American Journal of Otolaryngology and Head and Neck Surgery

Research Article
Published: 01 Oct, 2022

Important Notes about Prestina

*Jan Myjkowski**

Otolaryngology Clinic in Mielec, Poland

Abstract

The OHC transmembrane protein responsible for the transport of chlorine and anions through the cell membrane has been recognized as a molecular engine according to numerous studies. The work performed in the form of OHC contractions is supplied with the energy of the electric potential of the cell membrane. On the cytoplazmatic side, prestin has a chloride and anion level sensor. Changes in the level of chlorine in the cell are associated with OHC depolarization, which affects the conformational changes of the transmembrane protein and cell contraction. The frequency of prestin's conformational changes depends on depolarization and this depends on the work of ion channels of the lateral and lower OHC surfaces.

The frequency of depolarization is limited by the time the cell's ion channels work. If the magnitude of the membrane potential changes is constants, then there is a problem with amplifying the soft tones. The contraction is proportional to the membrane potential and depolarization. Each contraction of the OHC by pulling on the basilar membrane strengthens the vibration of the basilar membrane. There is no mechanism for regulating OHC contractions.

Keywords: Acoustic cells; Amplification; Receptor; Ionic canals

Operation Mechanism

Prestine belongs to the family of chlorine and anion transporters through cell membranes. It is encoded by gene SLC26A5 in chromosome 7. This is a transmembrane, polytope protein which passes through OHC cell membrane many times [1]. Encoding takes place in the karyon, while production in ribosome's and the endoplasmic reticulum. The spatial structure of the polypeptide prestine chain is determined by the sequence according to which amino acids are arranged. A prestine particle is made of approx. 740 amino acids. Its diameter amounts to 12 nm to 15 nm. 6,000 prestine particles can be arranged on 1 μm^2 of cell membrane. A particle chain forms 10 to 12 domains, passing across the cell membrane. The final plicate prestine structure produced in the cell, *viz.* conformation, depends on proper energy of the chemical bonds of polypeptide, and its free energy is usually the lowest. Alien proteins, called chaperones, help the protein plicate in order to arrive at the most convenient conformation possible. So prepared prestine is transported to the cell membrane. Its minimum free energy cannot be the source of force required for performing a cyclical work in the form of OHC contractions. It was ascertained in the year 2000 that prestine is a molecular motor, responsible for OHC contractions and an amplification of a sound wave signal by 30 dB to 40 dB [2]. Molecular motors: Myosin, kinesin and dynein do work due to external energy, taken from high energy phosphorus compounds, mainly ATP and GTP [3]. It was assumed that prestine takes energy from the cell membrane potential. It is endowed with a sensor of variable chlorine and anions levels in the cell. An elevated chlorine level in the cell, after cell depolarization, affects conformation changes in prestine, which is to cause OHC shortening. OHC depolarization means an outflow of Cl- from the cell. Yet, there emerges a problem since the chlorine level in a cell is 4 mM to 10 mM, whereas in endolymph - 130 mM, and in perilymph - 125 mM. Moreover, due to cell depolarization, the potential of the cell membrane is close to zero while the chlorine level in the cell increases. This potential is to be the driving force of OHC contractions. A cell contraction follows depolarization which depends upon the operation of ion channels of sodium, potassium, calcium and chlorine in the lateral and inferior area of an auditory cell. Tension dependent ion channels operate according to a certain rhythm: Closing and stimulation, opening and inactivation - when a channel is inactive to stimulation. To the greatest extent, the cell membrane potential depends on the ion channels of sodium. Activation time of a channel: 10 μs, opening time = 0.5 ms to 1.0 ms, then inactivation time (refraction) = 0.2 ms to 0.5 ms. Depolarization + repolarization need some time; an OHC contraction depends upon the driving force in the form of changes of membrane potential, and it cannot occur within microseconds [4]. Investigations into OHC contractions with electric current stimulations are not reliable since they do not regard the work of ion channels. Basing upon

OPEN ACCESS

Correspondence:
Jan Myjkowski, Otolaryngology Clinic in Mielec, Poland,
E-mail: janmyjkowski@poczta.onet.pl

Received Date: *05 Sep 2022*
Accepted Date: *25 Sep 2022*
Published Date: *01 Oct 2022*

Citation:
Myjkowski J. Important Notes about Prestina. Am J Otolaryngol Head Neck Surg. 2022; 5(8): 1207.

Copyright *© 2022 Jan Myjkowski. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.*

those investigations, an OHC may contract up to 60,000/s. The work of OHC ion channels have been omitted here intentionally.

The energy for the gating mechanism of mechanosensitive channels of auditory cell hairs is encoded and conveyed from the sound wave energy. It serves for the regulation of opening of a mechanosensitive potassium ion channel up to 0.3 nm in the narrowest channel segment. Instead, the energy required for contracting an auditory cell - which is 50,000 nm long and 10,000 nm thick - is far and away higher. Each time OHC depolarization grows to reach the maximum after exceeding the excitability threshold of the receptor. Each OHC contraction is identical for being dependent upon the driving force. Decisive is the permeability of the cell membrane to tension dependent ions of sodium and potassium, and to a lesser extent - to calcium and chlorine. Exceeded the excitability threshold, there is an exponential process of opening more and more sodium channels accompanied by a rapidly growing cell depolarization. Reached the maximum value, the cell repolarization will start [3]. The cell potential falls to the lowest level and the membrane hyperpolarization will occur when the membrane potential is lower than at rest. At the time of repolarization, chlorine ions flow into the cell in line with electrochemical potential; those ions are recognized by specific prestine sensors. Chlorine ions or other anions combine with prestine and change its conformations, which is to lead to an OHC contraction [5]. It has not been elucidated, however, how a polypeptide chain which passes the cell membrane many times can change its conformation. Nor has it been explained why a contraction occurs at the time when the potential of depolarized cell membrane is close to zero. Therefore, how come that external energy for contractions, especially in the case of high frequencies - when the role of inertia becomes more and more significant - is proportional to intensity and squared frequency? In line with the theory of traveling wave, an OHC contraction causes an amplification of this quiet sound wave, already received, and when the signal has been already conveyed to the center [6].

Due to cell depolarization, a portion of transmitter is conveyed to an afferent synapse where post-synaptic exciting potential is generated, then conducted to the nervous cell of a spiral ganglion. This is where generated is also action potential, conducted to the center. OHC is endowed with afferent innervation. Instead, in compliance with the theory, an OHC contraction is to pull up the basilar membrane massif with the entire organ of Corti to the tectorial membrane, which releases a flow of fluid into the subtectorial space and the bending of the acoustic cell hairs. This process of pulling up and pushing of the basilar membrane has to amplify a sound wave at a frequency of up to 200 kHz. But what wave? Because there is no longer any primary wave entailing an amplification. There occurs a new, unknown wave which perhaps does not need amplifying. If those are quiet and loud multitones of various frequencies, then an amplification of the whole will entirely change the information. Can only quiet tones be amplified selectively? Of that new wave? What is the amplification limit? What is like the tuning mechanism of amplification at a constant OHC contraction value? This is not explained by the Hopf bifurcation theorem propagated by J. Hudspeth. If a quiet 20 dB sound is amplified by 30 dB, it will be heard as a 50 dB sound – still audible as quiet, whereas a 40 dB sound will be still perceived as a 40 dB tone - so it keeps on being a loud one. This is not normal. Each quiet tone is amplified by pulling at and pushing the basilar membrane. What mechanism prevents an amplification of a 100 dB sound at an identical OHC contraction? A mechanical amplification with a molecular drive with prestine is time-consuming. Into consideration must be taken the work of ion channels and speed differences of a sound wave in cochlear fluids and of a wave traveling on the basilar membrane, supported by OHC contractions (prestine) [7]. The speed of the traveling wave is on an average 30 to 50 times smaller than the speed of the sound wave [8]. That is why during an amplification of the primary tone the resonance of a new wave conveys to the basilar membrane completely new information, remote in time from the said primary amplified wave. In what way so mixed up information can be encoded and further conveyed to the center? How is it analyzed? There is a separation in time of loud and quiet pieces of the same information, and in addition, there occurs a superposition of the amplified information on new information which does not need an implication any longer. Subliminal tones cannot be amplified this way, since signals do not reach the receiver, there is no OHC depolarization nor cell contraction brought about by a molecular motor in the form of prestine. Nor is there any change to the OHC cell membrane potential [9].

Conclusion

Many creatures on earth can live due to a very fast and precise reception of auditory information, which cannot be ensured by a slow traveling wave and time-consuming procedures of amplification and transmission of auditory information *via* cochlear fluids. Those defects are not encountered on the signal path to the receptor through a cochlear bony housing as well as the molecular intracellular amplification commonly utilized in other sensory organs. It is probable that in an OHC - as distinct from a neuron - there is no one-time depolarization of the entire acoustic cell. Perhaps not all channels and not all synapses work exactly at the same time. Of importance are receptor fields in conjunction with temporal and space summation. Lack of high frequencies after stapedotomy indicates the importance of inertia in wave motion. Physiologically received are frequencies of up to 200 kHz [a bat]; that is why it should be assumed that the signal path to the receptor cannot run through cochlear fluids and the basilar membrane; nor can a signal be subject to mechanical amplification with prestine. Inertia either impedes or excludes the reception of high frequencies through cochlear fluids and their amplification. A sound wave is bereft of mass and cannot be thus conveyed directly to the receptor through soft issues and the cochlear bony housing.

References

1. He D, Lovas S, Ai Yu, Li Yi, Beisek K. Prestin at year 14: Progress and prospect. Hear Res. 2014;311:25-35.
2. sSantos-Sacchi J, Song L. Chloride anions regulate kinetics but not voltage-sensor qmax of the solute carrier SLC26a5. Biophys J. 2016;110(11):2551-61.
3. Myjkowski J, Przetwarzanie i przekazywanie informacji słuchowych, Otolaryngologia Polska Nr 2/2004, str. 377-383.
4. Santos-Sachci J, Tan W, Kinetyka preparatu Prestin ogranicza pasmo przenoszenia ruchliwości zależnej od napięcia zewnętrznych komórek włoskowatych. J. Neurosci. 2018;38(24):5495-506.
5. Fettiplace R. Hair cell transduction, tuning and synaptic transmission in the mammalians cochlea. Compr Physiol. 2017;7(4):1197-1227.
6. Dong W, Olsen S, Wykrywanie wzmocnienia ślimaka i jego aktywacja, Biophysical Journal Tom 105, 2013;106701078.
7. Santos-Sacchi J, Song L. The speed limit of outer hair cell electromechanical activity. HNO. 2019;67(3):159-64.

8. Zosuls A, Rupprecht LC, Mountain DC. Obrazowanie fal biegnących do przodu i do tyłu w ślimaku. bioRxiv.

9. Fallah E,Strimbu C, Olson E: Nieliniowość i amplifikacja w odpowiedzi ślimaka na bodziec jedno-i wielotonowe. Usłysz Res. 2019;377:271-81.