International Conference on Pure and Applied Chemistry

Chemistry for a Clean and Healthy Planet

Symposium II
Unravelling the Mysteries of Diabetes: Challenges, Complications and Future Directions

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Mauritius
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Preface

On 21st December 2006 the General Assembly of the United Nations declared diabetes was as an international public health issue. This unprecedented announcement rendered diabetes as the only second disease after HIV/AIDS to attain this urgent status, and thus, was born World Diabetes Day. Diabetes is a chronic disease currently affecting over 400 million people worldwide. This disease epidemic has gigantic cost implication. For the first time, international governments have acknowledged that a non-infectious disease can pose a serious health threat to world health as do infectious diseases such as tuberculosis, malaria and HIV/AIDS.

The paradise island of Mauritius has not been spared from the grip of diabetes and over the past decades, its prevalence has risen to 21% in adults aged 20-74 years, constituting a significant social and economic burden for the island. According to data reported by the World Health Organisation in 2017, diabetes-related deaths in Mauritius reached 2,546, accounting for 28.73% of total deaths. When converted into age-adjusted death rate, diabetes accounts for 167.64 deaths per 100,000 of the population, ranking Mauritius as number 2 worldwide for diabetes-associated deaths.

Obesity is a major risk factor for diabetes and other severe pathologies including cardiovascular disease. Over 390,000 Mauritians are overweight, with the incidence of obesity reaching 17.6% in 2015. Such level of obesity, along with possible impact from the maternal environment in utero during gestational diabetes, have likely contributed to the escalating disease prevalence on the island. Timely diagnosis and effective interventions are key factors to prevent diabetes-related complications which are still poorly controlled.

This workshop aims to increase knowledge of diabetes from prevention to treatment. The lectures will focus on the clinical care recommended for impaired blood glucose control and discuss some of the main complications of diabetes such as foot ulcers, non-alcoholic fatty liver and cardiovascular diseases. In the second session, we will give an overview on current diabetes research, from its state of art to future perspectives, exploring the latest advances in drug development, surgical treatment of diabetes and clinical trials. The final part of the workshop will offer an opportunity to the audience to engage with all the speakers in an open discussion session.
Programme
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Abstracts
The Role of Gut Hormones in Health, Diabetes and Weight-Loss Surgery

R. D. Ramracheya*

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In health, blood glucose levels are regulated by the joint actions of insulin and glucagon secreted from the pancreatic beta- and alpha-cells, respectively. Thus, hyperglycaemia does not arise due to insulin deficiency alone. Dysregulation of glucagon secretion occurs in all forms of diabetes and elevated glucagon levels can aggravate hyperglycaemia. However, unlike insulin secretion, the role of gut peptides such as GLP-1 and PYY on glucose-mediated glucagon release remains uncharacterised. GLP-1 potently inhibits glucagon secretion in isolated mouse and donor human islets. However, the underlying mechanism is unclear as GLP-1 receptor (GLP1R) expression levels are negligible in the alpha-cells. In parallel, we have also shown that peptide tyrosine tyrosine (PYY) is capable of suppressing glucagon release although PYY receptors are restricted to beta-cells, suggesting paracrine interactions involving insulin or somatostatin secretion. The inhibition of dipeptidyl peptidase-IV (DPP-IV), the proteolytic enzyme responsible for the degradation of GLP-1 and PYY, constitutes an effective diabetes therapy, but the benefits have been attributed to the prolongation of active GLP-1 only. The existence of a DPP-IV system within the islets has been documented and we demonstrate that its inhibition does not affect islet-derived GLP-1 but influences the local regulation of pancreatic PYY and islet secretory function.

Bariatric surgery is being offered as a treatment option for type 2 diabetes (T2D) as it leads to rapid and durable remission of the disease. This phenomenon occurs independently of weight loss via a combination of factors, including changes in gastrointestinal peptides. GLP-1 has been recognized as a critical factor. However, we have shown that although diabetic GK rats subjected to Roux-en-Y gastric bypass (RYGB) do not have increased circulating GLP-1 levels, they exhibit marked beneficial metabolic effects. In this rat model, restoration of deranged islet secretory function upon RYGB is linked to marked elevations in PYY and persists in the presence of GLP-1R inhibition. Moreover, chronic treatment of diabetic rat and human islets with exogenous PYY improves insulin and glucagon release. These findings suggest that PYY is the humoral factor which mediates the anti-diabetic effects of RYGB and restoration of dysregulated insulin and glucagon secretion in diabetes. Since impairment of glucagon regulation constitutes a major fifty percent of the pathogenesis of diabetes, addressing both the insulin and glucagon defects would effectively ‘cure’ the disease. To date, very few anti-diabetic drug therapies target both hormonal impairments. This is well illustrated by the remarkable success rate of GLP-1-based therapies. However, the unpleasant side-effects associated with these treatments have hampered their suitability for many patients. Thus, the fact that PYY is also capable of restoring both defective insulin and glucagon release, is of significant clinical relevance. This lecture will first, explore the regulation of pancreatic hormone release by GLP-1 and PYY, and subsequently discuss their roles in glucose homeostasis, diabetes and bariatric surgery.
Diabetes Care Model: A Patient Centre-Cared Approach

I. Ramracheya*

Consultant Diabetologist, Mauritius

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Aim: 2015 non-communicable disease data of Mauritius has showed a diabetes prevalence in adults at 22.8%. Diabetes complication rate in Mauritius remains worrisome. Education, medication compliance, availability of new oral hypoglycaemic drugs, appropriate follow-up and advice are some of the factors that account for this high prevalence. A personal and patient-centered care approach is believed to help deal with some of these issues, often culminating in better patient management and resulting in an improvement of glycaemic control which eventually helps in curbing the rise in diabetes complications. This equates to better quality of life and promotes general wellbeing.

Methods: Applying similar level and quality of care as I implemented in the UK, including education about diabetes, role of lifestyle interventions and individualised targeted therapy, outcomes post my interventions were compared to initial baselines parameters.

Results: Outcomes since my intervention, have demonstrated a substantial improvement in terms of type and amount of food consumption, decrease in weight, better control of not only glycaemic control but also of blood pressure and lipid profile. Diabetes patients are also more proactive in terms of maintaining their glycaemic control to an ideal level and are managing their cardiovascular risk factors to an optimal level. HbA1c levels are much better, lipids profile is satisfactory and their blood pressure are well within the target range.

Conclusion: There certainly are rooms for major improvements in diabetes care. My aim is to continuously improve patient satisfaction, demonstrate efficiency, and implement a patient-centred approach.
Non-Alcoholic Fatty Liver Disease in Patients with Diabetes: Novel Clinical and Research Insights into a Global Epidemic and Major Public Health Burden

A. Moolla*

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Non-alcoholic fatty liver disease (NAFLD) is a spectrum ranging from simple steatosis to inflammation (steatohepatitis/NASH), fibrosis and cirrhosis. It is the hepatic manifestation of metabolic syndrome and is tightly associated with insulin resistance and type 2 diabetes (T2DM), which are the principal risk factors for disease progression, liver failure and cardiovascular complications. Indeed, up to 70% of patients with T2DM have evidence of NAFLD and the majority of deaths in patients with NAFLD are due to cardiovascular disease.

Diagnosis and risk stratification of patients with NAFLD is challenging as the gold standard diagnostic and staging tool is liver biopsy, an invasive and resource intensive procedure which is not without complication and morbidity. Furthermore, there are presently no specific licensed therapies for NAFLD. Management aims to optimise metabolic risk factors through weight loss, as well as through pharmacological interventions for diabetes and cardiovascular disease.

A multidisciplinary approach, involving hepatologists and diabetologists working alongside allied health professionals, is thus advocated for the management of NAFLD. Interventions include dietary and lifestyle advice as well as pharmacological interventions for cardiovascular disease and diabetes.

This presentation will firstly describe experiences and lessons learned from a UK programme raising awareness of NAFLD in patients with T2DM amongst Diabetes professionals. In addition, it will describe lessons learned from studying the impact of a large, tertiary centre, multidisciplinary metabolic hepatology clinic at the Oxford University Hospitals NHS Trust, Oxford, UK over a 3-year period. This includes detailed evaluation of significant improvements to liver, cardio-metabolic and related health parameters including surrogate markers of metabolic syndrome, liver disease and cardiovascular risk.

Secondly, this presentation will outline research investigating novel non-invasive tools to accurately diagnose and stage NAFLD to reduce the need for liver biopsy. Based on the knowledge that steroid (glucocorticoid) metabolism is differentially dysregulated across the disease spectrum of NAFLD, these changes have been measured using the non-invasive urinary steroid metabolome. Furthermore, unbiased computational machine learning analysis of the urinary steroid metabolome in patients with NAFLD has shown excellent potential both as a diagnostic and risk stratification biomarker tool with initial results being far superior to existing non-invasive markers for NAFLD. Finally, this presentation will describe how this tool along with other non-invasive techniques such as imaging have been incorporated into clinical trials under way at the University of Oxford to investigate potential novel therapies, such as GLP-1 agonists, for the treatment of NAFLD.
Advanced NAFLD is Common in Bariatric Surgical Patients, Suboptimally Staged by Non-Invasive NAFLD Biomarkers and Associated with Adverse Post-Operative Outcomes

N. Dempster¹, I. Gerogiannis¹, R. Franklin², A. Tandon¹, L. Rickers¹, C. Fletcher¹, G. Tan², R. Gillies¹, J. Cobbold³, W. Rosenberg⁴, B. Sgromo¹, L. Hodson², J. Tomlinson² and J. D. Ryan³*

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Background
Non-alcoholic fatty liver disease (NAFLD) represents the hepatic manifestation of the metabolic syndrome, and the most common cause of liver disease in Western society. Its prevalence and severity have been variably reported in individuals undergoing bariatric surgery.

Aims
To determine the prevalence and severity of NAFLD in individuals undergoing bariatric surgery. To assess the accuracy of existing non-invasive NAFLD biomarkers of liver fibrosis. To assess whether advanced NAFLD is associated with adverse post-operative outcomes.

Methods
284 patients were recruited. 120 underwent sleeve gastrectomy and 164 underwent Roux-en-Y Gastric Bypass surgery. Intra-operative liver biopsies were taken in a series of 176 consecutive patients and histologically graded using the NAFLD Activity Score and Kleiner classifications. Biomarkers of NAFLD (including Enhanced Liver Fibrosis (ELF) score and Fib-4 Score), metabolic health markers and clinical data were recorded just prior to surgery, 6 and 12 months post-operatively.

Results
Steatosis was present in 84.6%, NASH in 11.9%, advanced fibrosis in 23.1% and cirrhosis in 4.1% of biopsies. All biomarkers poorly identified advanced fibrosis (AUROC=0.60-0.69). ELF best predicted cirrhosis (AUROC=0.73), however NICE-recommended cut-off thresholds failed to predict 80% of cirrhosis cases. Metabolic health markers improved in the first post-operative year (including HbA1c 6.2% to 5.3% p<0.001). In contrast, NAFLD biomarkers worsened (including AST/ALT 0.9 to 1.2 p=0.01). Liver-related complication rate was 2.3%, occurring a median 342 days post-operatively. These complications were associated with intraoperative biopsy-proven cirrhosis (p=0.01).

Conclusion
Advanced NAFLD is common in patients undergoing bariatric surgery. Current non-invasive tests suboptimally predict histological NAFLD severity, highlighting the need for biomarkers with greater diagnostic accuracy. Moreover, cirrhosis occurs in 4% of patients and is associated with significant post-operative adverse outcomes.
An Insight into Type 2 Diabetes and Cardiovascular Disease

D. Sookur$^{1,2,3}$

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Type 2 diabetes poses the highest risk factor for the development of cardiovascular disease. This presentation will offer an insight into how type 2 diabetes can affect the heart, cardiovascular complications and the burden of coronary disease and stroke. The interaction with inter-related risk factors and public health implications will also be discussed. Finally, therapeutic strategies which improve cardiovascular parameters, in addition to optimal blood glucose regulation will be highlighted.
Optimising Diabetes Foot Care: Minimising Amputation Rate

I. Ramracheya*

Consultant Diabetologist, Mauritius

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Aim: According to Ministry of Health and Quality of Life health statistics report 2015, a total of 563 amputations were done in 2015. Out of these 90% were in diabetes population. Foot amputation, often done for foot ulcers, non-healing ulcers, gangrenous foot lesions, can at times be managed conservatively with good outcome. Diabetic foot amputations exert a huge cost burden on the state and it costs anywhere between Rs 50,000 to 100,000 to look after each individual. Diabetes foot care in Mauritius is still in its embryonic stage.

Methods: I present two patients who, despite being offered surgical amputations, were treated successfully with conservative medical care.

Conclusion: Early diagnosis and prompt management of diabetic foot disease, with advice on foot hygiene, foot wear and regular follow-up, in addition to diabetes control, helps save a foot and reduces the need for unnecessary foot amputations.
Pilot Studies in Diabetes: Unraveling the Role of Glucagon from Bench to Bedside

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Diabetes is a multi-hormonal disorder characterized by insufficient insulin secretion and aberrant glucagon secretion, with fasting hyperglucagonemia leading to increased rates of hepatic glucose production, and insufficient secretion at low glucose predisposing to hypoglycaemia episodes. Sulfonylureas used at low concentrations have been shown to partially restore appropriate glucose-regulated glucagon secretion in islets isolated from donors with type 2 diabetes. In this series of 3 pilot, translational clinical trials, we aim to clarify the role of aberrant glucagon secretion in patients with type 2 diabetes, type 1 diabetes, and a monogenic form of diabetes (HNF1α/4α MODY), and to investigate whether pharmacological manipulation of endogenous glucagon secretion can lead to clinical benefit.

In the “LEGEND-A” trial (Low-dosE GlibENclamide in Diabetes – part A), we demonstrated for the first time that very low doses (1/20th the normal starting dose) of the sulfonylurea glibenclamide could reduce fasting hyperglucagonaemia in patients with type 2 diabetes by 30%. In the on-going “Glucagon in MODY” study, we are investigating the impact low doses of gliclazide (which is the preferred treatment choice for these patients) have on glucagon secretion during an oral glucose tolerance test, and we will present our preliminary findings. Finally, we will present our protocol for the new “DEPTH” (Dapagliflozin during Exercise for the PrevenTion of Hypos) trial, which will examine whether exercise-induced hypoglycaemia episodes in patients with type 1 diabetes can be improved using a sodium-glucose cotransporter 2 inhibitor.
Calcitonin Gene-Related Peptide: A Neuropeptide of Many Talents in the Cardiovascular System

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Sensory nerves contain and release the highly potent vasodilator calcitonin gene-related peptide (CGRP) [1,2]. Whilst blocking the action of CGRP does not influence blood pressure regulation in healthy individuals, deletion or blockade of CGRP activity can worsen cardiovascular diseases in various animal models. Transient receptor potential ankyrin-1 (TRPA1) are non-selective cation channels that are widely expressed on sensory nerves, and using a murine model of local environmental cold exposure, we demonstrated that TRPA1 acts a primary vascular cold sensor. The cold-induced vascular response consists of vasoconstriction followed by vasodilatation [2]. This vasodilator phase is critical for protecting the cutaneous tissues against cold injury. We have now identified that TRPA1 activation is required to initiate the constrictor response as well as the subsequent dilator response, mediated by the sensory nerve-derived dilator CGRP and nitric oxide. This highlights the major involvement of the TRPA1-CGRP dilator pathway in the physiological reflex to local cold exposure, and provides impetus for further research in developing therapeutic agents aimed at protecting the skin in peripheral vascular disease and adverse climates.

However, the influence of the TRPA1-CGRP pathway is less easy to determine systemically in the cardiovascular system. Whilst TRPA1 deletion had no effect on blood pressure changes in hypertension, CGRP deletion led to a worsened hypertensive phenotype. Understanding the extent of the hypotensive properties of CGRP on cardiovascular protection will enable us to develop feasible ways to increase CGRP activity as a potential effective therapy for cardiovascular diseases [3]. Our most recent findings supplemented this hypothesis; using a novel long lasting CGRP analogue in collaboration with Novo Nordisk we demonstrated that chronic treatment with a CGRP agonist protects against hypertension, reducing blood pressure, vascular, renal and cardiac hypertrophy, fibrosis and oxidative stress. These protective effects are consistent with further experiments in a model of heart failure where the CGRP agonist preserves cardiac function, and prevents cardiac remodelling and limits damage associated with the progression of heart failure. Whilst the activity of TRPA1 to release CGRP from sensory nerves appear to be site and stimulus specific, the role of CGRP, more generally when released endogenously or administered exogenously appears to be pivotal in cardiovascular disease. Our current findings provide evidence for a potential novel therapeutic strategy, with the concept that CGRP agonists are anti-hypertensive and cardioprotective, with limited adverse effects when treatment starts early onset of hypertension or heart failure.

References
Long Chain Fatty Acid Oxidation is Required for Basal Glucagon Secretion

L. J. B. Briant\textsuperscript{1}, M. S. Dodd\textsuperscript{2}, M. V. Chibalina\textsuperscript{1}, P. Carmeliet\textsuperscript{3}, P. Rorsman\textsuperscript{1} and J. G. Knudsen\textsuperscript{1*}

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Type 2 diabetes is characterised by deficient insulin secretion and signalling. However, it is becoming apparent that dysregulated glucagon secretion from α-cells is an important part of the diabetic aetiology. Despite the centrality of glucagon in the regulation of glucose homeostasis, the mechanisms, which regulate glucagon secretion in conditions of low glucose, remain unclear. Contrary to β-cells, α-cells retain the ability to secrete glucagon in low or in the complete absence of glucose. Therefore, we suggest that an alternative substrate may underlie the ATP production necessary to maintain α-cell secretory function when glucose is low. We show here that incubation with the carnitine palmitoyltransferase 1 (CPT1) inhibitor etomoxir or siRNA-mediated knockdown of CPT1a reduces long chain fatty acid (LCFA)-oxidation and ATP production in mouse, human islets and α-TC1-6 cells, resulting in a 50% reduction in glucagon secretion at low glucose. In mice with knockout of CPT1a specifically in the α-cells, we observed similar reductions in glucagon secretion from isolated islets. Unexpectedly, the reduction of α-cell LCFA-oxidation in the CPT1a KO mice as well as human and mouse islets treated with etomoxir caused a depolarisation of α-cell membrane potential and reduction in action potential amplitude. These changes occurred without changes in \(K_{ATP}\) channel activity and were mimicked by the \(Na^+/K^+\) pump inhibitor ouabain, which likewise lowered glucagon secretion. A mathematical model of membrane potential dynamics in α-cells demonstrates that a reduction in ATP supply to the \(Na^+/K^+\) pump results in changes in glucagon secretion and electrical activity consistent with the CPT1a KO data. Together these findings suggest that LCFA oxidation in α-cells energises \(Na^+/K^+\) pump activity, thereby maintaining cellular membrane potential dynamics and glucagon secretion in low glucose conditions.
The Role of PYY in the Surgical Control of Diabetes

C. Guida¹*, S. D. Stephen¹, D. Chen², A. Clark¹, P. Rorsman¹, J. D. Ryan³ and R. D. Ramracheya¹

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Bariatric surgeries are weight loss interventions, which result in a spectacular and long-lasting reversal of type 2 diabetes (T2D) and associated metabolic benefits in man. Among other factors, gut hormone changes are known to play a critical role in the surgery-associated benefits. In particular, increased levels of the intestinal hormone PYY, mainly known as an appetite regulator, have been recently proved to be crucial in rodents by restoring pancreatic islet functions within days after Roux-en-Y gastric bypass (RYGB). In addition to enteroendocrine cells, PYY is also produced in pancreatic islets alluding to a potential direct effect of the peptide on islet restoration. We have investigated the relevance and modulation of locally produced PYY in pancreatic islets and its impact on glucose-regulated insulin release. Specifically, we have addressed the localisation of PYY and its receptors in isolated human islets in comparison to rodent islets and studied the regulation of PYY activity by the proteolytic enzyme DPP-IV which is also highly expressed in islets. Like chronic PYY treatment, inhibition of DPP-IV results in enhanced glucose-stimulated insulin secretion in isolated islets. DPP-IV inhibition is already a successful anti-diabetes therapy, but its efficacy has been attributed so far to the prolongation of the half-life of another gut hormone: GLP-1. Our results indicate that the beneficial effects of DPP-IV inhibition are mediated by the prolongation of intra-islet PYY activity and not GLP-1. Furthermore, we show that in diabetes plasma PYY levels are markedly reduced and demonstrate for the first time, that intra-islet PYY content is also significantly lower. This reduction in islet PYY content is completely restored after RYGB, consistent with the elevations of PYY in circulation post-surgery. Finally, we also demonstrate that PYY is a key humoral factor in the early recovery of impaired islet secretory function following weight-loss surgery in humans and that bile acids and the short chain fatty acid propionate, which are elevated in bariatric surgery, can trigger its release from enteroendocrine cells as well as human pancreatic islets. These results have clinical relevance for the development of new non-surgical therapies for T2D correction.
Biography
Dr Reshma Ramracheya; BSc (Hons.); PhD

Reshma is an islet physiologist with 18 years of experience in diabetes research and academic industry. She holds a PhD from King’s College London where she studied the regulation of insulin secretion in human islets of Langerhans. Reshma has been a Principal Investigator at the University of Oxford with a strong background in translational research in type 2 diabetes, obesity, weight-loss surgery, and cellular, animal and human research models. Her work explores the (dys)regulation of insulin and glucagon secretion and the role of gut hormones in health, obesity, diabetes and metabolic surgery (https://www.rdm.ox.ac.uk/about/our-divisions/oxford-centre-for-diabetes-endocrinology-and-metabolism/oxford-centre-for-diabetes-endocrinology-and-metabolism-research/pancreatic-islet-and-gut-hormones-in-health-diabetes-and-metabolic-surgery). The clinical relevance of Reshma’s work has been repeatedly endorsed by the media (Daily Express), diabetes organisations (Diabetes UK, Diabetes Times) and prestigious journals (Nature Reviews Endocrinology; Cell Reports). Reshma has published over 30 original papers in top journals, and delivered award-winning presentations at multiple conferences. She is an active member of various academic committees, editorial boards and reviewer for top journals as well as international grant bodies. Reshma’s distinguished career in the medical field is highlighted by the various prestigious awards she has won including the Diabetes UK RD Lawrence Fellowship, Senior Research Fellowship at Wolfson College, University Research Lecturer at the University of Oxford and Scientific Membership of the first UK Clinical Study Group for Prevention, targets & therapies for type 2 diabetes.
Dr. Jakob Knudsen; MSc; PhD

Dr. Knudsen is currently a Novo Nordisk Postdoctoral fellow at the university of Oxford. He holds an MSc in cellular biology and physiology from the University of Copenhagen where he also obtained his PhD in molecular physiology. Dr. Knudsen’s PhD dissertation focused on the role of skeletal muscle as an endocrine organ and its role in the regulation of metabolism in response to acute exercise and exercise training. He came to Oxford in September 2015 to work with Professor Patrik Rorsman at the Oxford Centre for Diabetes, Endocrinology & Metabolism. His current research is focused on hyperglycaemic effects in α-cells, α-cell metabolism, and how regulation of glucagon secretion contributes to the development of diabetes.
Dr Aisah Aubdool: BSc (Hons.); PhD

Dr Aisah Aubdool is currently a postdoctoral research associate in Professor Adrian Hobbs’ laboratory at the Heart Centre, William Harvey Research Institute, Queen Mary University of London where she is studying the role of endothelial C-type natriuretic peptide in angiogenesis and vascular remodelling. Prior to this, she graduated with a BSc (Hons) in Pharmacology and completed her PhD studies in Cardiovascular Medical Research under the mentorship of Professor Susan Brain at King’s College London (KCL). Dr Aubdool’s latest published research focuses on investigating the role of sensory nerve and the neuropeptide calcitonin gene-related peptide (CGRP) in cardiovascular disease, conducted at KCL in Professor Susan Brain’s laboratory. Dr Aubdool is an ambassador for the British Pharmacological Society and an editorial board member for Pharmacology Matters.
Dr Dharmendra Sookur; MBChB; MRCP (UK); MD
CONSULTANT INTERVENTIONAL CARDIOLOGIST (CANADA)
CARDIAC CT CORONARY ANGIOGRAPHY SPECIALIST (USA)

Dr Sookur is a board certified interventional cardiologist from the Ottawa Heart Institute in Canada (2007) and also a cardiac CT specialist with credentials from Virginia USA (2008). He graduated from the University of Manchester UK in 1994, obtained his MRCP (UK) in 1998 and trained in post graduate cardiology in the South Manchester University Hospitals in the UK and became a consultant cardiologist in 2007. Currently he is consultant interventional cardiologist working in Mauritius since 2008 and is also a part time lecturer at the University of Mauritius in cardiology.
Dr Iswaraj Ramracheya; MBBS MRCGP (UK) MRCP (UK)
MRCP (Endocrinology & Diabetes)
CCT (General Practice)
CCT (Internal Medicine) CCT (Endocrinology & Diabetes)

Dr Iswaraj Ramracheya is a Consultant Diabetologist and Endocrinologist with extensive experience in diabetes, hormonal disturbances, metabolic disorders and internal medicine. Iswaraj completed his medical training in Oxford at the renowned Oxford Centre for Diabetes, Endocrinology & Metabolism (OCDEM), and has worked as a Consultant Diabetologist & Endocrinologist in Edinburg and Liverpool. To ease the burden of diabetes and associated complications in Mauritius, Iswaraj has recently been appointed as the Advisor in Diabetology and Endocrinology at the Ministry of Health & Quality of Life. In his new endeavour, Iswaraj proposes to review and innovate the current framework, implement international guidelines and introduce cutting-edge medical therapies in the island. He is currently championing to introduce evidence-based prevention programmes to reverse diabetes and shift the paradigm of diabetes complications towards meaningful reductions in limb amputations, kidney failure, retinopathy and strokes. Iswaraj’s vision is to eradicate Mauritius from the list of top countries with the highest incidence of diabetes by preventing onset of prediabetes, more efficient diagnosis and refining diabetes care.
Dr John Ryan is an NIHR Academic Clinical Lecturer in Gastroenterology, with a strong interest in clinical and academic Hepatology. He did his Undergraduate and Postgraduate training along with a PhD on iron regulation in liver disease in Dublin, Ireland, with time spent at the Mayo Clinic in the US and the University of Heidelberg in Germany. John subsequently completed a Clinical Fellowship in Gastroenterology in Oxford. He has worked at the Royal Free Hospital in London for a year in Transplant Hepatology. John’s chief focus now is on NAFLD, the most common cause of liver disease in Western society. He has helped to set up and co-run a dedicated Metabolic Hepatology/NAFLD Clinic in Oxford with Dr Jeremy Cobbold, and initiated several translational collaborations in Oxford between the TGU and the Oxford Centre for Diabetes, Endocrinology and Metabolism (OCDEM), the Oxford Bariatric Service, and the Weatherall Institute of Molecular Medicine (WIMM), as well as outside Oxford, with the Institute of Food Research (IFR) in Norwich, the Food & Nutrition Unit at Plymouth University and the Centre of Liver Research, University of Birmingham. John is an active young investigator of the European Association for the Study of Liver (EASL), is involved in several clinical trials in Hepatology and serves as an expert advisor to the World Health Organisation.
Dr Ahmad Moolla; BSc (Hons), MBBS (Hons) MEd MRCP
NOVO NORDISK CLINICAL RESEARCH TRAINING FELLOW & DPHIL STUDENT

I am a Specialist Registrar and Clinical Research Fellow in Diabetes, Endocrinology and Metabolism. My undergraduate training was undertaken at Imperial College London from where I hold a BSc in Pharmacology and Toxicology and graduated in Clinical Medicine with Distinction. My postgraduate training includes the award of NIHR Academic Clinical Fellowships at Imperial College London and at Bart’s and the London School of Medicine to pursue research in diabetes, obesity and metabolism, alongside my clinical practice. I also have considerable experience in medical education and clinical leadership. I hold a Masters in Education (MEd) and between 2010-11 I worked on secondment at the Department of Health as a Clinical Advisor to the National Medical Director for the NHS in England where my portfolio included work on quality improvement and clinical leadership programmes within the NHS.

My research is focused on non-alcoholic fatty liver disease (NAFLD), which is rapidly becoming the commonest cause of chronic liver disease worldwide and affects up to 70% of patients with Type 2 Diabetes Mellitus (T2DM). Based at the Oxford Centre for Diabetes, Endocrinology and Metabolism (OCDEM) and the University of Oxford Centre for Clinical Magnetic Resonance (OCMR), I am investigating new treatments for NAFLD, including the utility of GLP-1 analogues as novel therapy, as well as investigating novel non-invasive techniques with which to stage and grade NAFLD and with which to assess treatment response.
I am a clinical researcher and specialty registrar in diabetes and endocrinology in Oxford, with a background in molecular biology. I have been working in the field of islet physiology since 2010 alongside my clinical training, and am currently completing a PhD at the University of Oxford. I am also part of the clinical islet transplantation team. My work focuses on investigating the hormone secretion profiles of islets in various forms of diabetes, with an emphasis on translating in vitro work into pilot clinical trials. I have recently completed a CT-IMP (clinical trial of investigational medicinal product) of low-dose sulfonylureas in patients with type 2 diabetes, which demonstrated improvement in fasting hyperglucagonemia. I am now extending this work to clinical studies in patients with MODY (maturity onset diabetes of the young) and type 1 diabetes. My aim is to better understand the effect aberrant glucagon secretion has on the pathophysiology of diabetes, and the impact various pharmacological interventions have on this system.
Dr Claudia Guida; MSc; PhD
NOVO NORDISK POSTDOCTORAL RESEARCH FELLOW

I obtained a Master degree in Biomolecular Sciences and Technologies in 2009 at the University of Pisa (Italy) and continued my master-thesis research at the European Institute of Oncology in Milan studying the molecular regulation of mitotic checkpoint. I moved to Heidelberg (Germany) in 2010 and completed my PhD study in molecular biology at the European Molecular Biology Laboratory (EMBL) and the Heidelberg University in October 2014 working on disorders of iron metabolism in the lab of Prof. Martina Muckenhuber and Prof. Matthias Hentze. Particularly, I investigated the relationship between the regulation of iron metabolism and innate immunity during acute inflammatory condition. In 2016 I was awarded a Novo Nordisk Postdoctoral Research Fellowship in the laboratories of Dr Reshma Ramracheya and Prof Patrik Rorsman at the Oxford Centre for Diabetes Endocrinology & Metabolism at the University of Oxford. My research focuses on type 2 diabetes and the role of gut hormones in its remission following bariatric surgery. The metabolic benefits of surgery are so compelling that it is now being considered as a therapeutic option for type 2 diabetes in obese patients. However the underlying physiological mechanisms are still unknown. Increased levels of the intestinal hormone PYY have been proven to be crucial in rodents by restoring islet secretory functions within days after Roux-en-Y gastric bypass. I am now investigating the role of PYY in diabetes and islet function including insulin, glucagon and somatostatin release. Targeting PYY or its action may provide a novel, non-surgical therapy for diabetes.