Hosted by Vickie DeRose

Dept. of Chemistry and Biochemistry

Organic/Inorganic Seminar Series

# Christine S. Chow

Wayne State University

## Friday, November 9, 2018

2:30—3:30 pm, 331 KLA

Coffee reception @ 2:00 pm, 377 KLA

## *Interactions of platinum(II) complexes with RNA: impact of ligands on kinetics, structural integrity, and cytotoxicity*

Abstract: The potency of cisplatin for cancer treatment is complicated by both toxicity and resistance. RNA competes with DNA as a cisplatin target and is able to accumulate inert platinum adducts. Cisplatin can be modified with ligands of varying sizes, polarities, and charges. These features can affect kinetics of interaction with nucleic acids, the types of adducts formed, the preferred sites of coordination, and cell cytotoxicity. In this work, amino acid-based platinum analogues were examined. Kinetic studies show that ornithine-, arginine, and alanine-linked platinum complexes (OrnPt, ArgPt, and AlaPt) are reactive towards RNA and DNA nucleosides, but with different selectivities. Inductively coupled plasma mass spectrometry (ICPMS) quantification reveals different levels of accumulation of OrnPt and ArgPt on RNA and DNA. Platination by OrnPt and AlaPt at particular sites on the ribonucleosides (*e.g.*, N1, N3, or N7 on A residues) has varying impacts on glycosidic bond stabilities. Weakening of the glycosidic bond could accelerate depurination and ultimately contribute to cell cytotoxicity. Our results suggest that platinum adducts on RNA may play roles in drug toxicity and/or resistance.