Review of: "[Review] Contemporary Physical Methods in Studies of Lipid Phase Polymorphism"

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Potential competing interests: Legitimacy of opinion, with respect to affiliation.

The review article by Li and Gasanoff is a detailed technical appraisal of contemporary powerful biophysical methods which are commonly used in the studies of lipid phase polymorphism and functional role(s) of non-bilayer lipid structures in model and biological membranes.

The article analyses how the non-bilayer lipid phases and lipid phase polymorphism affects the structure and function of biological membranes of cells and organelles which has been a gradually developing area of biophysical research in membranology for the past 50 years. The authors describe in a chronological order that it has been established that non-bilayer lipid structures play a key role in the intermembrane exchange of lipids, membrane fusion and membrane fission. The review article also reports that proteolipid fraction isolated in 1993 from the bovine heart mitochondria made of F_0 subunit proteins and cardiolipin had the non-bilayer arranged cardiolipin molecules associated with proteins of F_0 subunit of ATP synthase. Following chronological order, the authors point out that non-bilayer lipid phase in the intact and fully functional mitochondria has been reported for the first time in 2015. The authors also describe in detail the breakthrough experimental evidence of 2018 that has revealed that the non-bilayer lipid structures in mitochondrial membranes facilitate mitochondrial ATP synthesis. Over the past five years it has been shown according to this review article that the cationic proteins rich in lysine reside such as cardiotoxins (aka cytotoxins) from the cobra venom and melittin from bee venom can trigger the formation of non-bilayer lipid phases in intact mitochondria leading to the increase in production of mitochondrial ATP.

This review article does not only describe contemporary powerful biophysical methods commonly used in the studies of lipid phase polymorphism and mechanistic details of dynamics and architecture of non-bilayer lipid structures in model and biological membranes of cells and organelles, but the article also focuses on non-bilayer structures which are triggered by native and synthetic cationic lysine-residue-rich proteins including cobra cardiotoxins and bee melittin. This review article discusses and suggests feasible mechanisms of non-bilayer lipid structures triggered by cationic proteins in modulation of mitochondrial ATP production. A particular attention is given to the potential application of cationic proteins in the advancement of novel drugs to be used in treatment of energy decline in cells during course of aging and diseases. The overall contribution of this review article is that it opens an intriguing avenue for development of cutting-edge novel pharmaceuticals to be used in treatment of pathologies associated with abnormal processes in physiology of lipid phase polymorphism.

I believe this review article is of a great interest to the experts in polymorphism of membrane lipid phase, bioenergetics, membrane biophysics and biochemistry and cardiological and neurodegenerative pathologies associated with the decline in mitochondrial ATP production. I do recommend this review article for publication in the peer review journal.