

**P009** The mechanism of specific interaction between Sushi peptides and bacterial membrane lipid mimics: structure-activity relationship

<sup>1</sup>Peng Li, <sup>1</sup>Miao Sun, <sup>2</sup>Thorsten Wohland, <sup>1,2</sup>Daiwen Yang, <sup>3</sup>Bow Ho and <sup>1</sup>Jeak Ling Ding

*Departments of Biological Sciences<sup>1</sup>, Chemistry<sup>2</sup> & Microbiology<sup>3</sup>, National University of Singapore, Singapore 117543*

Sushi peptides (S1 & S3), which are derived from the lipopolysaccharide (LPS)-binding sequence of Factor C, have been shown to interact with LPS. The intermolecular disulfide bonded S3 dimer is indispensable for its LPS-neutralising activity. Here, we studied the specific activity of the Sushi peptide by constructing phospholipid vesicles with POPG, which represents bacterial membrane; and POPC & POPE, which mimics the mammalian cell membrane. Our study shows that the peptides exhibit selective interaction with POPG (anionic phospholipids) rather than with POPC and POPE (zwitterionic phospholipids), suggesting that the peptides bind strongly and preferentially to anionic vesicles. Both electrostatic and hydrophobic interactions contribute to the specific binding of the peptides to POPG. Furthermore, being unsaturated, POPG confers fluidity to the lipid layer, and probably enhances the insertion of peptides into the inner membrane of the bacteria. CD spectrometry revealed that the S1 peptide underwent conformational change in the presence of POPG, transitioning from a random coil to  $\alpha$ -helix structure, but it remained unchanged in neutral vesicles. In contrast, S3 resumed a mixture of  $\beta$ -sheet and  $\alpha$ -helical structures in anionic phospholipids. Furthermore, by using rhodamine-entrapped vesicles, fluorescence quenching and FCS analyses suggest that the peptides disrupt POPG vesicles, thus yielding clues to the mechanism of specificity and selectivity of the peptides for bacterial membranes.