# METHODS TO GENERATE NOVEL ACYL-TRNA SPECIES

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## PATENT STATUS

| Country | Type | Number | Dated | Case |
|---|---|---|---|---|
| Patent Cooperation Treaty | Reference for National Filings | WO/2023/164676 | 08/31/2023 | 2022-095 |

Patent Pending

## BRIEF DESCRIPTION

The inventors have discovered PylRS enzymes that accept -thio acids, N-formyl-L-amino acids, and diverse -carboxyl acid monomers (malonic acids) that are formally precursors to polyketide natural products. These monomers are all accommodated and accepted by the translation apparatus in vitro. High-resolution structural analysis of the complex between one such PylRS enzyme and a meta-substituted 2-benzylmalonate derivative reveals an active site that discriminates pro-chiral carboxylates and accommodates the large size and distinct electrostatics of an -carboxyl acid substituent.

This discovery emphasizes the potential of PylRS for evolving new enzymes capable of encoding diverse non-L-amino acids in synergy with natural or evolved ribosomes. The absence of orthogonal aminoacyl-tRNA synthetase enzymes that accept non-L-amino acids is the primary bottleneck hindering the in vivo translation of sequence-defined hetero-oligomers.

## SUGGESTED USES

These enzymes could be used to develop keto-peptide hybrid molecules that are privileged scaffolds for drug design.

## ADVANTAGES

Towards the goal of charging tRNAs with non-L-α-amino acid monomers, PylRS enzymes have advantages of MjTyrRS in how they recognize the α-amine of their substrate.

## RELATED MATERIALS

### ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Nuclear Delivery and Transcriptional Repression with a Cell-penetrant MeCP2

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## OTHER INFORMATION

**KEYWORDS**

enzymes, in vivo

**CATEGORIZED AS**

» **Biotechnology**

» Health

» **Medical**

» Research Tools

» Therapeutics

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