



Contribution ID: 63

Type: **Talk**

Not just a fluidifying effect: omega-3 phospholipids induce formation of non-lamellar structures in biomembrane

Thursday, 10 June 2021 14:00 (20 minutes)

Polyunsaturated omega-3 fatty acid docosahexaenoic acid (DHA) is found in very high concentrations in a few peculiar tissues. DHA was proposed to affect the function of the cell membrane and related proteins through an indirect mechanism of action, based on the DHA-phospholipid effects on the bilayer structure. Most studies have focused on its influence on lipid-rafts, neglecting the effects on liquid disordered phases that constitute most of the cell membranes.

By combining NR, cryo-transmission electron microscopy, SANS, DLS and EPR, we characterize liquid disordered bilayers formed by the naturally 1-palmitoyl-2-oleoyl-snglycero-3 phosphocholine and different contents of a di-DHA glycerophosphocholine, 22:6-22:6PC, from both a molecular/microscopic and supramolecular/mesoscopic viewpoint. We show that, below a threshold concentration of about 40% molar percent, incorporation of 22:6-22:6PC in the membrane increases the lipid dynamics promoting the membrane deformation. Notably, beyond this threshold, 22:6-22:6PC disfavours the formation of lamellar phases, leading to a phase separation consisting mostly of small spherical particles that coexist with a minority portion of a lipid blob with water-filled cavities. From a molecular viewpoint, the polyunsaturated acyl chains tend to fold and expose the termini to the aqueous medium. We propose that this peculiar tendency is a key feature of the DHA-phospholipids making them able to modulate the local biomembranes morphology

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Session Classification: Biological membranes, surfaces and interfaces

Track Classification: Biological membranes, surfaces and interfaces