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REVIEW ARTICLE **OPEN ACCESS**

Prestin: Piezo-electric Mechanotransducer bridge in hearing

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ABSTRACT
Noise induced hearing loss involves non coordination of large number of cochlear proteins in the human ear. These cochlear proteins contribute maximally to the resilience of sound. Amidst of all these cochlear proteins, this review sheds light on motor protein prestin which ultimately contributes to electromotility of Outer Hair Cells. This sensory protein plays a role in anion transduction in mammals, but not in non mammals. Prestin based outer hair cell motility is responsible for the exquisite sensitivity and frequency selectivity seen in the mammalian cochlea. This review unravels the evolution of prestin and its difference in functioning among mammals and non mammals. This review also includes the protein's unique functions and mechanisms as a voltage to force converter. The effect of non-linear capacitance on this motor protein has also been substantially explained with examples. The prestin protein possesses a unique sequence motif named STAS. This motif has the hydrophobic domains of involved in inter and intermolecular interactions. This review summarizes the conformational changes that occur in prestin during translocation of anions and the structural and functional properties of this motor prestin protein for understanding the molecular mechanism of hearing.
Keywords: *Anion Transduction, Electromotility, Non-Linear Capacitance, STAS, Voltage-to-force.*

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INTRODUCTION

A loud sound, irritating, disturbing as well as unpleasant to hear for human being is commonly reported as Noise. High volume is one of the attractions in urban cities of every country around the globe. Noise is being reported as one of the major health issues in developing countries. In Indian scenario, noise pollution is a regular phenomenon, especially in urban suburbs. In ancient times, there was less noise pollution and most importantly nil exposure to hi-tech gadgets; therefore people were less prone to hearing loss. In contrast to this, sound pollution is increasing continuously in metro cities. This trouble mainly leads to mild to severe acoustic injuries. Noise induced hearing loss (NIHL) is ironically a silent disorder which develops gradually after months to years of industrial noise exposure without causing substantial pain to the hearing organs. This loud and disruptive noise waves over simulates sensitive hearing cells gradually leading to damage and death of the hair cells. As the populations tend to rise and demand for products increases eventually, the spread of industries collectively increase, making Occupational NIHL add to the major disability to the global burden. According to the statistics collected from various sectors in the world around the years, 16% of the hearing loss related cases found in the adults is registered as Occupational noise [1]. Occupational hearing loss affects an estimate 0.2 to 2% of the GDP, causing hearing problems one-thirds of the working population.

MECHANISM OF HEARING

It is quite interesting to know how are we able to hear so many sounds and interpret it within milliseconds. It is a complex mechanism of the mammalian ear which is in the temporal bone of the skull. Sounds enter through outermost soft funnel-like structure called pinna or auricle. The ear is divided into three parts to study the complex structure with an ease, namely outer ear, middle ear and inner ear. Pinna serves as a funnel which not only connects waves but filters and amplifies a little bit. The sound waves enter the auditory canal. It passes through auditory canal where it hits the tympanic membrane or the ear drum. The sound waves cause the tympanic membrane to vibrate with compression pushing the

membrane in and rare fractions pull it out. The sound energy is converted into mechanical energy, the form in which it will be transmitted through the rest of the ear. The tympanic membrane is attached to the head of the malleus and its vibrations are transmitted to the rest of the ossicular chain. The movement of ossicular chain within the tympanic cavity amplifies the energy transmitted. The ear drum has much larger surface area than the stapes even though the same amount of energy is being transferred with more energy applied over smaller surface area, thus it needs greater force. The middle ear is filled with air and inner ear is with liquid. Malleus acts as a lever to amplify the force with which the ossicular chain vibrates and it needs to be amplified because the rest of the ear is fluid-filled. Wave propagation in these mediums (air and fluid) will involve overcoming resistance and amplification. The foot of the stapes covers the oval window which is connection with the perilymph filled vestibule. The rocking motion of stapes over the oval window causes pressure waves in the perilymph fluid. The tympanic cavity is lined with mucosa and filled with air and the auditory ossicles consisting of three tiny bones called the malleus (hammer), incus (anvil), and stapes (stirrup) .As the auditory ossicles vibrate, the stapes pushes the oval window in and out. This is passed to inner ear and the cochlea, a fluid – filled, snail shaped structure which has a spiral organ of Corti, that is the receptor organ for hearing .Tiny hair cells- Outer hair cells (OHCs) and Inner hair cells (IHCs) in this organ convert the sound vibrations into electrical impulses that are transported to brain via sensory nerves. Sound amplification is achieved through two kinds of receptor cells; Outer hair cells (OHC) and inner hair cells (IHC). Outer hair cells (OHCs) are the cells of highly distinctive nature which provides Cochlear amplification [2]. Figure 1. Auditory sensory cells are the cells that are sensory receptors of both auditory system and the vestibular system in the ears of all vertebrates. In mammals, the auditory hair cells are located within the spiral organ of Corti on the thin basilar membrane in the cochlea of the inner ear. OHCs electromotility depends on novel type of force generating mechanism. Unlike OHCs, IHCs convey all the auditory information via afferent nerve to the brain. While OHCs are the sensory receptor cells that contain stereociliary filaments. The stereociliary are arranged in rows and connected by tip links which are elastic elements that mediates transduction channel. The stereocilia bring about deflection upon the movements of tectorial and basilar membrane. When the stereocilia moves towards striavascularis, tight junctions present between the neighbouring cells does allow protein diffusion between the hair cells. The endolymph present is low in Na^+ and Ca^{2+} but rich in K^+ ions. The striavascularis exports the K^+ to endolymph and generates endocochlear potential *i.e.* potential difference between endolymph and perilymph. This endocochlear potential as well as K^+ is responsible for mechanotransduction process performed by OHCs. When cilia displaces towards striavascularis, K^+ ions enter the cell leading to depolarisation. Simultaneously, Ca^{2+} enters the cell. Potassium channels close before the return of stereocilia which leads to rapid adaptation that is because ion channels are partially terminated. Whereas, slow adaptation displaces actin and myosin XVa filament of stereocilia. In the slow adaptation, the motor complex tries to climb up stereocilia that changes the position of tip link that increases tension. During positive signal, the motor complex slides down and decreases the tension thus closing the channel. This traps the Ca^{2+} in channel and creates a tension in the tip links that encourages the closure of channels. The trapped Ca^{2+} can affect the adaptation motor that is hooked to next tip link in same stereocilia molecule. After the entry of stereocilia through the transduction channels, Ca^{2+} is rapidly bound by Ca^{2+}chelators. These chelators prevent it from coming close to the mouth of channel. Ca^{2+} can be transferred back to the endolymph by plasma membrane calcium pumps (PMCA). The Ca^{2+}in endolymph is crucial for mechanotransduction, thus levels of the Ca^{2+}diminished affect the mechanotransduction currents. Stereociliary actin- mediated microvillar bundles which convert vibrational motion into electric current convey to the brain via afferent nerve endings. Proteins involved in the framework of IHCs, OHCs and stereocilia responsible for hearing acuity. Cochlear proteins such as myosin, cadherin23, otoferin, stereocilin, harmonin, protocadherin, radixin, whirlin, espin, prestin, worfferin, wolframin, connexin26, collagen, alpha tectorine makes the framework of cochlear integrity and different functions in hearing mechanism. Whirlin is a cytoplasmic protein that elongates and maintains stereocilia. It also controls actin polymerization of stereocilia. Myosin is localized in stereocilia in IHCs and OHCs and synaptic terminals. It maintains the framework of stereocilia along with cadherin 23. Cadherin 23 is first member of calcium binding proteins. It is expressed in IHCs and acts with myosin VIIIa and harmonin in hair cell differentiation. Harmonin is multimer scaffold protein prevalent in IHCs, OHCs and stereocilia. Harmonin b directs the cadherin 23 to stereocilia microelements and also acts along myosin VIIa in developing stereocilia. Connexin protein family are called connexions. They combine homomeric and heteromeric gap junctions. Connexin 26 maintains K^+ ion concentration in inner ear endolymph. Espin elicits microvillar elongation and mainly involved in maintenance of actin filaments. Wolframin type II transmembrane protein comprises of 890 amino acids and balances homeostasis of K^+ and Ca^{2+} in endoplasmic reticulum and regulates ion channels. Collagen IX maintains the integrity of type-A fiber of transmembrane domain which is straight, unbranched bundles parallel

with type –B which is highly branched and loosely packed. It also maintains inner ear integrity. Otoferin is involved in the synaptic vesicle – membrane fusion and in membrane trafficking for exocytosis. The otoferin protein is encoded by the OTOF gene which belongs to ferin family, associated with nonsyndromic deafness. Genetic mutation in otoferin leads to hearing impairment resulting from improper hair cells. This review is focused on the prestin protein which is abundant in OHCs and mainly responsible for electromotility. The evolutionary changes of the hearing mechanism of prestin molecule from non mammalian to mammalian was not focussed fully in previous reviews also the mechanism of hearing and role of prestin was scientifically put up but not reviewed and succinct. So this review has unique features to throw light on the importance of prestin molecule in resilience of sound. Loss of prestin protein can be a significant cause for sever to profound hearing loss [3-7]. Figure 1,2.

STRUCTURE OF PRESTIN

Prestin is 11nm bullet shaped particle with abundant cytoplasmic domain encoded by SLC26A gene (solute carrier family26) belongs to sulphur binding domain of anion transporter family that encode Na^+ independent anion transporters[8]. Prestin consists of 744 amino acids with molecular weight of 80kDa. The prestin gene was found to contain 20 exons and located at chromosome 7 in humans. It is known to appear the only responsible protein for hair cell motility, also known as OHC motor proteins [9]. The OHCs possess trilaminate structure that is composed of plasma membrane, cortical lattice and subsurface cisternae as depicted in figure 3. The plasma membrane is the outermost layer present laterally that encodes the motor protein present abundantly. Then, next is the cortical layer below the plasma layer that accounts for the cytoskeleton, which is actin based two dimensional structures. The innermost layer encodes for subsurface cisternae that accounts for endoplasmic reticulum as depicted in figure 4.

ASSOCIATION OF PRESTIN WITH STAS

Prestin drives voltage dependent electromotility in mammalian outer hair cells [9, 10].

Prestin possess unique sequence motif namely STAS (sulphate transporters and antisigma factor antagonists)that belongs to SulP family that are involved in intramolecular and intermolecular interactions [11]. However mammalian prestin shares its highly specific intracellular domain Sulfate transporter and anti- sigma antagonist (STAS) to the different members of the SLC26 family.This domain originates after transmembrane region and is located below lipid bilayer and can elongate much more than antisigma proteins. This STAS domain has ovoid shape composed of β strands with five α helices. Prestin posses 12 hydrophobic segments that expand the plasma membrane and the hydrophilic amino acid residues reside in cytoplasmic domain as depicted in the figure 5 and 6.

Presence of a correctly folded STAS domain is important for proper prestin function [12]. Liu Y. *et al* put forward a theory stating that in mammalian prestin, the anion binding sites in STAS domain consists of a reservoir of functionally ready anions, which increases the local anionic concentration, required for the high rate at which the molecular motor operates (upto 120 kHz) [13,14].Under physiological conditions, majority of the anion binding sites on STAS domain are engaged by Cl^- and hence prestin acts as dimer or tetramer structure [15, 16].

VOLTAGE TO FORCE TRANSDUCER MOLECULE

Prestin functions as a transducer and voltage sensor that analyses the changes occurring in transmembrane potential. Prestin consists of four subunits (tetramer) composed of six transmembrane regions from S1-S6. The first four subunits composed of voltage sensor domain and the last two forms the pore for K+ permeation [17]. S4 voltage sensor has positive charged amino acid that causes repulsion and closes the channel. Depolarization moves the helix and induces the conformational changes in prestin that open the channels. This opening of channels allows the ions to flow through the membrane. This mechanism of polarization and depolarization is performed by voltage sensor of motor protein .The OHCs doesn't operate in a motor as there is no domestic source of energy, rather OHC electromotility arises from an 'actuator' which is responsible for moving and controlling a mechanism. The cell changes between states when externally fulfilled by an energy source, showing a piezoelectric property *i.e* mechanical stress is applied to generate electric charge [18,19]. These two mechanisms show that prestin can work as both voltage sensor and actuator in a concomitant manner.

Schacchinger *et.al.* had notion whether a voltage acts intrinsically or extrinsically on prestin. He confirmed that the anion moves towards cytoplasm then area of the cell decreases (short state) and outside it increases (long state).

Voltage driven motility of the cell can be measured by Non linear capacitance (NLC).Prestin shows voltage-dependent charge transfer called NLC [20]. It includes gating current that causes dislocation of charge across the membrane. NLC is a substitute measure of motility, which is an electrical signature of

prestin action and can be carried out on a typical patch-clamp setup without additional equipment. To analyze the relation of NLC with the prestin, another mechanism was deduced that confirmed the NLC can only be diminished when absence of intracellular anion on prestin site. The advantage of NLC is more evident in the assessment of prestin function in transfected cell lines which often express much less prestin, but requires relatively fast measures to acquire large number of cells for statistics [21-23] .The monovalent intracellular anions such as Cl^-act as extrinsic voltage sensors that bind to the prestin molecule that triggers the conformational changes which is required for motility of OHCs. The anions binds with high affinity across the membrane called hyperpolarisation and when it gets translocated towards cytoplasmic side called depolarization [24]. Figure 5.

There are two factors responsible for NLC activities. Primilarily prestin has an intrinsic property of which diminishes due to absence of Cl^-. Secondarily, influences the expression of NLC is amino acids between last transmembrane region and C-terminus region. These amino acids interfere with the voltage regulated anion binding that induces the conformational change in the protein molecule. One of these amino acids sits at the entrance and control the entering of anions to interact with other amino acids. Determination of NLC dependent motility found that the charge movement shows conformational change in motor protein.

The effect of hydrophobic amino acids binding to anions to make conformational changes in prestin protein was studied by Schacchinger *et.al*. The recombinant gene was produced by fusing few segments of SulTP gene of one organism with the other segments of another organism. The different segments from Sul TP gene of rat prestin was fused with N and C terminals of zebra fish prestin, showed sufficient levels of NLC. On the contrary when Sul TP gene of zebra fish prestin fused with N and C terminals of rat prestin showed loss of NLC (Schacchinger et.al 2011). It was confirmed from the study of Schacchinger that Sul TP mediates NLC without the use of C terminal.

EVOLUTION OF PRESTIN FROM AN ANION TRANSPORTER TO A MOTOR PROTEIN

The acoustic tuning of the hair cells in the hearing machinery is believed to indulge different processes of kinetics of channel activation and fast adaptation. The quick adaptation and channel activation time window depends on the vast frequency range of hearing of the species.

In mammalian species, the kinetic process of channel activation is more in number and present in multiple (more than one) order of magnitude faster than in non-mammalian species and consistent with the sharp need of higher magnitude of frequency detection. The mammalian cochlea is arranged in a sequential tonotopical manner where the base hair cells are tuned to higher frequency and atop (apex) hair cells are tuned to lower frequency. The frequency tuning is enhanced further by the intrinsic properties of the hair cells. Surprisingly it is stated that the basal hair cells display faster kinetics than the apical ones.

Xiaodong Tan *et al* conducted a research on two aspects of physiological functions of prestin for which Zebrafish, Chicken, Platypus and Gerbil were used for study [25]. The motor and transport functions of the protein and its orthologs from different species under the sub phylum vertebrata were studied. To gain the better perspective, Platypus prestin is a major and important link between two classes. This provided a necessary peptide sequences and structural implications about the functioning of prestin and evolution from the non-mammalian vertebrate transporter to mammalian electromotility motor.

In the comparative studies, it was found that both the non-mammalian species of zebrafish and chicken prestins indicated weak NLC, with significant peak shifts towards the depolarization side. This was opposite with the mammalian samples of Platypus and Gerbil, where the prestins of the mentioned samples showed a robust NLC with peak shift towards the hyperpolarization side. The mammalian prestin samples also retained traces of transporter function compared to major anion transport capacities in the non mammalian prestin samples. The aptitude of OHCs to adjust the length of their cell bodies in reaction to a change in membrane potential is known as somatic motility or electromotility [26]. Somatic motility was found positive only in the Platypus and Gerbil samples. Therefore, The collected samples of prestin from Zebrafish and Chicken (non mammalians) are anion exchangers or transporters with no trace of motor function. This study implies that prestin might have evolved from an anion transporter of non-mammalian to mammalian. Mammalian prestin is an exclusive member in its gene family with ability to function as a suitable motor protein. Therefore it seems to show an inverse relationship between motor and anion transport functions during evolution of the protein. Motor function is observed to have emerged only in mammalian prestin and the gain of motor function is present with reduced transport capabilities [27].

Motility and NLC functions were measured from prestin-transfected HEK-293 cells by means of a voltage-clamp technique and photodiode-based displacement measurement system. Observations show inverse changes among the four selected samples, displaying diminished transport function from zebrafish to

gerbil, NLC becomes more even along with a typical shift of V1/2 from positive to negative voltages. The gain of NLC is supported with the gain of somatic motility in both Platypus and Gerbil prestins. But gain of electromotility showed to be concurrent with loss of anion transport function. Therefore it indicates an inverse relationship between NLC and anion transport capabilities, where motor function is seen to be active only in the mammalian prestin [28].

After reviewing various experiments, it was concluded that prestin protein evolved from non-mammalians to mammalians with significant changes in the function of the protein. The protein evolved among the species acting as an anion transporter in non mammalians into a motor protein, enhancing the hearing sense in mammals.

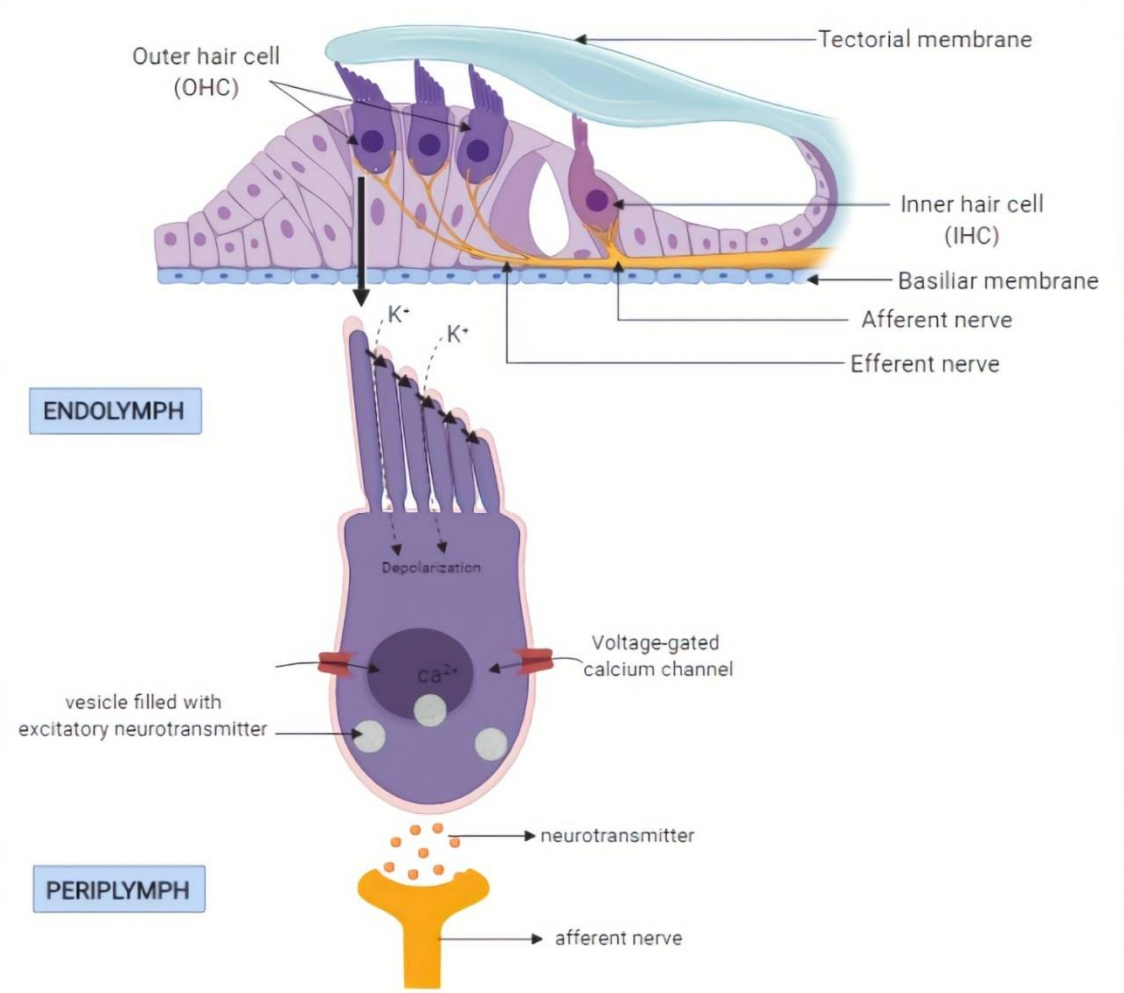


Figure 1: The first figure shows the arrangement of outer hair cells and inner hair cells between tectorial and basiliar membrane in the cochlea. Outer hair cells perform the electromotility essential for cochlear amplification. Inner hair cells send transduced auditory information via afferent nerve to the brain. The second figure shows the mechanism of transmission of neurotransmitter via afferent nerve to the brain. The stereocilia brings deflection upon movement between the basiliar and tectorial membrane. The stereocilia are connected by means of tip links that mediates the transduction channel. When stereocilia moves towards stria vascularis, the neighbouring cells doesn't allow protein diffusion between hair cells. The stria vascularis exports K^+ in endolymph in endocochlear potential responsible for mechanotransduction process. When cilia displaces towards stria vascularis, K^+ enters the cell causing depolarization. Simultaneously, Ca^{2+}ions enter the cell and gets trapped that sends signal to stereocilia for closure via tiplinks. $^+$. Ca^{2+} helps vesicle-filled neurotransmitter to come out of endolymph and reach afferent nerve via perilymph to the brain. Chelators are accumulated at the opening to prevent the escape of Ca^{2+}

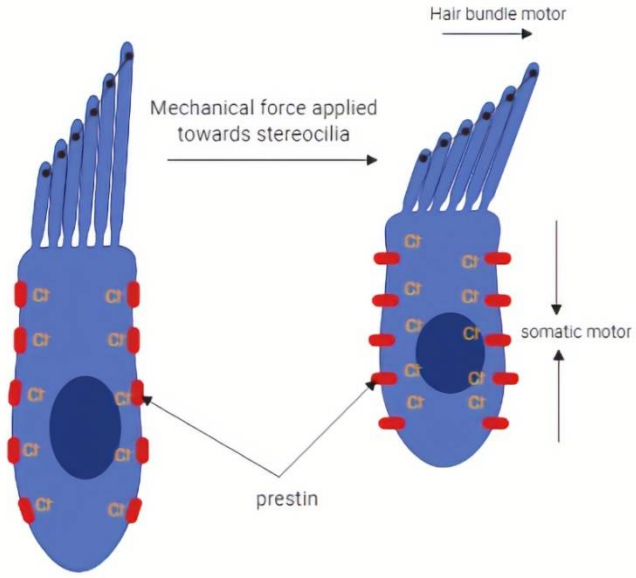


Figure 2: The chloride ions are bound on the surface of prestin site in OHC molecules. These chloride ions changes conformation of the cell from long state to short state that acts as a driving force for somatic motility. The stereocilia molecules are present on the surface of outer hair cells. These stereocilia molecules are deflected towards stria vascularis converting vibrational motion into electric current for bringing conformational changes in the cell.

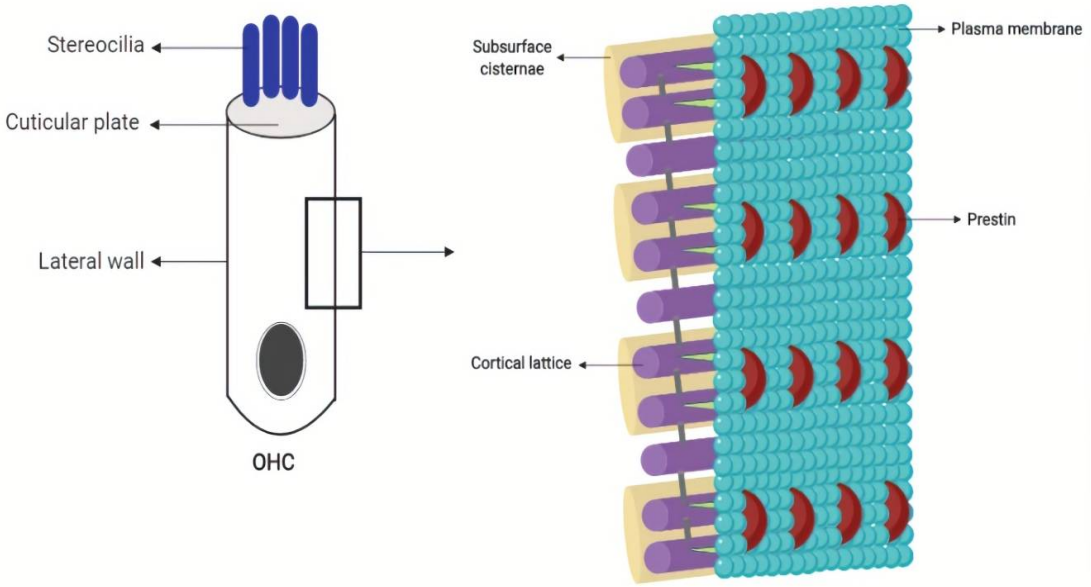


Figure 3: Trilaminar structure of OHCs- The OHC molecular structure is composed of three layers; plasma membrane, cortical lattice and subsurface cisternae. The plasma membrane has the motor protein that is present laterally on surface of OHCs which is depicted in red colour in the figure. The second layer is cortical lattice present below the plasma layer that has actin based two-dimensional structure present in form of bundles. The innermost layer is subsurface cisternae that have endoplasmic reticulum. Extrinsically, the stereocilia molecules are attached to the OHC molecules by means of a cuticular plate. These stereocilia are attached by means of tip links that convert vibrations into electric current.

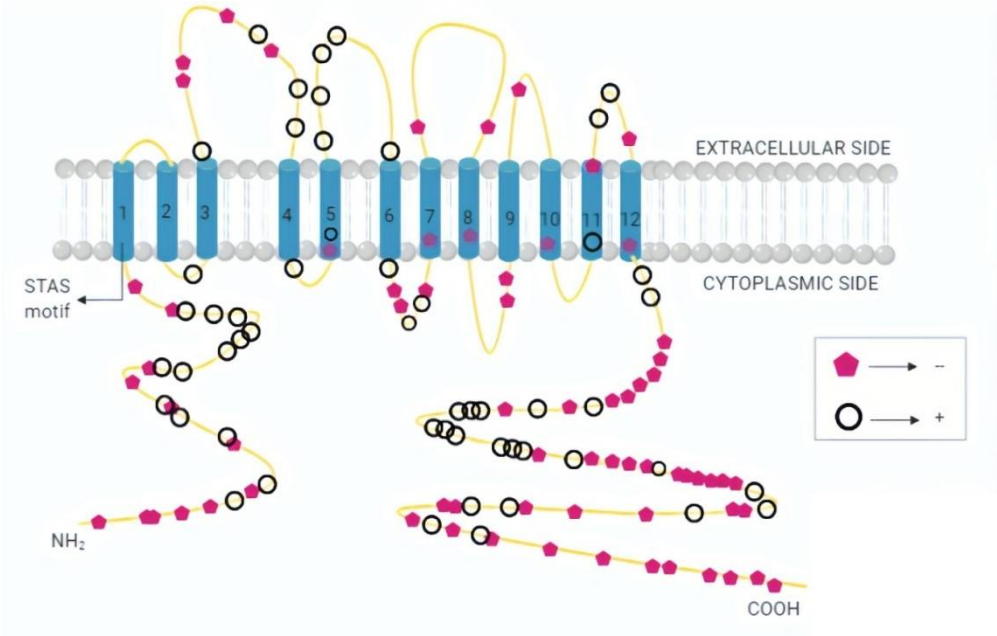


Figure 4: The illustrated cartoon depicts the arrangement of structure of the prestin protien. The structure consists of 1744 amino acids. The structure contains positively and negatively charged amino acids shown using black rings and pink pentagons respectively. Hydrophilic amino acids are positively charged present along the carboxy terminal and hydrophobic amino acids are negatively charged on the amino terminal. The 12 hydrophobic segments expand the plasma membrane showing high concentration of hydrophilic amino acid residues in cytoplasmic domains. The membrane across helix contains highly conserved STAS motif(sulphate transporters and antisigma-factor antagonists).STAS is an ovoid or cylindrical shaped embedded in the transmembrane region between extracellular side and cytoplasmic side. This STAS domain has the binding site for ions such chloride, bromide and nitrate ions responsible for intermolecular and intramolecular interactions.

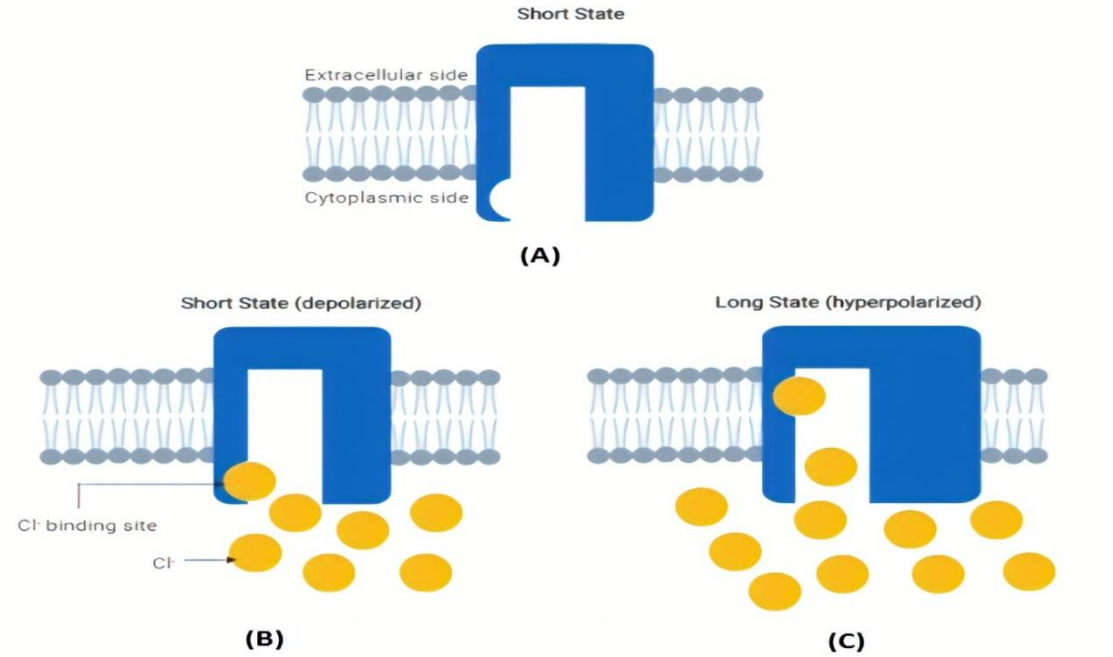
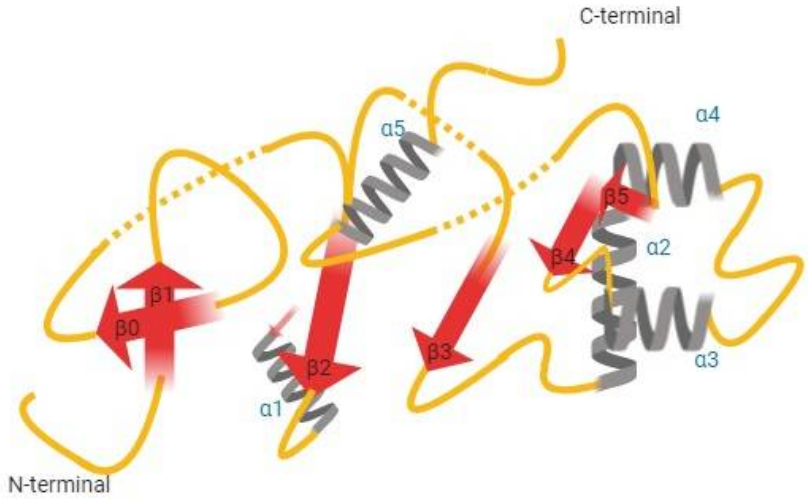


Figure 5: **Prestin protein works on an integral mechanism of internal Cl^- ions.**
(A)When Cl^- ion is absent, prestin protein attains a short state.(B) Here, the cell membrane is depolarized. Cl^- binds to the molecular site but stays at the cytoplasmic side of the membrane and retains the short state.(C) The cell membrane is hyperpolarized. Cl^- ions bound to the site is translocated across the molecule towards extracellular side. When the ion binds to the extracellular site , the molecular attains a

long conformational state. When the Cl^- ion travels back to cytoplasm, the molecule becomes short. The cell contraction due to depolarization is larger than cell elongation caused due to hyperpolarization.



Crystal structure of STAS domain

Figure 6: The 3D arrangement of STAS domain constructed from rat model illustrate a conserved folding core, constituted of a central β-sheet made of five to six β-strands, with five α-helices surrounding them. The 3D model of the transmembrane domain of mammalian prestin is identified as a central anion binding region in the domain, with a pathway leading to anions from the cytoplasm. The crystal modulated structure of STAS (rat model prestin) show that ions like Cl^-, Br^-,I^- ,$SCN^-$and $NO3^-$binds to the specific site of the STAS domain which is compatible in identification of the unique anion-binding site.

CONCLUSION

Prestin is a unique motor protein. Prestin is completely different from normal cellular motors which depend on enzymatic processes rather it works on voltage to displacement conversion and functions at microseconds rate quicker than other cellular proteins. The protein has been evolved for *myriteries* to transform from an anion transporter in non mammalians to become a motor protein in mammals. As NLC and electromotility measurements can be analysed from the prestin protein, it can be a suitable model for research on characteristics of anion transporting membrane protein. However prestin is a highly sensitive protein and due to excessive noise, slight damage in the protein can disturb the function and lead to improper transduction and amplification of sounds and lead to gradual permanent hearing loss.

Prestin has remarkable and unique piezo-electric properties, voltage controlled actuators and suitable for future nanotechnological advancements. Identification of the proper structural domains of protein is useful to create nanomotors which can be applied in vast fields of medicine, protein engineering etc.

With further modifications in the near future, malfunction in prestin protein which causes hearing loss can be successfully repaired by modified prestin probes which can be injected directly towards the micromachinery of the ear leading to self heal of the damaged site, which may revert the hearing sense back to normal.

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REFERENCES

1. Pingle S, Tumane R, Jawade A, Jain R, Thakkar L, Sishodiya P & Mandal B, (2013). "Evaluation of biomarkers for the early detection of noise induced hearing loss in the mine workers. Project Report Vol.(1)3:123

2. Ashmore JF, (1987). "A fast motile response in guinea-pig outer hair cells: the cellular basis of the cochlear amplifier" J Physiol. 388:323–347.
3. Nelson DI, Nelson RY, Concha-Barrientos M, Fingerhut M, (2005). "The global burden of occupational noise-induced hearing loss" Am J Ind Med: 48(6):446-58.
4. Azizi MH, (2010). "Occupational Noise-induced hearing loss" Int J Occup Environ Med. 1:116-23.
5. Occupational Exposure to Noise: Evaluation, Prevention and Control: NIOSH Cooperative Agreement with WHO for 1994-1995. Available from: http://www.who.int/ occupational_health /publications/noisebegin.pdf.
6. Fuente A, Hickson L, (2011). " Noise induced Hearing Loss in Asia" , International journal of Audiology: 50:53-510.
7. Zheng XY, Henderson D, Mcfadden, SL, Hu BH, (1997). "The role of the cochlear efferent system in acquired resistance to noise-induced hearing loss" Hear. Res: 104(1-2):191-203.
8. Dallos P, Fakler B, (2002). "Prestin, a new type of motor protein" Nat Rev Mol Cell Biol. 3:104–11
9. Zheng J, Shen W, He DZ, Long KB, Madison LD, Dallos P, (2000). "Prestin is the motor protein of cochlear outer hair cells" Nature. 405:49–155.
10. Pasqualetto E, Aiello R, Gesiot L, Bonetto G, Bellanda M and Battistutta R, (2010). "Structure of the cytosolic portion of the motor protein prestin and functional role of the STAS domain in SLC26/SulP anion transporters" J. Mol. Biol. 400:448–462
11. Santos-Sacchi J, Dilger JP, (1988). "Whole cell currents and mechanical responses of isolated outer hair cells" Hear Res. 35:143–150
12. Iwasa KH and Kachar B, (1989). "Fast in vitro movement of outer hair cells in an external electric field: effect of digitonin, a membrane permeabilizing agent" Hear Res. 40:247–254
13. Zheng J, Du GG, Matsuda K, Orem A, Aguinaga S, Deak L, Navarrete E, Madison LD and Dallos P, (2005). "The C-terminus of prestin influences nonlinear capacitance and plasma membrane targeting" J. Cell Sci. 118:2987–2996
14. Lolli G, Pasqualetto E, Costanzi E, Bonetto G, Battistutta R, (2016). "The STAS domain of mammalian SLC26A5 prestin harbours an anion-binding site" Biochem J. 15:473(4):365-70.
15. Liu Y, Rossiter SJ, Han X, Cotton JA and Zhang S, (2010). "Cetaceans on a molecular fast track to ultrasonic hearing" Curr. Biol. 20:1834–1839
16. Detro-Dassen S, Schanzler M, Lauks H, Martin I, zu Berstenhorst SM, Nothmann, D, Torres-Salazar D, Hidalgo P, Schmalzing G and Fahlke C, (2008). "Conserved dimeric subunit stoichiometry of SLC26 multifunctional anion exchangers" J. Biol. Chem. 283:4177–4188
17. Zheng J, Du GG, Anderson CT, Keller JP, Orem A, Dallos P and Cheatham M, (2006). "Analysis of the oligomeric structure of the motor protein prestin" J. Biol. Chem. 281:19916–1992
18. Bezanilla F, (2000). "The voltage sensor in voltage-dependent ion channels." Physiol Rev. 80:555–92
19. Dallos P, Corey ME, (1991). "The role of outer hair cell motility in cochlear tuning" Curr Opin Neurobiol 1:215–220.56.
20. Dallos P, Evans BN, (1995). "High-frequency motility of outer hair cells and the cochlear amplifier" Science 267: 2006–2009
21. Song L and Santos-Sacchi J, (2016). "A Walkthrough of Nonlinear Capacitance Measurement of Outer Hair Cells" Methods Mol Biol. 1427:501-12
22. Bai JP, Navaratnam D, Samaranayake H, Santos- Sacchi J, (2006). "En block C-terminal charge cluster reversals in prestin (SLC26A5): effects on voltage- dependent electromechanical activity" Neurosci Letts. 404:270–275
23. Bai JP, Surguchev A, Bian S *et al*, (2010). "Combinatorial cysteine mutagenesis reveals a critical intramonomer role for cysteines in prestin voltage sensing" Biophys J. 99:85–94
24. Bai JP, Surguchev A, Ogando Y, Song L, Bian S, Santos-Sacchi J, Navaratnam D, (2010). "Prestin surface expression and activity are augmented by interaction with MAP1S, a microtubule- associated protein" J Biol Chem. 285:20834–20843
25. Oliver D, He DZ, Klocker N, Ludwig J, Schulte U, Waldegger S, Ruppersberg JP, Dallos P, Fakler B, (2001). "Intracellular anions as the voltage sensor of prestin, the outer hair cell motor protein" Science. 292:2340–3
26. Tan X, Pecka JL, Tang J, Okoruwa OE, Zhang Q, Beisel KW, He DZ, (2011). "From zebrafish to mammal: functional evolution of prestin, the motor protein of cochlear outer hair cells" J Neurophysiol. 105(1):36-44
27. Brownell WE, Bader CR, Bertrand D, de Ribaupierre Y, (1985). "Evoked mechanical responses of isolated cochlear outer hair cells" Science 227(4683):194–196
28. Tan X, Pecka JL, Tang J, Lovas S, Beisel KW, He DZ, (2012). "A motif of eleven amino acids is a structural adaptation that facilitates motor capability of eutherian prestin" J Cell Sci. 125:1039–47
29. Albert JT, Winter H, Schaechinger TJ, Weber T, Wang X, He DZ, Hendrich O, Geisler HS, Zimmermann U, Oelmann K, Knipper M, Gopfert MC, Oliver D, (2007). "Voltage-sensitive prestin orthologue expressed in zebrafish hair cells" J Physiol. 580:451–61.

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