Faculty of Health Sciences

2021 Australian Government Research Training Program Scholarships

Strategic Project Profile

PROJECT TITLE: Cellular studies on the antidiabetic potential of lupin protein fractions

FIELD OF RESEARCH CODE: 0601

PROJECT SYNOPSIS:

Australia is the world's largest lupin seed producer and it is one of our largest legume crops. However lupin is undervalued as sold as animal feed and thus does not attract a premium. Lupin has many advantages for the Australian agri-food system being an ideal rotation crop in the Western Australian wheat belt, where its nitrogen fixation assists with soil quality. Due to its current low value, lupin has lost some favour with farmers, therefore it is vital that value-added human uses are found. Lupins are high in protein and human trials, though limited, have indicated that one protein, γ-conglutin may help in control of blood glucose through hypoglycaemic effects.

This study will provide new knowledge on the efficacy of γ-conglutin for control of blood glucose using cellular and animal model studies.

The cellular mechanism(s) leading to the hypoglycaemic action of γ-conglutin will be investigated in non-pancreatic tissues firstly by evaluating the effect of γ-conglutin peptides and the intact protein on a broad screen of the cellular kinome and phosphatome, the regulation of which is highly dynamic and absolutely central to normal and pathological states. It is conceivable that the hypoglycaemic action of γ-conglutin may derive from multiple effects across several different pathways, which may in themselves be different or overlapping with insulin. Therefore, the broad screen approach will be more informative than targeting a few individual enzymes within the specific insulin-signalling repertoire. Thus, as a first but comprehensive step, signal transduction phosphopeptide mapping will be undertaken to track over 100 phosphoproteins and kinases as well as 29 protein phosphatases with the assistance of the Kinetworks™ signal transduction protein profiling approach. Kinases and phosphatases shown to be commonly or differentially affected by γ-conglutin can be further investigated and detailed following the initial screens. In brief, cell cultures comprising HepG2 hepatocytes, 3T3-L1 adipocytes and Human skeletal muscle myoblasts (HSMM CC-2580, Lonza, Basel, Switzerland) will be used with regard to measurement of proliferation, differentiation, insulin responsiveness and bioenergetics. These cell lines will be treated with either 1) vehicle, 2) insulin, 3) purified γ-conglutin (native and peptide fractions following in vitro digestion/bioavailability procedures), or 4) a combination of insulin and γ-conglutin. Lysates of the treated cells will then be immunoblotted against a bank of specific antibodies targeting specific protein kinases and protein phosphatases, which will be resolved by 2D electrophoresis. This approach provides qualitative and semi-quantitative analyses of the expression of a broad array of specific protein kinases and cell signalling proteins in typical insulin sensitive, liver, fat and muscle cells. The selection of kinases and phosphatases includes many of those known to be specific to insulin action, including those targeting glucose transport, but extends across a broad range of other biochemical pathways. These studies will be performed on protein fractions generated during the γ-conglutin extraction/purification process development that have been exposed to in vitro digestion conditions. These methods will be used to monitor and ensure the bioactivity of the final product and to substantiate its glucose modulating bioactivity. In addition lupin globulin fractions (α, β) isolated by our conventional techniques will be evaluated along with γ-conglutin analogues from L. albus, soya bean and chickpea prepared by our already established lab scale methods and will serve as comparisons for γ-conglutin bioactivity. Also we will investigate, as part of research student training, the use of γ-conglutin encapsulated in acid resistant microcapsules to reduce digestibility; an area that CI Johnson is actively researching.

The most promising lead fractions will be tested in animal models of diabetes and insulin resistance, where determination of supplement effects on insulin resistance, beta cell function, glucose regulation, body weight gain and lipid profiles will be determined.

The results of this study may open up opportunities for external funding from the Federal Government (e.g. NHMRC) and commercial enterprises for post-doctoral recruitment to perform human trials on the efficacy of γ-conglutin for tight control of blood glucose.

Demonstration of the efficacy of γ-conglutin for the control of blood glucose has potential for wide ranging impacts and benefits such as: Increased financial returns on the lupin crop for farmers, stimulating increased planting and follow-on environmental benefits; development of a highly profitable new Australian manufacturing opportunity for γ-conglutin-based nutraceuticals; increased quality-of-life of consumers with chronic high blood glucose levels.

FEASIBILITY AND RESOURCING – DESCRIPTION OF THE SUPPORT THIS PROJECT WILL RECEIVE:

ARC-Linkage project LP190100130; “Process development for purification of the bioactive legume protein γ-conglutin as a nutraceutical for maintaining healthy blood glucose levels”

2020- 2022

The new student will be trained by the postdoc employed on the ARC grant (3 year position)

THE SIGNIFICANCE OF THE PROJECT/ PROGRAM FOR THE ENROLLING SCHOOL OR INSTITUTION:

Lead research areas in the Faculty include: ‘Biosciences and Metabolic Health’. This research area includes the following areas of priority:

Biomolecular Interactions, Cancer, Immunology, Molecular Microbiology, Neuroscience and of relevance to this proposal, ‘Vascular and metabolic disorders’

Priority areas of research for the School of Pharmacy and Biomedical Sciences and CHIRI include ‘Vascular and metabolic disorders’

Collaboration with A/Prof Stuart Johnson (Food Technology, Faculty of Science and Engineering) and A/Prof Ranjeet Utikar (WA School of Mines: Minerals, Energy and Chemical Engineering) will ensure this cross disciplinary project is supervised by experts in the relevant areas of research involved at various levels in the project described here

Students must express interest in this scholarship opportunity by emailing the Project Lead listed below. Please provide a copy of your current curriculum vitae and detail your suitability to be involved in this strategic project.

PROJECT LEAD CONTACT:

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