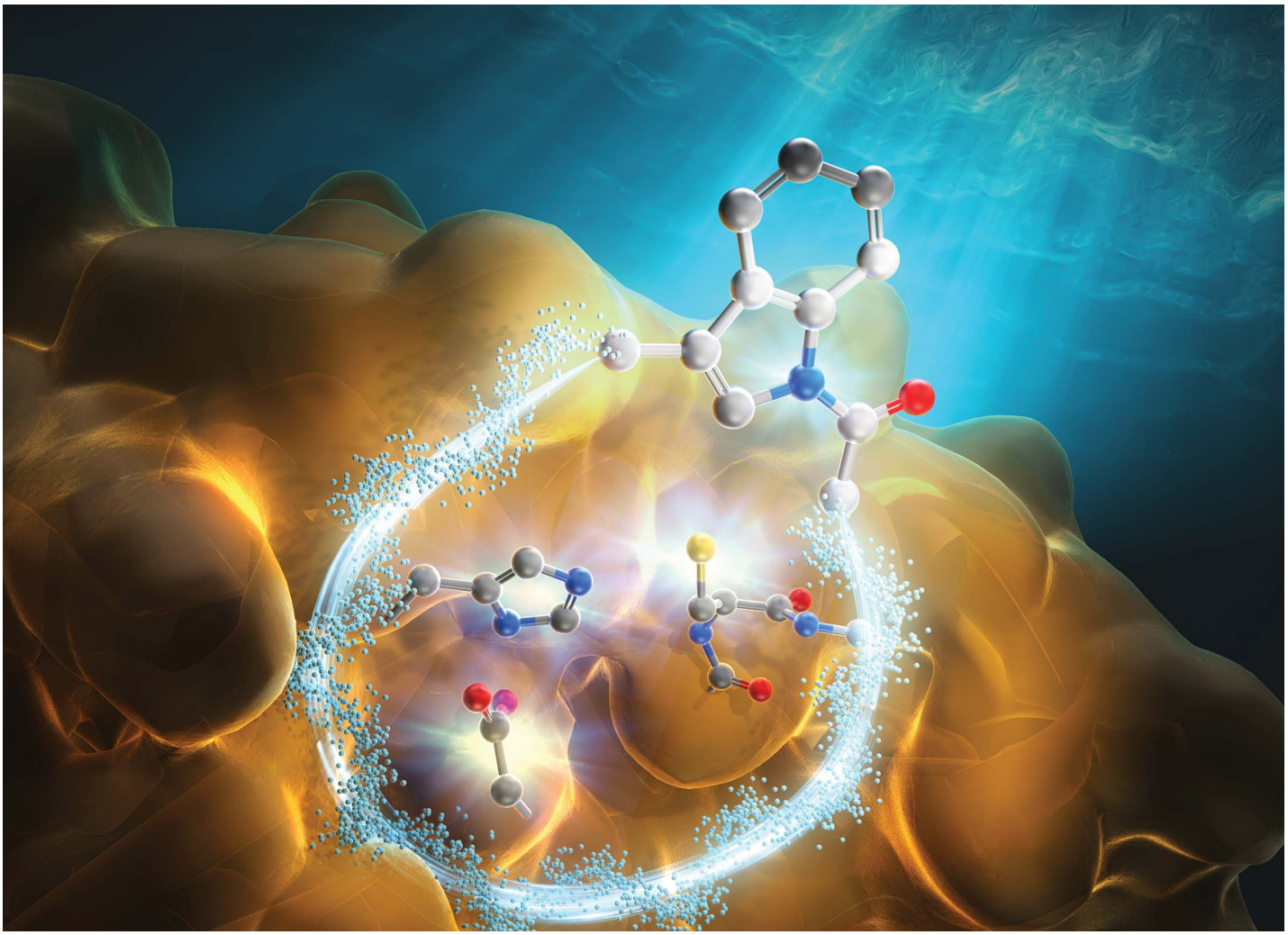

Showcasing research from Professor Wakimoto's laboratory, Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo, Japan.

Enzymatic peptide macrocyclization *via* indole-*N*-acylation

Indole-*N*-acylation is a challenging chemical transformation due to the low nucleophilicity of the indole nitrogen. In this study, we identified a unique thioesterase domain within the biosynthetic pathway of bulbiferamide—a non-ribosomal cyclic peptide—that catalyses peptide macrocyclization *via* *N*-acylindole linkage formation. Substrate scope analysis, structural modelling, and mutagenesis studies elucidated the basis of substrate recognition. These results offer valuable insights into the pivotal role of its catalytic residue in dictating nucleophile specificity.

As featured in:

See Kenichi Matsuda, Toshiyuki Wakimoto *et al.*, *Chem. Sci.*, 2025, **16**, 3872.

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