

## INVITED LECTURE H8

### Biophysics of cell mechanosensor at work: structure function of an MS channel protein

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Mechanosensitive (MS) channels are the only established molecular class of cell mechanosensors. Among them the bacterial MS channel MscL is the best studied one owing to the resolved 3D structure of its closed state. MscL is a homopentamer of the subunit having two transmembrane  $\alpha$ -helices (inner and outer) and neighboring inner helices cross each other near the cytoplasmic surface, thus forming the most constricted part (gate) of the channel. The remaining issue of MscL is to understand the mechanism underlying the gating (channel opening) process driven by tension in the membrane; more concretely where and how the channel protein receives forces and how the forces lead to channel opening. To identify the tension-sensing site, we made MD simulations and site-directed mutagenesis at each hydrophobic residue in the outer helix and found that the hydrophobic interaction between Phe78 and lipids near the periplasmic surface is essential to the tension sensing. Upon tension increase in the bilayer, the tension sensor Phe78 was dragged outwardly by lipids followed by a tilting of the helices and an outward sliding of the cross points between inner helices, leading to the gate opening of MscL.