equivalence of osmotic and dehydration pressures by NMR experimental measurements as well as thermodynamically [2]. The elastic area compressibility modulus (K_a) of bilayers is determined by employing different pressure techniques in combination with NMR and vapor pressure osmometry methods. Our findings agree well with the reported K_a value for DMPC [4] obtained with a much smaller range of osmotic pressures. However, we observe an additional variation in K_a determined at higher osmotic pressures, where the role of complex dynamics in the bilayer structural changes becomes more evident. We propose that the hierarchy of forces and motions is perturbed by membrane dehydration (osmotic pressure) due to the alteration of interlamellar spacings, with corresponding changes in elastic area compressibility moduli. Our findings have significant implications for the applicability of solid-state ^{2}H NMR spectroscopy together with membrane stress techniques for understanding the mechanisms of action of pressure-sensitive proteins.

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2581-Pos Board B351

Influence of the Interdigitated Gel Phase in Mixtures of Ether-Linked and Monofluorinated Ester-Linked Phospholipids

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To evaluate the thermodynamic phase behavior of 1,2-di-*O*-hexadecyl-phosphocholine (DHPC) and 1-palmitoyl-2-[16-fluoropalmitoyl]sn-glycero-3-phosphocholine (F-DPPC) mixtures, a combination of differential scanning calorimetry (DSC), fluorescence spectroscopy, and spectrophotometry was used. DHPC is the ether-linked analogue of DPPC and has a pretransition between the interdigitated gel phase (L_βI) and the ripple gel phase (P_β'). F-DPPC is identical to DPPC except for a single fluorine substitution on the terminal carbon of the *sn*-2 chain. As a result, F-DPPC has no pretransition and is fully interdigitated below the T_m. The mixtures of F-DPPC and DHPC were found to be highly miscible above and below the main transition temperature (T_m). The T_m hysteresis was found to increase steadily with a higher mole fraction of F-DPPC. Small amounts of F-DPPC increase the pretransition temperature (T_p) of DHPC between the L_βI and the P_β' phase until the pretransition merges with the main transition. These results support that incorporating F-DPPC progressively stabilizes the L_βI phase until the membrane is fully interdigitated below the T_m. The ability of both lipids to interdigitate is determined to be an important factor controlling gel phase miscibility. Our results demonstrate that ether- and ester-linked lipids can be highly miscible within the interdigitated gel phase, and the gel phase behavior of DHPC is highly sensitive to changes in its environment.

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Nanoparticle-Induced Holes in Model Membranes

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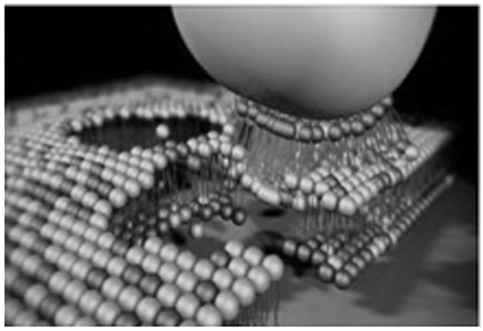
In vitro characterization of nanoparticles with respect to their interactions with biomolecules is becoming increasingly important due to the rapid development of novel applications for nanomaterials, both in nanomedical contexts as well as in various consumer products. Commonly, nanoparticles are simply characterized with respect to their size and zeta potential, along with cytotoxicity assays, and additional in vitro characterization of nanoparticles is needed to develop useful nanoparticle structure - activity relationships. It is highly interesting to characterize the interactions between nanoparticles and model interfaces, such as lipid membranes. We are developing a methodology to study such interactions using surface-sensitive analytical techniques, by forming first a supported lipid membrane on a sensor surface. This presentation describes results obtained for titania nanoparticles. It is shown by a combination of quartz crystal microbalance (QCM-D) and atomic force microscopy (AFM) that holes are introduced into the lipid membranes when interacting with the particles. An ion-mediated mechanism for these observations is discussed, see also [1].



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Calcium Signaling Proteins

2583-Pos Board B353

Spontaneous Ca^{2+} Oscillations in Beating Human Induced Pluripotent Stem Cell-Derived Cardiomyocytes (HIPSC-CM) and Rat Neonatal Cardiomyocytes (RN-CM)

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Isolated 4-6 day old RN-CM and HIPSC-CM beat spontaneously under culture conditions and appear to express all the ionic channels associated with the cardiac myocyte phenotype. Both Cell types continued spontaneous beating and Ca^{2+} oscillations at −60mV holding potentials where Na^+, K^+, I_f, and Ca^2 currents were not allowed to activate. Nevertheless, inward transients of NCX currents (I_{NCX}) occurred regularly (50-150 beats per minute at ~25 °C) with spontaneous releases of Ca^{2+}, using Cs^+-based dialyzing solutions containing 0.1-0.2 mM concentrations of Fura 2 or EGTA. Caffeine-induced Ca^{2+}-releases also activated large I_{NCX} in both RN-CM (1.7 pA/pF, n=13) and HIPSC-CM (3.9 pA/pF, n=9) that were 2-4 times larger than those of mature rat or human myocytes. The rate and magnitude of Ca^{2+}-oscillations and I_{NCX} increased on adrenergic stimulation, and rapid increases of $[Ca^{2+}]_o$ from 2-5 mM. Withdrawal of $[Ca^{2+}]_o$ and application of NCX-blocker (KBR-7943) or tetracaine also rapidly and reversibly inhibited spontaneous Ca^{2+}-oscillations. Xestospongine C, and 2-APB applications, to probe the role IP_3-signaling failed to alter spontaneous beating, as did Ca^{2+}-channel blocker (nifedipine) and NO-synthase inhibitor L-NAME. Surprisingly, application of low concentrations of mitochondrial uncouplers (5-50 nM FCCP or 100-200 μM DNP) suppressed the spontaneous Ca^{2+}-oscillations rapidly and reversibly in both cell types and inhibited the rate of uptake of caffeine-induced release of Ca^{2+}. Blockers of mitochondrial-uniporter, or mitochondrial NCX were ineffective in modulating the frequency of spontaneous beating. Our data suggests that mechanisms of spontaneous pacing are similar in HIPSC-CM and RN-CM, and are mediated by possible Ca^{2+}cross-talk between NCX, RyR/SR, and mitochondria. It is as yet unclear whether the mitochondrial Ca^{2+} cycling primarily initiates or modulates the spontaneous Ca^{2+}-oscillations and beating. (NIH HL16152 and HL 107600).

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Ca^{2+} Signaling in Cardiomyocytes Derived from Human Induced Pluripotent Stem Cells (hIPSC)

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iPSCS were created from skin biopsies of control subjects and a patient with catecholaminergic polymorphic ventricular tachycardia associated with point mutation (F2483I) in the FKBP12.6 binding domain of RYR2. Here we used rapid 2-dimensional confocal fluorescence imaging in patch-clamped cells to investigate Ca^{2+} signaling in hIPSCs in which cardiac phenotype was indicated by spontaneous beating, I_{Ca}-gated Ca^{2+} release, and protein expression. hIPSC shapes varied from spherical to elongated with a sarcomeric pattern. The I_{Ca}-gated Ca^{2+} release in patient-derived IPSCs occurred first at the periphery of the cells, but unlike control cells, continued even after deactivation of I_{Ca}. Exposures to cAMP and forskolin suppressed I_{Ca}-gated Ca^{2+} release, even though caffeine-induced release showed that SR Ca^{2+} stores were intact. In elongated cells, I_{Ca}-gated Ca^{2+} release caused brief localized Ca^{2+} releases (sparks) in a sarcomeric pattern, somewhat similar to mature ventricular cardiomyocytes, but sparking activity continued long after repolarization, consistent with over-active RyRs. In some round-shaped cells, clamped at −60 mV, spontaneous Ca^{2+} release activity, of variable frequency and loci, were frequently observed. In other voltage clamped cells we found propagated Ca^{2+} waves of random distribution and dispersion. Our results suggest that hIPSC-derived cardiomyocytes produce cardiac-type I_{ca}-gated Ca^{2+}-signaling in control and in patient-derived cells, but the mutant hIPSCs show Ca^{2+}-signaling phenotype consistent with over-active RyRs and the pathology of the CPVT disease. (Supported by NIH HL16152 and HL 107600).