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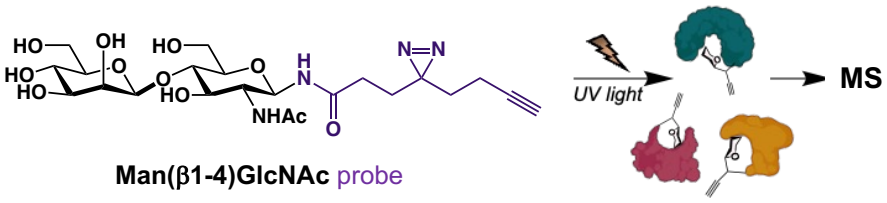
Grant Title: Chemoproteomic mapping of the Man(β1-4)GlcNAc disaccharide interactome in cells

Abstract

Some autoimmune diseases, including systemic lupus erythematosus or "lupus," are now known to occur because of the pathogenic excess of an intracellular disaccharide called Man(β1-4)GlcNAc. The accumulation of this autogenous disaccharide in cells can lead to the erroneous activation of immune responses, leading to autoimmunity. The molecular mechanisms through which Man(β1-4)GlcNAc regulate autoimmunity remain unknown, due to the difficulties of capturing the intracellular interactors and receptors of free oligosaccharides, like Man(β1-4)GlcNAc. We will apply modern chemical strategies to access synthetic derivatives of this important disaccharide in a stereoselective manner and use a chemoproteomic mass spectrometry-based approach to elucidate the interactome of Man(β1-4)GlcNAc to identify its functional receptors in cells. The accomplishments resulting from this work will result in an enhanced understanding of aberrant glycosylation and the bioactivity of free Man(β1-4)GlcNAc, as well as pave the pathway for studying the interactomes and molecular mechanisms of intracellular free oligosaccharides.



Man(β1-4)GlcNAc probe