

Professor **David Charles Wright, PhD, MSc**

Place of employment and host institution: University of Guelph, Canada

Host principal investigator: Professor Jørgen Wojtaszewski, University of Copenhagen, Department of Nutrition, Exercise and Sports

Title of project: Targeting Skeletal Muscle AMPK to Offset the Acute Hyperglycemic Effects of Antipsychotic Drugs

Abstract

Second generation antipsychotic drugs (SGAs) are used in the management of schizophrenia and a growing number of other conditions such as anxiety, bi-polar disorder and depression. SGAs cause weight gain and increase the risk for developing type 2 diabetes and cardiovascular disease. An important negative side effect of SGAs is that they cause direct and rapid increases in blood glucose following each dose of drug. These repeated excursions in blood glucose increase the risk of developing type 2 diabetes. Increases in liver glucose production and decreases in insulin sensitivity and secretion are thought to be linked to the development of SGA-induced hyperglycemia. The purpose of the proposed Danish Diabetes Academy Visiting Professorship application is to determine if manipulating the activity of the energy sensing enzyme 5'AMP activated protein kinase (AMPK) in skeletal muscle, impacts SGA-induced disturbances in glucose homeostasis. This project will be done in collaboration, and in the laboratories of, Dr. Jorgen Wojtaszewski and Dr. Henriette Pilegaard, internationally recognized experts in skeletal muscle glucose metabolism. We hypothesize that reducing skeletal muscle AMPK activity will worsen acute SGA-induced metabolic dysfunction, while the activation of AMPK in skeletal muscle will attenuate the SGA-induced increases in blood glucose. To test these hypotheses we will utilize inducible, muscle specific, AMPK knockout mice and pharmacological activators of AMPK. In addition to the proposed experimental work, planning meetings will be held with clinical and basic researchers from Canada and Denmark to establish the framework of a clinical study examining the relationship between single nucleotide polymorphisms in AMPK subunits and the development of impaired glucose metabolism in those treated with SGAs. The proposed Visiting Professorship application has clear relevance to the etiology and treatment of type 2 diabetes and fulfills the mandate of the Danish Diabetes Academy of international, interdisciplinary and across sector collaboration.