Yeongju Lee, Assistant Professor

Department of Chemistry,
Pusan National University, Busan, 46241, Korea.
Tel: +82-51-510-2868
Email: lyj0308@pusan.ac.kr

2022- Present	Assistant Professor, Pusan National University
2020-2022	Postdoctoral Researcher, The Scripps Research Institute, USA
2019-2020	Postdoctoral Researcher, POSTECH, Korea
2019 PhD	POSTECH, Korea
2014 BS	POSTECH, Korea

Research Interests:

RNA-targeting Small Molecule, Drug Discovery, Proteolysis-Targeting Chimeras, Ribonuclease-Targeting Chimeras

Selected Publications:

1. Tong, Y.† ; **Lee, Y.** † ; Liu X. †; Child-Disney, J. †; Suresh, B.M.; Benhanou, R. I.; Sievers, S.; Grefe, M.; Crynen, G.; Meter, M. V.; Costales, M. G.; Abegg, D.; Haniff, H. S.; Wegner, T.; Paulisch, T. O.; Adibekian, A.; Lekah, E.; Glorius, F.; Waldmann, H.; Disney, M. D; "Biologically inactive RNA binding small molecules are rendered bioactive when converted into degraders" Nature, 2023, 618, 169-179. † equally contributed

2. **Lee, Y.**; Heo, J.; Jeong, H.; Hong, K. T.; Kwon, D. H.; Shin, M. H.; Oh, M.; Sable, G. A.; Ahn, G.; Lee, J. S.; Lim, H. S. "Targeted Degradation of Transcription Co-activator SRC-1 through the N- Degron Pathway." Angew. Chem. Int. Ed. 2020, 59, 17548-17555.

3. **Lee, Y.**; Im, H.; Oh, M.; Lee, J. H.; Das, S.; Ham, S.; Lim, H. S. "Bridged α-helix mimetic small molecules." Chem. Commun. 2019, 55, 13311-13314.

4. **Lee, Y.**; Chung, B.; Ko, D. S.; Lim, H. S. "A solid-phase method for synthesis of dimeric and trimeric ligands: Identification of potent bivalent ligands of 14-3-3σ." Bioorg. Chem. 2019, 91, 103141.

5. **Lee, Y.**; Yoon, H.; Hwang, S. M.; Shin, M. K.; Lee, J. H.; Oh, M.; Im, S. H.; Song, J.; Lim, H. S. "Targeted Inhibition of the NCOA1/STAT6 Protein-Protein Interaction." J. Am. Chem. Soc. 2017, 139, 16056-16059.

Small Molecule Approaches to Targeting Disease-Associated RNAs

Yeongju Lee
Department of Chemistry, Institute for Future Earth, Pusan National University, Busan, 46241, Korea

Abstract

Target occupancy is often insufficient to elicit biological activity, particularly for RNA, compounded by the longstanding challenges surrounding the molecular recognition of RNA structures by small molecules. Here we studied molecular recognition patterns between a natural-product-inspired small-molecule collection and three-dimensionally folded RNA structures. Mapping these interaction landscapes across the human transcriptome defined structure–activity relationships. Although RNA-binding compounds that bind to functional sites were expected to elicit a biological response, most identified interactions were predicted to be biologically inert as they bind elsewhere. We reasoned that, for such cases, an alternative strategy to modulate RNA biology is to cleave the target through a ribonuclease-targeting chimera, where an RNA-binding molecule is appended to a heterocycle that binds to and locally activates RNase L. Overlay of the substrate specificity for RNase L with the binding landscape of small molecules revealed many favourable candidate binders that might be bioactive when converted into degraders. We provide a proof of concept, designing selective degraders for the precursor to the disease-associated microRNA-155 (pre-miR-155), JUN mRNA and MYC mRNA. Thus, small-molecule RNA-targeted degradation can be leveraged to convert strong, yet inactive, binding interactions into potent and specific modulators of RNA function.

1. Tong, Y.† ; **Lee, Y.** † ; Liu X. †; Child-Disney, J. †; Suresh, B.M.; Benhanou, R. I.; Sievers, S.; Grefe, M.; Crynen, G.; Meter, M. V.; Costales, M. G.; Abegg, D.; Haniff, H. S.; Wegner, T.; Paulisch, T. O.; Adibekian, A.; Lekah, E.; Glorius, F.; Waldmann, H.; Disney, M. D; "Biologically inactive RNA binding small molecules are rendered bioactive when converted into degraders" Nature, 2023, 618, 169-179. † equally contributed