Developmental highlights of the human inner ear

0day zygote
5day cleavage → blastula
13day gastrulation → trilaminar embryo

       endoderm → gut, airway
       mesoderm → connective tissue, muscle, bone, blood
       ectoderm → nerve cells, skin (neural tube → CNS; neural fold and adjacent region → neural crest and placodes, which generate the sensory structures that provide inputs to the CNS

       All layers of the gastrula contribute to ear and vocal tissue. Cells in different layers interact via inductions. For example, mesoderm secretes FGF-19, which induces Wnt8c expression in the adjacent neural plate, and, in turn, both induce the formation of the otic placode. (See attached diagram.)

The otic placode arises from a common placodal field adjacent to the neural plate. All placodes arise from this field. These include the hypophyseal, olfactory (I), lens, trigeminal(V), otic(VIII), and epibranchial (geniculate (VII), petrosal(IX), nodose(X)) placodes. Experiments that include removing, transplanting, and applying test compounds have produced preliminary models of how placodes are induced and how they are controlled to produce organs.)

Neural crest cells are a special class of ectodermally derived tissue that form melanocytes (in ear and skin), peripheral neurons (DRG), Schwann cells, autonomic neurons, adrenal medulla, and sclera of the eye.
Melanocytes in the labyrinth are unique to mammals.

26 day branchial arches appear
28 day otic placode appears
4 weeks begins embryonic period (period of great vulnerability for induced birth defects)
4th week otocyst forms, vestibular/auditory ganglion cells separate from epithelium, chondrogenesis in periotic mesenchyme begins, probably induced by otocyst
5th week auditory nerve enters brainstem, vestibular and auditory ganglia separate
6 weeks saccule/cochlea emerges from utricle, walls of utricular outpocketings fuse to form semicircular canals, central auditory brainstem nuclei identifiable
7 weeks one cochlear turn formed
8 weeks 2.5 cochlear turns formed, semicircular canals complete, cartilage surrounding the membranous labyrinth has formed from mesenchyme.
8 weeks is end of embryonic period, beginning of fetal period
9 weeks peripheral processes of ganglion cells penetrate cochlear epithelium
(N.B. The central processes entered the brain at week 5. Tonotopic organization is obviously organized without the aid of acoustic input.)

10 weeks hair cells in basal turn differentiate, accompanied by neural plexus immediately beneath them, which suggests an inductive influence. It is unclear if these nerve fibers are afferent and/or efferent.

(Efferent fibers initially take a similar path as do VIIth n. fibers. They join the vestibular tract and follow it to the vestibular-cochlear anastomosis, where the auditory efferents pass to the cochlea and spiral apicalward within the spiral ganglion in the intraganglionic spiral bundle. There is ambiguity regarding the identity of nerve fibers beneath developing hair cells because immature efferent fibers need not have abundant synaptic vesicles and immature ganglion cells stain positively for acetylcholinesterase.)

Inner hair cells form within greater epithelial ridge, OHCs in lesser epithelial ridge of Koelliker's organ.

Perilymphatic spaces form from mesenchyme surrounding the cochlear duct

16 weeks ossification begins

23 weeks ossification centers fuse to form petrous bone. Adult size of the inner has been reached.

26-28 weeks fetus begins to respond to external sounds

8 months mesenchyme cleared from middle ear space

The formation of the head and neck is the product of the development of the branchial (pharyngeal) arches. Each has an associated cleft. Each arch produces bones, muscles, and other tissue specific to it. Each carries with it a cranial nerve, which activates the muscles and a separate vascular supply.

Branchial arches

BA 1 forms jaws, incus, malleus, muscles of mastication, trigeminal (Vth) nerve (motor and sensory)

BA2 forms stapes, styloid process, hyoid bones, facial (VIIth) nerve (motor, facial expression; and sensory, taste from anterior tongue)

BA3 forms parts of hyoid bone, muscles of pharynx, and glossopharyngeal (IX) nerve

BA4 forms laryngeal cartilage, heart vessels, vocal constrictor muscles, and superior laryngeal (X) nerve

BA5 forms laryngeal cartilages, intrinsic laryngeal muscles, and recurrent laryngeal (X) nerve

The pharyngeal pouches extend from the pharynx to form the Eustachian (acoustic) tube and middle ear space (forming an endodermal lining of the middle ear and its contents), the palatine tonsils, the parathyroid glands and the thymus. Genetic defects that affect development of these tissues and of branchial arch-derived tissues (e.g., Down's syndrome and DiGeorge syndrome) also result in malformed inner ears. The inner ear tissues are epithelial tissues derived from the otic placode. The fact that inner ears are malformed in Down's and DiGeorge patients (Mondini dysplasia) is one line of evidence indicating that the final product of inner ear development is the result of multiple interactions between the growing ear and its surrounding mesenchyme. On the other hand, mutations in the gene the controls production of pendrin, an ion transporter found in the cochlear epithelium, also results in Mondini dysplasia.

There is also control of ear development by induction via signals from the developing brain. The otic vesicle migrates to the junction of the 5th and 6th rhombomeres (divisions of the developing brainstem). The invariant location of the developing otocyst at these locations indicates that there is some attractant factor that guides the migrating otocyst to that location. The transcription factor bZIP is normally expressed in r5 and r6. In the Kreisler mouse mutation it's presence in the developing brain is disrupted and the cochlea is grossly deformed. Fibroblast growth factor 3 is expressed in r5 and r6. Fgf3 knockout mice lack an endolymphatic duct, have few VIII N ganglion cells, and have a dysmorphic cochlea.