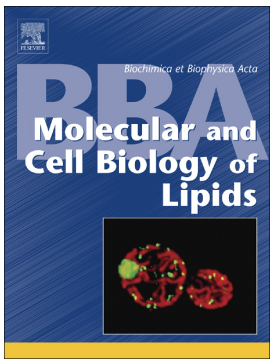

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Hydroxysteroid dehydrogenase family proteins on lipid droplets through bacteria, *C. elegans*, and mammals

Yangli Liu[1,2#], Shimeng Xu[1#], Congyan Zhang[1,2#], Xiaotong Zhu[1], Mirza Ahmed Hammad[1,2], Xuelin Zhang[3], Mark Christian[4], Hong Zhang[1,2], Pingsheng Liu[1,2*]

[1]National Laboratory of Biomacromolecules, CAS Center for Excellence in Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China
[2]University of Chinese Academy of Sciences, Beijing 100049, China
[3]School of Kinesiology and Health, Capital University of Physical Education and Sports, Beijing, 100191, China
[4]Division of Metabolic and Vascular Health, Warwick Medical School, University of Warwick, Coventry, CV4 7AL, UK.

[#]Equal contribution
*Corresponding author: Pingsheng Liu, E-mail: pliu@ibp.ac.cn

Abstract

Lipid droplets (LDs) are the main fat storing sites in almost all species from bacteria to humans. The perilipin family has been found as LD proteins in mammals, *Drosophila*, and a couple of slime molds, but no bacterial LD proteins containing sequence conservation were identified. In this study, we reported that the hydroxysteroid dehydrogenase (HSD) family was found on LDs across all organisms by LD proteomic analysis. Imaging experiments confirmed LD targeting of three representative HSD proteins including ro01416 in RHA1, DHS-3 in *C. elegans*, and 17β-HSD11 in human cells. In *C. elegans*, 17β-HSD11 family proteins (DHS-3, DHS-4 and DHS-19) were localized on LDs in distinct tissues. In intestinal cells of *C. elegans*, DHS-3 targeted to cytoplasmic LDs, while DHS-9 labeled nuclear LDs. Furthermore, the N-terminal hydrophobic domains of 17β-HSD11 family were necessary for their targeting to LDs. Last, 17β-HSD11 family proteins induced LD aggregation, and deletion of DHS-3 in *C. elegans* caused lipid decrease. Independent of their presumptive catalytic sites, 17β-HSD11 family proteins regulated LD dynamics and lipid metabolism through affecting the LD-associated ATGL, which was conserved between *C. elegans* and humans. Together, these findings for HSDs provide a new insight not only into the mechanistic studies of the dynamics and functions of LDs in multiple organisms, but also into understanding the evolutionary history of the organelle.

Keywords

Lipid droplet, hydroxysteroid dehydrogenases (HSDs), short-chain