METHODS FOR THE SYNTHESIS OF SEQUENCE-DEFINED HETEROPOLYMER BACKBONES

Tech ID: 33354 / UC Case 2024-055-0

PATENT STATUS

Patent Pending

BRIEF DESCRIPTION

Biological systems naturally synthesize precise, sequence-defined polymers—proteins and nucleic acids—that perform a staggering array of functions. However, the chemical diversity of these polymers is limited by the set of twenty canonical α-amino acids. To overcome this limitation, researchers at UC Berkeley have pioneered a method for the programmed biosynthesis of heteropolymers with expanded backbones. By engineering orthogonal aminoacyl-tRNA synthetases (aaRS), such as variants of the pyrrolysyl-tRNA synthetase, the system can charge tRNAs with non-natural $\beta 2$-backbone substrates. These substrates are then incorporated by the ribosome into a growing polymer chain in vivo. This breakthrough allows for the creation of sequence-defined biomaterials that possess structural and chemical properties far beyond those of traditional proteins, including enhanced stability and novel folding patterns.

SUGGESTED USES

» Stabilized Biologic Therapeutics: Developing peptide-based drugs with beta-backbone segments that are resistant to proteolysis, significantly extending their half-life within the human body.

» Next-Generation Bioplastics: Synthesizing biodegradable polyesters and polyhydroxyalkanoates with precise, genetically encoded monomer sequences for tailored mechanical properties.

» Molecular Data Storage: Utilizing the high-density information capacity of sequence-defined polymers to store digital data in a stable, compact, and long-lasting chemical format.

» Custom Foldamer Design: Engineering synthetic macromolecules that fold into specific, predictable three-dimensional shapes for use as catalysts or selective binding agents.

» Advanced Bioremediation: Creating specialized proteins with expanded chemical functional groups capable of sequestering or breaking down environmental toxins that natural enzymes cannot process.

ADVANTAGES

» Genetic Programmability: Leverages the precision of cellular translation to produce polymers with exact sequences and lengths, which is difficult to achieve via conventional chemical synthesis.

» Increased Metabolic Stability: The introduction of non-canonical backbones makes these heteropolymers inherently resistant to the enzymes that normally degrade proteins.

» Broad Chemical Space: Opens the door to incorporating a wide variety of non-natural monomers, allowing for the fine-tuning of polymer hydrophobicity, charge, and reactivity.

» Scalable In Vivo Production: Enables the cost-effective "growing" of complex polymers inside engineered microbial cells rather than relying on expensive, labor-intensive benchtop synthesis.

» High Structural Diversity: The expanded $\beta 2$-backbone architecture provides new degrees of freedom for molecular folding, leading to the discovery of novel secondary and tertiary structures.

RELATED MATERIALS

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Improved Vehicles For Endosomal Escape
- Ribosomal Synthesis Of Ketone-Containing Peptide Backbone Via O To C Acyl Shift
- Methods To Generate Novel Acyl-Trna Species
- Nuclear Delivery and Transcriptional Repression with a Cell-penetrant MeCP2
- Methods For The Synthesis Of Peptide Macrocycles With Embedded Heterocycles

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OTHER INFORMATION

CATEGORIZED AS

» **Biotechnology**
» Proteomics
» **Materials & Chemicals**
» Polymers
» **Research Tools**
» Protein Synthesis

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