

Publication

Structure and Mechanism of Ergothionase from *Treponema denticola*

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Ergothioneine is a sulfur-containing histidine derivative that emerges from microbial biosynthesis and enters the human body through intestinal uptake and regulated distribution into specific tissues. Although the proteins involved in biosynthesis and uptake are well characterized, less is known about the degradative pathways of ergothioneine. This report describes the crystal structure of the active form of ergothionase from the oral pathogen *Treponema denticola* complexed with the substrate analogue desmethyl-ergothioneine sulfonic acid. This enzyme catalyzes the 1,2-elimination of trimethylamine from ergothioneine and ergothioneine sulfonic acid by using a unique mode of substrate activation combined with acid/base catalysis. This structural and mechanistic investigation revealed four essential catalytic residues, which are strictly conserved in homologous proteins from common gastrointestinal bacteria and numerous pathogenic bacteria, suggesting that bacterial activity may play an important role in determining the availability of ergothioneine in healthy and diseased human tissue.

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