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Abstract

MitoNEET is a recently discovered [2Fe-2S] protein that binds to the anti-diabetic drug pioglitazone. MitoNEET contains a unique ligation of three cysteines and one histidine, but its function is unknown. Previous members of the Konkle lab discovered that mitoNEET binds to and activates bovine glutamate dehydrogenase (GDH1). My project utilizes enzyme kinetics to analyze mitoNEET and GDH1 with the addition of physiologically relevant effector molecules that were found to allosterically control GDH1. These include activators leucine and ADP, and deactivators palmitoyl-CoA, epigallocatechin gallate (EGCG), and GTP. NAD+ not only serves as a cofactor but may alter the secondary structure of mitoNEET through binding at an allosteric site. I examined the impact of the protein mitoNEET on the allostery of GDH1 to determine if these two classes of regulators act with synergy or are independent of each other. The data suggest that mitoNEET has a “rescue” effect on the overall rate of the reaction but does not completely overcome any deactivation of the enzyme. Likewise, order of addition of mitoNEET and the ligand does not appear to influence the rate recovery. Trials where NAD+ was added after mitoNEET while pre-bound to GDH1 exhibited even higher “rescue” effects with some assay rates nearing the initial activated rate. Additionally, GDH1 may be able to metabolize the product of a mitoNEET catalyzed reaction. With this project, I have learned to experience life outside of my comfort zone and have added to work that will help further elucidate the interplay of these two proteins *in vitro*. This work may be furthered on by others in order to understand how this combination contributes to type-2 diabetes and will hopefully inspire others to work towards answering the world’s unknown questions.

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