

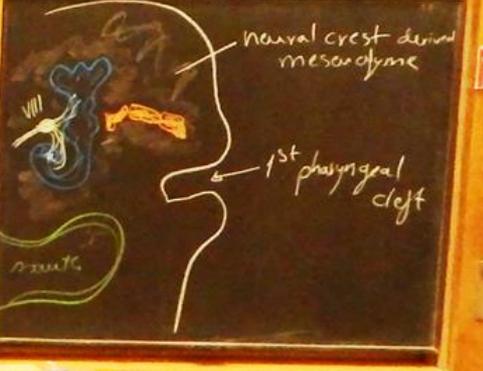
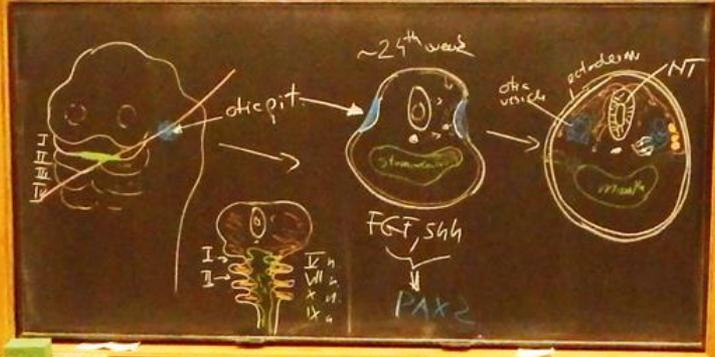
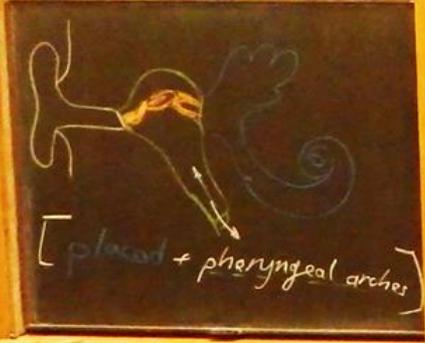
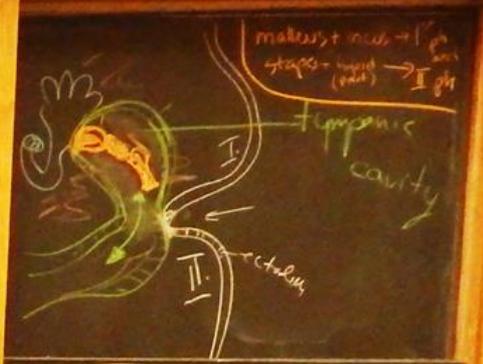
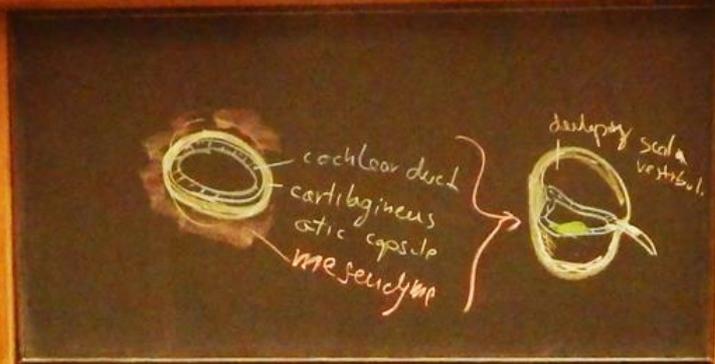
Development of the auditory system

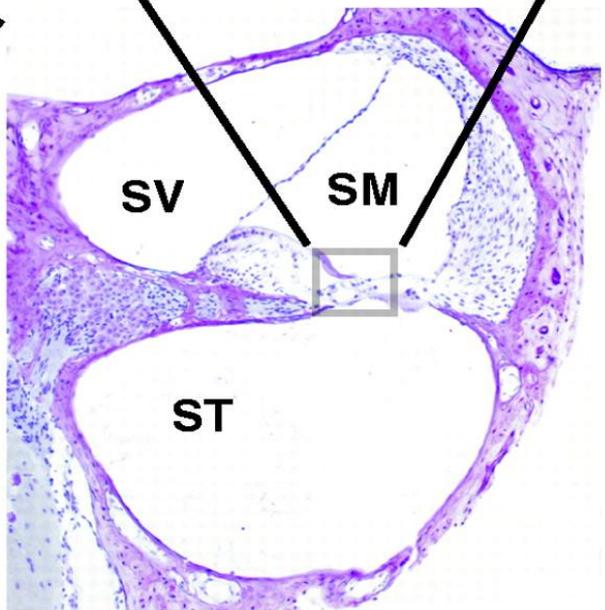
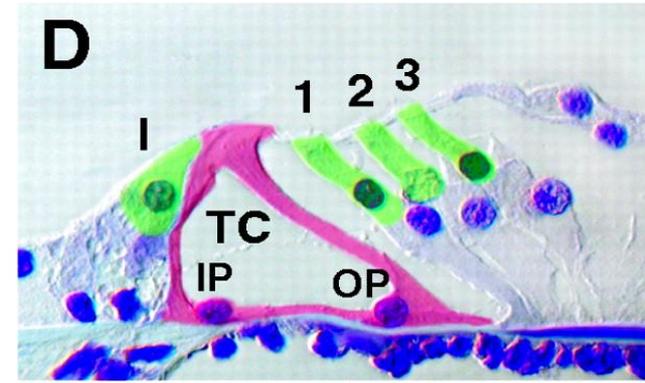
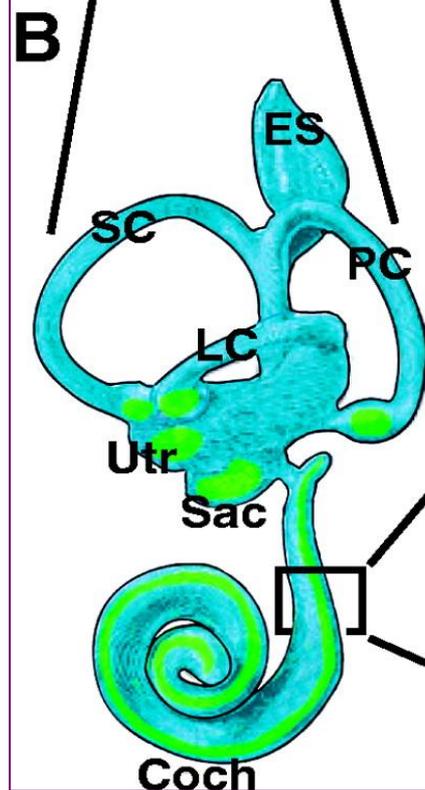
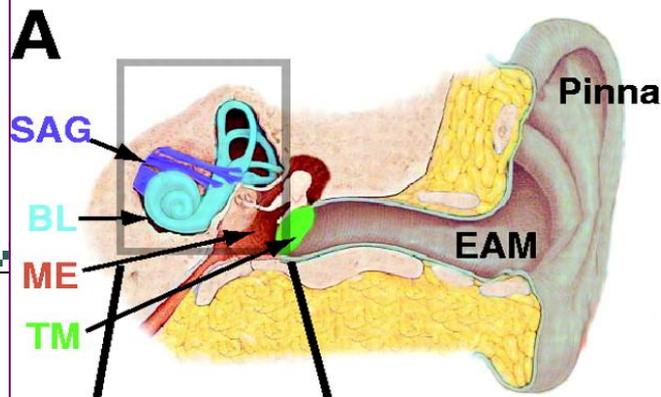
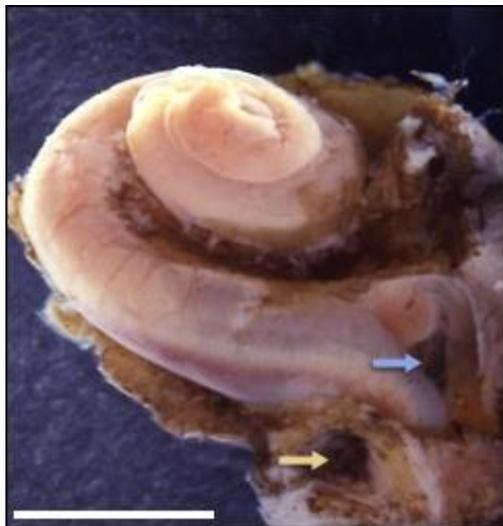
Dr. Nandor Nagy



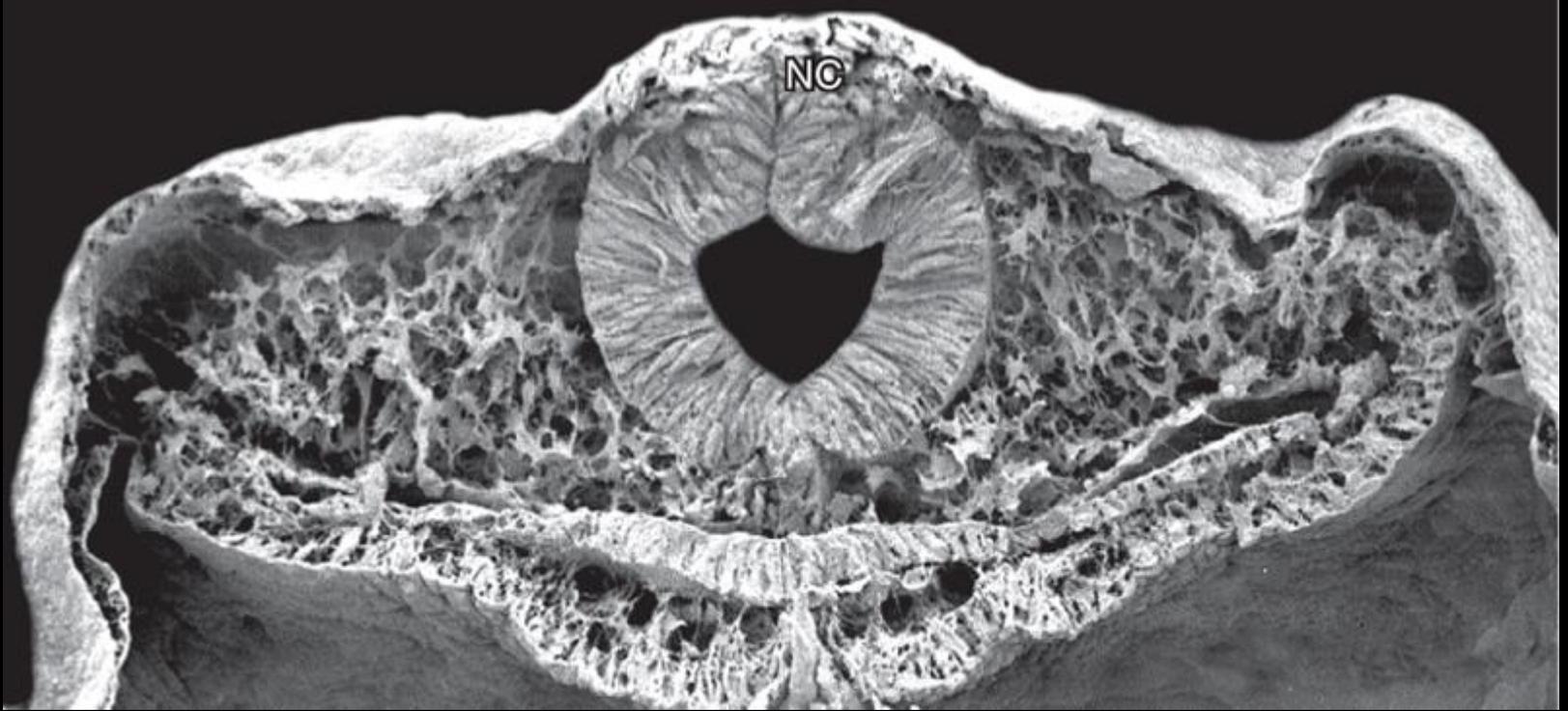
Semmelweis University, Budapest

vestibulo-cochlear ganglion
 cochlear duct
 cartilaginous otic capsule
 mesenchyme
 neural crest → ossicles



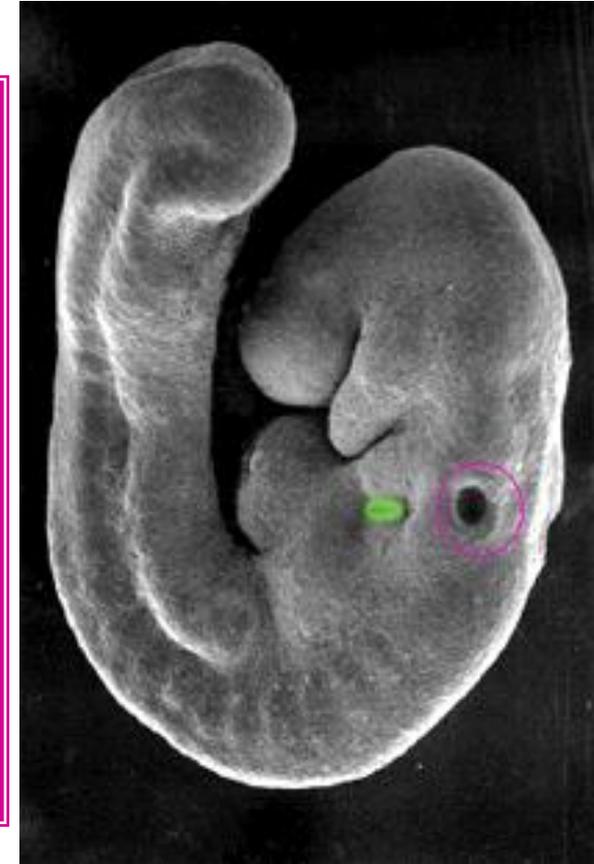
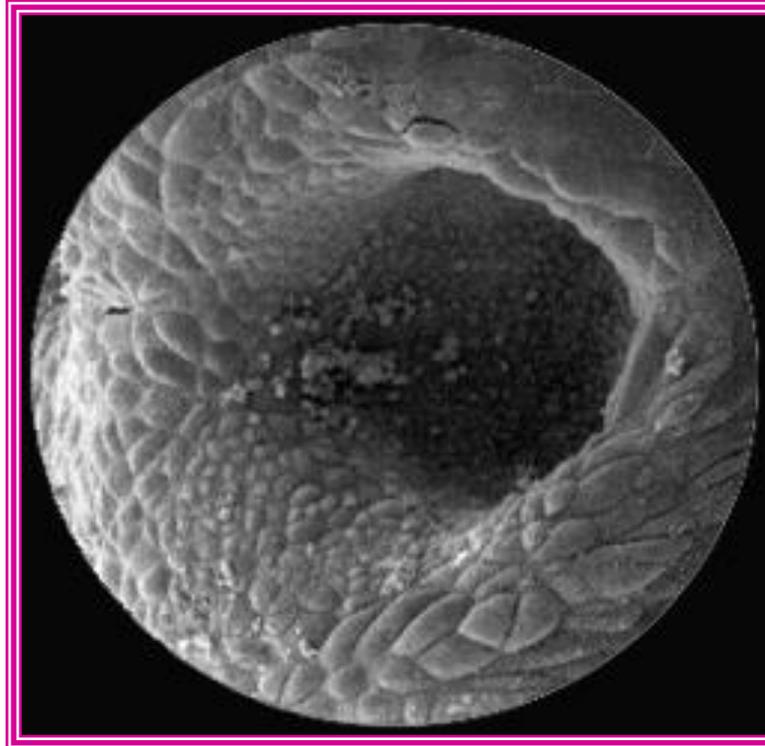


Barald, K. F. et al. *Development* 2004;131:4119-4130

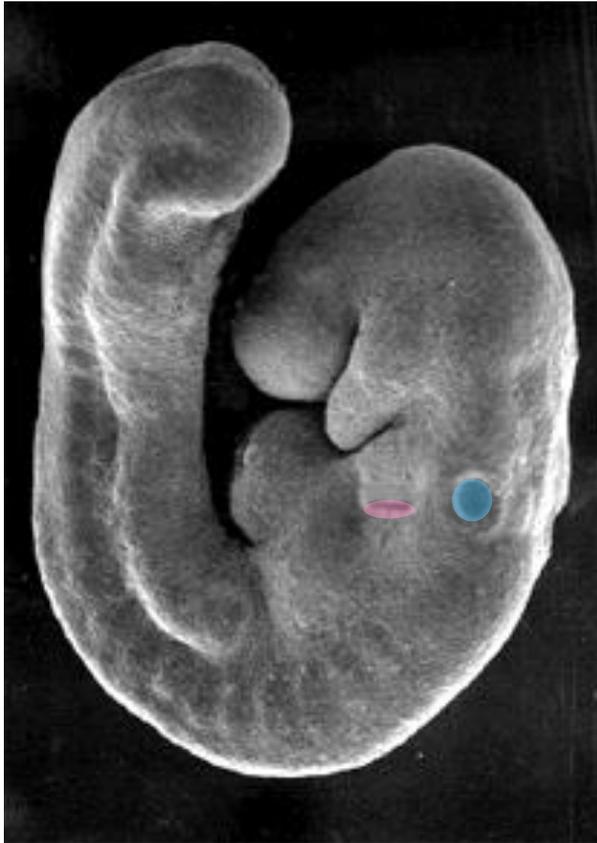


Development of Inner Ear

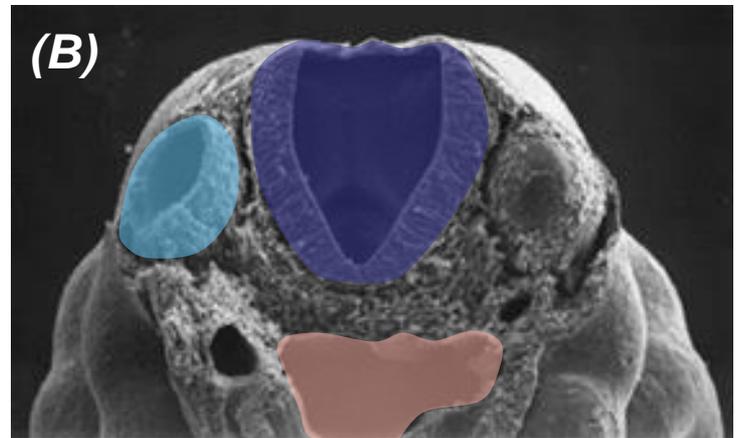
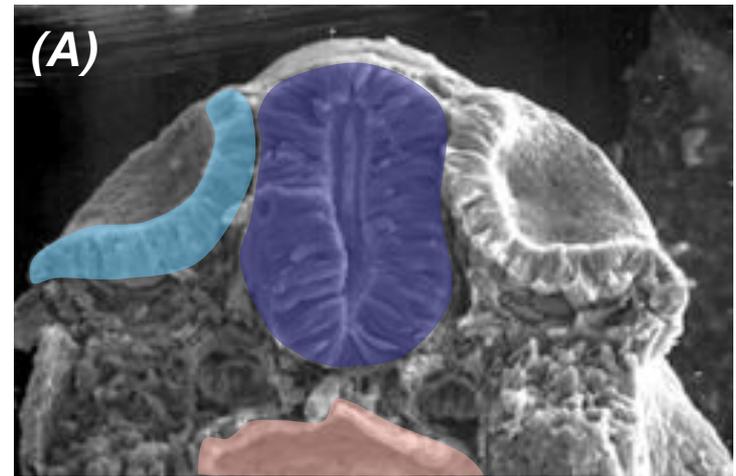
-all of the inner ear derivatives arise from ectoderm



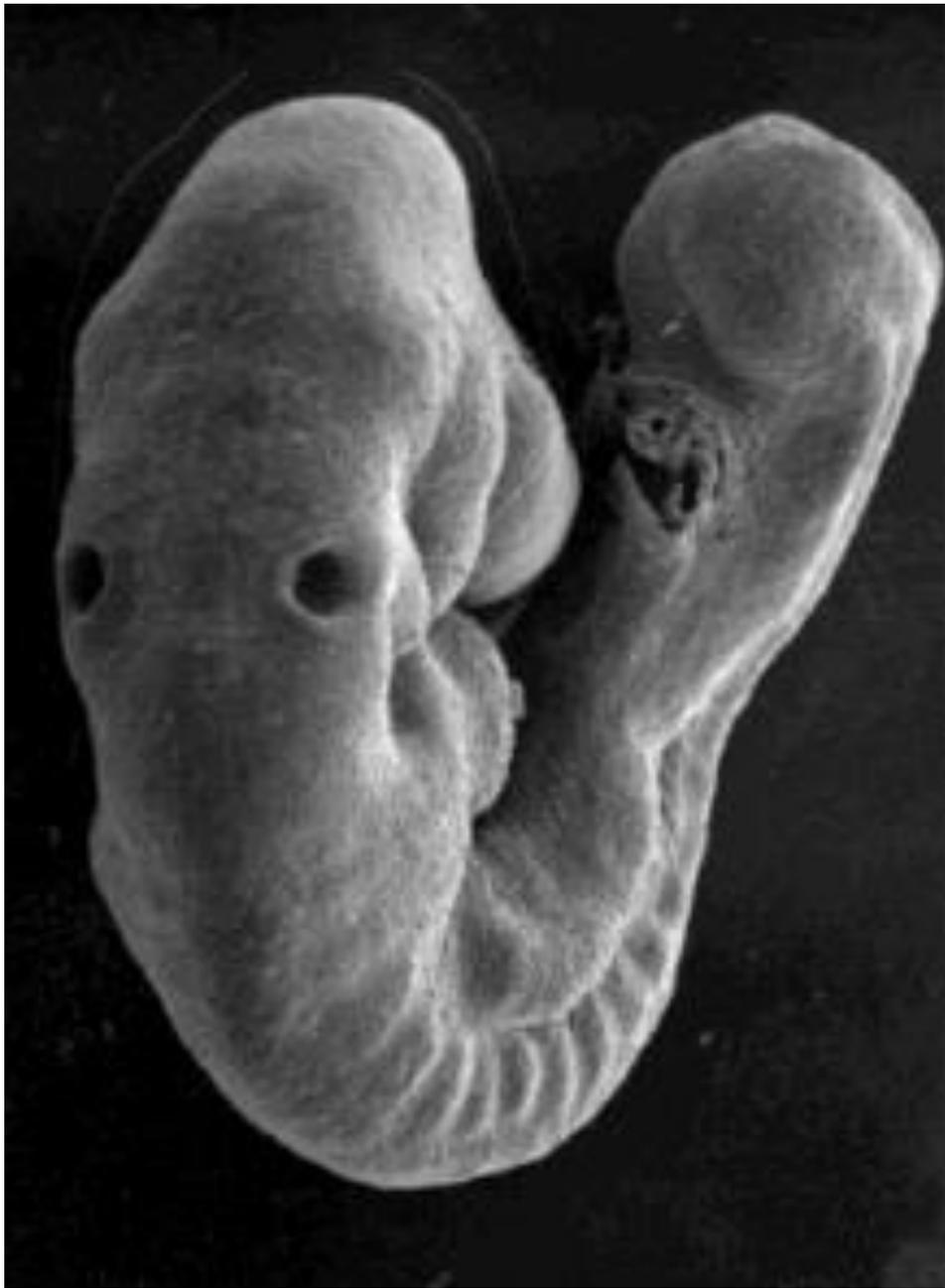
The otic pit forms as this thickened (placodal) ectoderm invaginates 26 E



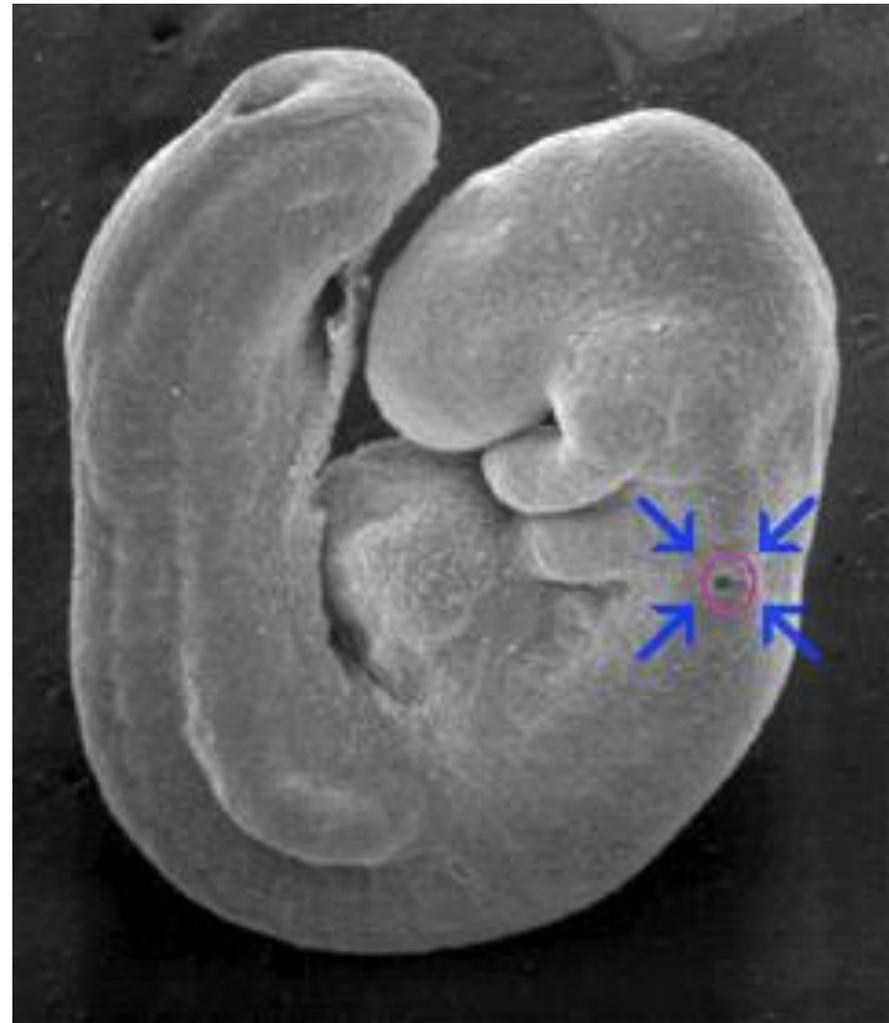
*The otic placode invaginates to form an **otic pit** and finally the **otic vesicle**. Its surface aspect is dorsal to the **2nd branchial cleft***



*The **neural tube** in the region of the **hindbrain** induces formation of the **otic placode** (A) and then **otic vesicle** (B), dorsolateral to the **pharynx***

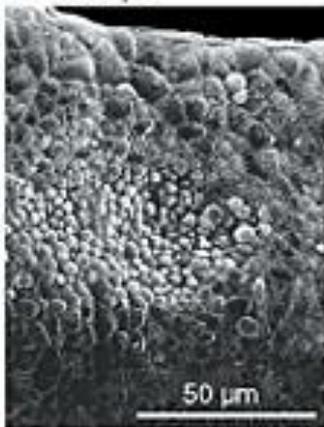


The otic pit is located dorsal to the second pharyngeal cleft.

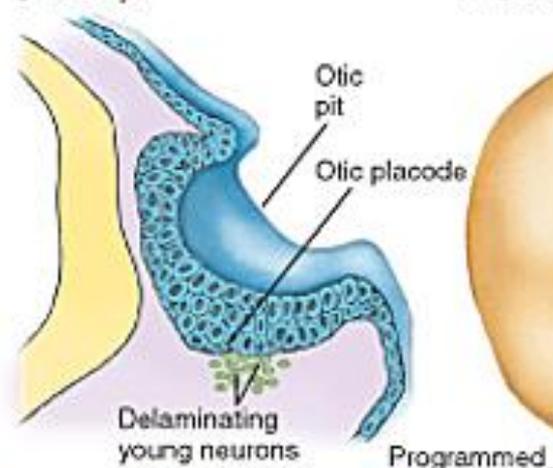


The otic pit deepens and pinches off from the surface.

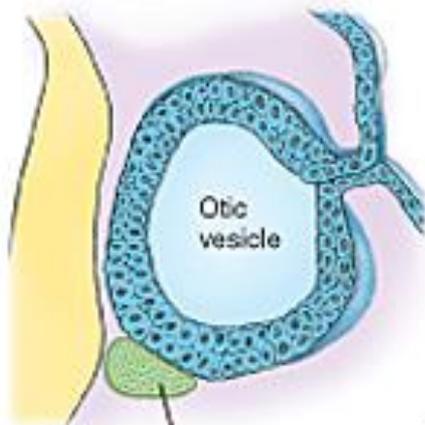
B 25 days



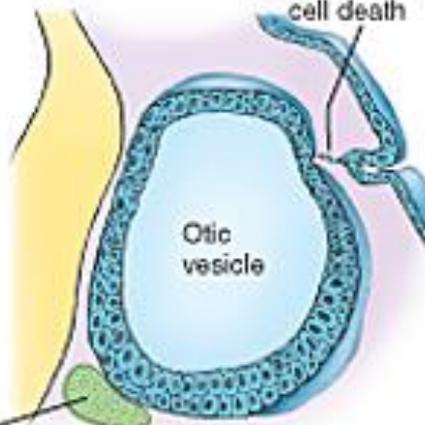
C 25 days



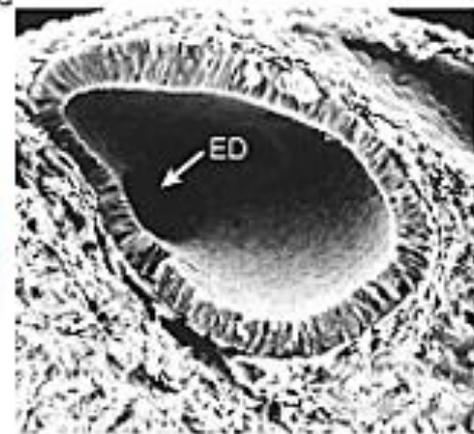
D 25 days



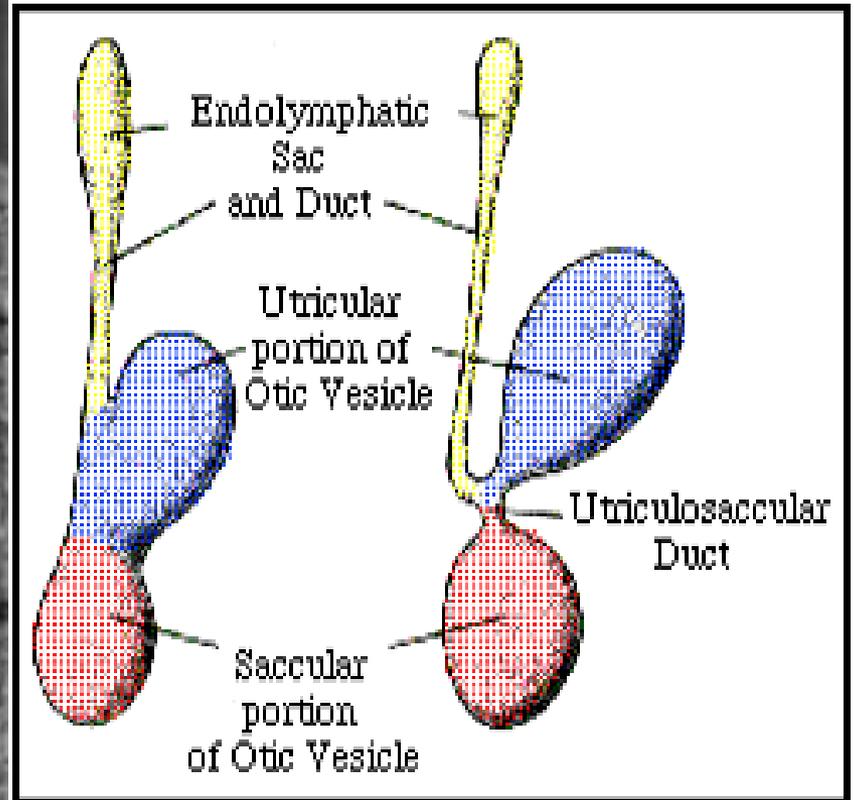
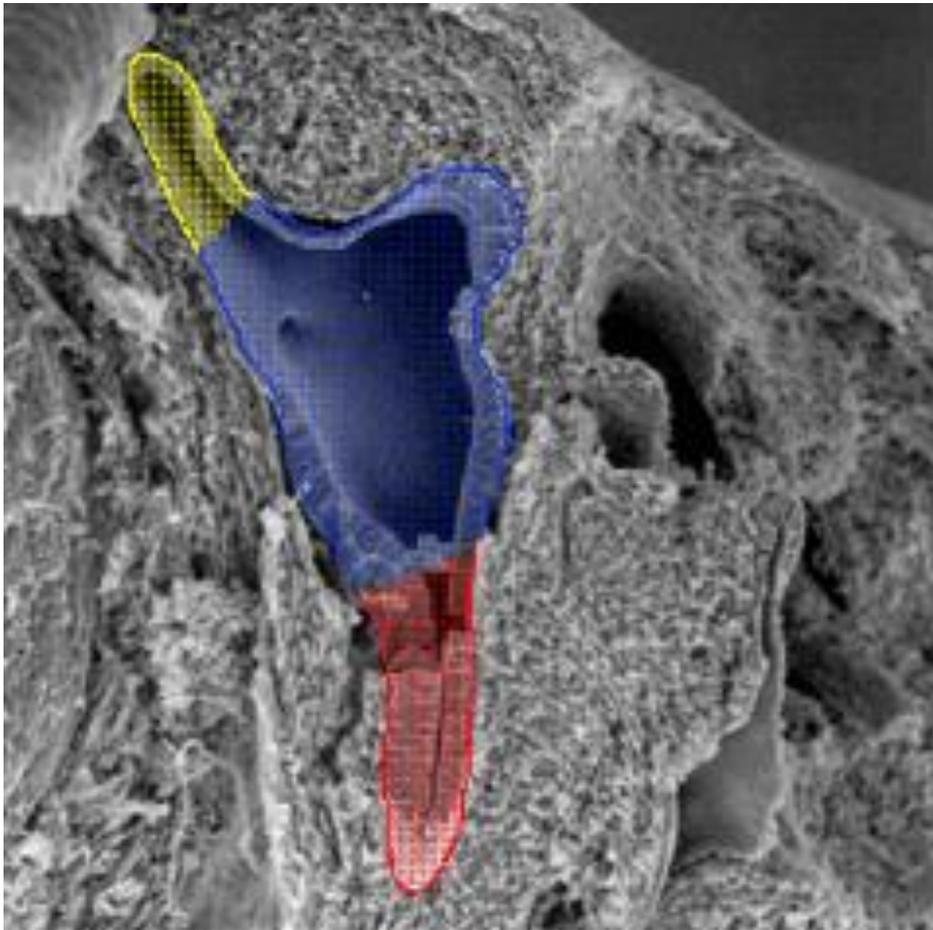
E 28 days



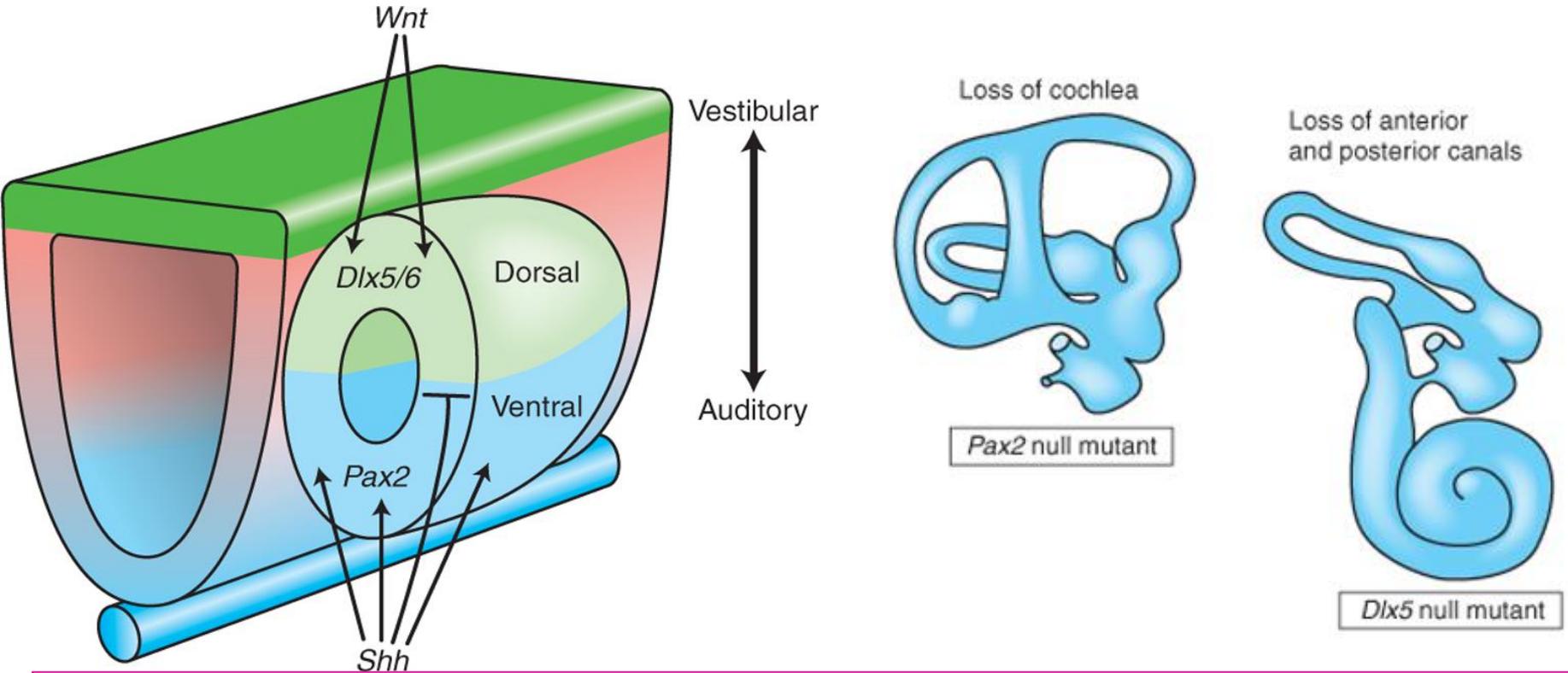
F 28 days



G 28 days



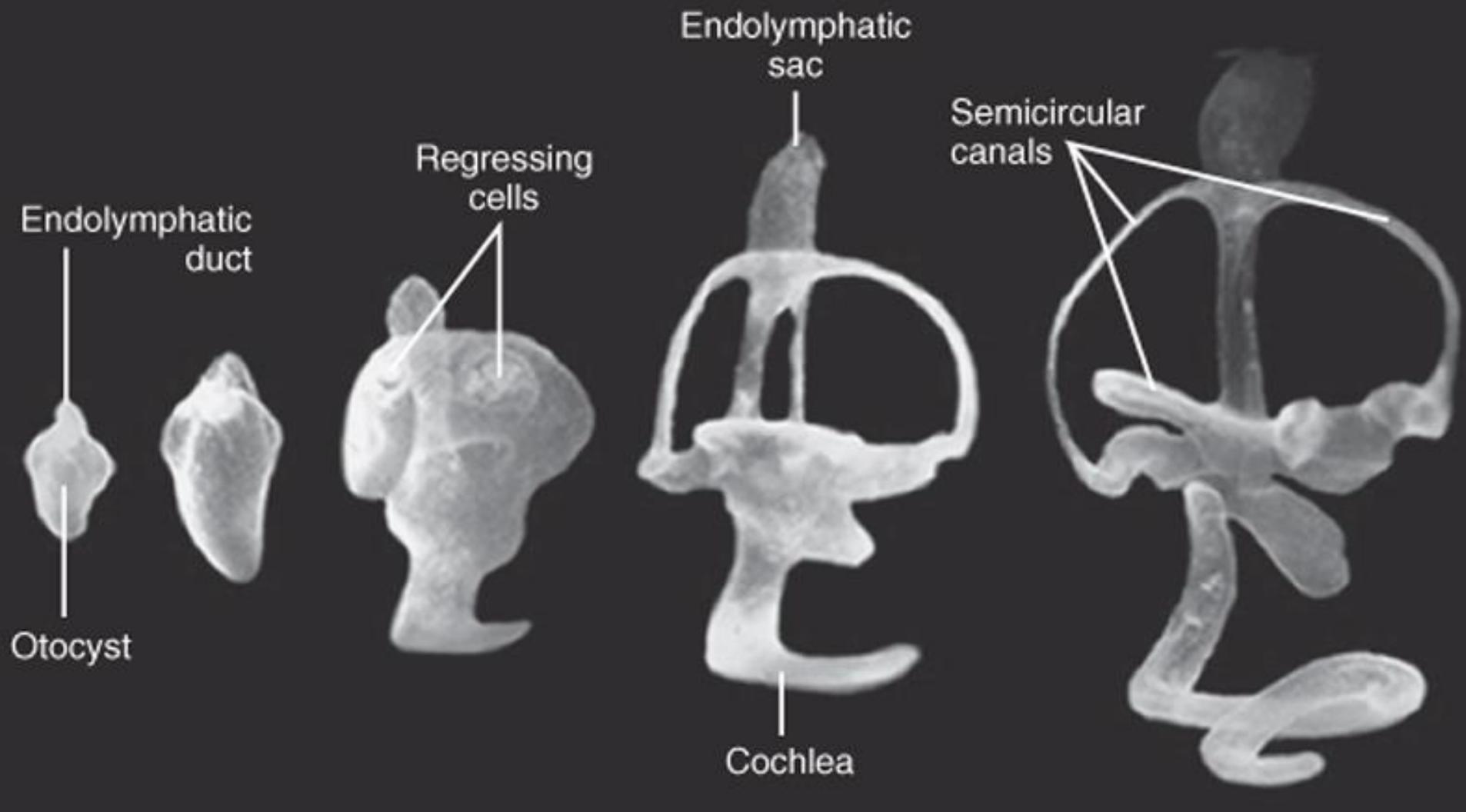
Differentiation of the otic vesicle yields three major subdivisions of the inner ear: the **endolymphatic sac and duct** and the **utricular** and **saccular** portions.
-approx. Human Age: 36 days



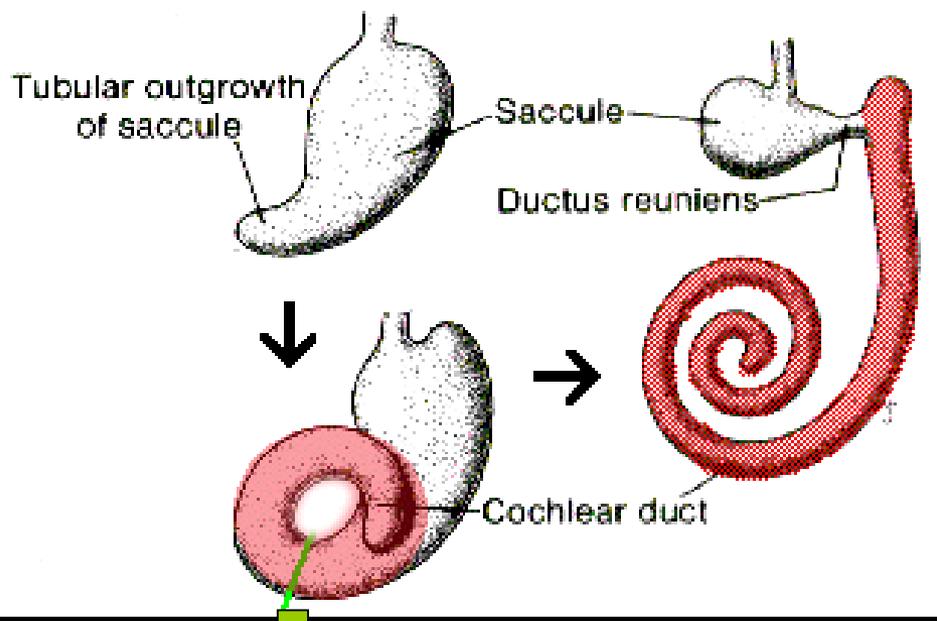
Malformations of inner ear:

-a syndrome characterized by vestibulocochlear dysplasias is **CHARGE syndrome** (coloboma of the eye, hear defects, atresia of the choanae, retarded growth and development, genital and urinary anomalies, and ear anomalies and hearing loss), often caused by mutations in *CHD7*

-Conditions such as **rubella** can lead to maldevelopment of the organ of Corti, causing inner ear deafness

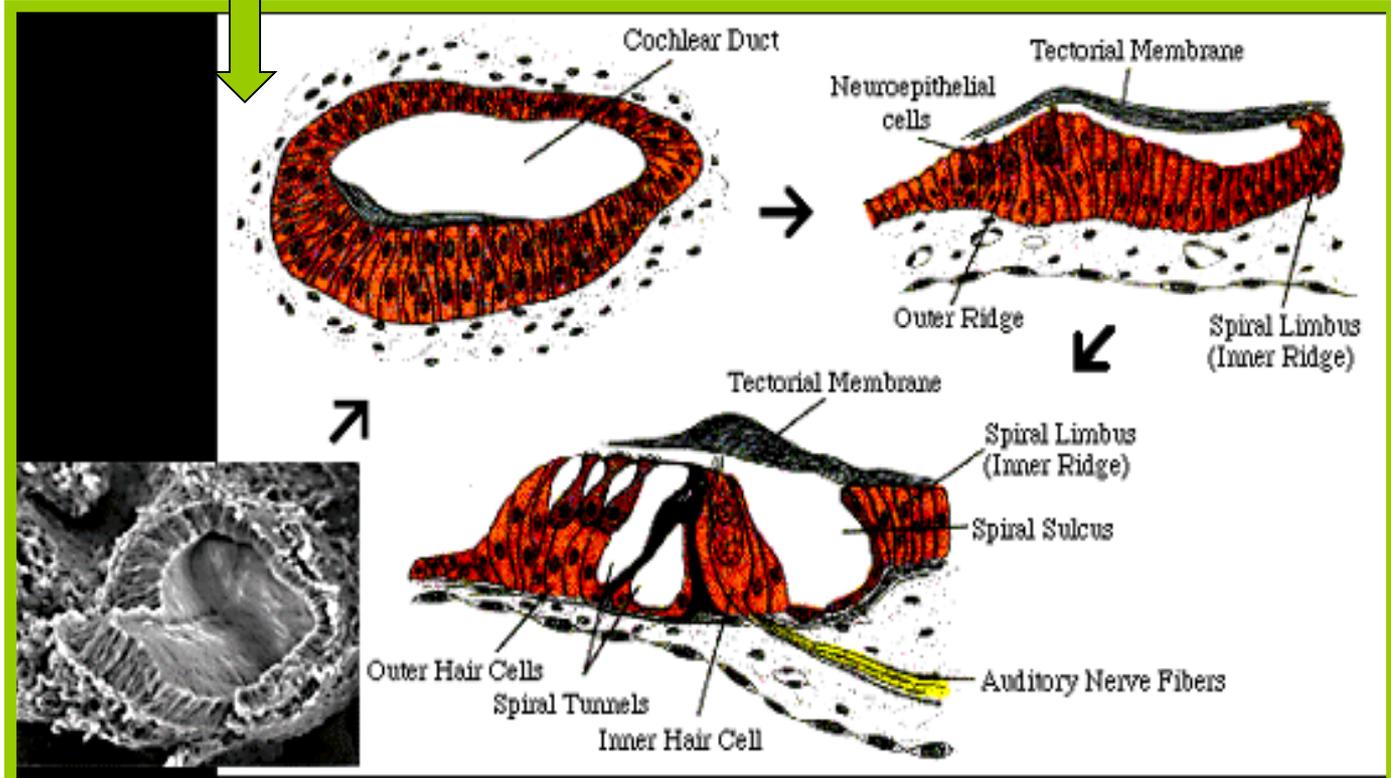


Morphogenesis of the mouse inner ear over a 7-day period in embryogenesis, revealed by filling the cavity of the developing otocyst with opaque paint.

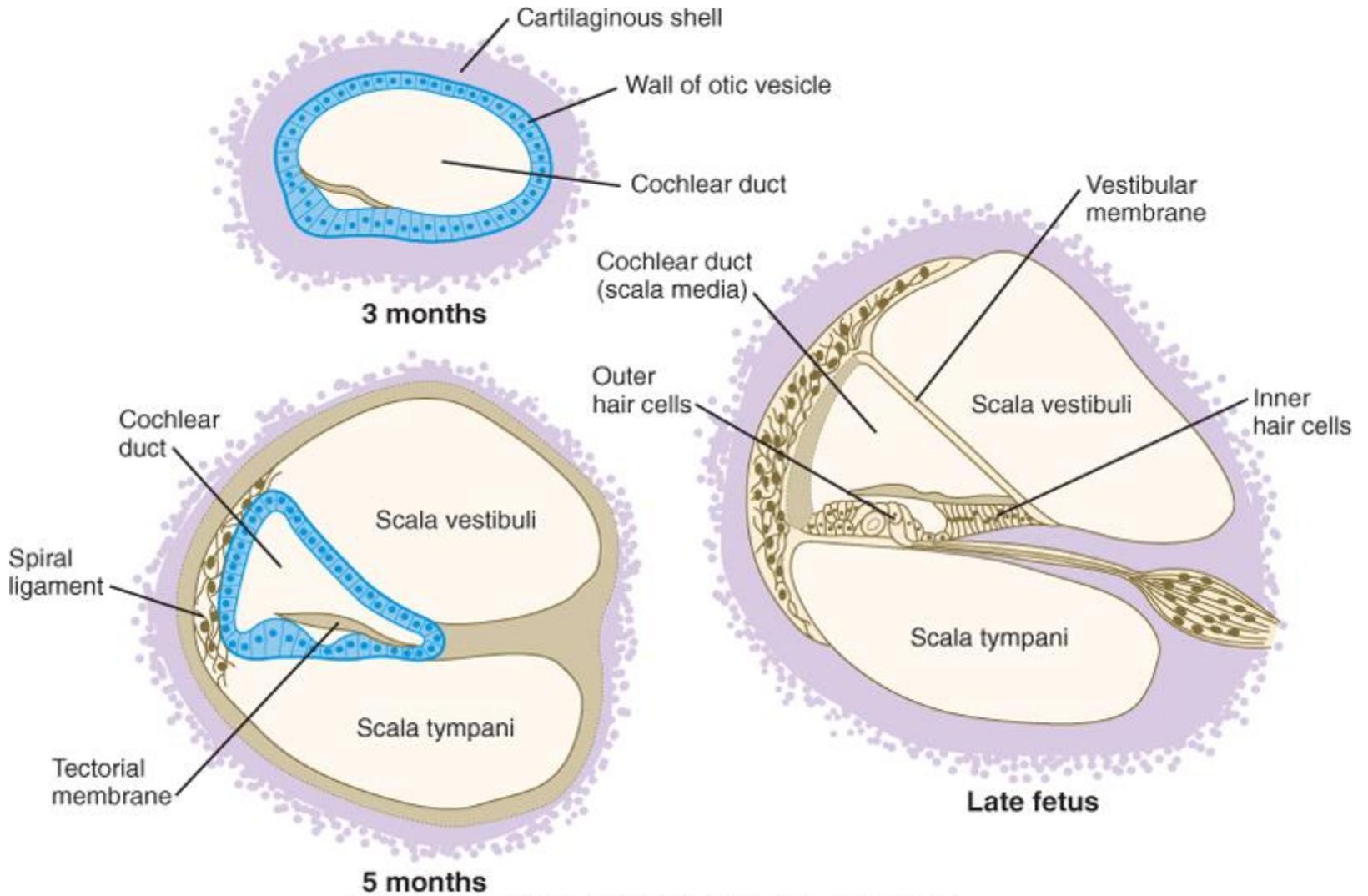


An outgrowth of the saccule forms the **cochlear duct**.

9th week of embryogenesis

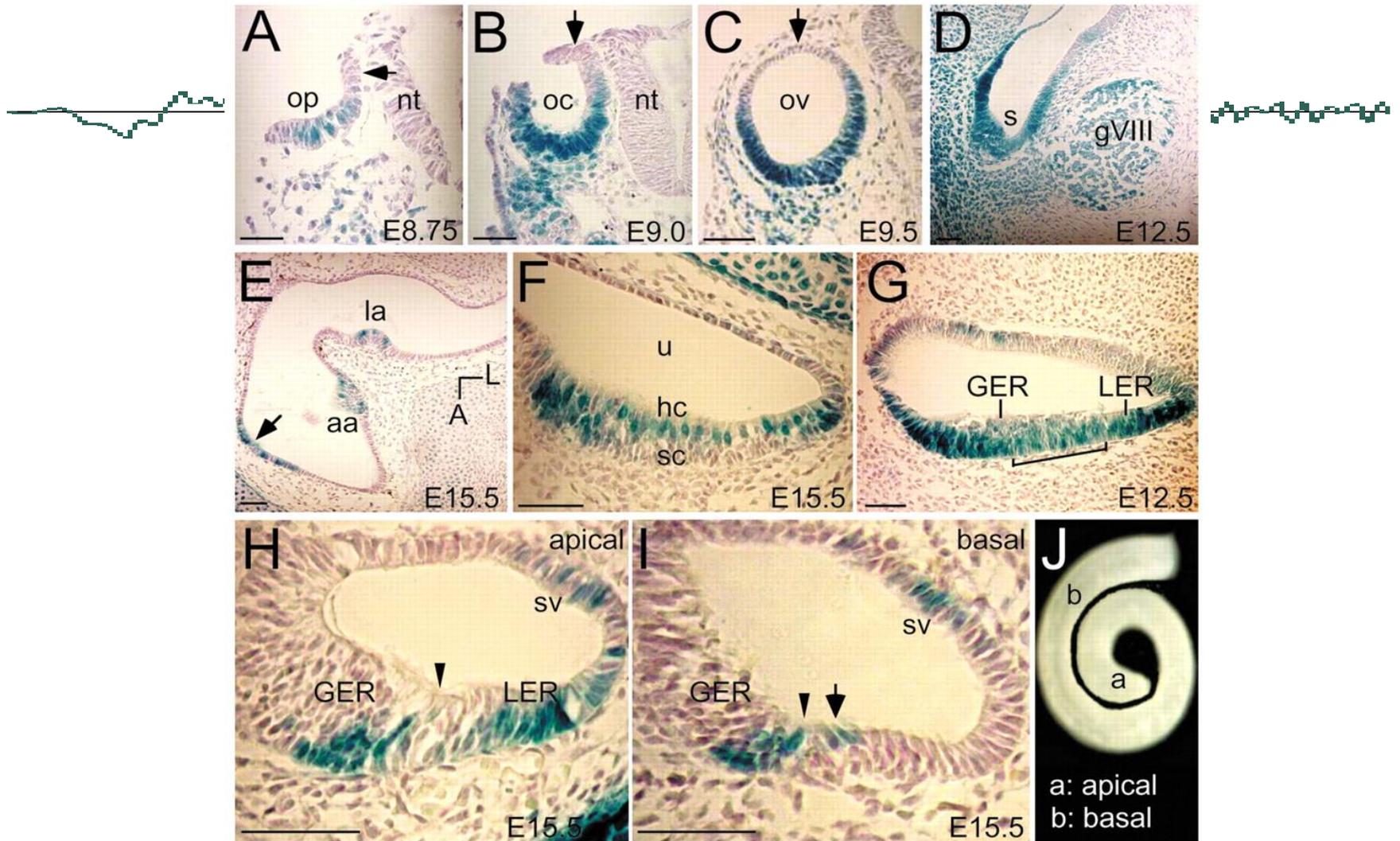


The **tall, columnar epithelial cells** of the growing cochlear duct become the Organ of Corti (the hearing receptors).



Carlson: Human Embryology and Developmental Biology, 4th Edition.
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Six1 expression during inner ear development

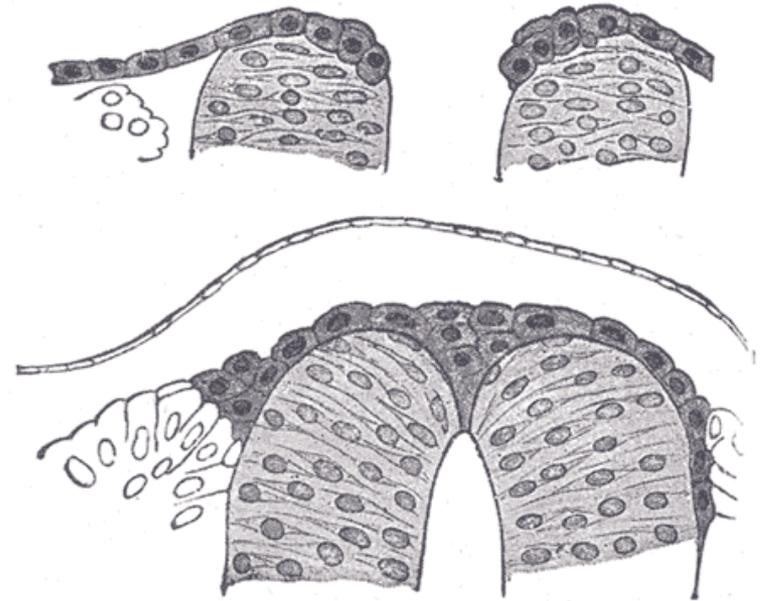


Zheng, W. et al. *Development* 2003;130:3989-4000

Embryonic Development of the Ear

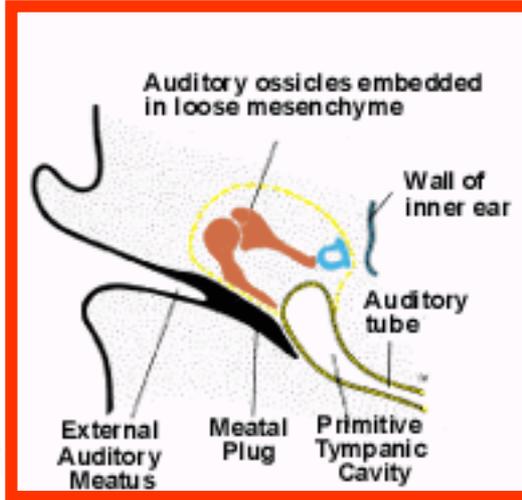
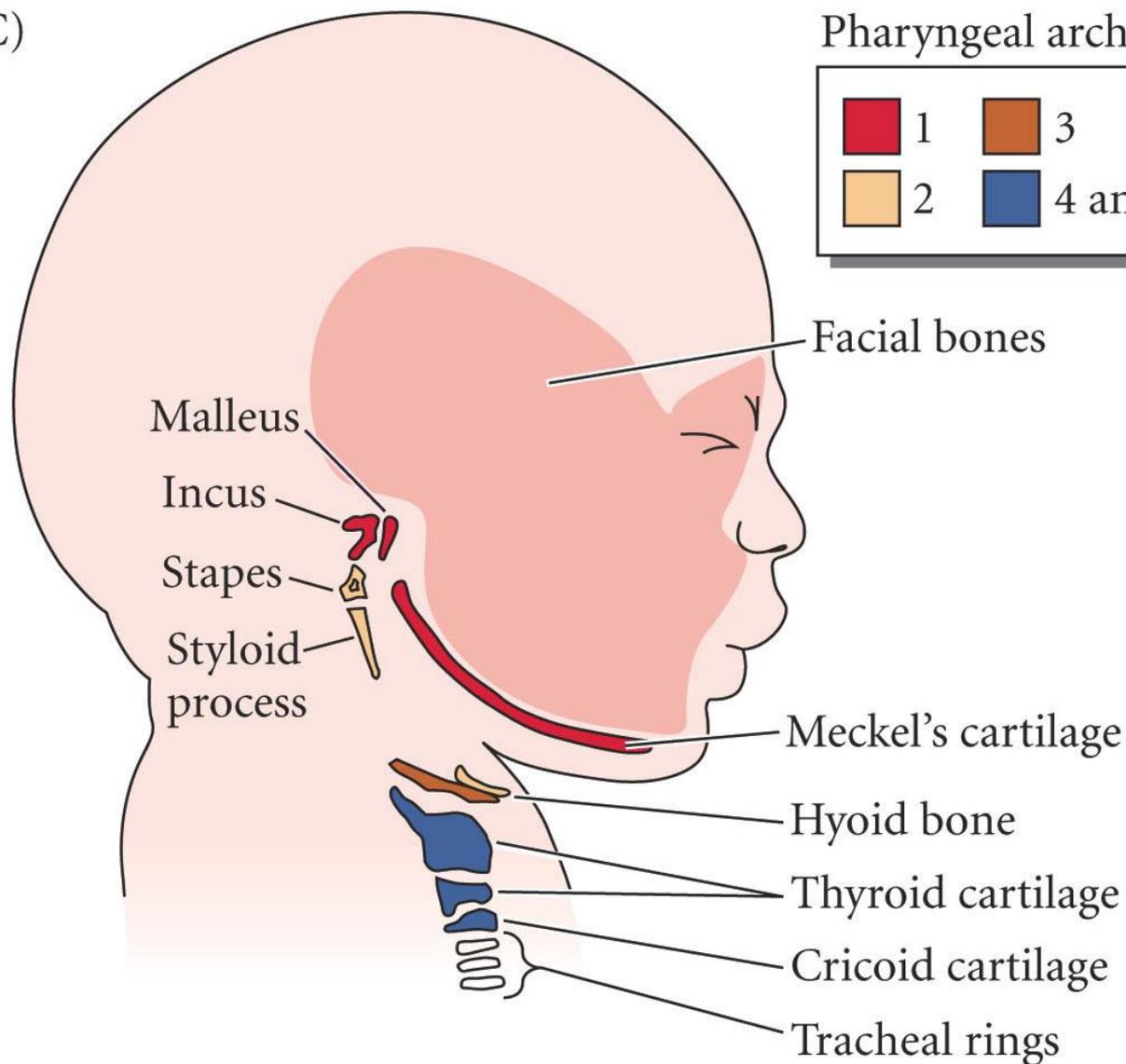
- Begins in the fourth week of development
- The inner ear forms from **ectoderm**
- The middle ear forms from the **first pharyngeal pouches (endoderm)**
- Ear ossicles develop from cartilage (**neural crest**)
- The external ear differentiates from the **first branchial groove (ectoderm)**

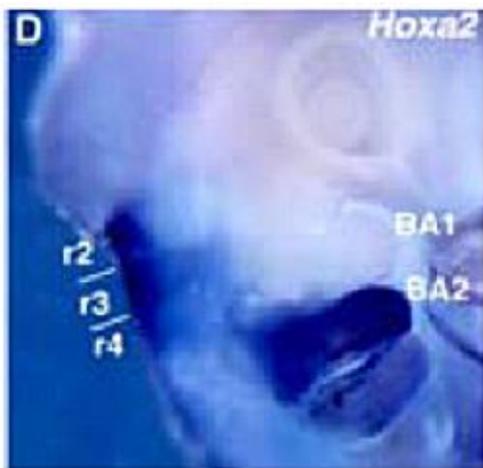
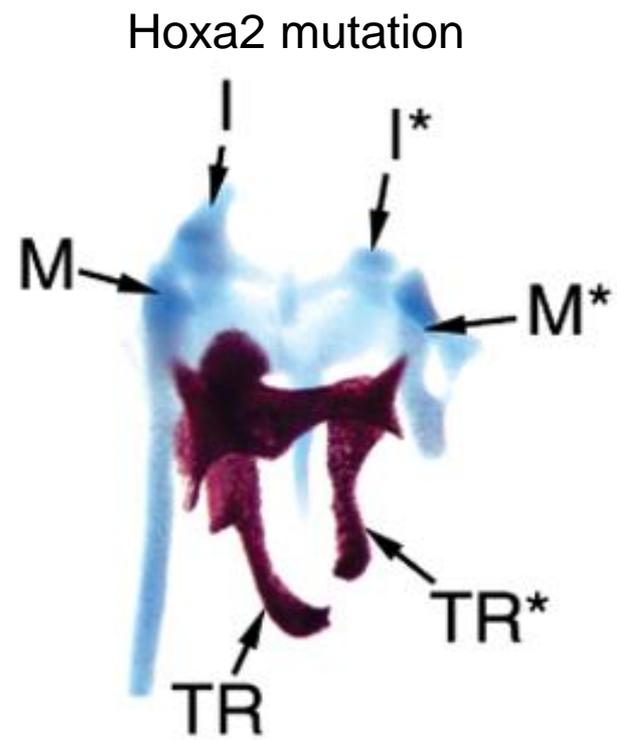
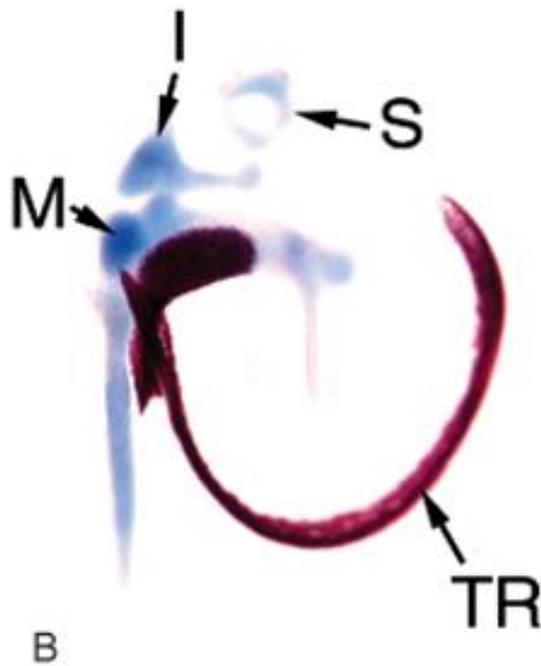
Development of Middle Ear

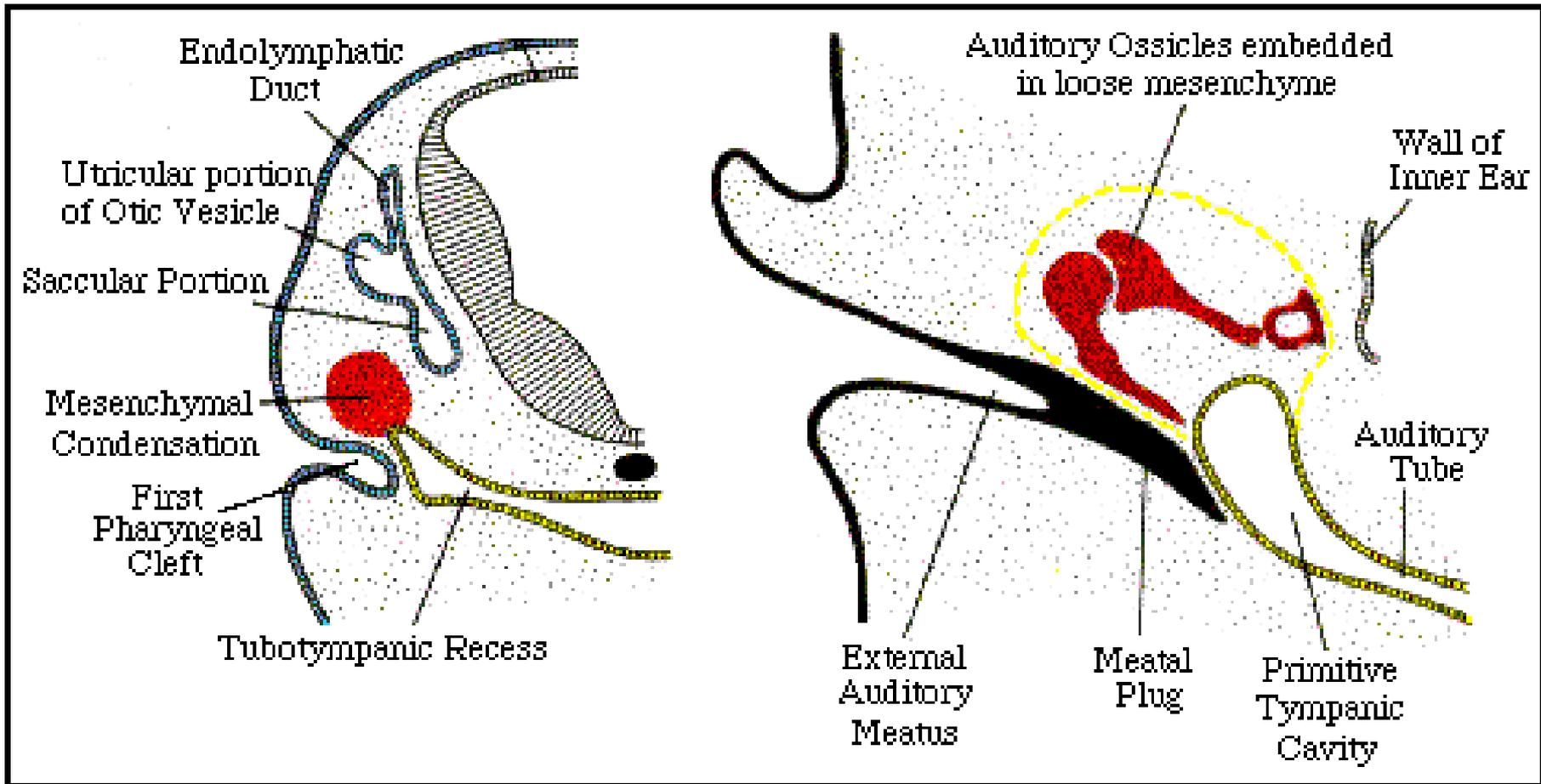


The bones of the middle ear are derived from the cartilage (*cranial neural crest derivatives*) of the first and second arch.

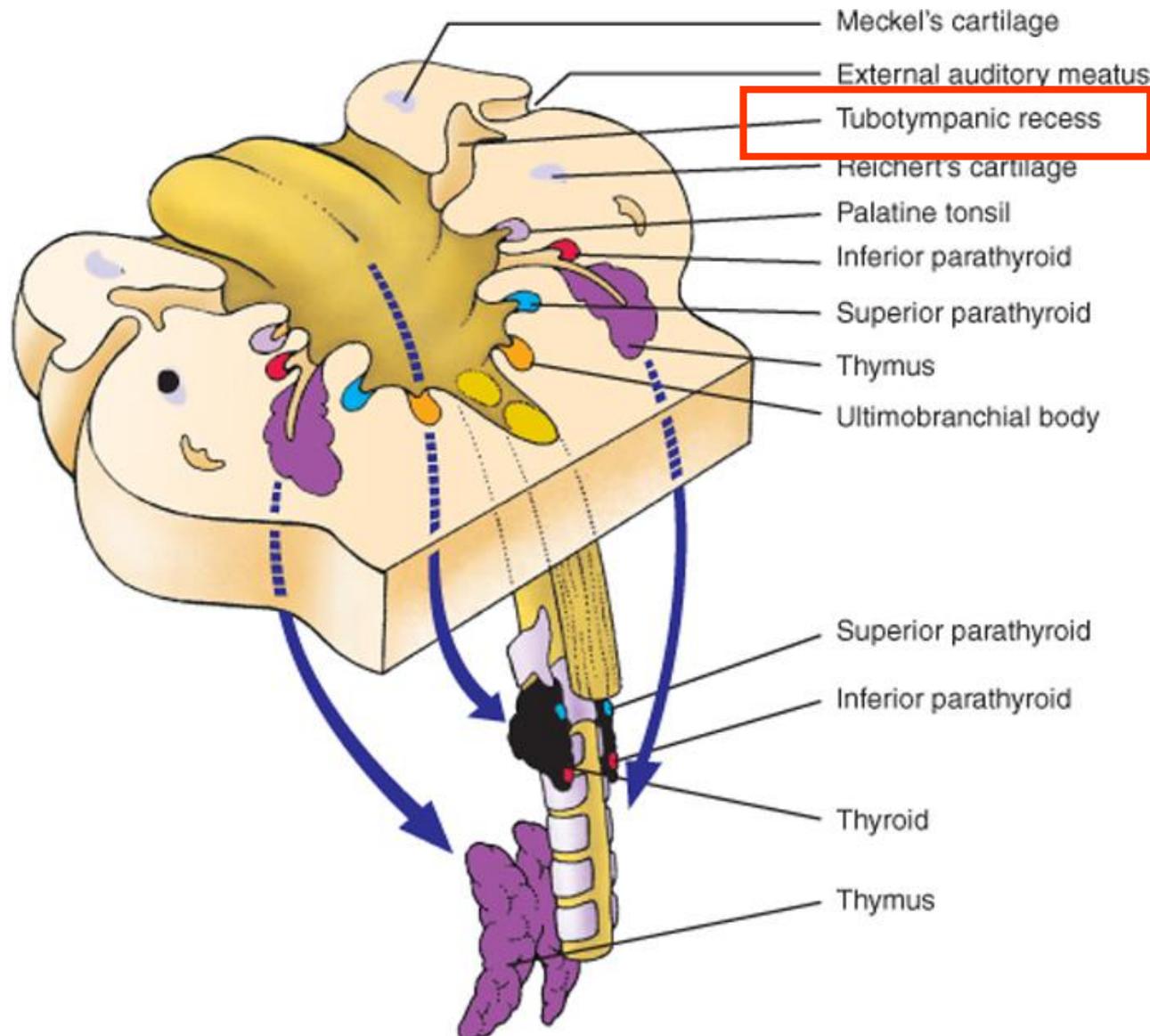
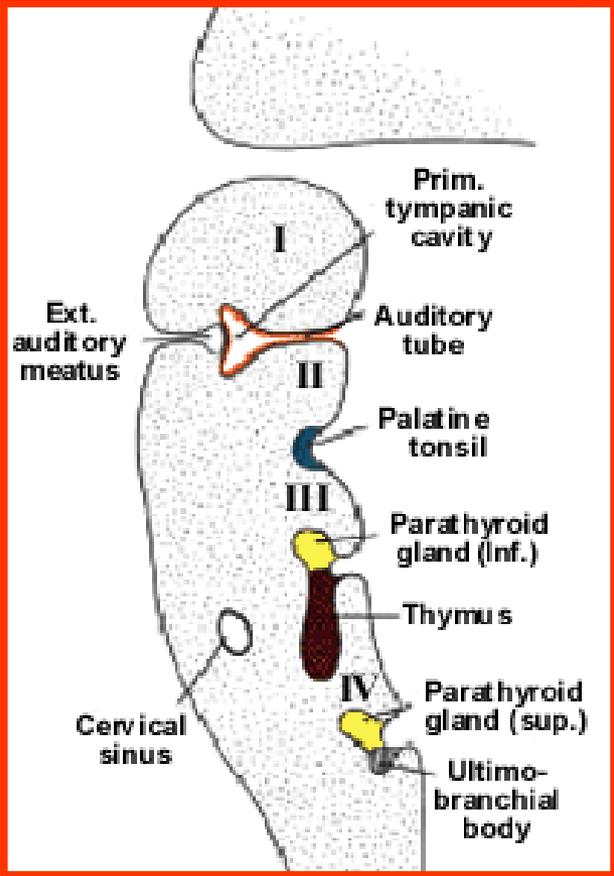
(C)





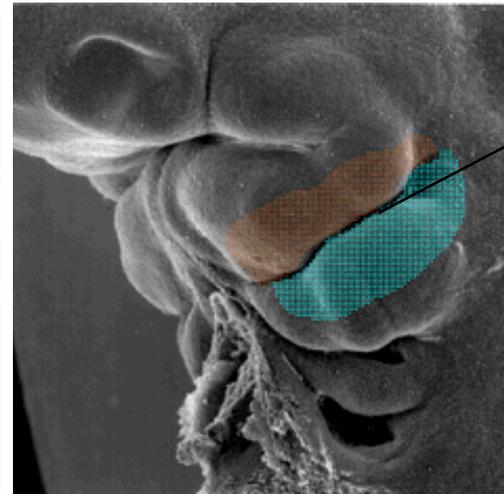
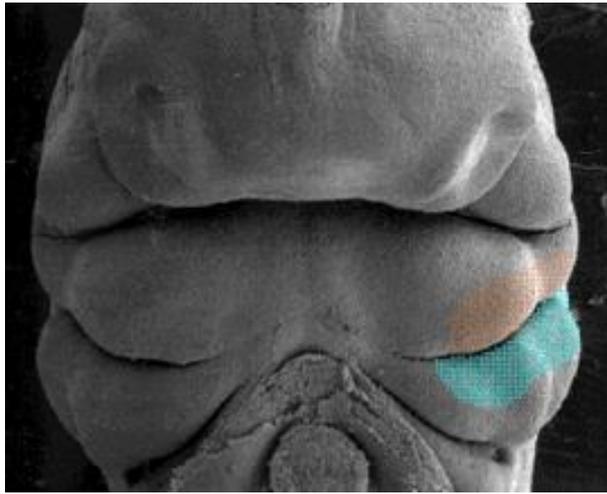


As the inner ear differentiates, the middle ear forms. The endoderm of the first pharyngeal pouch will line the middle ear cavity and auditory tube.



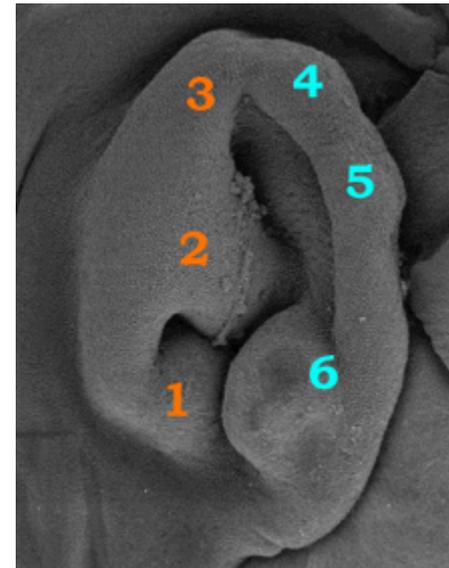
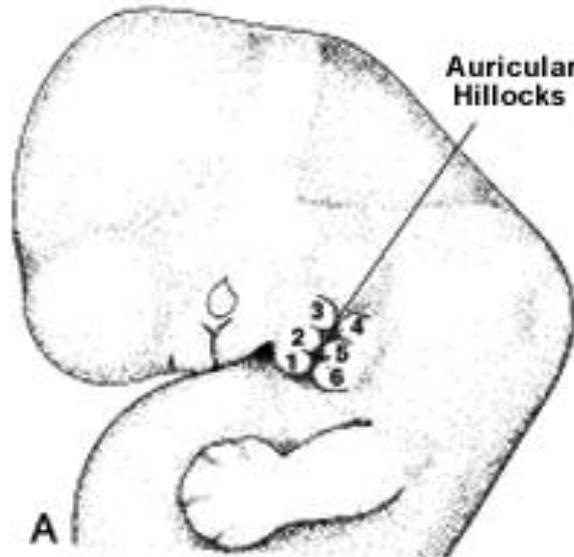
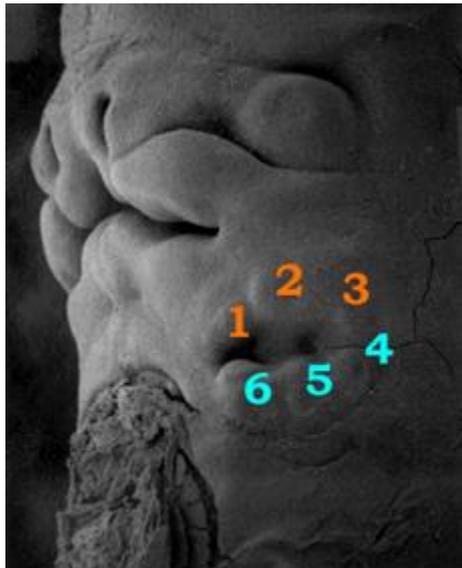
The pharyngeal pouches contain the primordia of a number of different adult structures

Development of external ear



1st pharyngeal cleft

The external ear also forms from tissues of the **first** and **second** pharyngeal arches.



hillock #1 forms the tragus and **hillock #6** forms the antitragus, as well as part of the helix

Anomalies of the external ear: microtia (small auricle; [Fig. A, B](#)) or **anotia** (absence of the auricle) (Fig C)



Fig. D and F: external ear of a boy with BOR syndrome. The upper arrow indicates a preauricular pit and the lower arrow indicates a cervical fistula



A



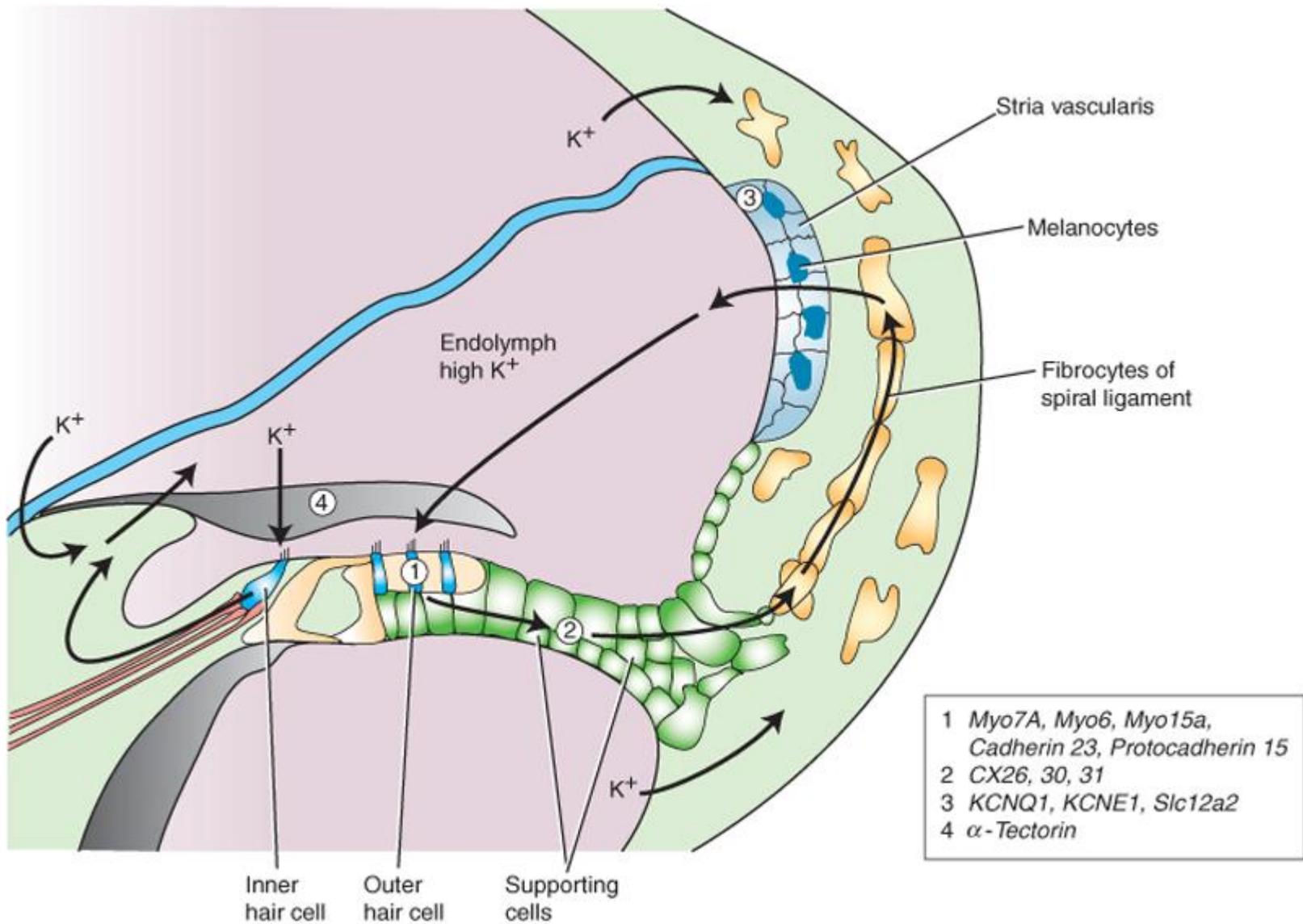
B

-branchio-oto-renal (BOR) syndrome

(mutation in the *EYA1* gene).

-the cup-shaped ears and branchial cysts (arrow). Preauricular pits and tags sometimes accompany the syndrome

-also known as Melnick-Frasier syndrome, BOR is most often caused by mutations in the *EYES ABSENT HOMOLOG 1 (EYA1)* gene. As the name suggests, mutations in the *Drosophila* homolog of this gene (*Eya*) affect the eyes



Hearing loss can result from mutations of the many different genes expressed in the inner ear.