MMPL-Family Proteins in Bacteria, Protozoa, Fungi, Plants and Animals: A Bioinformatics and Structural Investigation

Eric Oldfield[1] and Satish R. Malwal[1]

[1]University of Illinois at Urbana-Champaign Department of Chemistry

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Abstract

Lipid transporters play an important role in most if not all organisms, ranging from bacteria to humans. For example, in *Mycobacterium tuberculosis*, the trehalose monomycolate transporter MmpL3 is involved in cell wall biosynthesis, while in humans, cholesterol transporters are involved in normal cell function as well as in disease. Here, using structural and bioinformatics information, we propose that there are proteins that also contain "MmpL3-like" (MMPL) transmembrane (TM) domains in many protozoa, including *Trypanosoma cruzi,* as well as in the bacterium *Staphylococcus aureus*, where the fatty acid transporter FarE has the same set of "active-site" residues as those found in the mycobacterial MmpL3s, and in *T. cruzi.* We also show that there are strong sequence and predicted structural similarities between the TM proton-translocation domain seen in the X-ray structures of mycobacterial MmpL3s and several human as well as fungal lipid transporters, leading to the proposal that there are similar proteins in apicomplexan parasites, and in plants. The animal, fungal, apicomplexan and plant proteins have larger extra-membrane domains than are found in the bacterial MmpL3, but they have a similar TM domain architecture, with the introduction of a (catalytically essential) Phe>His residue change, and a Ser/Thr H-bond network, involved in H^+-transport. Overall, the results are of interest since they show that MMPL-family proteins are present in essentially all life-forms: archaea, bacteria, protozoa, fungi, plants and animals and, where known, they are involved in "lipid" (glycolipid, phospholipid, sphingolipid, fatty acid, cholesterol, ergosterol) transport, powered by transmembrane molecular pumps having similar structures.

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