



COLLOQUIUM SEMINAR SERIES

CHEMICAL TOOLS FOR RNA STRUCTURE AND DRUGGABILITY



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RNA is a highly versatile molecule and exhibits many diverse functions.^{1,2} Our lab explores new approaches and chemistries to study RNA structure and druggability. Controlling RNA in a cellular context to dissect its role in biological processes has remained challenging. During this talk, new chemical tools are presented that can selectively modify biologically relevant RNA molecules in cells to aid in elucidating RNA structure.^{3,4} For example, our newly devised method Spatial 2'-Hydroxyl Acylation Reversible Crosslinking (SHARC) allows to measure nucleotides in close proximity in cellular RNA, which establishes a strategy for measuring RNA 3D distances and alternative conformations in their native cellular context.³

Furthermore, using customized affinity-based profiling tools we study RNA structural folding and small molecule ligand binding.⁴ Applying these tools to structured RNA, we can determine ligand binding sites with single nucleotide resolution. Lastly, combining our tools with qPCR allows us to measure binding of RNA targeting drugs in live cells.

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(2) Cech, T. R.; Steitz, J. A. The Noncoding RNA Revolution - Trashing Old Rules to Forge New Ones. *Cell* 2014, 157 (1), 77-94. <https://doi.org/10.1016/j.cell.2014.03.008>.

(3) Van Damme, R.; Li, K.; Zhang, M.; Bai, J.; Lee, W. H.; Yesselman, J. D.; Lu, Z.; Velema, W. A. Chemical Reversible Crosslinking Enables Measurement of RNA 3D Distances and Alternative Conformations in Cells. *Nature Communications* 2022, 13 (1), 911. <https://doi.org/10.1038/s41467-022-28602-3>.

(4) Crielaard, S.; Maassen, R.; Vosman, T.; Rempeken, I.; Velema, W. A. Affinity-Based Profiling of the Flavin Mononucleotide Riboswitch. *J. Am. Chem. Soc.* 2022, 144 (23), 10462-10470. <https://doi.org/10.1021/jacs.2c02685>.

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Wednesday, October 25, 2023 | 3:30pm | CCT2150