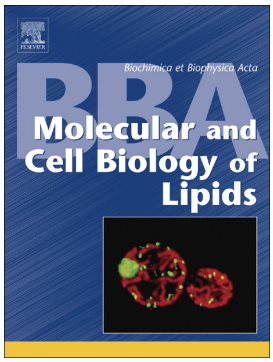

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PII: S1388-1981(18)30122-7
DOI: doi:10.1016/j.bbalip.2018.06.001
Reference: BBAMCB 58306

To appear in: *BBA - Molecular and Cell Biology of Lipids*

Received date: 16 January 2018
Revised date: 10 May 2018
Accepted date: 1 June 2018

Please cite this article as: Meng Zhang, Xiaobo Zhai, Jinping Li, John J. Albers, Simona Vuletic, Gang Ren , Structural basis of the lipid transfer mechanism of phospholipid transfer protein (PLTP). Bbamcb (2018), doi:10.1016/j.bbalip.2018.06.001

Structural basis of the lipid transfer mechanism of phospholipid transfer protein (PLTP)

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Running title: PLTP's interactions with lipoproteins

KEYWORDS: PLTP, phospholipid transfer protein, PLTP bound to HDL, PLTP bound to liposome, electron microscopy, HDL, liposome

ABSTRACT

Human phospholipid transfer protein (PLTP) mediates the transfer of phospholipids among atheroprotective high-density lipoproteins (HDL) and atherogenic low-density lipoproteins (LDL) by an unknown mechanism. Delineating this mechanism would represent the first step towards understanding PLTP-mediated lipid transfers, which may be important for treating lipoprotein abnormalities and cardiovascular disease. Here, using various electron microscopy techniques, PLTP is revealed to have a banana-shaped structure similar to cholesteryl ester transfer protein (CETP). We provide evidence that PLTP penetrates into the HDL and LDL surfaces, respectively, and then forms a ternary complex with HDL and LDL. . Insights into the interaction of PLTP with lipoproteins at the molecular level provide a basis to understand the PLTP-dependent lipid transfer mechanisms for dyslipidemia treatment.