Molecular insight into bacterial cleavage of oceanic dimethylsulfoniopropionate (DMSP) into dimethyl sulfide (DMS)

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The microbial cleavage of dimethylsulfoniopropionate (DMSP) generates volatile dimethylsulfide (DMS) through the action of DMSP lyases and is important in the global sulfur and carbon cycles. When released into the atmosphere from the oceans, DMS is oxidized, forming cloud condensation nuclei that may influence weather and climate. Six different DMSP lyase genes are found in taxonomically diverse microorganisms, and *dddP* and *dddQ* are among the most abundant in marine metagenomes. DddP belongs to the M24 peptidase family as suggested by sequence alignment. Peptidases hydrolyze C-N bonds, but DddP is deduced to cleave C-S bonds. Mechanisms responsible for this striking functional shift are currently unknown. DddQ belongs to the cupin superfamily. Here, we examine the molecular mechanisms of DMSP cleavage by DMSP lyases, DddP and DddQ, from *Ruegeria lacuscaerulensis* ITI_1157. We determined the structures of DddP bound to inhibitory 2-(*N*-morpholino)ethanesulfonic acid or PO_4^{3-} and of two mutants bound to acrylate. The structures of DddQ bound to an inhibitory molecule 2-(*N*-morpholino)ethanesulfonic acid and of DddQ inactivated by a Tyr131Ala mutation and bound to DMSP were also solved. Based on structural, mutational and biochemical analyses, the molecular mechanisms for DMS production through DMSP cleavage by DddP and DddQ were proposed for the first time. DddP adopts a new ion-shift catalytic mechanism to cleave DMSP, while for DddQ, Tyr131 undergoes a conformational change during catalysis, acting as a base to initiate the β-elimination reaction in DMSP lysis. Furthermore, we suggested the structural mechanism leading to the loss of peptidase activity and the subsequent development of DMSP lyase activity in DddP. Our study provides important insight into the mechanism involved in the conversion of DMSP into DMS, which should lead to a better understanding of this globally-important biogeochemical reaction.