Synthesis of tetraether membrane lipids in archaea

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One of the most unique properties of archaea is the chemical composition of their cellular membranes. While bacteria and eukaryotes have ester linked fatty acid based bilayer membranes, archaeal membranes are composed of ether linked isoprenoidal lipids. In addition, several archaea generate membrane spanning monolayers, known as glycerol dibiphytanyl glycerol tetraethers (GDGTs), which can be further modified by the addition of cyclopentane rings. It has been observed that the average number of GDGT cyclizations increase as growth temperature increases and this is proposed to be a mechanism to adjust membrane rigidity at higher temperatures. This physiological adaptation is the basis for GDGT-based paleotemperature proxies such as TEX_{86}. Core GDGTs occur in sedimentary rocks dating as far back as the mid-Cretaceous and are used to reconstruct sea surface temperatures over a variety of geologic timescales.

The robustness of GDGT-based biomarkers, however, depends on a full understanding of their biosynthesis and physiology in modern organisms. Currently, the biochemical mechanisms and proteins required for forming the core GDGT as well as the introduction of the various rings are unknown. Further, recent physiological studies of marine Thaumarchaeota, on which the TEX_{86} paleotemperature proxy is based, demonstrate that GDGT cyclization may be influenced by other metabolic parameters besides temperature and conclude that more studies are needed to further constrain GDGT-based proxies. In this study, we take a comparative genomics approach coupled with gene deletion analyses to address some of these unanswered biosynthetic questions in the thermoacidophilic archaeon *Sulfolobus acidocaldarius*. We have identified two distinct radical SAM proteins, GrsA and GrsB, necessary for the introduction of the pentacyclic rings into the GDGT core structure. Deletion of these GDGT ring synthases results in the production of GDGT lipids with no rings and results in reduced growth of *S. acidocaldarius*. Complementation studies demonstrates that these proteins cyclize distinct GDGT substrates at specific locations. Taken together, these studies begin to provide answers to some of the more perplexing enzymatic and physiological questions regarding archaeal membranes.