

Wednesday, January 29th, 2014

LSC 3 - Life Sciences Centre

2350 Health Sciences Mall

12-1pm



Dr. David Vocadlo

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“Chemical biology of the O-GlcNAc post-translational modification: from probes to Alzheimer disease.”

N-acetylglucosamine O-linked to serine and threonine residues (O-GlcNAc) is an abundant form of protein glycosylation found within the nucleus and cytoplasm of multicellular eukaryotes. This post-translational modification is reversible and its levels within cells vary in response to various stimuli including glucose availability and cellular stress. O-GlcNAc is particularly abundant in brain tissue and is present on many proteins including both tau and the amyloid precursor protein. The nutrient responsiveness of O-GlcNAc is notable in the context of Alzheimer disease (AD) given that impaired glucose utilization is an early feature in the brains of AD patients. Consistent with these observations, AD patients have been shown to have lower levels of brain O-GlcNAc and, interestingly, neurofibrillary tangles composed of tau bear no O-GlcNAc. Here I will discuss the generation of inhibitors that slow removal of O-GlcNAc, the protective effects of such inhibitors in cellular and transgenic mouse models of Alzheimer disease, and touch on the processes by which increased O-GlcNAc protects against tau-induced neurodegeneration.

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