

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

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

This review paper provides an overview on the biological relevance of the reversed hexagonal lipid phase transitions.

Comments:

Authors promised to introduce latest concepts to link non-bilayer structures to biological activity and related physiological activities. Nonetheless, in subsequent sections there is no such conceptual background from which the reader could link functional role of reversed hexagonal phase and non-bilayer phase transitions.

Authors promised a list of protein and peptides that promote non-bilayer phase transitions, which contains 5 examples: Cyt C, mitochondrial creatine kinase, and Shetty-Schiller tetrapeptides, and CTII, and mellitin. From these examples it is difficult to identify the physicochemical principles that promote non-bilayer transitions. For example, cardiolipins seem to be a typical lipid environment in non-bilayer phase transition, could the authors explain the cardiolipins properties that promote such transitions?

Authors mention NMR reports for describing phase-transitions. What about FTIR, neutron scattering, X-Ray studies? See for example: Ruthven N.A.H. Lewis, Ronald N. McElhaney *Biochimica et Biophysica Acta* 1828 (2013) 2347–2358; R.N.A.H. Lewis, R.N. McElhaney, The mesomorphic phase behaviour of lipid bilayers, in: P.L. Yeagle (Ed.), *The structure of biological membranes*, CRC Press, Boca Raton, 2012, pp. 177–201; C Doe, HS Jang, SR Kline, SM Choi *Macromolecules* 2009, 42, 7, 2645–2650; Rappolt, M., Hickel, A., Bringezu, F., & Lohner, K. (2003). Mechanism of the lamellar/inverse hexagonal phase transition examined by high resolution x-ray diffraction. *Biophysical journal*, 84(5), 3111–3122.

As a review paper, authors may include a discussion of the state-of-the-art topics on non-bilayer transitions, in addition to the historical perspective. So, readers could benefit from a self-contained discussion. This review paper may be considered for publication after a critical discussion of the recent literature on the field.

Specific comments

-TM not defined (Thylakoid Membrane/Transmembrane)

-IMM not defined. (Inner Mitochondria Membrane)

-PC, PE not defined (phosphocholine/phosphoethanolamine)

