CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Mythri Ambatipudi

Project Number

35733

Project Title

Investigating the Power of AMPK Regulation on Cell Signaling Pathways to Treat Neurodegenerative Diseases and Cancer

Abstract

Objectives/Goals

Biological homeostasis imbalance has been identified as the root cause of neurodegenerative diseases, cancer and diabetes as it causes intracellular accumulation of abnormal proteins, chronic inflammation, mitochondrial dysfunction and hyperglycemia. The objective of my project is to investigate effects of AMPK regulation on homeostasis restoration and inhibition of Parkinson's (PD), ALS, Alzheimer's (AD), cancer and diabetes. The objective is to test the AMPK regulatory abilities of mitochondrial inhibitors, allosteric modulators, anthocyanins, hormones and nutrients by simulating diseases in model organisms with AMPK homologs and orthologs.

Methods/Materials

A.Thaliana containing SnRK1 (AMPK-ortholog) was used to simulate all diseases except cancer, for which S.Cerevisiae containing SNF1 (AMPK-homolog) was used. Spraying plants with concentrated H(2)O(2) oxidized SOD1, simulating mutant SOD1 in fALS. Spraying with Methylglyoxal (MG) and Glyoxal (GO) glycated DJ-1, simulating mutant DJ-1 in PD. Other diseases were simulated similarly. SnRK1 activation was confirmed with glycogen assay and compared by measuring Trichome (TL) and Root Hair lengths (RHL) using a homemade microscope. Lipid, starch and amino acid levels were measured through Sudan III, Iodine and Ninhydrin tests using a homemade spectrophotometer and Beer Lambert's Law.

Results

SNF1/SnRK1 activation alleviated all diseases, but inhibition benefited ALS. All regulators activated SNF1/SnRK1, but T6P inhibited. In AD simulation, leptin improved TL and RHL by 176.7% and 33.0% and reduced transmembrane protein cleaving by 75.6%. In PD, resveratrol improved TL (35.1% MG, 13.4% GO) and RHL (45.3% MG, 55.9% GO). In sALS, T6P improved TL (77.6% MSG, 53.3% Aspartame) and RHL (87.0% MSG, 48.1% Aspartame). In fALS, T6P improved TL and RHL by 57.6% and 9.5%. In cancer, goat's rue reduced colony growth and lipid content by 62.8% and 89.6%. In diabetes, goat's rue reduced starch and lipid content by 70.9% and 74.1%. Cell signaling pathways showing the effects of AMPK were derived.

Conclusions/Discussion

This project has identified AMPK's ideal regulatory mode (activation/inhibition), downstream substrates, cell signaling pathways and AMPK regulators for mitigating PD, ALS, AD, cancer and diabetes. Leptin is the best activator for AD, resveratrol for PD and goat's rue for cancer and diabetes. High calorie diet and inhibited AMPK may be beneficial for ALS.

Summary Statement

This project aims to identify AMPK regulation as a potential solution for restoring homeostasis and for alleviating PD, AD, ALS, Cancer and Diabetes symptoms.

Help Received

My science teacher, Mrs. Segal provided valuable guidance. My parents purchased all the materials and provided encouragement.

Preliminary