Ekaterina Shishova, J Glycobiol 2018, Volume 7
DOI: 10.4172/2168-958X-C1-012

Biochemical and structural characterization of STARD10, a phospholipid binding protein

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Phospholipids are the major structural components of biological membranes and mediators of signal transduction. In cells, these water insoluble molecules are exchanged between membranes via a group of transport proteins known as steroidogenic acute regulatory protein–related transfer (START) domain superfamily of proteins. Proteins containing START domain function in many physiological processes, such as lipid transfer between intracellular compartments, lipid metabolism, and cell signaling events. One such lipid transporter is StARD10, a 33 kDa protein, originally identified as a protein overexpressed in breast cancer. While its physiological role is still not clearly understood, studies suggests that StARD10 is highly expressed in liver and the mammary gland, may be used as a biomarker for cancer, and it is also required for normal insulin secretion. Closely related to StARD2, a phosphatidylcholine transfer protein, StARD10 was reported to bind and transfer both phosphatidylcholine and phosphatidylethanolamine. Here, we report a study in which recombinant human StARD10 was purified and tested for phospholipid transfer activity using an in vitro fluorescence quench assay for intermembrane transfer of 7-nitro-2,1,3-benzoxadiazol-4-yl (NBD) labeled phosphatidylcholine, phosphatidylethanolamine and phosphatidylserine. The protein showed higher transfer activity for a phosphatidylcholine with NBD labeled head group, followed by about four fold reduced activity for head group labeled phosphatidylethanolamine, and only a negligent transfer activity for a tail labeled phosphatidylcholine. There was no transfer activity observed for phosphatidylserine. Through analysis of closely related phosphatidylcholine transfer protein StarD2 three dimensional structure and primary sequence alignment with StARD10, the key phospholipid binding amino acids evolutionary conserved in both StARD2 and StARD10 were identified. Further, 3-dimensional homology models of StARD10 without and with phospholipid substrates were generated by SWISS MODEL and SWISS Dock, respectively, and provide a useful insight into the substrate binding mode in StARD10 active site.

Biography

Ekaterina Shishova is an Assistant Professor of Biochemistry at the Sage Colleges in Troy, NY. She has expertise in structural biochemistry. She hold a Ph.D. in chemistry from the University of Pennsylvania where she completed research on X-ray crystallographic studies of metallo-enzymes. Further, she received post-doctoral training at Brigham and Women's Hospital and Harvard Medical School where she worked on biochemical characterization and development of small molecule inhibitors of lipid binding proteins.

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