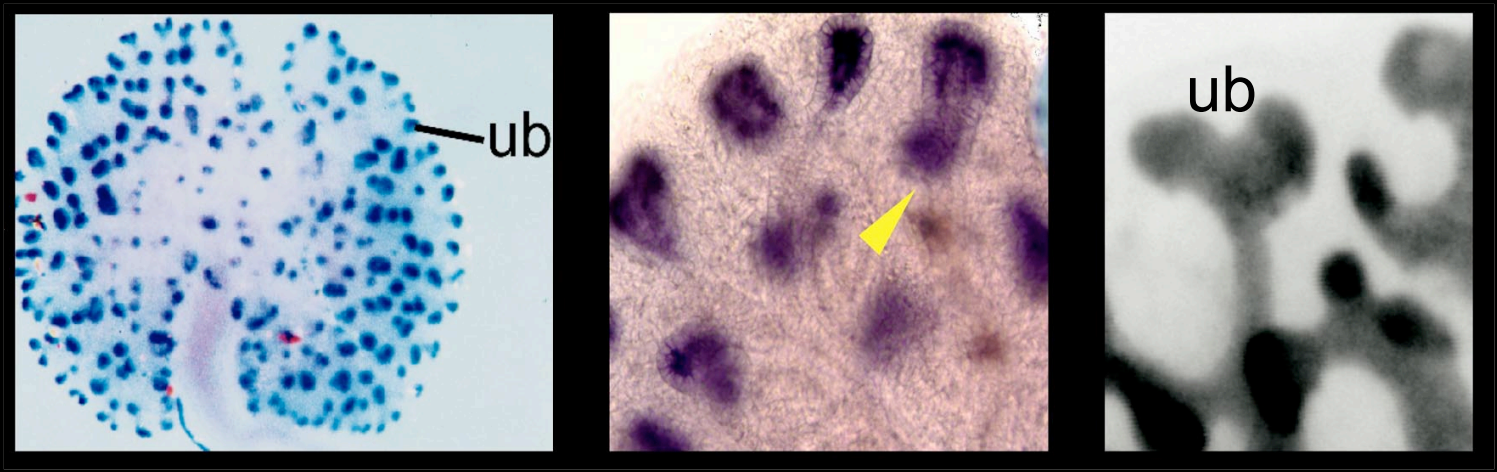
•no nephron progenitors, no branching morphogenesis



signals from the ureteric bud control nephron induction

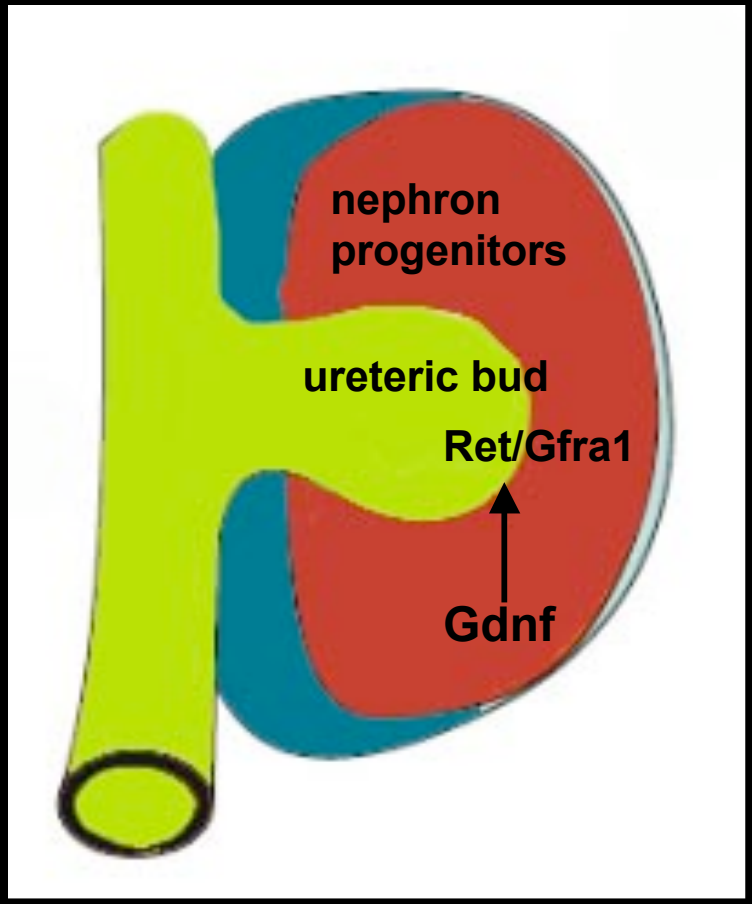
signals from nephron progenitors control branching morphogenesis

Ret/Gdnf signaling exemplifies a reciprocal loop

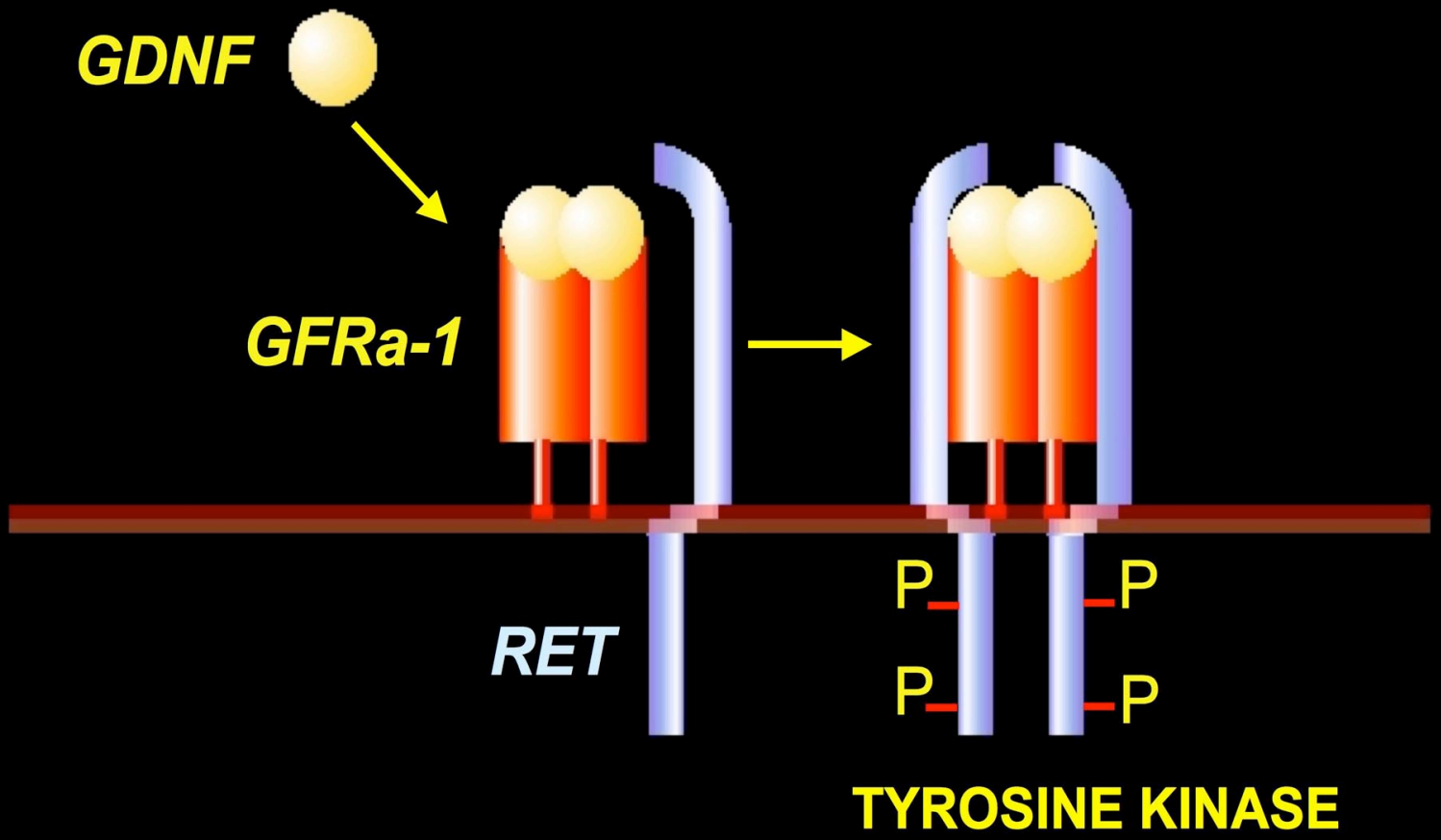


The *Ret gene* is expressed in ureteric bud tips where it control branching morphogenesis

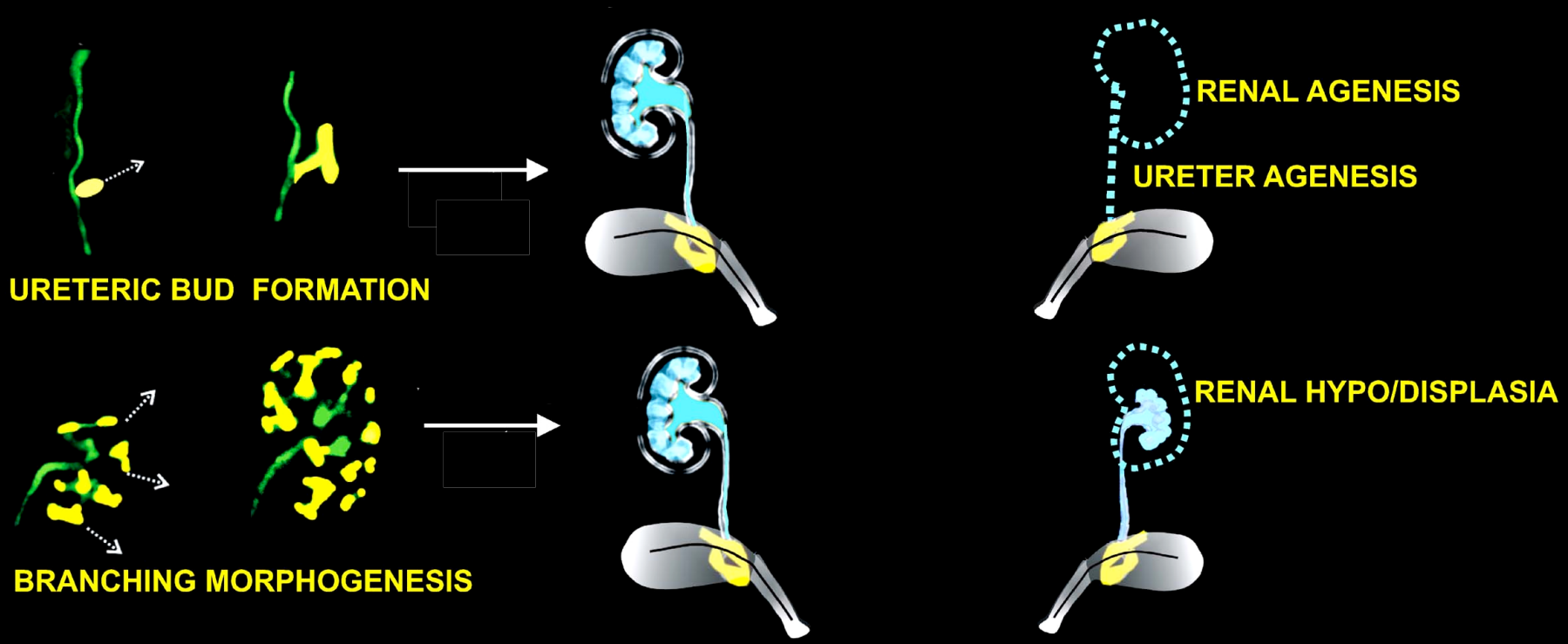
Gdnf secreted by nephron progenitors binds to Ret via the Ret receptor (Gfra1) inducing branching morphogenesis



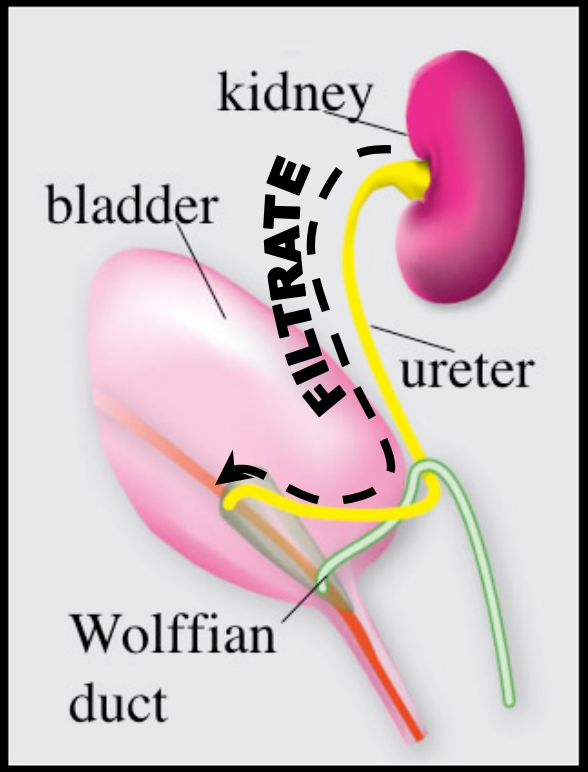
GDNF signals *through GFRa-1* and *RET*



deletion of Ret, Gdnf or the Ret receptor Gfra1 results in renal agenesis or hypoplasia

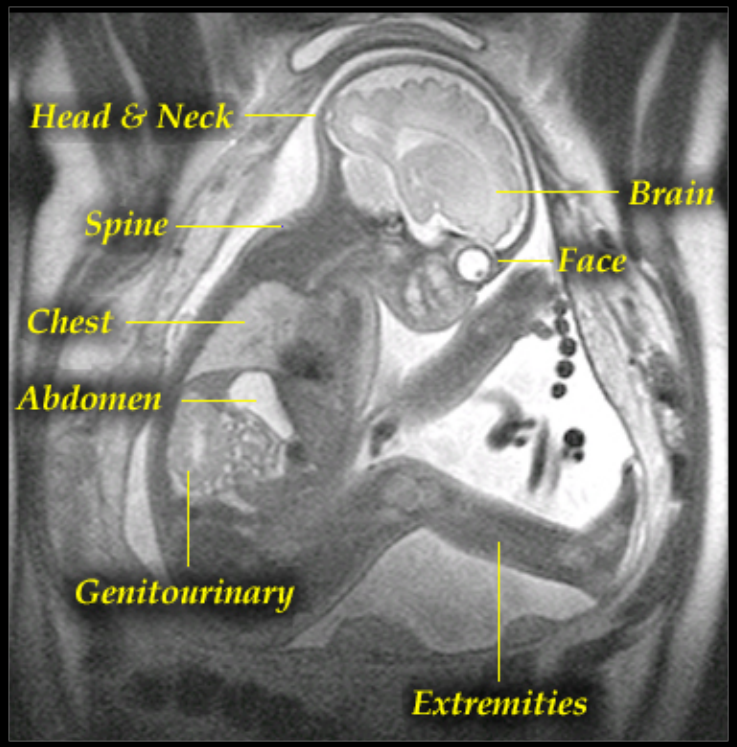


Connecting the upper and lower urinary tract



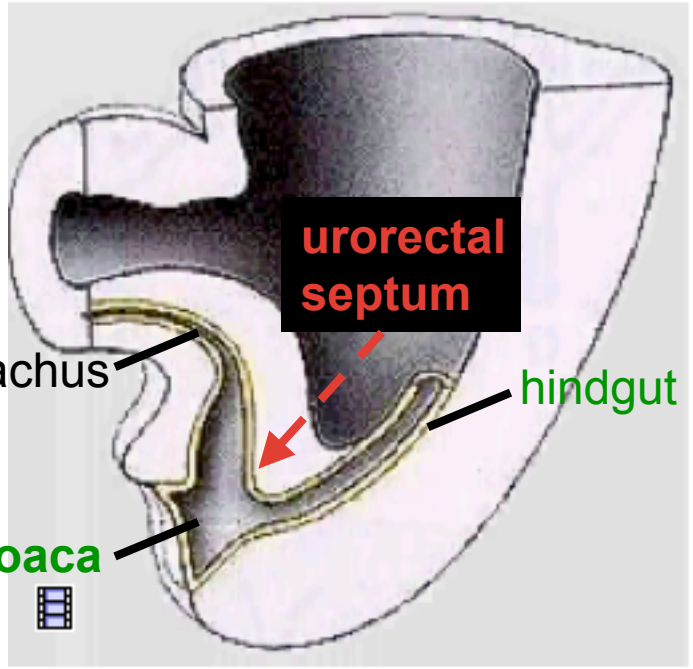
renal filtrate must be efficiently propelled to the bladder for storage and excretion

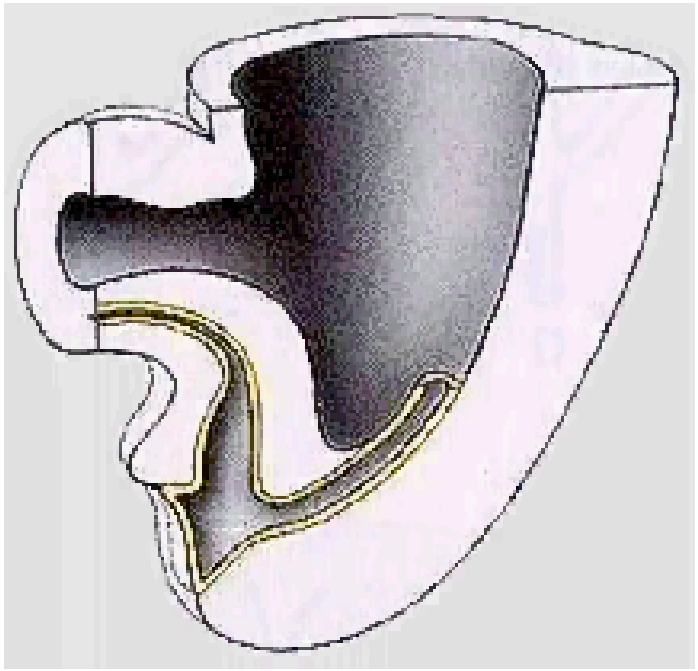
physical or functional blockage that impedes urine flow can cause renal scarring, hydronephrosis or end state renal disease



hydronephrosis *in utero*

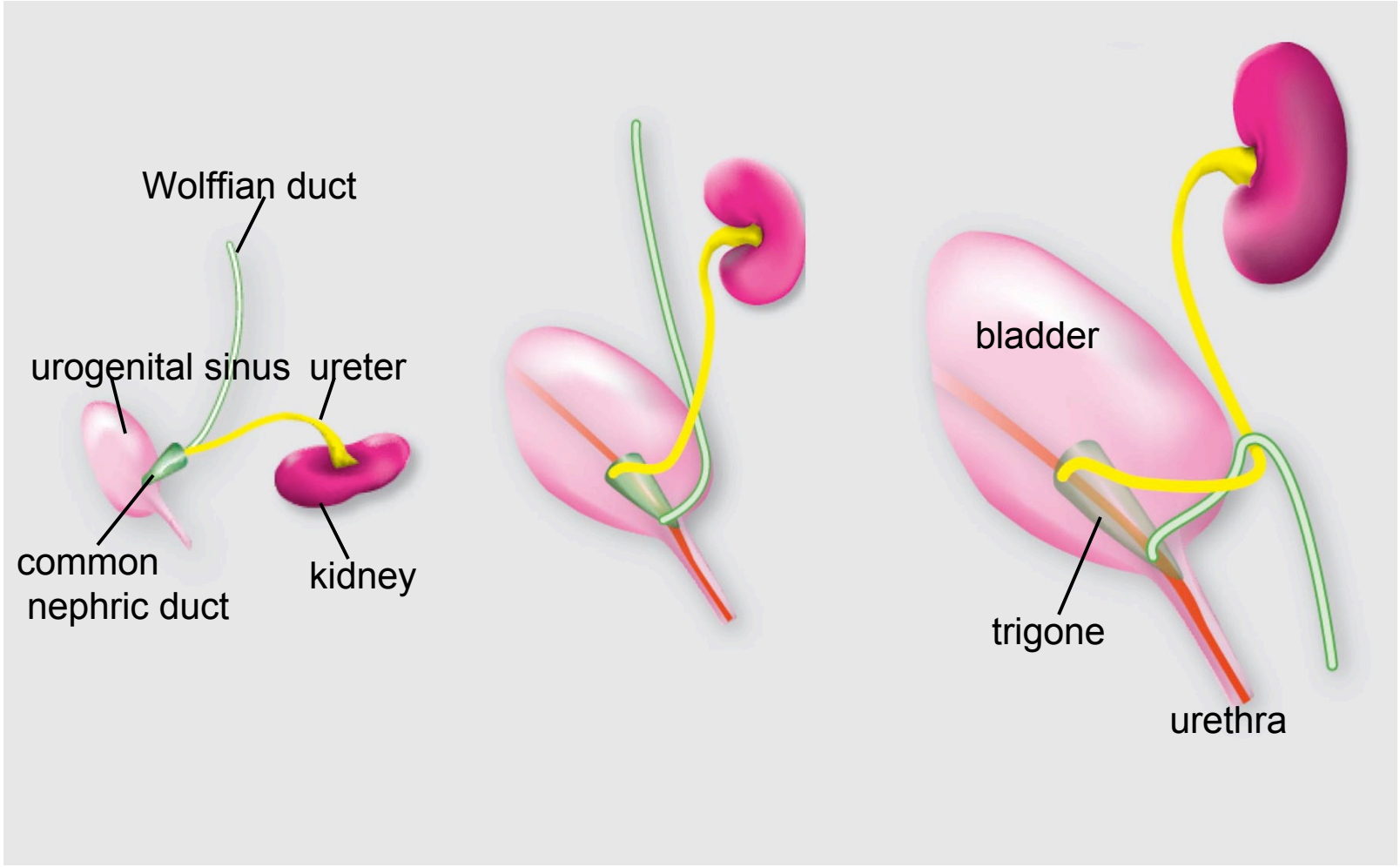
How does the lower urinary tract form?



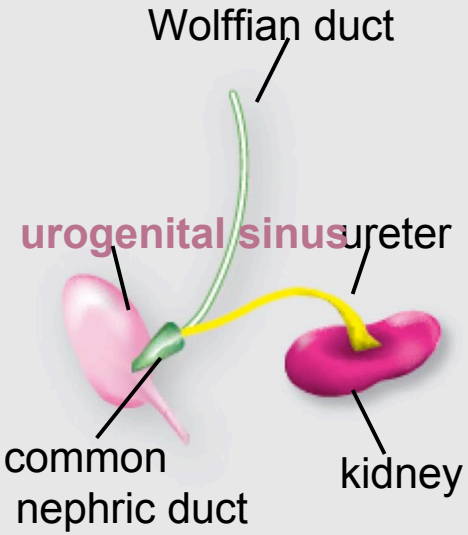


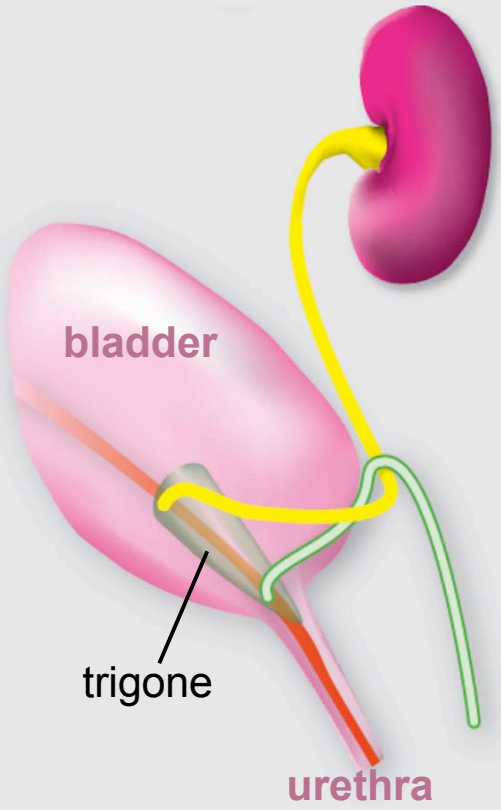
the **cloaca** is partitioned into the **hindgut** and **urogenital sinus** by the **urorectal septum**

As the embryo grows, the ureters lengthen, and the **kidneys rotate** and **ascend** along the dorsal body wall

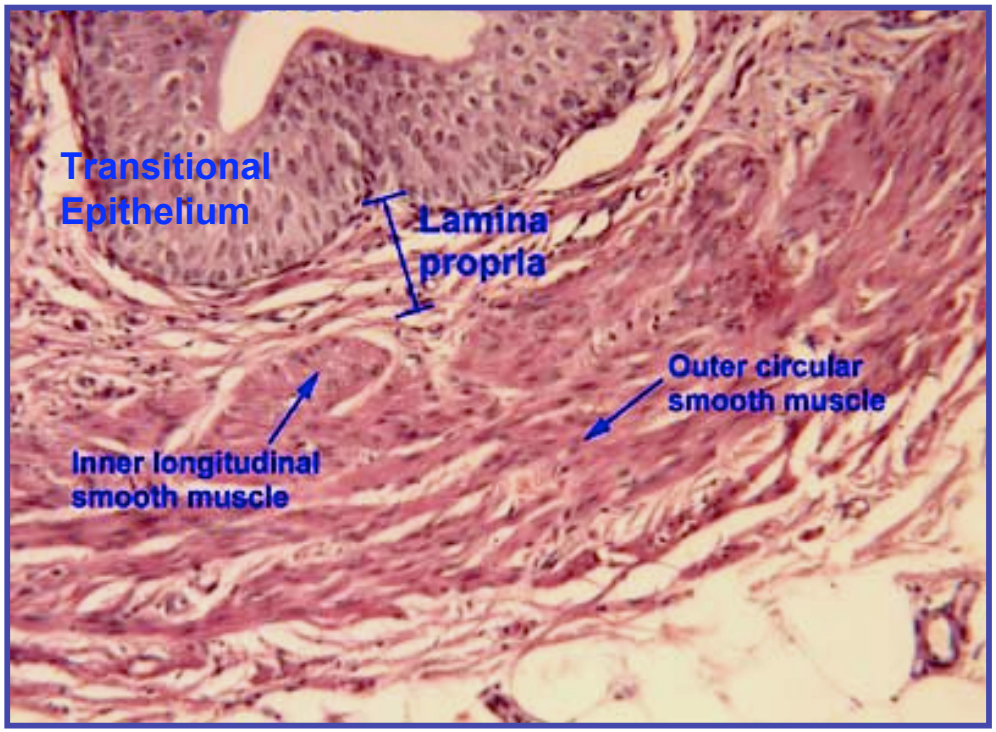


The urogenital sinus forms the **bladder** and the **urethra**





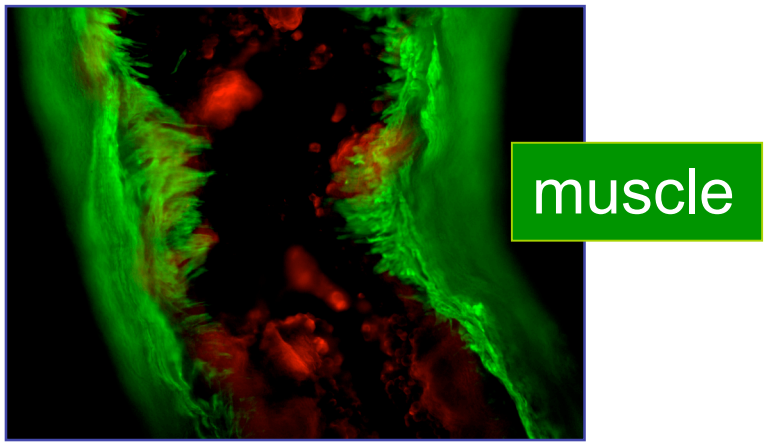
The renal pelvis, ureters and bladder are lined with a a transitional epithelium (the urothelium)



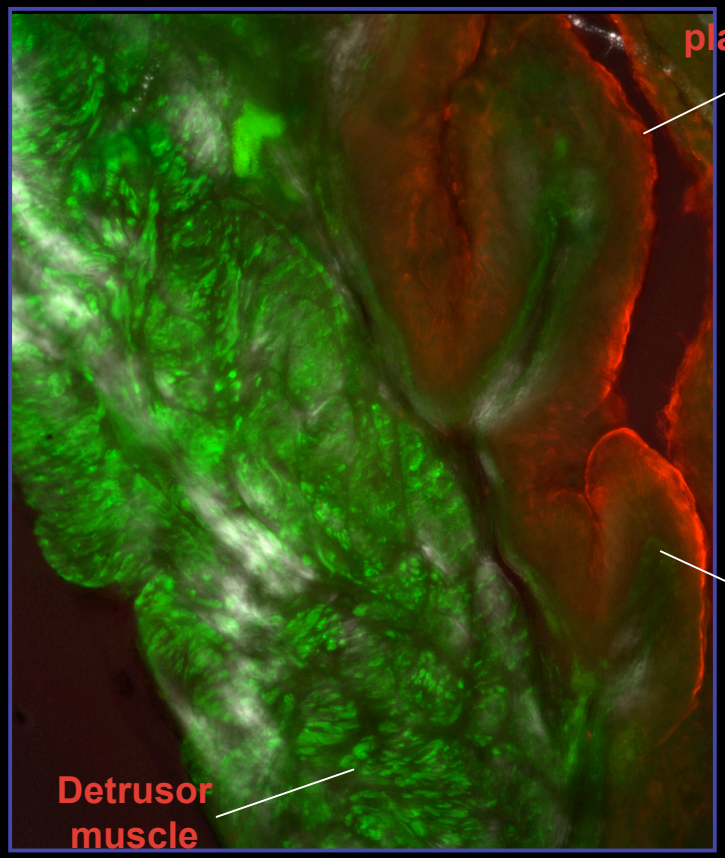
Urine transport depends on peristalsis

ureters are surrounded by 2-3 coats of longitudinal and circular muscle that mediate myogenic peristalsis

myogenic peristalsis is initiated in the renal pelvis moving a bolus of urine to the ureter then to the bladder.



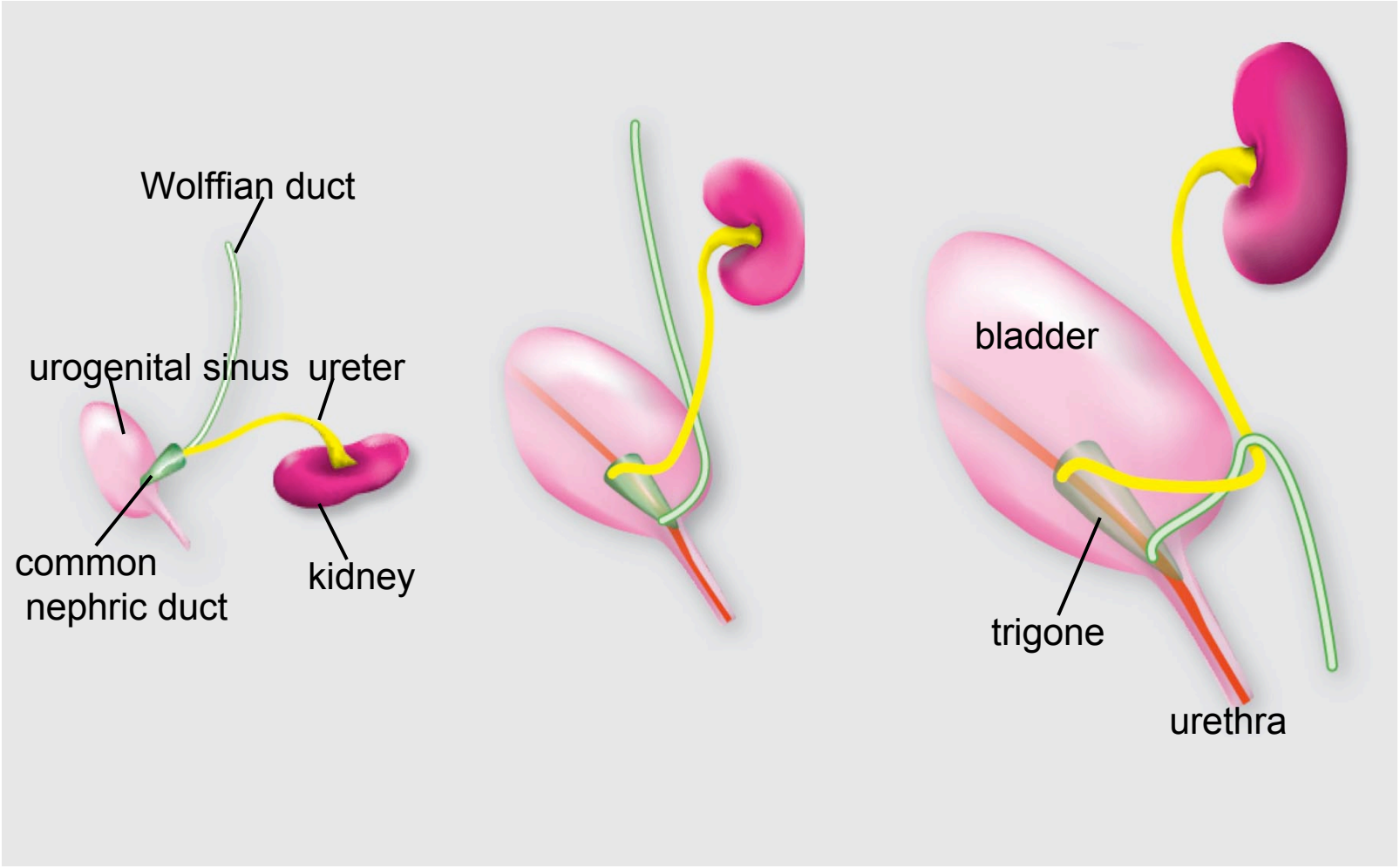
The Bladder



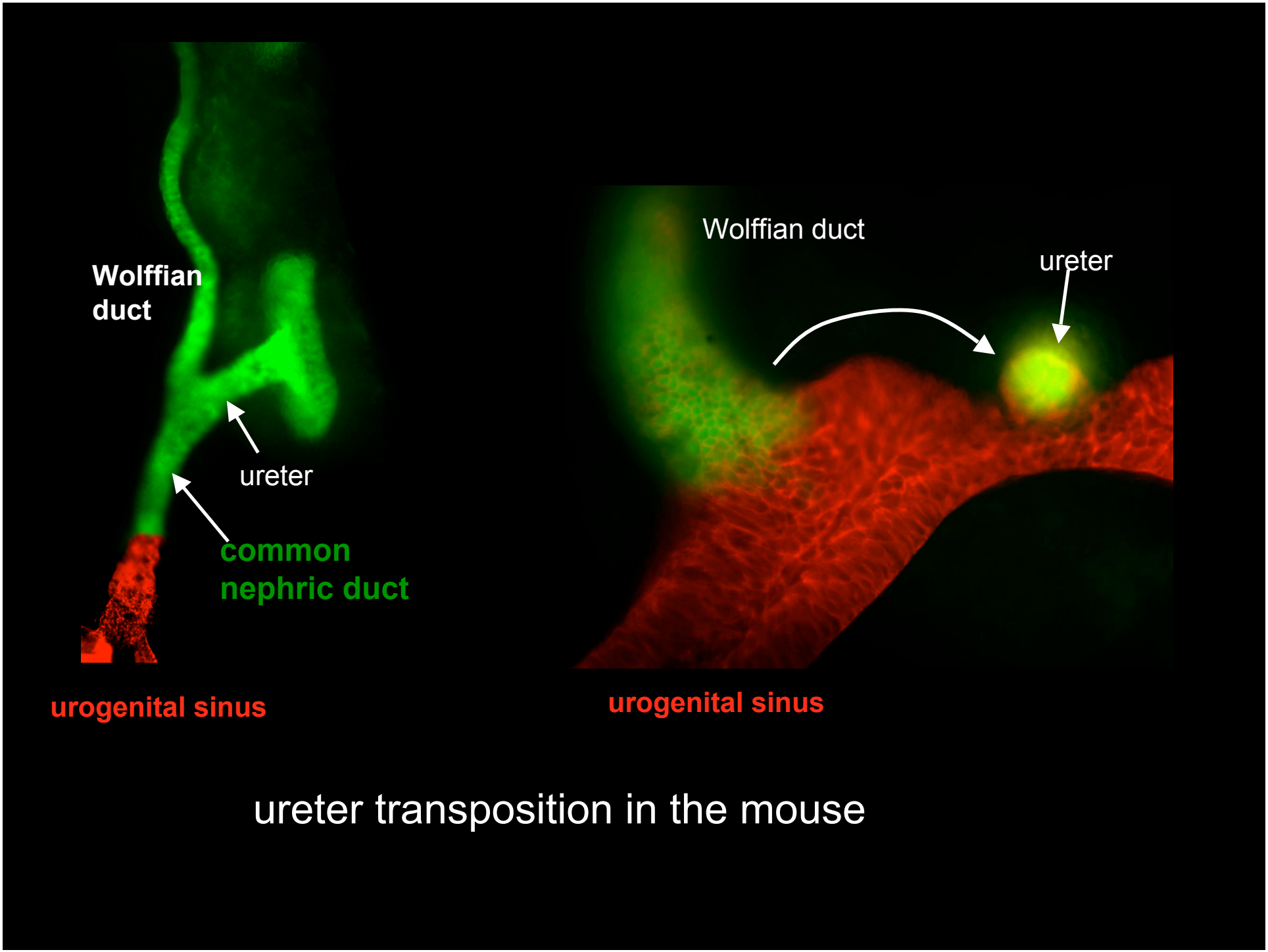
Epithelium lined with **uroplakin plaques** that form a water-proof barrier

rugae (folds)
allow expansion of the bladder as it fills

The ureter is initially joined to the Wolffian duct (future vas-deferens) not to the bladder



Mature connections are established when the ureter orifice is **transposed** from the posterior Wolffian duct (**the common nephric duct)** to the bladder

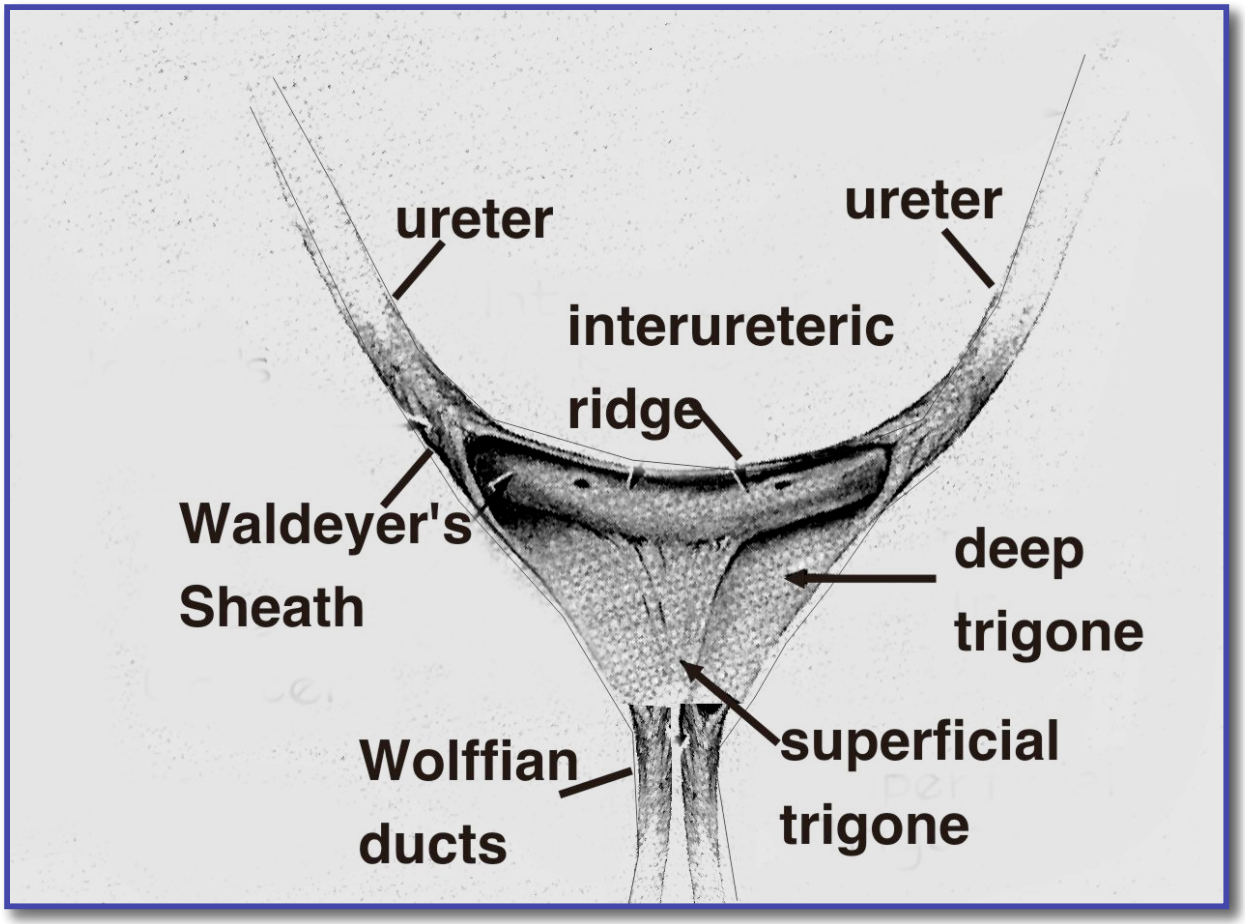


ureter transposition in the mouse

Accepted model of ureter transposition

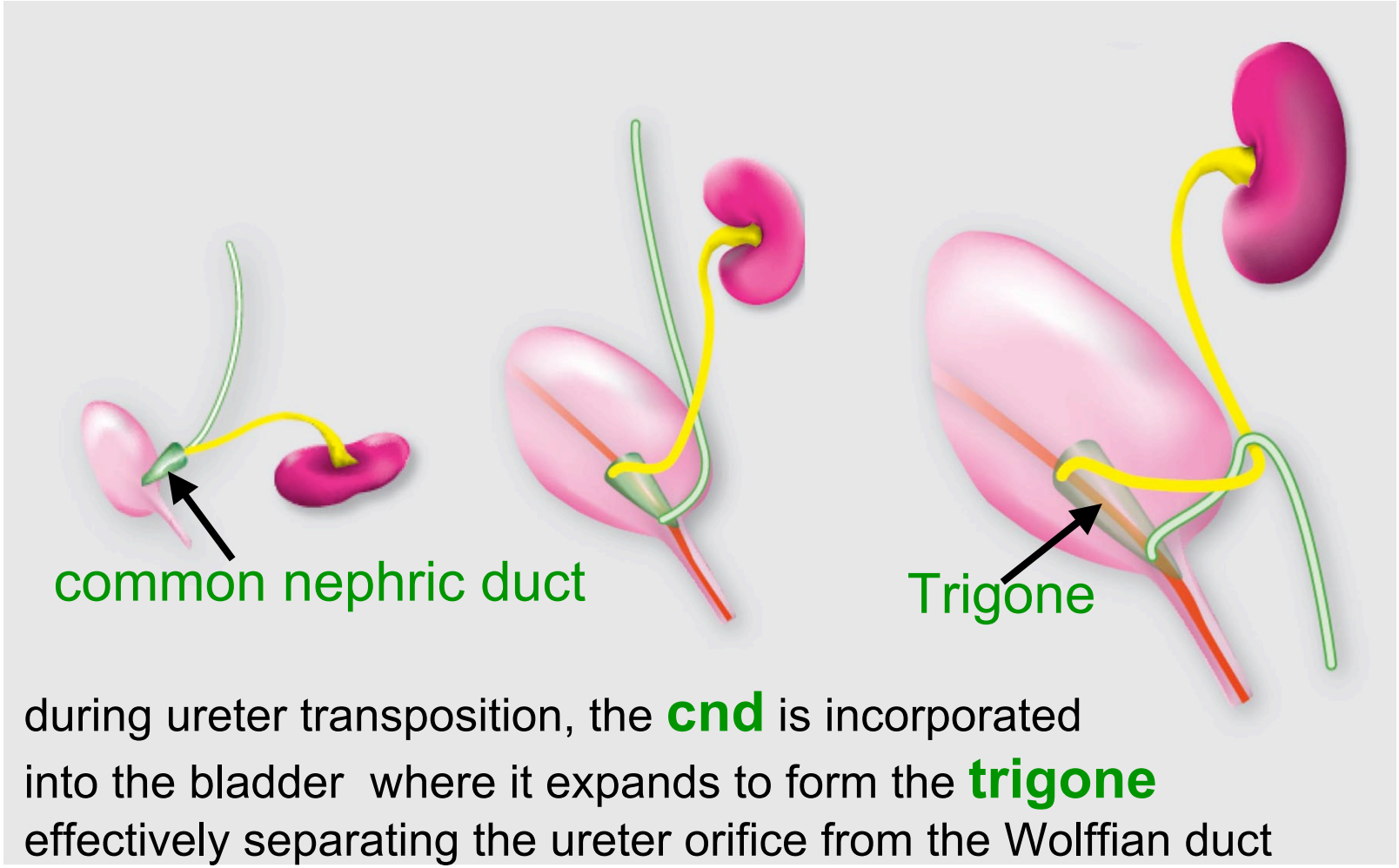
formation of the **trigone** from the **common nephric duct** repositions the ureters in the bladder

Urine transport depends on proper connections between the ureters and the **bladder trigone**



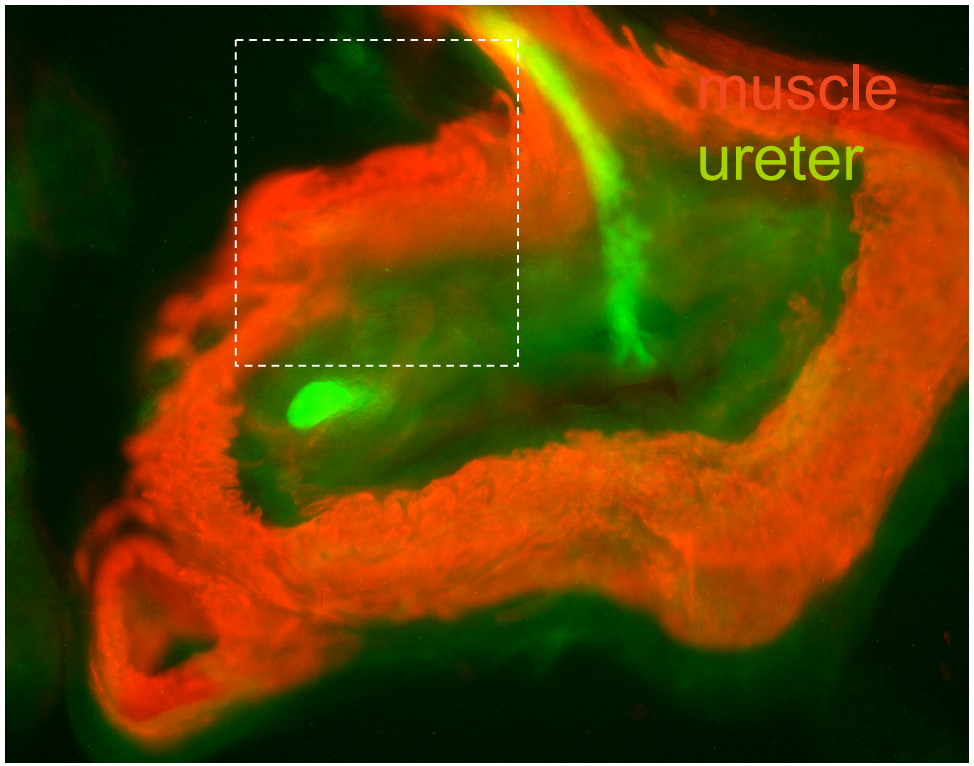
The **trigone** is defined as the portion of the urogenital sinus that lies between the ureters and sex ducts

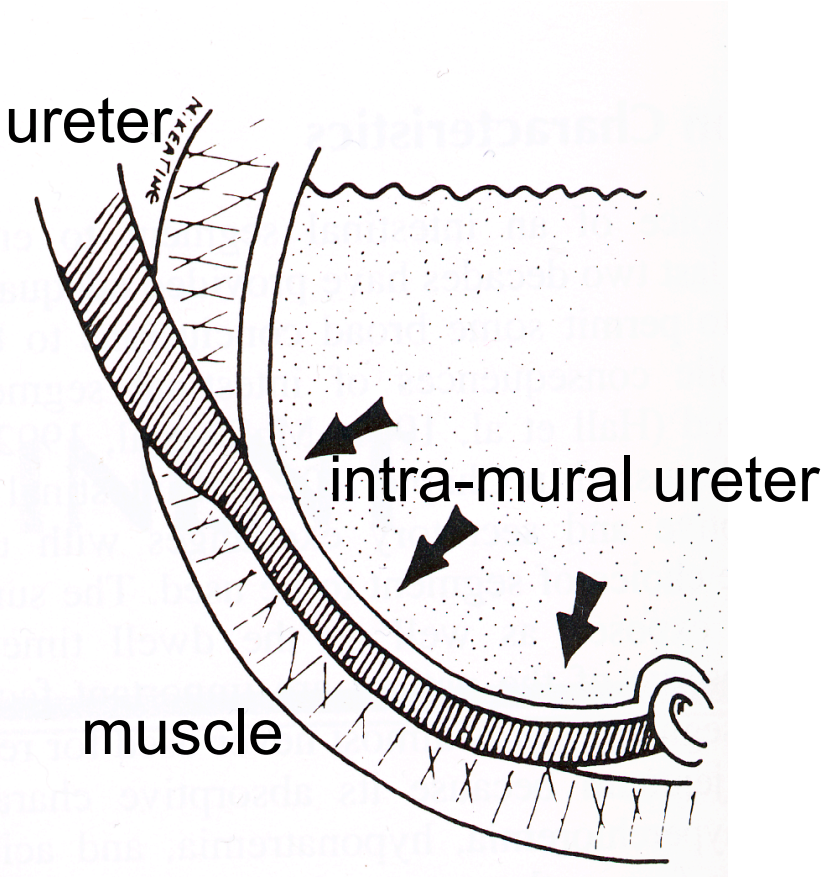
According to the accepted model, trigone formation is considered to be crucial for repositioning the ureter orifice



during ureter transposition, the **cnd** is incorporated into the bladder where it expands to form the **trigone** effectively separating the ureter orifice from the Wolffian duct

the **flap valve** is an anti-reflux mechanism that prevents urine back flow



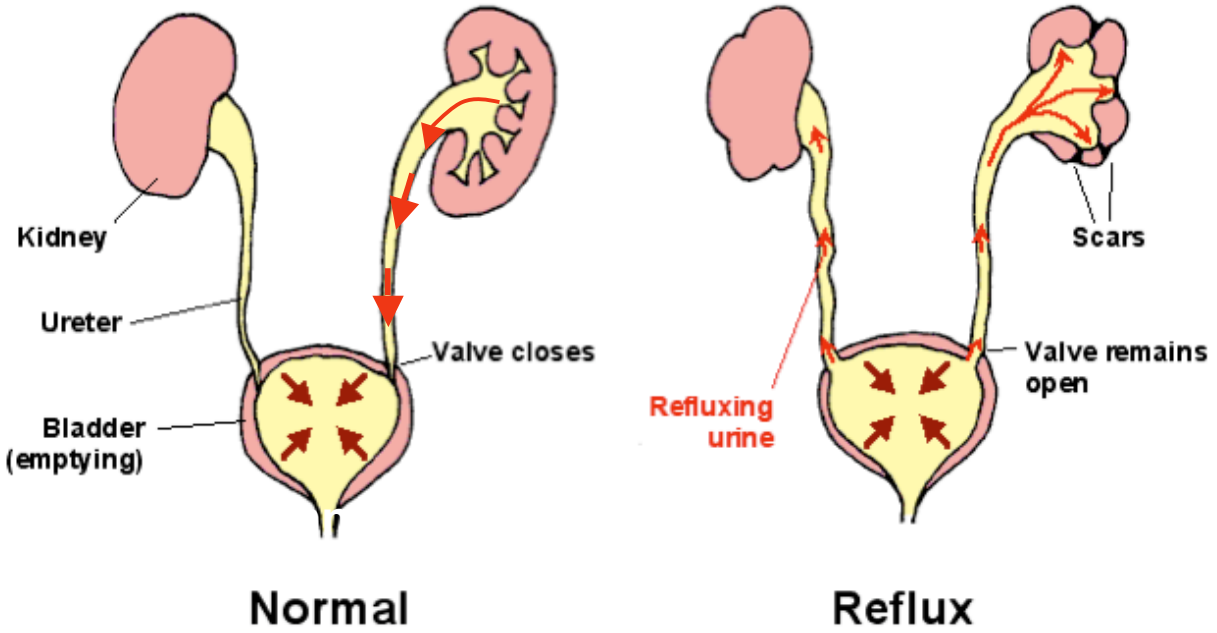


its function depends on proper insertion of the ureter orifice in the bladder

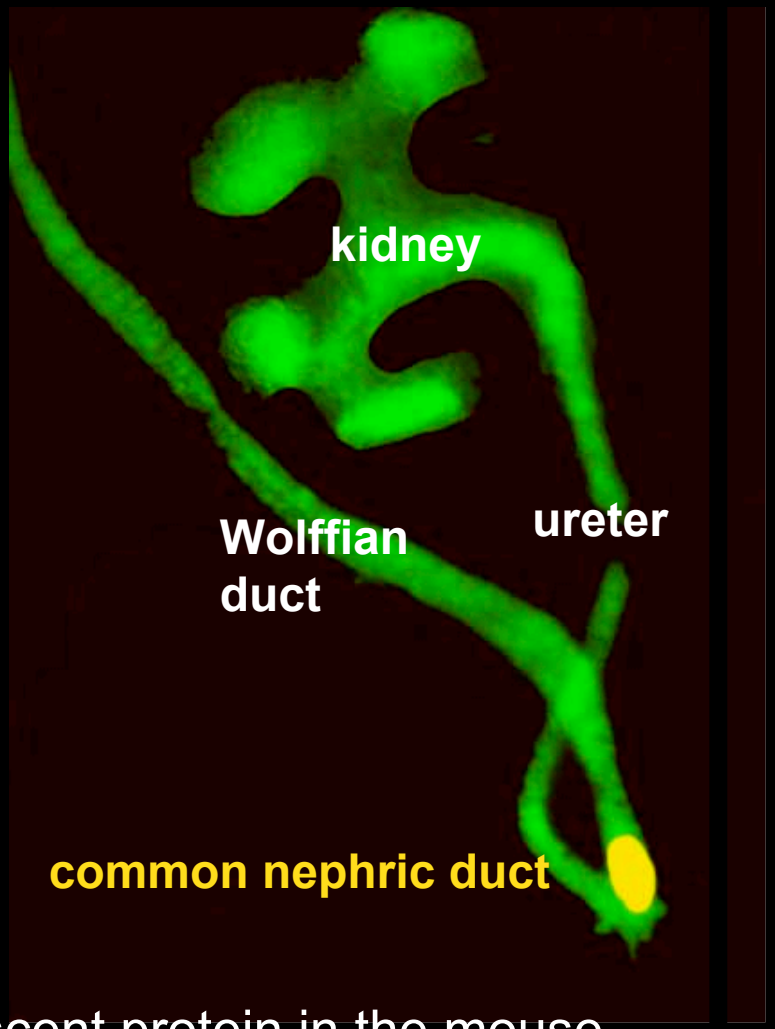
proper positioning of the ureter orifice is necessary for:

- formation of patent connections along the outflow tract
- preventing reflux

defects in position, can cause obstruction or reflux, inducing severe renal damage



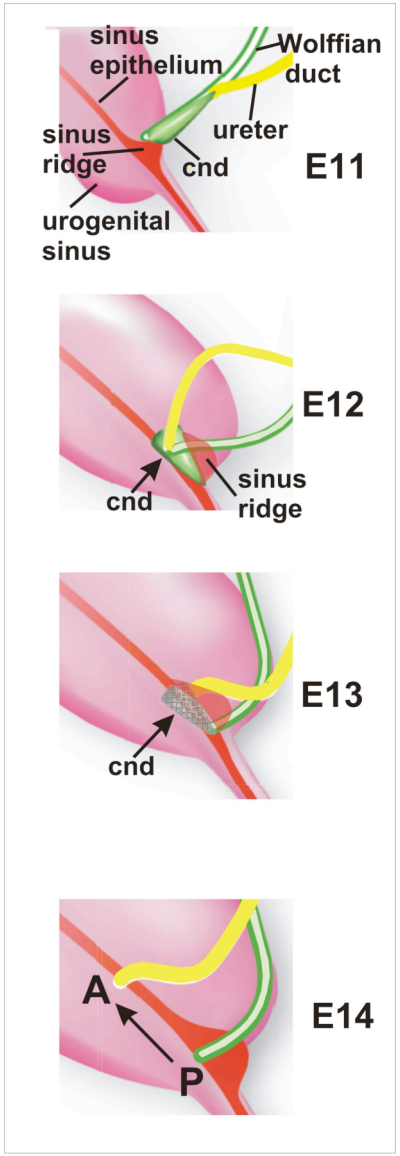
using mouse models to re-assess the mechanism of ureter transposition:



expression of Jelly Fish green fluorescent protein in the mouse common nephric duct of this transgenic mouse enables us to follow its fate during ureter insertion

Ureter transposition depends on apoptosis of the **common nephric duct**, **which does not form the trigone**

A revised model of ureter transposition



the common nephric duct is absorbed into the expanding urogenital sinus. The ureter makes direct contact with and inserts into the urogenital sinus

apoptosis of the common nephric duct enables the ureter orifice to detach from the Wolffian duct

continued growth and expansion of the urogenital sinus moves the ureter orifice further anterior to the bladder neck

**forget this revised model of ureter transposition when you take your boards; the new model is published but not in the text books yet. Remember it however as an example of how modern tools will allow us to directly examine other embryological models of organogenesis!!