# Complex Combination of Diabetes and Covid-19: Role of Glycolytic Inhibitors in the Treatment

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The purpose of this project is to identify the role of glycolytic inhibitors as repurposed drugs for the cure of Covid-19 through virtual screening and test their efficacy against the inhibition of glycolytic enzymes, mainly hexokinase 2. Method: Reports show an upregulation of many glycolysis-associated genes in the lungs of Covid-19 patients and increased glycolysis is specific to SARS-Cov-2. Since, hexokinase 2 (HKII), a rate-limiting and first key enzyme of glycolysis are upregulated in SARS-CoV-2 infection, glycolytic inhibitors that have the potential to inhibit HKII may not only offer protection against the viral infection but also could prevent metabolic complications in diabetic patients. For this project, several glycolytic inhibitors (ligands) were docked against HKII protein and their binding affinities are evaluated. PyRX AutoDock vina tool was used to dock the compounds with HKII protein and their inhibitory property was determined based on their binding affinities. The hit compounds with high binding affinities for HKII protein were further evaluated in vitro hexokinase assay and covid-19 spike-ACE2 binding assay to evaluate their protection against viral infection. Results: The glycolytic inhibitors like 2-deoxyglucose, Benserazide, Pachymic acid displayed a high binding affinity for hexokinase II with high docking scores. When analyzed in hexokinase activity assay, these compounds showed strong inhibition of HK and spike2-ACE2 protein binding. Conclusion: Combined techniques of virtual screening and enzyme assays, helped to evaluate the efficacy of existing glycolytic inhibitors that could be repurposed and used as potential target drugs for Covid-19 as we explore treatment options for this ongoing pandemic.

**Awards Won:**