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## ACCEPTED MANUSCRIPT

#### Modification of Membrane Lipid Compositions in Single-celled Organisms– from Basics to Applications

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#### Abstract (250 words)

All intact cells, and their organelles, are surrounded by a  $\sim 30$  Å hydrophobic film that typically separates the interior from the environment. This film is composed of lipid bilayers that form from a pool of structurally highly diverse, amphipathic lipids. The specific composition and nature of these lipids strongly contributes to many different processes in the cell by influencing membrane structures, membrane protein sorting and functionalities. In this review, we discuss strategies to alter membrane lipid compositions of organelles and plasma membranes in different organisms, focusing on microbial cells. Reflecting the many essential roles of lipids in cellular regulation, we delineate diverse cellular processes affected by membrane lipid modifications and discuss possible applications in a biotechnological and biomedical context. A major motivation for membrane lipid engineering has been the improvement of expression, translocation and activity of heterologous membrane proteins, which can facilitate the biochemical and structural characterization of this challenging class of proteins. Additionally, better expression of membrane proteins or membrane lipid engineering - or a combination of both - led to improved production of high-value compounds and food additives, e.g. polyunsaturated fatty acids and glycolipids, in diverse hosts. More recently it has been shown that diverse cellular pathologies such as cancer and Alzheimer's disease are associated with lipid alterations. Hence, the progress in our understanding of membrane structure, function and protein-lipid interactions, and the resulting possibilities regarding the engineering of membrane lipid composition clearly enable novel nutraceutical and pharmaceutical interventions to be developed. Significant progress in this important area of research is highlighted in this review.

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