The Glycation, Nutrition & Metabolism Laboratory focuses on dietary factors and disorders in mitochondrial energy generation pathways leading to the onset and/or progression of diabetes, its complications and of other chronic diseases.

Research Brief

It is becoming increasingly recognized that excess intake of processed foods is involved in the development of chronic diseases such as diabetes. Since the diet is comprised of a multitude of molecules capable of regulating diverse biological processes, it is plausible that certain constituents of the diet are responsible for the initiation of pathways of disease. A major goal of the Glycation, Nutrition & Metabolism Laboratory is to understand which constituents of the modern diet initiate pathological processes. This is achieved through laboratory based nutrition science using dietary intervention studies in rodent models and elucidating mechanisms at the biochemical and molecular level using a multidisciplinary approach.

Diabetes-associated kidney disease is the major cause of end-stage renal disease, requiring dialysis or kidney transplantation for survival. There is an urgent need to understand the factors that trigger kidney damage in diabetes, and also to develop new therapies that can be applied early in the disease to stop the progression to end stage renal disease. A key aim of the laboratory is to develop better treatment strategies for individuals with diabetic nephropathy by studying biochemical mechanisms in genetically modified mouse models and in cell culture. Pre-clinical discoveries are directly translated to human disease by investigating relevant markers of these pathways in human renal biopsies, plasma and urine from well characterised cohorts.

Methodologies

- Nutrient intervention studies
- Rodent models of diabetes, including pre-clinical testing of novel compounds and metabolic phenotyping
- Cell culture studies of human primary cultures and viral gene delivery
- Mitochondrial bioenergetics and cell signalling

Selected Publications


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Excess dietary intake of advanced glycation end products (AGEs) results in impaired pancreatic and renal function and disruption in the incretin signalling axis.

Rats fed a diet high in AGES for 24 weeks demonstrated (a) reduced glucose-stimulated insulin secretion from the pancreas during intravenous glucose tolerance testing, increased (b) urinary albumin excretion (AER) and (c) creatinine clearance, and (d) a decline in circulating GLP-1. Data are n=8 rats per group, *p<0.05. Coughlan MT et al., Diabetes 2011; Forbes JM…Coughlan MT J Nutr Biochem 2013.

Mitochondrial dysfunction in diabetic nephropathy coincides with onset of the renal phenotype

Mapping the development of diabetic nephropathy (DN) and mitochondrial function. Control and diabetic Sprague dawley rats were followed for 4, 8, 16 or 32 wk and the onset and progression of DN and kidney mitochondrial function was monitored (a) Albumin excretion rate (b) GSI (c) Mitochondrial H2O2 production (d) Mitochondrial oxygen consumption. Mean±SEM, n=5 rats/group *P<0.05 vs control.

High glucose promotes mitophagy

High glucose promotes mitophagy in human proximal tubule epithelial cells (PTEC). Mitochondria within human PTECs were labelled with mitotracker red (MTR; shown in red), hoechst nuclear dye (blue), and immunolabelled for LC3 (magenta) and PINK1 (green). Scale bar represents 10 µm.