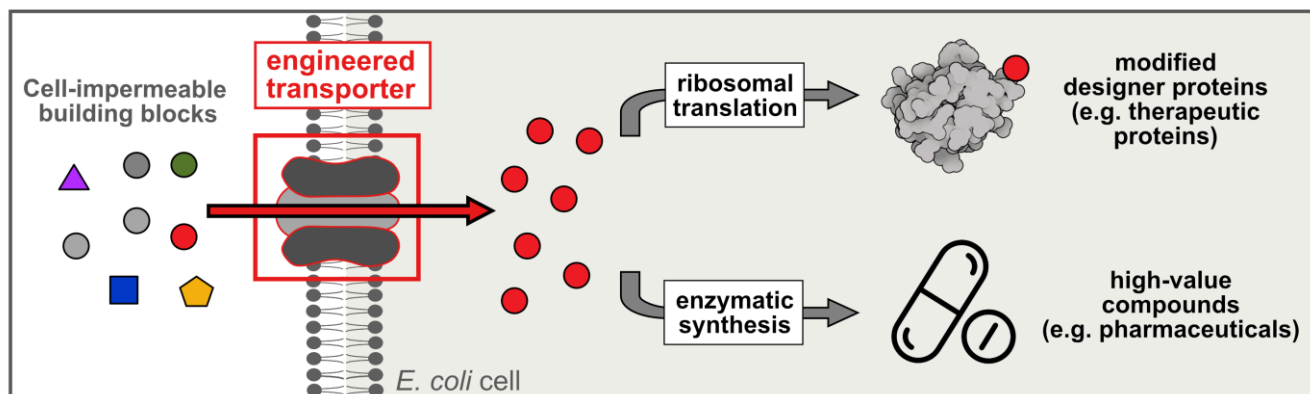


Licensing Opportunity

Production platform for proteins containing non-canonical amino acids



Application

This programmable import system delivers previously impermeable building blocks into microbial cells. The excellent transport-yield lowers the cost of microbial protein synthesis as less building block material is needed in the process. The import system offers, thus, an economical way to produce next-generation therapeutic proteins based on high-value building blocks.

Features & Benefits

- Cheap, scalable production of modified designer proteins
- Enabling efficient bioorthogonal crosslinking with non-canonical amino acids
- Post-translational modifications and chemoenzymatic conjugation

Publication

- "Hijacking a bacterial ABC transporter for genetic code expansion", Nature 647, 1045–1053 (2025) <https://doi.org/10.1038/s41586-025-09576-w>
- Patent pending

Background

Site-specific encoding of non-canonical amino acids (ncAAs) via genetic code expansion enables the production of proteins with defined chemical modifications, such as post-translational modifications, bioorthogonal handles, and crosslinkers. While promising, the incorporation of ncAAs often suffers from low protein expression yields. This is due in part to the limited permeability of ncAAs across the cell membrane. In addition, ncAA synthesis can be expensive, which - when combined with low incorporation yields can drastically limit the production of ncAA-containing proteins in industrial applications.

Invention

Novel *E. coli* strains with custom membrane transporters, engineered through high-throughput directed evolution, actively import non-canonical amino acids into cells. This enables high intracellular levels of previously impermeable building blocks for efficient production of proteins with novel chemical modifications.

In a proof-of-concept study, production of a nanobody bearing a site-specifically placed bioconjugation handle (for accessing ADC-like therapeutics) gave wild-type like expression yields, 60% higher than previous systems.



ETH transfer

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 Reference 2024-108

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Technology Readiness Level

