Review Article

Morphological aspects of Kölliker's organ in the developing Mammalian Cochlea: A review

Valeria Caragli

Department of Biomedical, Metabolic, and Neuroscience Sciences, Otorhinolaryngology-Head and Neck Surgery, Audiology Program, University of Modena and Reggio Emilia, Modena, Italy

Abstract

The development of the mammalian auditory system is a complex process characterized by cellular differentiation and morphological changes. It begins during embryogenesis and continues postnatally. This study focuses on Kölliker's organ (KO), a transient structure which is essential for cochlea maturation and auditory function. A comprehensive literature search on the morphological features of KO in mammals was conducted across different databases. Following strict inclusion criteria, nine studies were selected for review. In addition, a histological analysis on murine embryos across various postnatal stages (P0, P5, P10, P15, P20, and P22) was performed, using traditional histochemical techniques. Images were stored from the Bioacoustics Laboratory at the University of Padua. From our study, it emerged that KO originates from the ectoderm. KO is characterized by closely spaced columnar cells with specific morphological traits, including extensive intercellular gap junctions, composed of Connexins. Significant cellular transformations occur in KO as its cells transit from columnar to cuboidal forms, ultimately leading to their disappearance by P15. This morphological progression is critical for the Corti's organ formation and for the maturation of the auditory pathway. KO is also important for structural support, ATP signaling, and synapse formation in the inner hair cells. Thus, KO plays a pivotal role in cochlear maturation, and it is potentially involved in auditory disorders.

Keywords: Auditory development, Kölliker's organ, morphology

Address for correspondence: Dr. Valeria Caragli, Otorhinolaryngology-Head and Neck Surgery, Audiology Program, University of Modena and Reggio Emilia, Modena 41125, Italy.
E-mail: valeria.caragli@unimore.it
Submitted: 14-Apr-2025 **Revised:** 18-May-2025 **Accepted:** 21-May-2025 **Published:** 02-Aug-2025

INTRODUCTION

The development of the mammal auditory system starts during the embryological stages and completely ends in a wide range of time after birth, depending on the species. During the gestational weeks, different events occur, including cell differentiation, morphological changes, and fiber myelinization. These processes lead, from the embryological Kölliker's organ (KO), to the formation of the mature auditory organ, named Corti's organ (CO), which is able to rightly process sounds and conduct them along the acoustic pathways.[1] Thus, KO is crucial for cochlea maturation and auditory function.[2]

The organ of Kölliker was first described by the Swiss-born German histologist, anatomist, embryologist, and physiologist Albert von Kölliker. Kölliker's early

Access this article online	
Quick Response Code:	Website: https://journals.lww.com/hbcm
	DOI: 10.4103/HBC.HBC_10_25

How to cite this article: Caragli V. Morphological aspects of Kölliker's organ in the developing Mammalian Cochlea: A review. Hear Balance Commun 2025;23:52-8.

observations of the organ, derived from an older calf embryo, revealed "an epithelial bulge consisting of a simple layer of fairly large and generally vertical cells," which exhibited specific shape and positional peculiarities. He identified two distinct types of cells within KO: the first type rose from the holes of the habenula perforata on a broad, triangular, nucleated base, oriented outwards with a tapered end, while the second type turned its narrower end toward the first, presenting a broader nucleated base externally. These cells' features were considered by Kölliker himself as the outer and inner cortical fibers. The fibers were at that moment quite steeply, but later they would move apart with their bases, depending on the growth in length of the cells themselves or their base, the membrana basilaris.[3]

Few later, Hensen,[4] while studying KO in cats, noted that the tall-columnar cells were only present during embryonic stages and then replaced by cuboidal cells in the internal sulcus. He observed a loss of many columnar cells he but could not ascertain their fate. Similarly, Bast and Anson[5] reported complete cell replacement in humans by the 25th week of gestation, yet the nature of this process remained poorly understood.

Current research suggests that KO comprises different supporting cells involved in morphological and numerical changes during the embryonic and postnatal periods.[6,7] According to Lim and Anniko,[8] cell degeneration and disappearance occur after the opening of the external auditory canal, the establishment of endocochlear potential, and the cochlea's exposure to external acoustic stimuli. Noteworthy advancements in the understanding of KO came from Tritsch *et al.*,[9] who demonstrated that KO is responsible for the spontaneous release of adenosine triphosphate (ATP). The ATP release increases intracellular Ca^{2+} levels in inner hair cells (IHC) via intercellular gap junction protein hemichannels, ultimately triggering the release of the neurotransmitter glutamate and exciting afferent nerve fibers. In this capacity, KO supporting cells convey crucial temporal and spatial information which are necessary for cochlear development, promoting the formation of fine-tuned synaptic connections within the auditory pathway, and aiding cochlear maturation and auditory acquisition.[6,9]

As a transient structure, KO undergoes considerable remodeling during embryonic and early postnatal stages, altering its morphology before transforming into the inner sulcus region of the organ of Corti, once the sensory structures become responsive to external sound. This raises the intriguing hypothesis that delayed degeneration of KO and/or its dysfunction may lead to abnormal cochlear hearing development[10] and could be linked to auditory disorders.

The aim of this study is to provide a comprehensive overview of the current knowledge on KO, focusing on its morphological aspects. This investigation seeks to synthesize existing literature on KO across mammalian species, reporting the relevance of KO in auditory physiology and also addressing the significant gaps in knowledge on this topic.

MATERIALS AND METHODS

A comprehensive literature search was conducted on PubMed, Embase, CINAHL, and Scopus databases, using the term "Kölliker's organ" and without imposing any temporal constraints. Last search was performed on March 2024. Inclusion criteria were: (1) English studies; (2) studies on mammals or humans; and (3) studies reporting morphological features of KO. Following the selection of studies, data were extracted. Duplicate studies were removed. Articles were first screened for abstract and titles; studies not matching the inclusion criteria were removed. Secondly, selected articles were full-text read to be included in the review.

To describe the morphological characteristics of KO using properly methods, the images obtained from murine embryos tissues, made available by the archives of the Bioacoustics Laboratory research group of the Department of Neuroscience at the University of Padua (formerly the Bioacoustics Centre at the University of Ferrara) and in collaboration with the I-ApproVE Centre (International Auditory Processing Project in Venice, University of Padua), were evaluated. Images were obtained using a traditional histochemical method for ultrastructural analysis of biological samples. The biological samples were embedded in epoxy resin, sectioned using an ultramicrotome, and stained with toluidine blue. The analysis was performed at P0, P5, P15, P20, and P22, using an electron transmission microscope.

RESULTS

A total of 500 studies were identified through databases search. After title and abstract examination, 35 studies were considered. The full-text reading led to finally include 9 studies in the review. Figure 1 reports the selecting article process.

Morphological characteristics of Kölliker's organ supporting cells during auditory development

KO is recognized as the earliest visible epithelial structure

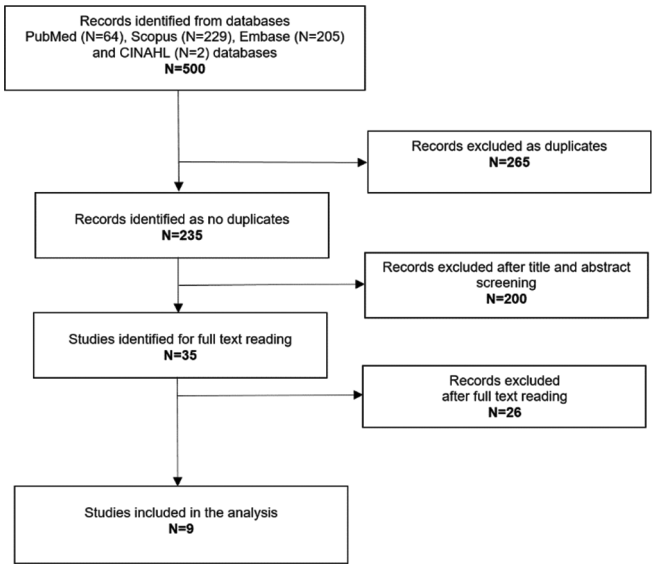

Figure 1: Selecting articles process

in the embryonic inner ear. It originates from ectoderm and it is enveloped in mesenchymal tissue, which persists throughout the late embryonic and early postnatal periods (postnatal day 0 – P0 to postnatal day 14 – P14) in mice. The cochlea develops in a temporally dependent manner from its base to apex, both structurally and functionally.[7,8]

The differentiated KO comprises closely spaced columnar cells, characterized by a dense distribution of nuclei, typically localized at the base of the cells, which results in a stratified appearance in cross-sectional slices. The KO supporting cells exhibit elongated cytoplasmic extensions, often separated by an extracellular space measuring approximately 200 Å, with some gaps reduced to as little as 30 Å. These cells possess either bipolar or unipolar protrusions at their apex, with microvilli approximately 3–4 μm in length visible at their tips, emerging within the first 10 days after birth. Although an occasional kinocilium has been noted on the surfaces of these epithelial cells, some studies have posited that all cells within KO possess kinocilia surrounded by microvilli.[10] The cytoplasm at the apical or luminal end of these cells is rich in organelles, including mitochondria, endoplasmic reticulum, and secretory vesicles, suggesting a functional role in the secretion of the tectorial membrane. KO cells are extensively interconnected via gap junctions, forming a functional syncytium. These gap junctions consist of two connexin hemichannels from adjacent cells, each composed of six subunits containing four transmembrane regions. The KO gap junctions are primarily composed of connexin 26 (Cx26) and connexin 30 (Cx30) subunits, which are capable of forming heteromeric channels and which are established before the functional maturation of the cochlea.[7]

During the early developmental stages, particularly at birth in mice, the tectorial membrane is closely associated with KO through a network of fine filaments, which later detach, as development progresses. Approximately 2 weeks after birth, the tectorial membrane extends toward the outer hair cell region.[10] The transformation of KO appears to be sensitive to thyroid hormone levels; deficiency in this hormone has been associated with prolonged survival of KO cells in rats up to 30 days old, and to the presence of CO structure malformation, particularly affecting the tectorial membrane.[7]

Notably, certain KO cells exhibit mitotic activity during the late embryonic and early postnatal stages, demonstrating the potential for transdifferentiation into hair cells.[7,11] Thus, KO supporting cells undergo programmed morphological changes during embryonic development and postnatal maturation.

On this regard, the evaluation of KO in mice, performed at the Bioacoustics Laboratory, revealed, at postnatal day 0 [Figure 2a], an epithelial bulge consisting of a simple layer of relatively large, predominantly vertical cells. It comprises two distinct cell types: one type exhibits a triangular shape with a nucleated base originating directly from the habenula perforata, while the other type displays a narrower free end oriented toward the first type, with a broader nucleated base facing outward [Figure 2b]. This initial formation and differentiation of cells in the auditory organ correspond to the early stages of KO, characterized by the presence of columnar epithelial cells undergoing substantial remodeling.

At postnatal day 5 [Figure 2c], the cells retain a morphology similar to that observed at postnatal day 0. However, by postnatal day 10 [Figure 2d], noticeable morphological changes begin to manifest, and the original columnar cells are replaced with cuboidal cells within the internal sulcus, leading to the formation of the mature inner sulcus. By postnatal day 15 [Figure 2e], the distinct morphology of the organ of Corti becomes apparent, as the columnar cells undergo a dramatic reduction in number, ultimately leading to their disappearance.

From around embryonic day 16 in mice, the epithelium forms two distinct domains: the greater epithelial ridge (GER), which contains KO on its medial aspect, and the lesser epithelial ridge (LER) on the lateral side. The epithelial cells that demarcate these two regions differentiate into the inner and outer pillar cells of CO.[9] While it is posited that inner ear cells originate from the GER, outer hair cells arise from the LER. The differentiation process

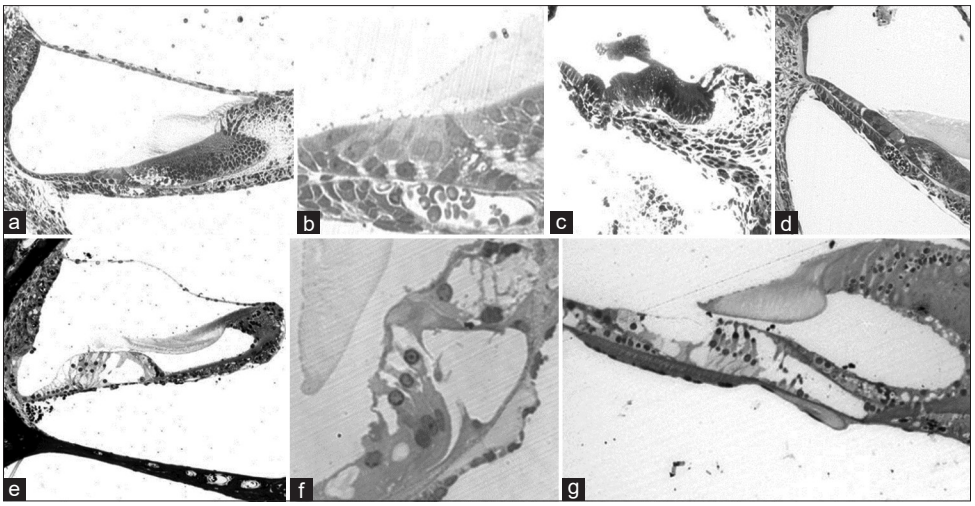

Figure 2: Histochemical images of Kölliker's organ (KO) in murine embryos at different stages; (a) KO at P0; (b) KO at P0-closer observation; (c) KO at P5; (d) KO at P10; (e) KO at P15; (f) KO at P20; (g) KO at P22. Courtesy of Prof. L. Astolfi and Prof. Martini – Archives of Bioacoustics Laboratory research group of the Department of Neuroscience at the University of Padua, and I–ApproVE Centre

between sensory and nonsensory cells initiates without discernible morphological differences, as nerve fibers begin to invade specific areas of the GER.[12,13]

Further investigations identified distinct cellular subtypes within KO supporting cells.[14] Specifically, Chen *et al*.[14] identified four cell subsets between postnatal days 1 and 14, with a gradual decrease in cell numbers, alongside four additional subsets that proliferate from postnatal days 1 to 7 and disappear by postnatal day 14. Kamiya *et al*.[15] observed that both apoptosis and mitosis coexist in KO supporting cells at postnatal day 7, indicating that cellular degeneration and regeneration occur simultaneously before their disappearance around postnatal day 12.[15] This suggests that mitotic proliferation of KO supporting cells is not confined to embryonic development, but it also occurs postnatally, during normal auditory system development.[15]

As mentioned before, during this critical developmental period, the columnar cells of KO undergo significant degeneration, with their population declining to approximately 12% of the original cell count in the adult cochlea. Specifically, cytoplasmic retraction from the cell membrane, development of cellular folds, and an increase in intercellular gaps are observed. By postnatal days 20 [Figure 2f] and 22 [Figure 2g], the organ of Corti in mice is fully developed, reflecting the developmental progression of KO.

This maturation process is instrumental in the development of spontaneous activity within the auditory system, which is crucial for the refinement of neural connections. This transition leads to the maturation of the cochlea, both in morphological structure and auditory function.[6]

DISCUSSION

This study analyses the morphological aspects of KO, reviewing the current literature on this topic. Data suggest the essential role of KO in cochlear development, which emerged in time.

From the first description by Kölliker normal auditory system development [3] and the subsequent observations, KO has been recognized as a transient, yet pivotal, structure in auditory development. While KO and CO share some fundamental similarities in their roles within the cochlear structure and auditory system, they exhibit distinct morphological features and cellular compositions, tailored to their specific functions in hearing. Specifically, KO is primarily involved in early developmental processes and supporting roles, while CO is specialized for sound transduction, housing the sensory hair cells responsible for converting mechanical stimuli into neural signals.[16]

KO represents the earliest visible epithelial structure in the embryonic inner ear and guides the formation of the mature organ of Corti. As described by Lim and Anniko[8] and confirmed by our results, KO initially presents as a dense cluster of columnar cells, characterized by stratified nuclei and extensive intercellular gap junctions, predominantly composed of Cx26 and Cx30. This configuration supports the notion of KO functioning as a syncytium, facilitating ion exchange and intracellular communication critical to early cochlear activity.[7]

Data show that KO facilitates spontaneous ATP release, initiating calcium signaling cascades in IHC.[6] This mechanism primes synaptic connections and fosters

auditory pathway maturation, underscoring KO's role as more than a structural precursor. The dense organelle composition and microvilli-rich apex of KO cells, particularly in early postnatal stages, suggest an active secretory function, contributing to the tectorial membrane's formation and positioning.[10] This aligns with prior studies, identifying KO as a key player in shaping the cochlear environment before the onset of sound-evoked activity.

The morphological observations from P0 to P22 in mice demonstrate a progressive transformation of KO cells, corroborating Lim[17] and Bast and Anson.[5] The gradual replacement of columnar cells with cuboidal ones in the internal sulcus by P10, and their eventual disappearance by P15, parallels the timeline reported by Kamiya *et al*.,[15] who observed simultaneous mitosis and apoptosis within KO. Notably, the persistence of KO cells under thyroid hormone deficiency[7] emphasizes the hormonal sensitivity of this remodeling process, suggesting potential links to congenital auditory pathologies.

The biphasic morphology identified in this study (triangular nucleated cells juxtaposed with narrower counterparts) mirrors Kölliker's original histological description and supports Chen *et al*.,[14] who characterized distinct KO cell subsets. The coexistence of proliferative and degenerative cells further supports the hypothesis of KO as a dynamic, self-renewing structure during early cochlear development, with potential for hair cell transdifferentiation.[11]

The transition from KO to the mature inner sulcus is a key developmental milestone, marking the cochlea's readiness for acoustic stimulation. Data affirm Pujol *et al*.[12] and Majumder *et al*.,[13] highlighting the GER-LER differentiation into sensory and nonsensory cell domains. This supports the emerging view that KO's fate is tightly orchestrated to ensure the precise organization of pillar cells and hair cells within the organ of Corti.

Moreover, the delayed degeneration or dysfunction of KO, as proposed by Lim,[17] remains an intriguing area for future research. Given KO's role in initiating spontaneous activity and synaptogenesis, its persistence or aberrant remodeling could underlie auditory processing disorders. Our study reinforces this hypothesis, demonstrating that KO's morphological progression directly parallels cochlear maturation stages, with any deviation potentially disrupting auditory development.

Kölliker's organ versus Corti's organ

KO and COs are both crucial structures within the inner ear, playing significant roles in hearing. However, they differ in morphology, cellular composition, time, and type of functioning.

Both structures are located within the cochlear duct of the inner ear, contributing to the auditory system's overall function. Moreover, they both are composed of epithelial cells that have specialized roles in hearing, and both organs contain supporting cells that provide structural integrity and potentially facilitate regeneration or repair processes.

Nonetheless, many differences occur between the two organs.

The structure of KO comprises closely spaced columnar epithelial cells with a stratified appearance. Conversely, in CO, a complex-layered structure, with multiple cell types and distinct spatial organization, can be detected.[10,16]

KO cell type primarily consists of supporting cells characterized by bipolar or unipolar protrusions and microvilli. On the other hand, CO contains sensory hair cells and several types of supporting cells (Deiters' cells, Hensen's cells, etc.). KO provides to the development of CO, including the secretion of the tectorial membrane and cellular communication through gap junctions. When the cochlea is mature, CO is responsible for sound transduction, converting mechanical vibrations into electrical signals.[10,16]

KO undergoes significant degeneration and cellular reorganization, with a reduction in the number of columnar cells during postnatal maturation. Conversely, CO maintains a more stable structure postnatally, with differentiated sensory and supporting cells becoming more specialized.[15,16]

Some KO cells may possess kinocilia surrounded by microvilli, indicating a role in auditory development. IHC have a kinocilium during development, while outer hair cells possess stereocilia, which are engaged in CO mechanotransduction.[10,16]

As regarding to the gap junctions, KO presents extensively interconnected cells via gap junctions, primarily composed of Cx26 and Cx30, forming a syncytium. CO supporting cells and hair cells are not as interconnected; instead, they form a tight junction network in the reticular lamina that separates endolymph from perilymph.[7,16]

Finally, KO shows mitotic activity during late embryonic and early postnatal stages, indicating potential for transdifferentiation into hair cells. Conversely, CO hair

cells do not regenerate in mammals, and they are terminally differentiated.[11,16] Table 1 reports the comparative analysis between KO and CO.

LIMITATIONS AND FUTURE DIRECTIONS

Despite providing a comprehensive overview of KO's morphological features across mammalian species, this study has certain limitations. Primarily, the reliance on ultrastructural analysis from murine models may not fully capture the variability present in other species, including humans, due to interspecies differences in cochlear development. In addition, while detailed ultrastructural analyses provide valuable insights into cellular features and developmental changes, the functional implications of these morphological characteristics remain only partially understood. Future research should aim to integrate molecular and genetic approaches to elucidate the signaling pathways regulating KO development and degeneration, as well as its potential for transdifferentiation into hair cells. Longitudinal studies combining morphological, electrophysiological, and molecular data could better clarify how disruptions in KO remodeling contribute to auditory disorders. Furthermore, exploring the influence of hormonal, environmental, and genetic factors on KO maturation may reveal targets for therapeutic intervention. Expanding research to include human tissues and clinical correlations would also enhance the translational relevance of these findings, ultimately advancing strategies for hearing restoration and congenital hearing loss prevention.

CONCLUSIONS

By synthesizing historical and contemporary findings, this study underscores KO's dynamic remodeling as a critical determinant of auditory system development. Further exploration into KO's molecular signaling networks and their disruption may illuminate novel pathways for addressing congenital and acquired hearing impairments. This understanding of KO's morphological and functional dynamics may ultimately inform the development of targeted therapeutic strategies for congenital hearing loss and cochlear regenerative treatments.

Acknowledgment

Me, I would like to express my gratitude to Prof. L. Astolfi and the Bioacoustics Laboratory research group at the Department of Neuroscience, University of Padua, as well as the I-ApproVE Centre, for their generous courtesy in providing the images used in this work. Their support greatly enhances the quality of this study.

I would like also to express my sincere gratitude to Professor A. Martini, Director of the Bioacoustics Laboratory in Ferrara (FE), Italy, for his invaluable scientific guidance and unwavering support throughout the course of this study. His patience and insightful feedback

Table 1: Comparative analysis between Kolliker and Corti's organs

Features	KO	CO
Location	Medial wall of the cochlear duct; GER	Basilar membrane within cochlear duct
Developmental timing	Present during embryonic and early postnatal stages; transient	Appears during late embryogenesis and persists throughout life
Main function	Supports cochlear development (e.g., tectorial membrane secretion and spontaneous activity)	Responsible for mechanoelectrical transduction of sound
Cell types	Mainly supporting epithelial cells with columnar morphology; some cells with kinocilia and microvilli	Inner and outer hair cells (sensory) + several supporting cells (Deiters', Hensen's, and pillar cells)
Cellular arrangement	Stratified appearance due to dense basal nuclei; aligned vertical cells	Highly organized architecture with distinct rows of hair and supporting cells
Apical specializations	Microvilli (~3–4 μm); occasional kinocilium	Hair cells with stereocilia (OHCs) and kinocilium (IHCs during development)
Gap junctions	Extensive gap junctions (C×26, C×30); forms a functional syncytium	Tight junctions in the reticular lamina; limited gap junctions
Mitotic activity	Yes – both mitosis and apoptosis occur postnatally; some transdifferentiation potential	No – cells are terminally differentiated; very limited regenerative capacity
Degeneration	Undergoes degeneration by~P15 (in mice); transforms into inner sulcus	Stable postnatal structure with minimal morphological changes
Hormonal sensitivity	Highly sensitive to thyroid hormone and hypothyroidism delays degeneration	Less directly affected by thyroid hormone levels
Role in spontaneous activity	Yes – releases ATP → ↑Ca^{2+} in IHCs → triggers glutamate release → stimulates afferents	No intrinsic spontaneous activity generation; receives synaptic input
Function in tectorial membrane	Contributes to secretion and positioning of tectorial membrane	Anchors tectorial membrane; OHC stereocilia embed into it
Morphological transition	Replaced by cuboidal cells of the inner sulcus during cochlear maturation	Maintains complex architecture through life

↑increase KO: Kölliker's Organ, CO: Corti's Organ, IHCs: Inner hair cells, Cx30: Connexin 30, Cx26: Connexin 26, OHCs: Outer hair cells, GER: Greater epithelial ridge, ATP: Adenosine triphosphate

have profoundly contributed to the development of this project.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Hudspeth AJ. How hearing happens. Neuron 1997;19:947-50.
2. Caragli, V.; Di Pasquale Fiasca, V.M.; Genovese, E.; Martini, A. Kolliker's Organ and Its Functional Role in the Development of Corti's Organ and Auditory Systems. Audiol. Res 2025;15:75.
3. Kölliker A. Bau der Schnecke. In: Handbuch der Gewebelehre des Menschen. Leipzig, Germany: Wilhelm Engelmann. 1863;4:708.
4. Hensen V. On the morphology of the cochlea of humans and mammals. Journal of Scientific Zoology. Z Wiss Zoo1 1863;13:481.
5. Bast TH, Anson BJ. The Temporal Bone and the Ear. Springfield, Illinois: Charles C. Thomas, Springfield, Illinois; 1949.
6. Tritsch NX, Bergles DE. Developmental regulation of spontaneous activity in the Mammalian cochlea. J Neurosci 2010;30:1539-50.
7. Dayaratne MW, Vlajkovic SM, Lipski J, Thorne PR. Kölliker's organ and the development of spontaneous activity in the auditory system: Implications for hearing dysfunction. Biomed Res Int 2014;2014:367939.
8. Lim DJ, Anniko M. Developmental morphology of the mouse inner ear. A scanning electron microscopic observation. Acta Otolaryngol Suppl 1985;422:1-69.
9. Tritsch NX, Yi E, Gale JE, Glowatzki E, Bergles DE. The origin of spontaneous activity in the developing auditory system. Nature 2007;450:50-5.
10. Hinojosa R. A note on development of Corti's organ. Acta Otolaryngol 1977;84:238-51.
11. Wu DK, Kelley MW. Molecular mechanisms of inner ear development. Cold Spring Harb Perspect Biol 2012;4:a008409.
12. Pujol R, Lavigne-Rebillard M, Lenoir M. Development of sensory and neural structures in the mammalian cochlea. In: Rubel EW, Popper AN, Fay RR, editors. Development of the Auditory System Springer Handbook of Auditory Research. Vol. 9. New York, NY, USA: Springer; 1998. p. 146-92.
13. Majumder P, Crispino G, Rodriguez L, Ciubotaru CD, Anselmi F, Piazza V, *et al.* ATP-mediated cell-cell signaling in the organ of Corti: The role of connexin channels. Purinergic Signal 2010;6:167-87.
14. Chen J, Gao D, Chen J, Hou S, He B, Li Y, *et al.* Single-cell RNA sequencing analysis reveals greater epithelial ridge cells degeneration during postnatal development of cochlea in rats. Front Cell Dev Biol 2021;9:719491.
15. Kamiya K, Takahashi K, Kitamura K, Momoi T, Yoshikawa Y. Mitosis and apoptosis in postnatal auditory system of the C3H/He strain. Brain Res 2001;901:296-302.
16. Raphael Y, Altschuler RA. Structure and innervation of the cochlea. Brain Res Bull 2003;60:397-422.
17. Lim DJ. Functional structure of the organ of Corti: A review. Hear Res 1986;22:117-46.