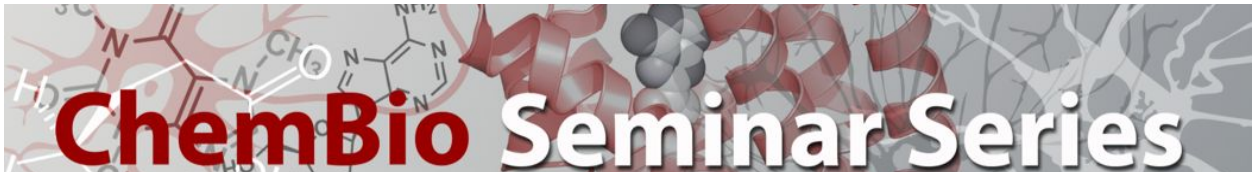

Thursday, April 18, 2019, 12:30 pm
Seaver Science Auditorium, Room 150
SSC Auditorium next to the library

Professor Hien Nguyen

Department of Chemistry
Wayne State University

Specific Inhibition of Heparanase by Glycopolymers for Cancer Therapeutics

Heparanase, the heparan sulfate polysaccharide degrading endoglycosidase enzyme, has been correlated to tumor angiogenesis and metastasis and therefore has become a potential target for anticancer drug development. In this systematic study, the sulfation pattern of pendant disaccharide moiety on synthetic glycopolymers was synthetically manipulated to achieve optimal heparanase inhibition. Upon evaluation, glycopolymer with 12 repeating units was determined to be the most potent inhibitor of heparanase (IC_{50} = 0.10 ± 0.36 nM). This glycopolymer was further examined for cross-bioactivity, using a solution-based competitive biolayer interferometry assay, with other HS-binding proteins (growth factors, P-selectin, and platelet factor 4), which are responsible for mediating angiogenic activity, cell metastasis, and antibody-induced thrombocytopenia. The synthetic glycopolymer has low affinity for these HS-binding proteins compared to natural heparin. In addition, the glycopolymer possessed no proliferative properties towards human umbilical endothelial cells (HUVEC) and a potent antimetastatic effect against 4T1 mammary carcinoma cells. Thus, our study not only establishes a specific inhibitor of heparanase with high affinity, but also illustrates the high effectiveness of this multivalent heparanase inhibitor in inhibiting experimental metastasis *in vivo*.

Hosted by Professor Matt Pratt

The scientific community is invited

USC Department of Chemistry
chem.usc.edu