

PS and gangliosides GM3 and GD3 in cell membranes on the cytotoxic activity of HDPs. Lipid monolayers at the air-liquid interface and supported lipid bilayers composed of DPPC and GD3, GM3, or DPPS at different ratios were used to model plasma membrane of cancer cells. The electron density profiles across the films, derived from X-ray reflectivity data, demonstrate that HDPs penetrate into all DPPC/anionic lipid monolayers, however with a different propensity. The HDPs' membrane-insertion propensity rises with increase in concentration of anionic lipids in the films and is the highest for GD3 and the lowest for DPPS. Grazing incidence X-ray diffraction data together with AFM indicate that HDPs can degrade effectively ordering of anionic lipids in the membranes. Our results suggest that the molecular mechanisms underlying the antibacterial and anticancer activities of HDPs may be the same.

1819-Pos Board B729

N-BAR Induced Tubulation of Phase-Separated Vesicles

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We investigate experimentally the energetics and dynamics of the deformation of lipid-bilayer membranes by curvature-sensing proteins. We focus on the membrane-binding domain N-BAR (Bin1/Amphiphysin/RVS167), residues 1-247 from *Drosophila melanogaster* amphiphysin. Giant unilamellar vesicles were prepared using electroformation with a ternary mixture of phosphatidylcholine, cholesterol, and sphingomyelin. As samples were cooled, homogeneous vesicles phase-separated, forming two fluid phases with distinct compositions. The N-BAR was added to solution with the vesicles in controlled amounts. The resulting deformations were recorded using both differential interference contrast and fluorescence microscopies. Rapid, spontaneous formation of fine tubules was observed to initiate at the boundary between the liquid-ordered and liquid-disordered phases, and the tubules were composed preferentially of lipid from the liquid-disordered phase. The role of the lipid composition on the membrane deformation will be discussed. We will also discuss micropipette aspiration experiments, with which we explore the role of membrane tension on tubule formation.

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The Effect of Aminoacylated Phospholipids on Membrane Binding of the Antimicrobial Peptides Cecropin A and Mastoparan X

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Aminoacylated phosphatidylglycerols are common lipids in the cytoplasmic membranes of Gram-positive bacteria. Their presence in staphylococcal cytoplasmic membranes has been linked to increased resistance to antimicrobial peptides. We showed previously that physiological lysyl-phosphatidylglycerol (lysyl-PG) concentrations did not reduce membrane binding of a synthetic peptide modeled on the C-terminal microbicidal domain of the mammalian platelet factor-4. Here, we addressed two additional questions. First, we investigated if that behavior is observed only for 6W-RP-1 or also for other antimicrobial peptides. Second, we explored the importance of the charge of the aminoacylated-phospholipid on peptide binding to lipid membranes. Binding of cecropin A and mastoparan X to unilamellar lipid vesicles composed of 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) and 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphoglycerol (POPG) was measured as a function of the concentration of an aminoacylated phosphatidylethanolamine (PE), a stable analog of the corresponding PG-derivative. Cecropin A and mastoparan X are well characterized antimicrobial peptides that form amphipathic α -helices when bound at the membrane-water interface. Peptide binding was measured through fluorescence energy transfer from the intrinsic tryptophan residue in the peptides to an acceptor fluorophore embedded in the membrane at low concentrations. Two aminoacylated PEs were used to explore the effect of lipid charge on peptide binding: lysyl-PE, a cationic phospholipid, and glutamyl-PE, a zwitterionic derivative. We found that as long as the concentration of aminoacylated PEs did not exceed 30 mol%, binding of both peptides was not significantly altered. In an attempt to understand these observations, we discuss the interplay between lipid charge and headgroup size on the activity of antimicrobial peptides.

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The Effect of Curcumin on the Antimicrobial Peptides Pore Formation in DOPC

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Interaction of curcumin with antimicrobial peptide is not well understood. A recent experiment showed that curcumin significantly affected the single channel lifetime of gramicidin in a DOPC bilayer without affecting its single

channel conductance. In this paper, we not only study the lifetime longer for gramicidin on DOPC, but also study the curcumin effect on the mechanism of the kill microbial cell by melittin peptide, too. We performed two experiments in order to understand those results. By X-ray lamellar diffraction, we measured the thickness change of DOPC bilayers as a function of curcumin-lipid ratio. By oriented circular dichroism, we found the critical concentration *P/L decrease with the C/L increase that indicates the curcumin will induce the melittin more easily to formation the insertion state in DOPC membrane. We results show that curcumin not only thins the lipid bilayer, it might also weaken its elasticity moduli and it can enhance the lifetime of gramicidin, but also induce the antimicrobial peptide more easily to kill the microbial cell.

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Amyloid Oligomers Increase the Lifetime and Single Channel Conductance of Gramicidin Channels

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Our previous data suggest that A β does not itself contribute a new intrinsic conductance to the membrane but soluble A β oligomers increase the bilayer conductance by altering physical properties of the membrane specifically increasing the apparent dielectric constant of hydrocarbon region. This change could in turn affect the properties of membrane ion channels.

In order to test this notion we compared the effects of amyloid oligomers prepared with the HFIP method on the single channel conductance and mean open time of gramicidin in 2 M NaCl and CsCl using DOPC and a series brominated lipids that change the dielectric properties of lipid bilayer at different depths into the membrane (11,12- bromo-16:0, 10,9- bromo-16:0 and 7,6- bromo-16:0, PC). Amyloid oligomers always increase the single channel conductance and mean open time both in 2 M NaCl and CsCl regardless of the nature of lipid used. The single channel conductance of gramicidin in brominated lipid membranes is lower in CsCl solutions and higher in NaCl solutions than that in DOPC membranes.

In addition we tested A β oligomers prepared in NaOH solution (HFIP-free). These oligomers did not affect the bilayer conductance but their effects on gramicidin channels were different compared to the effects of HFIP-prepared A β oligomers. These oligomers decrease the single channel conductance and increase the mean open time of gramicidin channels.

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Showing the Potential of the Lifetime-Based Dye Leakage Assay: All-Or-None Membrane Permeabilization by Fungicidal Lipopeptides from *Bacillus Subtilis* QST 713

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The fungicidal activity of *Bacillus subtilis* QST713, based mainly on the production of cyclic lipopeptides of the fengycin (FEs), surfactin, and iturin families, has been utilized for the highly effective and environmentally safe protection of crops against a variety of pathogens. The mixed population of native FEs forms micelles which solubilize individual FEs such as agrastatin 1 (AS1) that are otherwise rather insoluble on their own but promote the membrane permeabilizing activity of the mixture. Fluorescence lifetime-based calcein (Softmatter, 2009, 5, 2849-51) efflux measurements, isothermal titration calorimetry and electron microscopy show that these FEs show a unique scenario of membrane permeabilization. Poor miscibility of FEs with lipid induces stable, long-lived pores in 10% of the vesicles at only \approx 1 μ M free FE and in 15% of the vesicles at 10 μ M. We explain why this all-or-none leakage accounts for the killing of virtually all fungi whereas the same extent of graded leakage would likely be biologically irrelevant. Then, crystallization of AS1 and micellization of plipastatins cause a cut-off in leakage at 15% that might regulate the biological activity of FEs, protecting *Bacillus* and plant membranes. The fact that FE micelles solubilize only about 10 mol-% fluid lipid resembles the behavior of detergent resistance.

1824-Pos Board B734

The Effects of Salts and Sugars on the Plasma Membrane Permeabilizing Activity of Polycationic Peptides Derived from Protoxins

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Polycationic peptides with high activity in mitochondria permeabilization were derived from natural protoxins. Their capacity to permeabilize the plasma membrane was studied using red blood cells incubated in isotonic media with different salts (LiCl, NaCl, KCl, choline chloride) and/or sugars (mannitol, sucrose, raffinose). The addition of valinomycin induced high membrane potential (negative inside) and caused cell shrinkage with the rate that seemed