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Artificial Ribosomes for Fully Programmable Synthesis of Nonribosomal Bioactive Compounds

Nonribosomal peptides are bioactive and highly diverse compounds, usually produced by microorganisms, which comprise some of the most important drugs in use today, including antimicrobials, immunosuppressants and anticancer compounds. These compounds are synthesized by nonribosomal peptide synthetases (NRPSs) which can incorporate over 300 different amino acid residues into the peptides and can structurally modify the compounds to increase bioactivity. There have been significant efforts to reconstitute NRPSs in vitro, however, a scalable method has not been developed that affords the same sequence programming precision as that achieved by ribosomes.

Prof. Alexander Green of the Biodesign Institute is developing artificial ribosome systems that can synthesize potent and structurally diverse nonribosomal bioactive compounds with full control over sequence programming. Using this strategy, compounds can be synthesized in a test tube and potentially in living cells in a scalable manner. Although nonribosomal peptides are the initial focus, these systems can be extended to the synthesis of other important classes of compounds, namely polyketides and fatty acids. These artificial ribosome systems can enable the generation of diverse libraries of new drug candidates and open up new frontiers in chemical synthesis.

This strategy enables the scalable synthesis of an enormous range of therapeutic compounds that could have transformative potential in drug development and clinical applications.

Potential Applications

- Synthesis of nonribosomal bioactive compounds
 - o Drug discovery for the pharmaceutical industry
 - o On-demand drug synthesis
- Protecting warfighters from biowarfare agents
- Humanitarian operations

- Pharmaceutical research
- Hospitals

Benefits and Advantages

- Scalable
- Precise and controllable sequence programming
- Can be programmed to take on any geometry
- Diverse library generation as a valuable source of new drug candidates
- Can create nonribosomal peptides, polyketides and fatty acids
- Different configurations provide for different degrees of complexity and modularity
- High degree of modularity for NRP synthesis
- Production in living cells or cell-free in vitro systems

For more information about the inventor(s) and their research, please see [Dr. Green's departmental webpage](#)