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Metallopterin-Dependent Sulfurase From The Abyss

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PURPOSE OF THE ABSTRACT

Metallopretin-dependent proteins contain transition metals molybdenum or tungsten in the active site and catalyze essential processes in living organisms. The most diverse class of these enzymes, the dimethyl sulfoxide (DMSO) reductase superfamily, facilitates a wide range of chemical transformations that mainly implicate oxygen atom installation, removal, and transfer [1]. Here, we describe a novel enzyme from the DMSO reductase superfamily involved in the anaerobic biosynthesis of the natural antioxidant ergothioneine [2]. Metallopterin-dependent ergothioneine synthase (MES) contains two domains: an N-terminal metallopterin-binding sulfurase, and a C-terminal domain, which is a functional cysteine desulfurase. The two modules interact to transfer sulfur from cysteine onto the imidazole ring of trimethylhistidine (TMH) via an intramolecular persulfide relay (Figure 1). The C–S bond-forming activity of MES is unprecedented among metallopretin-containing enzymes and adds to the potential utility of these enzymes in biocatalysis. In addition, this discovery documents the second case of the independent emergence of anaerobic ergothioneine biosynthesis along with two alternative oxygen-dependent pathways [3], providing additional evidence for the importance of this widely-distributed metabolite in early anaerobic cell life.

FIGURES

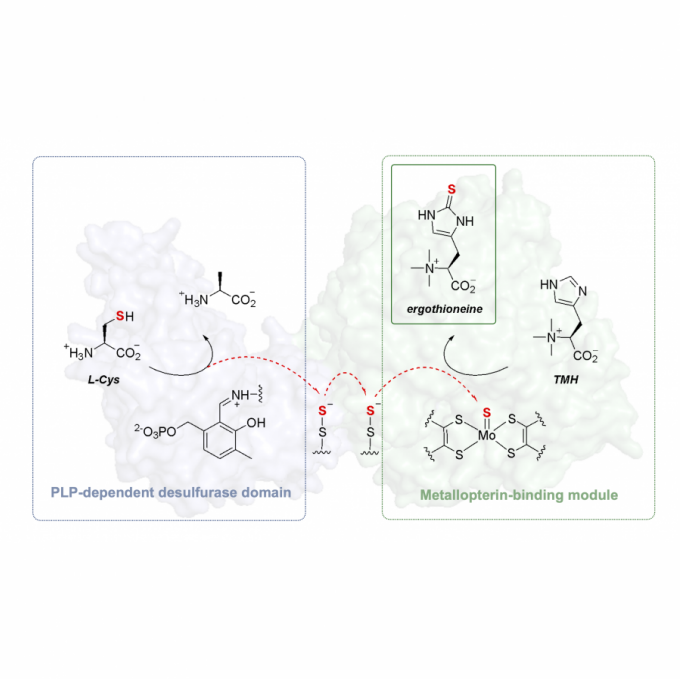

FIGURE 1

Scheme of ergothioneine biosynthesis by MES.

PLP-dependent desulfurase domain extracts sulfur from L-cysteine, which is then transported via the transient formation of persulfides on two cysteine residues to the N-terminal metallopterin-binding module that mediates oxidative sulfurization of TMH.

FIGURE 2

KEYWORDS

sulfurase | ergothioneine | sulfur metabolism | metallopterin-dependent enzyme

BIBLIOGRAPHY

[1] C. Le, M. Bae, S. Kiamehr, E. P. Balskus, Annu. Rev. Biochem., 2022, 91, 475-504.

[2] M. A. Beliaeva, F. P. Seebeck, JACS Au, 2022, 2, 2098-2107.

[3] A. R. Stampfli, W. Blankenfeldt, F. P. Seebeck, COSB, 2020, 65, 1-8.