Chemical & Physical Sciences
**UNIVERSITY OF TORONTO**
MISSISSAUGA

**Colloquium Seminar Series**
**Wednesday, November 13, 2024**
**3:15PM in CC3150**

# MODULATING THE CONFORMATION AND FUNCTION OF DISEASE-RELEVANT RNA WITH SMALL MOLECULES

featuring
## Amanda Hargrove, PhD
Chemical and Physical Sciences Dept
**University of Toronto, UTM**

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. We have used organic synthesis, machine learning and a variety of biophysical and cell-based assays to reveal patterns in the chemical and structural properties of bioactive RNA ligands as well as RNA topological space privileged for differentiation. We have applied these principles to several disease-relevant systems. For example, we were able to tune diiminazene-based small molecules to functionally modulate different RNA tertiary structures in the oncogenic long noncoding RNA MALAT1, leading to monofunctional degraders or tailored manipulation of RNA:protein interactions, respectively. We have also developed RNA-targeted antivirals for enterovirus (EV71) and SARS-CoV-2, revealing a novel allosteric mechanism of small molecule: RNA targeting.