

# AMANDA E. HARGROVE

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Thursday, January 18<sup>th</sup>

10:30am - 11:30am

Steele 006

## “Modulating the conformation and function of disease-relevant RNA with small molecules”

**Abstract:** Small molecules offer a unique opportunity to target structural and regulatory elements in therapeutically relevant RNAs, but understanding functional selectivity has been a recurrent challenge in small molecule:RNA recognition. RNAs offer less differentiating chemical functionality than proteins and sample multiple conformations that can individually impact function. The first and only small molecule drug targeting RNA other than the bacterial ribosome was approved by the US FDA in August of 2020, and our recent survey of the literature revealed less than two hundred reported chemical probes that target non-ribosomal RNA in biological systems.

As part of our efforts to improve small molecule targeting strategies and gain fundamental insights into small molecule:RNA recognition, we have analyzed patterns in both RNA-biased small molecule chemical space and RNA topological space privileged for differentiation. We have applied these principles to functionally modulate conformations of 3'-triple helix of the long noncoding RNA MALAT1, leading to small molecule degraders, as well as in the development of RNA-targeted antivirals for enterovirus (EV71) and SARS-CoV-2.

**Bio:** Amanda E. Hargrove is a Professor of Chemistry at Duke University. Prof. Hargrove earned her Ph.D. in Organic Chemistry from the University of Texas at Austin followed by an NIH postdoctoral fellowship at Caltech. Prof. Hargrove's laboratory focuses on developing small molecule probes to investigate the structure and function of RNA molecules relevant to human disease. The lab works to understand the fundamental drivers of selective small molecule:RNA recognition and to use this knowledge to functionally modulate viral and oncogenic RNA structures. Congruent with the interdisciplinary nature of this program, Prof. Hargrove holds a secondary appointment in the Biochemistry Department and membership in the Duke Cancer Institute, the Pharmaceutical Sciences Training Program, and the Center for Biological and Tissue Engineering. Recent honors include the RNA Society Elisa Izaurralde Award for Innovation in Research, Teaching, and Service, the Sloan Research Fellowship, the American Chemical Society Women Chemists Committee Rising Star Award, and the Cram Lehn Pedersen Prize in Supramolecular Chemistry. Prof. Hargrove serves as Editor-in-Chief of Medicinal Research Reviews and is a member of the ChemComm, Current Protocols, and Supramolecular Chemistry editorial advisory boards. In July 2024, the Hargrove lab will move to the University of Toronto Center for Medicinal Chemistry in Mississauga.