Purification of Glycerol-3-Phosphate Dehydrogenase and Testing Its Sensitivity to Metformin

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Metformin is the most widely prescribed drug worldwide for treating diabetes and it is becoming a promising drug for the treatment of a multitude of conditions including metabolic syndrome, pre-diabetes, obesity, cancer and other diseases. However, the percent of patients that fail to respond to metformin therapy can reach as high as 35%. An unexplored contributor to variability in metformin efficacy is the human gut microbiome. The objective of this project is to test the hypothesis that bacterial glycerol-3-phosphate dehydrogenase (GlpD) or glycerol kinase (GlpK) are targets for metformin. Previously research showed that metformin inhibits bacterial growth on glycerol, a process that requires the function of both of these enzymes. Both GlpK and GlpD were purified by generating recombinant proteins that contained an affinity tag (polyhistidine-tag). Assays conducted to measure GlpD and GlpK activity in the presence of metformin showed that metformin has no effect on GlpK activity and increased GlpD activity. Further studies are required to determine how increased activity of GlpD would have a negative effect on bacterial growth on glycerol.

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