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Fig. 1 Structures and biosynthetic gene clusters of thiopeptins and thiostrepton. (A) Structures of thiopeptins and thiostrepton. The (thio) amide moiety is shown in red, and the first residue is shown in blue. (B) Biosynthetic gene clusters of thiopeptins and thiostrepton. Homologous genes are indicated by dashed lines.

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Fig. 2 Sequence similarity networks of YcaO enzymes. A sequence similarity network (SSN) of PFAM 02624 is generated. The total number of sequences is 10 333. The SSN was generated using the Enzyme Function Initiative Enzyme Similarity Tool (EFI-EST) and visualized with Cytoscape. Each node is conflated at the 75% identity level, that is, the sequences that share more than 75% identity are represented by a single node.





Fig. 3 (A) Characterization of the role of TppX₂ in thioamidation. *In vivo* assays of TppX₂ activity. HPLC analyses of the culture extracts from the mutant $\Delta tppX_2$ (i) and the wild-type *S. tateyamensis* (ii). (B) Characterization of the roles of TppX₁ and TppX₂ in thioamidation. HPLC-HR-MS analyses of the culture extracts from the wild-type *S. laurentii* (i), the wild-type *S. laurentii* with the integrative plasmid containing $tppX_1$ (ii), the wild-type *S. laurentii* with the integrative plasmid containing $tppX_2$ (iii), the wild-type *S. laurentii* with the integrative plasmid containing $tppX_1$ (ii), the wild-type *S. laurentii* with the integrative plasmid containing $tppX_1$ and $tppX_2$ (iv), the mutant $\Delta tsrB$ with the integrative plasmid containing $tppX_1$ (v), the mutant $\Delta tsrB$ with the integrative plasmid containing $tppX_2$ (vi), the mutant $\Delta tsrB$ with the integrative plasmid containing $tppX_1$ and $tppX_2$ (vi).



Communication

Organic & Biomolecular Chemistry

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 $\mathbf{f}\mathbf{f}$ $\mathbf{f}\mathbf{f}$,

S. tateyamensis 2 †),

> 20 2 S. tateyamensis

8 (. .), $\Delta tsrP$ (tsrP . 0) (. . †), S. tateyamensis 2 1

2 8,

1 2, Escherichia coli 21(3). 1 2 $tppX_1$ $tppX_2$

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~1 1 2†). 2 (~ 3) (1 (~) . . 2

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Fig. 4 Structure of compound 8.

2+_ (e.g., 1 1 1 2) M. kandleri 3†), . 1 2 8 4 (2 .

4 8 in vivo.

Conclusions

in vivo , $tppX_1$ $tppX_2$ $\mathbf{f}\mathbf{f}$, S. tateyamensis 8 . , S. tateyamensis $tppX_2$

Conflicts of interest . 2)

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Notes and	references
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