

## **Lipid and lyso-lipid effects on the mechanosensitivity of co-reconstituted MscS and MscL**

Takeshi Nomura<sup>1,2</sup>, Andrew R Battle<sup>1,3</sup>, Masahiro Sokabe<sup>2,4</sup>, and Boris Martinac<sup>1,5</sup>

<sup>1</sup>Victor Chang Cardiac Research Institute, Australia, <sup>2</sup>ICORP/SORST, Cell Mechanosensing Project, Japan Science and Technology Agency, Japan, <sup>3</sup>Department of Physiology and Pharmacology, The University of Queensland, Australia, <sup>4</sup>Department of Physiology, Nagoya University Graduate School of Medicine, Japan, <sup>5</sup>St. Vincent's Clinical School, The University of New South Wales, Australia.

The bacterial mechanosensitive channels of small (MscS) and large (MscL) conductance are governed by membrane-stretch which induces conformational changes and allows flow of ions and water to prevent cell lysis. Although the “mechanosensor” of both channel proteins has already been proposed, much less is known about how lipids surrounding the channels in cell membrane influence their mechanosensitivity. Recently, our laboratory has succeeded in patch clamp recording of co-reconstituted both channels into liposomes. Here, we examined the effects of different types of phospholipids, acyl chain length and lyso-lipids on the mechanosensitivity of both channels co-reconstituted into liposomes using patch-clamp technique. Co-reconstitution into liposomes having 16 hydrocarbons (PE16:PC16), dramatically decreased the threshold activation ratio. Addition of 5-30% cholesterol, which is known to affect the bilayer thickness, led to a decrease of the threshold activation ratio. In contrast, application of lysophosphatidylcholine (LPC), which is known to activate channel opening, led to an increase of the threshold activation ratio. These findings suggest that the length of acyl chain and cholesterol induced difference in membrane thickness and the change in intrinsic lipid bilayer curvature induced by LPC affect mechanosensitivity of both channels to a different extent and by a different mechanism.