Title – O-GlcNAc Transferase May Affect the Activity of Succinate Dehydrogenase

Program of Study – Biochemistry

Presentation Type – Print Poster

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Category – Basic

Abstract

Cellular communication occurs in a variety of ways such as through the initiation of signaling cascades and regulation of gene expression. Another such process that can impact cellular signaling is post-translational modification. Post-translational modification of proteins by enzymes can affect the functionality of the protein by playing a role in the activation or inactivation of it. Examples of post-translational modifications include phosphorylation and glycosylation. O-linked N-acetylglucosamine Transferase (OGT) is one such example of an enzyme that carries out post-translational glycosylation, in which it adds an N-acetylglucosamine moiety to Ser and Thr residues of target proteins. The removal of this sugar moiety is catalyzed by O-GlcNAcase (OGA). Through OGT and OGA working tandem, a cycling of the O-GlcNAc modification is created. Additionally, this modification can occur on the same amino acid residue as phosphorylation, thus potentially blocking the phosphorylation and activation of a protein.

One potential target of OGT glycosylation is succinate dehydrogenase (SDH), or complex II of the mitochondrial respiration chain. Additionally, SDH functions within the citric acid cycle in the conversion of succinate to fumarate. Thus, SDH is integral to cellular metabolism through both mitochondrial respiration the citric acid cycle. It is hypothesized that OGT modification of key residues on SDH may affect its activity. This will be investigated through key sites on SDH
within a plasmid being mutated and then transfection of the mutated SDH into a human cell line. A redox enzymatic assay allows SDH activity to be examined. Due to the integral nature of SDH in cellular metabolism, investigation of how OGT affects SDH may lead to knowledge into the mechanisms of various metabolic syndromes.