Review of: "[Review] The Studies of Lipid Phase Polymorphism in Model Membranes"

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The short review in reference was written by Han and Gasanoff, which was based on the role of non-blaiyer lipid structures in the structure-function relationship in biological membranes with a particular focus on the tentative novel concept on modulation of bioenergetic status of mitochondrial membranes by the transient bilayer to non-bilayer evolutions in the lipid phase of membranes.

The authors describe the major findings of the extensive research done by Gasanoff over the course of 35 years of studies focused on the formation of non-bilayer lipid structures in model and biological membranes triggered by cationic cytotoxins, which are also known as cardiotoxins, which are isolated from cobra venom. The authors briefly describe biophysical methods which were used in characterization of non-bilayer lipid structures induced by cardiotoxins and the methods of studies which lead to the elucidation of molecular mechanisms of non-bilayer structure formation and how non-bilayer structures affect functional activities of biological membranes.

In this review the authors summarize their experimental and theoretical studies along with the studies of other researchers in this field to compile a comprehensive mechanism described in Figure 1 which proposes translocation of cationic proteins through the lipid phase of membranes via formation of inverted micelles at the intermembrane junctions between the plasma membranes and extracellular lysosomes pointing out on importance of non-bilayer structures such as inverted micelles in translocation of cationic proteins via plasma membranes and membranes of intracellular organelles and extracellular lysosomes.

The authors discuss the studies of other researchers involving formation of non-bilayer structures triggered by natural and synthetic cationic proteins and peptides and the authors suggest that mechanism of non-bilayer structure formation triggered by natural and synthetic cationic proteins likely resembles the mechanism elucidated by studies focused on interaction of cardiotoxins with model membranes. Authors also analyze their own results on melittin, another cationic protein isolated from bee venom, which can also induce formation of non-bilayer structures in membranes containing acidic phospholipids.

Interestingly, the authors of this articles suggest the structural features of cationic peptides which include the basic amino acid residues and hydrophobic residues which facilitates the targeting of cardiolipin (a major phospholipid of inner mitochondrial membranes), by these specific cationic proteins/peptides.

The authors also discuss the non-bilayer structures induced by cationic proteins with the specific structural features which

facilitate changes in membrane dynamics and tendency to polymorphic transitions leading to changes in functional activities of biological membranes including rejuvenation of mitochondrial functions.

Overall, the review possesses surgically precise timing, as it will indeed play a significant role in the rising interpretations of polymorphic transitions and particularly in non-bilayer structures triggered by specific cationic proteins, as the aforementioned field of study draws more and more attention from membranologists and experts in bioenergetics. One of the important features of this review article pays a special attention to polymorphism in mitochondrial membranes which suggests possible pharmaceutical applications to treat pathologies associated with decline in cellular energy production. Thus, I do recommend this review article by Han and Gasanoff for publication in a suitable peer-review journal.