The gating of mechanosensitive ion channels

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Mechanosensitive (MS) ion channels are a special type of integral membrane proteins activated by membrane deformation caused by mechanical stimuli experienced by living cells. They convert mechanical stimuli into electrical and/or chemical intracellular signals. There is a great diversity of these channels in terms of ionic conductance, selectivity or voltage dependence. These channels have been found in all types of prokaryotic and eukaryotic cells. In animals and humans they play a role in hearing, touch, proprioception or regulation of blood pressure. In plants they may function as gravity sensors in gravitropism, whereas in bacteria they constitute a mechanism that prevents excessive water inflow and build-up of excessive turgor pressure by acting as mechano-electrical switches, which open in response to cell membrane deformations caused by osmotic forces under hypotonic conditions. Among the MS channels studied to date the best characterised are bacterial MscL and MscS channels, the MS channels of large (L) and small (S) conductance (Martinac, 2004). Their 3D structure was determined by X-ray crystallography allowing for in-depth studies of the gating mechanism in these channels. In particular, the structure, function and structural dynamics of MscL channel has been well characterized by a number of techniques including the patch-clamp technique, electronparamagnetic resonance (EPR) spectroscopy, molecular dynamics simulations and most recently FRET spectroscopy. MscL and other prokaryotic MS channels are gated by bilayer deformation forces indicating that mechanism of mechanotransduction in these channels is defined by both local and global asymmetries in the transbilayer pressure profile and/or bilayer curvature at the lipid protein interface (Perozo *et al.*, 2002a, 2002b). Moreover, eukaryotic MS ion channels found in non-specialized mechanotransducer cells, such as TREK-1 (Patel *et al.*, 2001) and TRPC1 (Maroto *et al.*, 2005), have also been shown to be gated by membrane tension purely developed in the lipid bilayer. The implication of these findings is that the lipid bilayer is much more than a neutral solvent by actively modulating the specificity and fidelity of signalling by membrane proteins.

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