

---

## Asia 3 Roundtable on Nucleic Acids 2024

---

### Joongoo Lee, Professor

Department of Chemical Engineering,  
POSTECH, Pohang, 37673, Korea.

Tel: +82-2-279-2269

Email: [jgoolee@postech.ac.kr](mailto:jgoolee@postech.ac.kr)



---

2021-Present     Assistant Professor, POSTECH, Pohang, Rep. of Korea  
2016-2021       Postdoctoral Researcher, Northwestern University, Evanston, USA  
2015 PhD         University of Oxford, UK  
2008 MS         KAIST, Rep. of Korea  
2006 BS         Yonsei University, Rep. of Korea

#### Research Interests:

Ribosome, cell-free protein expression, genetic-code reprogramming, pharmacophore.

#### Selected Publications:

1. J. Lee, J. N. Coronado, N. Cho, J. Lim, B. M. Hosford, S. Seo, D. S. Kim, C. Kofman, J. S. Moore, A. D. Ellington, E. V. Anslyn, M. C. Jewett, Ribosome-mediated biosynthesis of pyridazinone oligomers in vitro, *Nat. Commun.* 2022, 13, 6322.
2. J. Lee, K. J. Schwarz, D. S. Kim, J. S. Moore, M. C. Jewett, Ribosome-mediated incorporation of long-carbon chain and cyclic amino acids into peptides in vitro, *Nat. Commun.* 2020, 11, 4304.
3. J. Lee, K. E. Schwieter, A. M. Watkins, D. S. Kim, H. Yu, K. J. Schwarz, J. Lim, J. Coronado, M. Byrom, E. V. Anslyn, A. D. Ellington, J. S. Moore, M. C. Jewett, Expanding the limits of the second genetic code with ribozymes, *Nat. Commun.* 2019, 10, 5097.
4. J. Lee, A. J. Boersma, M. A. Boudreau, S. Cheley, O. Daltrop, J. Li, H. Tamagaki, H. Bayley, Semisynthetic nanoreactor for reversible single-molecule covalent chemistry. *ACS Nano* 2016, 10, 8843
5. J. Lee, H. Bayley, Semisynthetic protein nanoreactor for single-molecule chemistry. *Proc. Natl. Acad. Sci. U.S.A.* 2015, 112, 13768

# **Expanded ribosomal synthesis of non-standard cyclic backbones in vitro**

Joongoo Lee

Department of Chemical Engineering, POSTECH, Pohang, 37673, Rep. of Korea

## **Abstract**

The ribosome polymerizes L- $\alpha$ -amino acids into polypeptides, catalyzing peptide bond formation through aminolysis. This process is facilitated by entropy trapping within its peptidyl transferase center (PTC). Based on our previous results published last year, which showed that the ribosome forms 6-membered pyridazinone backbones rather than traditional peptide bonds, we further investigated its ability to create more diverse cyclic backbones during polymerization.

To explore this, we designed a new set of various non-canonical monomers, charged them onto tRNA using ribozymes, and demonstrated that these monomers produce novel cyclic backbones through two consecutive chemical reactions within the ribosome. Furthermore, we examined the regioselectivity of these cyclic backbones, revealing that the ribosome favors the  $\alpha$ -nitrogen for covalent bond formation as it incorporates  $\alpha$ -amino acids as building blocks within the cell.