Editorial

iMedPub Journals
www.imedpub.com

Journal of Molecular Sciences

2017
Vol. 1 No. 1: 1

Mechanosensitive Ion Channels

Nuhan Purali*

Department of Biophysics, Hacettepe University, Turkey

Received: August 16, 2017; **Accepted:** August 17, 2017; **Published:** August 24, 2017

***Corresponding author:**
Nuhan Purali

npurali@hacettepe.edu.tr

Department of Biophysics, Medical Faculty, Hacettepe University, Turkey

Tel: 90 3123051494
Fax: 903123051492

Citation: Purali N (2017) Mechanosensitive Ion Channels. J Mol Sci. Vol. 1 No. 1: 1.

Senses supply the necessary information to construct the human made image of the world and universe. Philosophically, perception of the world is limited mainly by the variance of the sensory information. The subject has been so interesting that it has attracted many philosophers and scientists since the ancient times. Touch, which is based on mechanosensation, is perhaps the most ancient one among all the senses as Aristotle has mentioned about the importance of the tactile sensation for humans in his book De Anima III many centuries ago. Considering the phylogenetic point of view; mechanosensation is present in all the species ranging from bacteria to mammalians. For example: A Mechanosensitive (MS) ionic current or ion channels has been reported in bacteria wall [1], paramecium membrane [2], and vertebrate [3] and mammalian [4] cells. The principle component of the mechanosensation is a distinct type of transducer ion channel, opening (or closing) in response to a mechanical deformation of the cell membrane, the mechanosensitive ion channel. MS ion channels constitute another class of ion channels in addition to the voltage and agonist gated channels. In humans (or mammalians) it has been reported that MS channels are involved in several important physiologic functions such as sensation of tactile stimulus, pain, hearing, proprioreception, synaptogenesis, regulation of cell volume and heart rate [5-9]. Further, disfunction of the MS ion channels has been associated to various disease states like arrhythmia, pulmonary hypertension, muscular dystrophy, polycystic kidney disease, mechanical allodynia, anemia, peripheral paresthesia, tumor metastasis [10-17].

Presently, molecular properties of the voltage or agonist gated channels has been well documented in many species and the number of the family members are above 400 in humans. However, very few information is available about the molecular properties of the MS ion channels in contrast to the physiological relevance and homogeneous distribution among the species. The only available information related to the molecular properties of the MS channels is solely confined to those in bacteria wall and some invertebrate sensory neurons [18-20]. Thus, it is apparent that molecular properties of the MS ion channel and a component of mechantransduction process has not been comprehensively investigated yet.

The research in the area moves slowly due to several factors, discussed in the following section. Mechanosensation might have evolved differently in various body parts. Thus, mechanotransduction components in the skin touch receptors and hair cells of the inner ear would not be the same. Thus, a substantial amount of variance is expected in the molecular properties of MS channels within those structures, evolved to transduce the mechanical force into a different sensory modalities. Majority of the functional studies, related to the MS channels, are based on recording of the electrical responses to a form of mechanical stimulation [3,4,21-25] or blockage of the responses by some chemicals [26,27]. Keeping the stability of the recording configuration is a major problem during the mechanical stimulations. Thus, those kind of functional experiments are extremely difficult to conduct at the cellular and subcellular level. Further, presence of any form of mechanosensation capacity alone would not be a reliable indicator of a MS channel. Recent, reports indicates that a large group of voltage or agonist gated ion channels are also mechanosensitive. Nav1.5 [28], Nav1.6 [29], Cav1.2 [30], Kv1 [31], Kv7 [32], KATP [33], DEG/ENaC [34], TREK-1 [35], TRAAK [36], TRP [37-39], NMDA [41], CFTR [42] and TMC [43] channels may respond to a mechanical stimulation. By a careful inspection of the published results it might be proposed that sufficiently convincing data may be available only for TMC, TRP, DEG/ENaC channels. In addition to those multimodal channels, MscS channels of the bacteria wall and Piezo channels, firstly described in invertebrates and then mammalians, are the two mechanosensitive ion channels available at present [44,45]. It is apparent that a large group of ion channel has been associated to mechanotransduction process. However, the molecular structure of those channels are extremely heterogeneous. Neither structural architecture nor the amino acid sequences of any of those channels are similar. Further, physiological functions, pharmacological properties and the gating machinery of the MS channels differ substantially. For example MscL, TRAAK,

Piezo1 type channels can be blocked by ruthenium red or more specifically by Grammasutola Toxin (GT) [46-49]. It has been proposed that GT blocks the MS channel by changing the profile of the lipid bilayer as documented in the gating mechanism of TRAAK channel [48] where at resting state lipid chains shown to block the ion passage by filling the channel pore. Mechanical deformation removes the lipid chains and moves the channel to a conducting state. GT interferes with the lipid bilayer so that mechanical stimulus fail to remove the lipid chains from the channel pore. Such a gating mechanism is defined as the "bilayer model". However, GT fails to block all kinds of mechanosensitive channels or currents indicating that the lipid bilayer model would not be the only gating mechanism. In hair cells of inner ear different types of structural proteins like actin, protocadherin, ankyrin are necessary to activate the MS current (i.e. MS channel) [50]. MS current could not be initiated when any of those proteins are eliminated. Unlike the previous model in hair cell MS channel should be attached to cytoskeleton or intercellular matrix by those proteins. The model is called "tethered model" [50-52]. Apparently, in the tethered model instead of a single ion channel molecule we should be dealing with a "mechanosensitive ion channel complex", consisted of structural proteins and channel molecule in a certain configuration to convert mechanical force into ionic current.

It is evident that putative MS channels differ substantially with refer to gating and pharmacological properties. In order to contrast the degree of variance; we may recall that the whole voltage gated ion channel family might have reportedly been evolved from a single primordial member and the molecular architecture of the whole group could be assigned into four basic models [53,54]. None of those properties are relevant for MS channels. Presently, in contrast to the extensive research in the area molecular properties of only bacterial MS channel and Piezo channels are known. Bacterial channels are not present in humans and Piezo 2 is reported only in epidermal Merkell cells [55]. Further, mutations in piezo1 and piezo2 genes caused hereditary xerocytosis and loss of proprioreception in humans, respectively [56]. Though, Piezo channels seems as the most promising candidate member for MS channel family, however fails to cover the entire physiological functions based on MS ion channels or channel complex, ranging from sensation of tactile stimulus to hearing.

MS properties of rest of the channels, already discussed above, might be a matter of debate. For example TMC channel has been proposed as the MS transducer channel in the hair cells since a certain form of deafness is observed in individuals having mutations in the related gene [57]. The theory has been supported by the observation that the transducer current is not present in the knock out animals when the hair cell were stretched towards the direction of activation [58]. However, in another study it was reported that the transducer current could be observed in knock out animals if mechanical stimulus was applied in the direction of inactivation [59].

As it is discussed in this short editorial article MS channel or channel complex is perhaps the most complicated transducer channel group with respect to physiological, pharmacological and structural properties. Though, many candidates has been proposed a lot more information is required to explore the molecular basis of mechanotransduction.

References

1 Sukharev SI, Blount P, Martinac B, Blattner FR, Kung C (1994) A large conductance mechanosensitive channel in *E. coli* encoded by mscLalone. Nature 368: 265-268.

2 Zhou XL, Kung C (1992) A mechanosensitive ion channel in schizo *Saccharomyces-pombe*. Embo J 11: 2869-2875.

3 Guharay F, Sachs F (1984) Stretch activated single ion channel currents in myelinated nevre fibres of *Xenopus laevis*. J Physiol 352: 685-701.

4 Hamill OP (2007) Current topics in membrane.

5 Gu Y, Gu C (2014) Physiological and pathological functions of mechanosensitive ion channels. Mol Neurobiol 50: 339-347.

6 Woo SH, Ranade S, Weyer AD, Dubin AE, Baba Y, et al. (2014) Piezo2 is required for Merkel-cell mechanotransduction. Nature 509: 622-626.

7 Baumgarten CM, Clemo HF (2003) Swelling-activated chloride channels in cardiac physiology and pathophysiology. Prog Biophys Mol Biol 82: 25-42.

8 Tyler WJ (2012) The mechanobiology of brain function. Nat Rev Neurosci 13: 867-878.

9 Takahashi K, Kakimoto Y, Toda K, Naruse K (2013) Mechanobiology in cardiac physiology and diseases. J Cell Mol Med 17: 225-232.

10 Bett GC, Sachs F (2000) Whole-cell mechanosensitive currents in rat ventricular myocytes activated by direct stimulation. J Membr Biol 173: 255-263.

11 Song S, Yamamura A, Yamamura H, Ayon RJ, Smith KA, et al. (2014) Flow shear stress enhances intracellular Ca^{2+} signaling in pulmonary artery smooth muscle cells from patients with pulmonary arterial hypertension. Am J Physiol Cell Physiol 307: C373-C383.

12 Lansman JB, Franco-Obregon A (2006) Mechanosensitive ion channels in skeletal muscle: a link in the membrane pathology of muscular dystrophy. Clin Exp Pharmacol Physiol 33: 649-656.

13 Nauli SM, Alenghat FJ, Luo Y, Williams E, Vassilev P, et al. (2003) Polycystins 1 and 2 mediate mechanosensation in the primary cilium of kidney cells. Nat Genet 33: 129-137.

14 Lolignier S, Eijkelkamp N, Wood JN (2015) Mechanical allodynia. Pflugers Arch-Eur J Physiol 467: 133-139.

15 Zarychanski R, Schulz VP, Houston BL, Maksimova Y, Houston DS, et al. (2012) Mutations in the mechanotransduction protein PIEZO1 are associated with hereditary xerocytosis. Blood 120: 1908-1915.

16 Lennertz RC, Tsunozaki M, Bautista DM, Stucky CL (2010) Physiological Basis of Tingling Paresthesia Evoked by Hydroxy-α-Sanshool. The Journal of Neuroscience, March 30: 4353-4361.

17 Chen YF, Chen YT, Chiu WT, Shen MR (2013) Remodeling of calcium signaling in tumor progression. J Biomed Sci 20: 23.

18 Cox CD, Nakayama Y, Nomura T, Martinac B (2015) The evolutionary 'tinkering' of MscS-like channels: generation of structural and functional diversity. Pflugers Arch Eur J Physiol 467: 3-13.

19 Liu C, Montell C (2015) Forcing open TRP channels: Mechanical gating as a unifying activation mechanism. Biochemical Biophysical Research Communications 460: 22-25.

20 Schafer WR (2015) Mechanosensory molecules and circuits in *C. elegans*. Pflugers Arch Eur J Physiol 467: 39-48.

21 Wiersma CAG, Furshpan E, Florey E (1953) Physiological and pharmacological observations on muscle receptor organs of the crayfish. Cambarus clarkii Gerard. J Exp Biol 30: 136-150.

22 Rydqvist B, Purali N (1993) Transducer properties of the rapidly adapting stretch receptor neuron in the crayfish. J Physiol 469: 193-211.

23 Delmas P, Hao J, Rodat-Despoix L (2011) Molecular mechanisms of mechanotransduction in mammalian sensory neurons. Nature Reviews 12: 139-153.

24 Erxleben C (1989) Sretch activated current through single ion channels in the abdominal stretch receptor organ of the crayfish. J Gen Physiol 39: 87-113.

25 Hamil OP, McBridge DW (1992) Rapid adaptation of single mechanosensitive channels in *Xenopus* oocytes. Proc Natl Acad Sci USA 89: 7462-7466.

26 Swerup C, Purali N, Rydqvist B (1994) Block of receptor response in the stretch receptor neuron of the crayfish. Acta Physiol Scand 143: 21-26.

27 Suchyna TM, Johnson HJ, Hamer K, Leykam JF, Gage DA, et al. (2000) Identification of a peptide toxin from *grammostola spatulata* spider venom that blocks cation-selective stretch-activated channels. J Gen Physiol 115: 583-598.

28 Beyder A, Rae JL, Bernard CE, Strege PE, Sachs F, et al. (2010) Mechanosensitivity of Nav 1.5, a voltage-sensitive sodium channel. J Physiol 588: 4969-4985.

29 Wang JA, Lin W, Morris T, Banderali U, Juranka PF, et al. (2009) Membrane trauma and Na^+ leak from Nav1.6 channels. Am J Physiol Cell Physiol 297: C823-834.

30 Just S, Heppelmann B (2003) Voltage-gated calcium channels may be involved in the regulation of the mechanosensitivity of slowly conducting knee joint afferents in rat. Exp Brain Res 150: 379-384.

31 Tabarean IV, Morris CE (2002) Membrane stretch accelerates activation and slow inactivation in Shaker channels with S3-S4 linker deletions. Biophys J 82: 2982-2994.

32 Heidenreich M, Lechner SG, Vardanyan V, Wetzel C, Cremers CW, et al. (2012) KCNQ4 K(+) channels tune mechanoreceptors for normal touch sensation in mouse and man. Nat Neurosci 15: 138-145.

33 33.Van Wagoner DR (1993) Mechanosensitive gating of atrial ATP-sensitive potassium channels. Circ Res 72: 973-983.

34 Eastwood AL, Goodman MB (2012) Insight into DEG/ENaC channel gating from genetics and structure. Physiology (Bethesda) 27: 282-290.

35 Maingret F, Patel AJ, Lesage F, Lazdunski M, Honoré E (1999) Mechano or acid stimulation, two interactive modes of activation of the TREK-1 potassium channel. J Biol Chem 274: 26691-26696.

36 Brohawn SG, del Marmol J, MacKinnon R (2012) Crystal structure of the human K2P TRAAK, a lipid- and mechano-sensitive K+ ion channel. Science 335: 436-441.

37 Corey DP, García-Añoveros J, Holt JR, Kwan KY, Lin SY, et al. (2004) TRPA1 is a candidate for the mechanosensitive transduction channel of vertebrate hair cells. Nature 432: 723-730.

38 Shenton FC, Pyner S (2014) Expression of transient receptor potential channels TRPC1 and TRPV4 in venoatrial endocardium of the rat heart. Neuroscience 267: 195-204.

39 Fabian A, Fortmann T, Dieterich P, Riethmüller C, Schön P, et al. (2008) TRPC1 channels regulate directionality of migrating cells. Pflugers Arch 457: 475-484.

40 Clapham DE (2003) TRP channels as cellular sensors. Nature 426: 517-524.

41 Kloda A, Lua L, Hall R, Adams DJ, Martinac B (2007) Liposome reconstitution and modulation of recombinant N-methyl-D-aspartate receptor channels by membrane stretch. Proc Natl Acad Sci USA 104: 1540-1545.

42 Zhang WK, Wang D, Duan Y, Loy MM, Chan HC, et al. (2010) Mechanosensitive gating of CFTR. Nat Cell Biol 12: 812.

43 Kawashima Y, Kurima K, Pan B, Griffith AJ, Holt JR (2014) Transmembrane channel-like (TMC) genes are required for auditory and vestibular mechanosensation. Pflugers Arch-Eur J Physiol 467: 85-94.

44 Martinac B, Buechner M, Delcour AH, Adler J, Kung C (1987) Pressure-sensitive ion channel in *Escherichia coli*. Proc Natl Acad Sci USA 84: 2297-2301.

45 Coste B (2010) Piezo1 and piezo2 are essential components of distinct mechanically activated cation channels. Science 330: 55-60.

46 Oswald RE, Suchyna TM, McFeeters R, Gottlieb P, Sachs F (2002) Solution structure of peptide toxins that block mechanosensitive ion channels. J Biol Chem 277: 34443-34450.

47 Bae C, Sachs F, Gottlieb PA (2011) The mechanosensitive ion channel Piezo1 is inhibited by the peptide GsMTx4. Biochemistry 50: 6295-300.

48 Brohawn SG, Campbell EB, MacKinnon R (2014) Physical mechanism for gating and mechanosensitivity of the human TRAAK K^+ channel. Nature 516: 126-130.

49 Yoo J, Cui Q (2009) Curvature generation and pressure profile modulation in membrane by lysolipids: insights from coarse-grained simulations. Biophys J 97: 2267-2276.

50 Thomas Effertz, Alexandra LS, Anthony JR (2015) The how and why of identifying the hair cell mechano-electrical transduction channel. Pflugers Arch-Eur J Physiol 467: 73-84.

51 Cueva JG, Mulholland A, Goodman MB (2007) Nanoscale organization of the MEC-4 DEG/ENaC sensory mechanotransduction channel in *Caenorhabditis elegans* touch receptor neurons. J Neurosci 27: 14089-14098.

52 52 Zhang W, Cheng LE, Kittelmann M (2015) Ankyrin repeats convey force to gate the NOMPC mechanotransduction channel. Cell 162: 1391-1403.

53 Catterall WA, Gutman G (2005) Introduction to the IUPHAR compendium of voltage-gated ion channels. Pharmacol Rev 57: 385.

54 Yu FH, Yarov-Yarovoy V, Gutman GA, Catterall WA (2004) Overview of Molecular Relationships in theVoltage-Gated Ion Channel Superfamily. Pharmacol Rev 57: 387-395.

55 Nakatani M, Maksimovic S, Baba Y, Lumpkin AL (2015) Mechanotransduction in epidermal merkel cells. Pflugers Arch- Eur J Physiol 467: 101-108.

56 Wu J, Lewis AH, Grandl J (2017) Touch, tension, and transduction- The function and regulation of piezo ion channels. Trends in Biochemical Sciences 42: 57-71.

57 Kurima K, Peters LM, Yang Y, Riazuddin S, Ahmed ZM, et al. (2002) Dominant and recessive deafness caused by mutations of a novel gene, TMC1, required for cochlear hair-cell function. Nat Genet 30: 277-284.

58 Kawashima Y, Geleoc GS, Kurima K, Labay V, Lelli A, et al. (2011) Mechanotransduction in mouse inner ear hair cells requires transmembrane channel-like genes. J Clin Invest 121: 4796-4809.

59 Kim KX, Beurg M, Hackney CM, Furness DN, Mahendrasingam S, et al. (2013) The role of transmembrane channel-like proteins in the operation of hair cell mechanotransducer channels. J Gen Physiol 142: 493-505.