Poly(ADP-ribose) (PAR) is a natural polymer composed of ADP-ribose (ADPr) units. PAR is produced from $\beta$-NAD$^+$ by poly(ADP-ribose) polymerase (PARP) enzyme. The size of PAR polymers can be in between 2 – 200 units with branching in every 20 – 50 units. PAR is involved in many biological processes such as DNA damage repair, transcription, mitosis, and apoptosis.\(^\text{1}\) There are hundreds of proteins that contain PAR-binding domains, however, the interactions between PAR and proteins at the molecular level are still poorly understood due to the difficulty to obtain homogeneous PAR and in quantitative scale. We have developed a multifunctional neoglycoside auxiliary with the purpose to facilitate the isolation and fractionation of PAR polymers. The auxiliary was synthesized in 3 steps starting with a zinc catalyzed, one-pot tetrazine condensation followed by the introduction of the methylhydroxylamine via a Mitsunobu reaction and deprotection sequence. This auxiliary demonstrated many advantages in applications related to glycomic research including isolation and purification of complex carbohydrates and direct conjugation to chemical probes. Another approach to access the homogeneous PAR is to modify the substrate $\beta$-NAD$^+$ by utilizing a photoremovable protecting group. The synthesis of photocaged $\beta$-NAD$^+$ analogue in which 2'-OH on the adenosine is protected with the photoremovable 2-nitrobenzyl will be discussed. This $\beta$-NAD$^+$ analogue will be used as a substrate to produce highly branched PAR polymers.

Reference:

Room 316 Aubert Hall @ 11:00 a.m.
Tuesday, March 5, 2019
Light refreshments available.