Channels are not proteins: lessons from mechanosensitive ion channels

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Mechanosensitive ion channels (MSCs) are ubiquitous, spanning the evolutionary tree. They fall into two classes: those activated by stress in fibrous proteins connected to the channels and those activated by stress in the lipid bilayer. The former are associated with specialized receptors such as cochlear hair cells and the others with cellular receptors not linked to the CNS. This talk addresses the latter class.

Eukaryotes have a common MSC that is cation selective, but none of the members of the family appear to have been cloned. In general, the channels inactivate with time, but the inactivation is not adaptation and it requires an intact cytoskeleton. Activation, on the other hand does not. The only specific inhibitor known for MSCs is a small, basic, pentavalent peptide(Ostrow et al., 2003 ;Oswald et al., 2002) called GsMTx4 isolated from tarantula venom(Suchyna et al., 2000). Its mechanism of action is to shift the gating curve to higher tensions, not to plug the pore. The dogma for peptide/channel interactions claim the mode of action is via a lock and key mechanism that provides specificity and efficacy. However, we synthesized the D enantiomer of GsMTx4 and it works as well as the L form(Suchyna et al., 2004). Thus, the peptide acts specifically on a subclass of eukaryotic MSCs but without a dependence on chirality. This suggests an interaction with the boundary lipids, i.e. the functional unit is not just the protein, but the protein plus the boundary lipids.

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