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Ribosome as a molecular machine

Ribosomes are molecular machines that have evolved to polymerize L-alpha amino acids into peptides or proteins with amide linkages. Here, I discuss our recent investigation into leveraging the ribosome's polymerization ability to produce a novel chemical motif, pyridazinone, on a cell-free platform instead of via a peptide bond. Specifically, I explain a ribosomecatalyzed cyclocondensation reaction between activated y-keto and α -hydrazino ester monomers. This reaction demonstrates the ribosome's catalytic mechanism is plastic, as observed in both remnants of evolution and current efforts to expand genetic codes. Based on this result, we anticipate that rational designs of non-canonical monomers and engineering of the machinery in the system may open translational new opportunities for developing genetically encoded chemistry, transforming drug discovery practices beyond traditional boundaries.

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