“New Approaches to 1,2-Cis-2-Aminosugars and Well-Defined Heparan Sulfate Neo-Glycopolymers as Heparanase Inhibitors for Cancer Applications”

In this seminar, Dr. Nguyen will present new approaches to novel carbohydrate coupling methods that utilize transition-metals as the efficient catalyst to stereoselectively promote the formation of high purity 1,2-cis-2-aminosugars, one of the most important classes of naturally occurring complex carbohydrates and glycoproteins. The newly-developed glycosylation methods are then applied to the construction of sulfated glycopolymers. The synthetic glycopolymers are subsequently investigated as potential heparanase inhibitors. These compounds showed very good heparanase inhibition with IC$_{50}$ values of 1 - 2 nM using TR-FRET assay. Heparanase is an endo-$\beta$-D-glycosidase that cleaves heparan sulfate (HS) side chains of proteoglycans thereby altering the structural integrity of the extracellular matrix. These actions dynamically impact multiple regulatory pathways, most notably by accelerating cell invasion and augmenting the bioavailability of growth factors and cytokines bound to HS. Its overexpression in tumor cells supports several pathological scenarios, such as increasing tumor size, tumor angiogenesis, enhancing metastasis, poor patient prognosis, and tissue inflammation.