From Cubic Membranes to Plasmalogen Nanomaterials: Unraveling the Role in Cell Survival, Aging, and Neurodegenerative Disorders

Yuru Deng[1], Angelina Angelova[2]
[1]*Wenzhou Institute, University of Chinese Academy of Sciences, No.1, Jinlian Road, Longwan District, Wenzhou, Zhejiang 325001, China*
[2]*Université Paris-Saclay, CNRS, Institut Galien Paris-Saclay, F-91400 Orsay, France*
*email: dengyr@wibe.ac.cn; angelina.angelova@universite-paris-saclay.fr

Lipids may self-assemble into dynamic and complex membrane architectures ranging from simple, double, and multiple bilayer networks depicted by 3-dimensional periodic level surfaces termed "Cubic Membranes (CM)". The membrane structural dynamics is central to the diversity of roles they play in biological system, and cell membrane homeostasis might be the missing link in aging and age-related ailments, especially multiple inflammation-mediated neurodegenerative disorders. Here we introduce CM followed by CM-derived phospholipids – specifically plasmalogens (Pls), their shared properties together with CM as antioxidant and potentially anti-inflammatory function with implications in cell survival and organismal longevity [1]. We further discuss the observations of lowered levels of Pls measured across different neurodegenerative and metabolic disorders, as well as a potential strategy of restoring Pls levels via Pls replacement therapy to relieve illness and recover membrane architecture and homeostasis, and eventually promote human health. Two selected cell models with gyroid-CM mitochondria in: (1) cone photoreceptor of small mammals treeshrew (*Tupaia belangeri*), and (2) free-living giant amoeba (*Chaos carolinense*) will be presented. The advantages of plasmalogen-based self-assembled lipid nanomaterials (Fig. 1) and biomimetic nanotechnology inspired by cubic membranes will also be discussed [2,3].

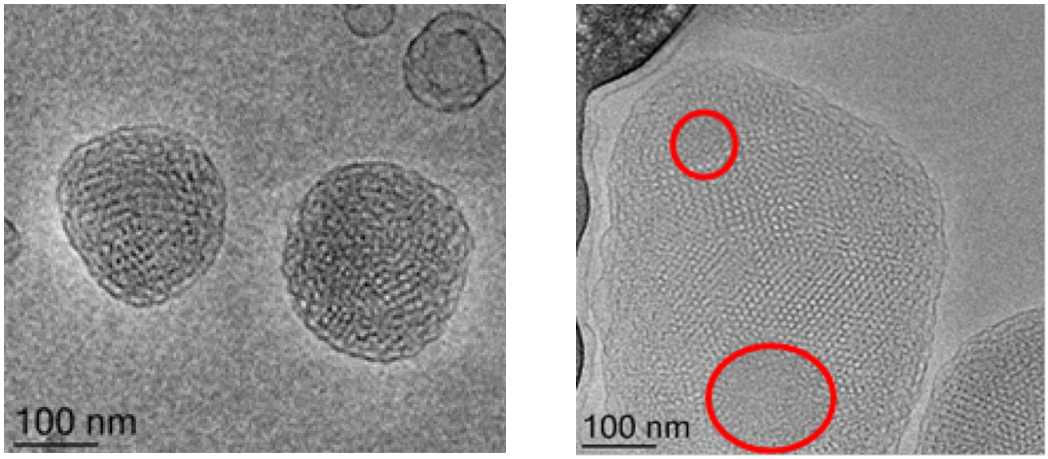

Figure 1 Liquid crystalline lipid nanoparticles (cubosomes) derived from self-assembled lipid cubic membrane phases. (Left) Plasmalogen-based cubosomes obtained by dispersion of a mixed amphiphilic mixture. (Right) Nanodomains with modified structural order induced by encapsulated drug molecules in the cubosome nanocarriers.

This work was supported by the Grant No. WIUCASQD2019005.

[1] Y. Deng, A. Angelova, *Front Cell Dev Biol.* **9**, 630242 (2021). doi: 10.3389/fcell.2021.630242.
[2] A. Angelova, B. Angelov, M. Drechsler, T. Bizien, Y.E. Gorshkova, Y. Deng, *Front Cell Dev Biol.* **9**, 617984 (2021). doi: 10.3389/fcell.2021.617984.
[3] Y. Wu, J. Wang, Y. Deng, B. Angelov, T. Fujino, M. S. Hossain, M. A. Angelova, *Adv Healthc Mater.* **13**(14), e2304588 (2024). doi: 10.1002/adhm.202304588.