

# Review of: "[Review] Structural and Functional Roles of Non-bilayer Lipid Phase in Mitochondria"

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**Potential competing interests:** No potential competing interests to declare.

This is an excellent review. It is based mainly in the solid and extensive work of the authors and the contribution of many others is also presented. Besides describing the role of cardiolipin and phosphatidyl ethanolamine, the review introduces the reader to a whole new and vast field related to the importance of shape and structure in the functioning of the respiratory chain. After the revolutionary concept of proton translocation introduced by Peter Mitchel, it became clear that participation of particular lipids is not a simple detail in the sense of activation or inhibition of enzymes and transporters mediated by the binding to specific sites in the proteins. Instead, they are involved in a much more general issue which is the regulation by reshaping and large structural changes. This idea (also revolutionary) is clearly conveyed in the review.

Still, I think we should be careful about incorporating some knowledge that is taken for granted. In some paragraphs the authors mention some mechanisms as if they were already well accepted facts (see for example "...via a mechanism described previously [7] [11] [34] [54]"). Nevertheless, when we go to the cited articles, from the very beginning of the title we find "The possible role...". Of course, the experimental evidence cited by the authors is comprehensive and the best we have at this time, but some issues remain hypothetical.

Regarding the discovery of no-lamellar phases in thylakoids and mitochondria, it could be useful to mention the large evidence about the existence of these structures shown in the book "The Language of Shape" by S. Hyde et al. (I am very grateful to my colleague Dr. Rafael Oliveira who recently let me know about this book).

Just to keep the formalisms, it would be correct to define the acronyms when they appear in the text, OPA1, MICOS, for example.

"annual" lipids should be "annular"

Is it DCCD-DPF a mistake or it is another protein?