SPECIAL DEPARTMENAL SEMINAR

Molecular Genetics
UNIVERSITY OF TORONTO

Strategies to modulate the conformation and function of RNA with small molecules

Prof. Amanda E. Hargrove, Ph.D.
University of Toronto; Mississauga, Ontario, Canada

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 each 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. We have tuned diiminazene-based small molecules to functionally modulate different RNA tertiary structures in the oncogenic long noncoding RNA MALAT1, leading to either 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.

Date: Monday, October 21st, 2024
Time:3:00 PM
Place: Galbraith Building 35 St. George Street. Room 220