

**10<sup>th</sup> ANNUAL**

**BRIP**

BIOMEDICAL RESEARCH AND  
INNOVATION PLATFORM

**SYMPOSIUM**

**SCIENTIFIC  
PROGRAMME**

**19 & 20 OCTOBER 2020**





# Next-generation scientists addressing national health challenges

**10<sup>th</sup> Annual Biomedical Research and Innovation Platform Symposium**  
**Scientific Programme**  
**19 & 20 October 2020**



## Foreword

It is my honor to welcome delegates and participants to the 10<sup>th</sup> Biomedical Research and Innovation Platform Symposium to be held 19 – 20 October 2020.

In the spirit of the quote by S Finlayson “Life is not about waiting for the storm to pass; it’s about learning to dance in the rain”, it is the first time that the meeting will be virtual. Although we will not be able to welcome our colleagues and friends personally, it is our hope that the meeting will retain the same warm and meaningful interaction between the researchers and students.

A major goal of the Symposium is to offer young, aspiring scientists the opportunity to showcase their research within a constructive learning environment that encourages scientific exchange and the sharing of knowledge. We look forward to the opening remarks by the SAMRC President, Prof Glenda Gray, and the exciting program featuring invited speakers and post-graduate student presentations on a wide range of topics in medical science.

I would like to thank the Symposium organizing and program committee members for all the arrangements and their hard work. To the delegates, a big thank you for your support and participation. I hope your experience with our 10<sup>th</sup> Biomedical Research and Innovation Platform Symposium is a memorable one.

**Christo Muller**  
**Interim Director**  
**Biomedical Research and Innovation Platform**

# Organising committee



*Dr Babalwa Jack*



*Dr Stephanie Dias*



*Dr Nireslmi Chellan*



*Ms Oelfah Patel*



*Dr Lawrence Mabasa*



*Ms Noluxabiso Mangwana*



*Dr Sylvia Riedel-van Heerden*



*Prof Rabia Johnson*

# 10<sup>th</sup> Annual Biomedical Research and Innovation Platform Symposium

19-20 October, 2020

## Scientific Programme

### Day 1

8h30 – 8h45	Registration/log-in	
8h45 – 9h00	Welcome and Opening: Prof Christo JF Muller	
<b>SESSION 1</b>		
Session Chairs: Drs Tarryn Willmer & Stephanie Dias		
9h00 – 9h30	Key note speaker: Prof Megan Shaw, University of the Western Cape <b>The quest to find drugs for SARS-CoV-2</b>	
9h30 – 9h45	The expression and methylation of Slc27a3 is altered in visceral adipose tissue of high fat, high sugar fed male Wistar rats	Amscha Viraragavan (PhD)
9h45 – 10h00	Connecting the dots: Investigating ATM down-regulation as the potential link between adipose tissue and the heart in obesity and insulin resistance	Danelle Botha (MSc)
10h00 – 10h15	10-year audit of pregnancies affected by diabetic ketoacidosis at the Pretoria Academic Complex	Dr Ncamsile Maseko (MMed)
10h15 – 10h30	Mitochondrial function affects insulin signalling in skeletal muscle cells	Sinenhlanhla Mthembu (MSc)
10h30 – 10h45	Tea break	
<b>SESSION 2</b>		
Session Chairs: Drs Ebrahim Samodien & Yonela Ntamo		
10h45 – 11h15	Plenary speaker: Dr Phiwayinkosi Dlodla, SAMRC <b>Cardioprotective potential of phytochemicals and micronutrients against diabetic dyslipidemia.</b>	
11h15 – 11h30	Oxidative stress in the male reproductive system and the proteins that may cause it: a proteomic investigation into oxidative damage in obesity-induced male fertility	Bongekile Skosana (PhD)
11h30 – 11h45	Development of an individualized genetic drug therapy for diabetic and hypertensive patients in Cape Admixed Population	Zhytoeniesa Brophy (MSc)
11h45 – 12h00	Effect of LPS-induced inflammation on skeletal muscle differentiation and function	Nnini Obonye (MSc)
12h00 – 12h30	Discussion and closing for the day	

## Day 2

8h40 – 8h50	<b>Registration/log-in</b>	
8h50 – 9h00	<b>Welcome and Opening:</b> Prof Christo Muller	
<b>SESSION 3</b>		
<b>Session Chairs: Drs Pritika Ramharack &amp; Pieter Venter</b>		
9h00 – 9h30	<b>Key note speaker:</b> Prof Glenda Gray, SAMRC President and CEO <b>A journey in HIV research</b>	
9h30 – 9h45	Whole genome bisulfite sequencing in South Africa	Tracey Jooste (PhD)
9h45 – 10h00	An evaluation of the role of platelet activation in HIV-related cardiovascular diseases onset	Leanne Dominick (MSc)
10h00 – 10h15	Repurposing drugs that target the interaction between HPV and TBX3 to treat cervical cancer	Saif Khan (PhD)
10h15 – 10h30	Potential anti-cancer activity of the chloroform fraction of <i>Bidens pilosa</i> in MCF-7 breast cancer cell line	Olga Raboshakga (MSc)
10h30 – 10h45	Tea break	
<b>SESSION 4</b>		
<b>Session Chairs: Drs Kwazi Gabuza &amp; Babalwa Jack</b>		
10h45 – 11h15	<b>Plenary speaker:</b> Prof Oscar Lorenzo, Universidad Autónoma, Madrid, Spain <b>New prognostic biomarkers for cardiac dysfunction in diabetes</b>	
11h15 – 11h30	"It's only one tool, it's not the holy grail": Stakeholder perspectives on food label health information	Melvi Todd (PhD)
11h30 – 11h45	Investigating high-density lipoprotein (HDL) functionality, composition and subclass in HIV patients	Peter Hudson (MSc)
11h45 – 12h00	<i>Momordica balsamina</i> induces pro-apoptotic activities associated with cell cycle arrest in HT-29 colon cancer cells	Kholofelo Malemela (PhD)
12h00 – 12h30	<b>Discussion</b>	
12h30 – 12h45	<b>Prize giving and closing</b>	

Venue: Microsoft Teams



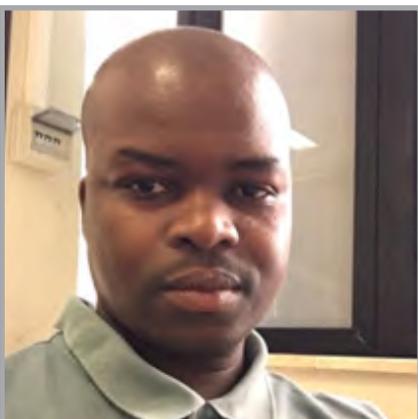
## Guest speaker: Prof Glenda Elisabeth Gray,

**MBBCH, FCPaedS (SA), DSc (honoris causa SFU), DSc (honoris causa SUN), LL.D (Rhodes). President and CEO of the South African Medical Research Council, Cape Town, South Africa**  
**Email: [Glenda.Gray@mrc.ac.za](mailto:Glenda.Gray@mrc.ac.za)**

CEO and President of the South African Medical Research Council (SAMRC), Research Professor of Paediatrics, University of the Witwatersrand and Professor in the Vaccine and Infectious Disease Division, Fred Hutch Cancer Research

Center is the Co-PI of the HIV Vaccine Trails Network (HVTN) and Director of HVTN Africa Programs. Gray is a NRF A-rated scientist, qualified paediatrician and co-founder of the internationally recognised Perinatal HIV Research Unit in Soweto, South Africa and is the CTU PI of the Soweto/PHRU site at the Chris Hani Baragwanath Hospital. Gray became involved in HIV Vaccine research in 2000, and led the first clinical trials involving HIV vaccines in the Republic of South Africa (RSA). She was the Protocol Chair for the first phase 2B HIV vaccine trial to be conducted in sub-Saharan Africa, and was in charge of the early clinical development of South Africa's first two candidate DNA and MVA HIV vaccines, which have been tested in both the USA and RSA under FDA and MCC regulations. She was the International Vice Chair for Vaccines for the NIH-funded IMPAACT network until 2010. She has published extensively in the field of HIV. Glenda's global profile: She is a member of the Academy of Science in South Africa, and chaired their Standing Committee on Health and has served on a number of expert panels for the Academy in the field of infant health, nutrition and HIV. She was elected as a foreign associate into the US National Academy of Medicine and served on their Board of Global Health. She is also a Fellow of the American Academy of Microbiology. She is a member of the African Academy of Science and The World Academy of Science (TWAS). She is a member of the GARDP Board, and the past Chair of the Global alliance for Chronic Diseases.

She received South Africa's highest honour - the Order of Mapungubwe - for her pioneering research in PMTCT. Other prestigious accolades include the Nelson Mandela Health and Human Rights Award for her significant contributions in the field of mother-to-child transmission of HIV. Selected as one of Time's 100 Most Influential People in the World, and Forbes top 50 most influential women in Africa, Gray is a recognised leader in her field.



## Guest Speaker: Dr Phwayinkosi V. Dladla,

**SAMRC, Cape Town,**  
**Email: [Phwayinkosi.Dladla@mrc.ac.za](mailto:Phwayinkosi.Dladla@mrc.ac.za)**

Dr Phwayinkosi Dladla is a Specialist Scientist with the South African Medical Research Council (SAMRC), holding an MSc in Biochemistry (University of Zululand), and a PhD in Medical Physiology (Stellenbosch University). His areas of expertise are based on understanding the pathophysiological mechanisms implicated in the development of metabolic diseases, with the special focus

on type 2 diabetes. Within this pathology of pandemic relevance, metabolic complications such as cardiovascular diseases represent a major health concern linked with the high morbidity and mortality rate. In this respect Dr Dladla has shown a keen interest to uncover novel therapeutics, especially dietary supplements or plant derived compounds

to protect against metabolic complications or to enhance and limit side effects of available pharmacological treatments. In fact, Dr Dłudla is currently completing his Postdoctoral Fellowship with Polytechnic University of Marche (Italy), where he is training in advanced laboratory techniques relating to nutritional biochemistry, especially the impact of dietary compounds on cholesterol metabolism, low-density lipoprotein oxidation and coenzyme Q10 biosynthesis. These basic science approaches have become important for application in the development of functional food and functional feed for human and animal wellbeing.



## Guest Speaker: Prof Megan Shaw,

**University of the Western Cape, Bellville, South Africa**  
**Email: [mshaw@uwc.ac.za](mailto:mshaw@uwc.ac.za)**

Prof Shaw studied Biochemistry and Microbiology at the University of Cape Town and received her Ph.D. in Virology from the University of Glasgow, Scotland in 2002. She then joined Dr. Peter Palese's laboratory at Mount Sinai School of Medicine in New York, USA as a postdoctoral fellow where she specialized in influenza viruses, and viral innate immune signaling. Prof Shaw became a faculty member at Mount Sinai in 2008 and started an independent laboratory with a focus on virus-host interactions and antiviral drug discovery. In 2019 she returned to South Africa and joined the Dept. of Medical Biosciences as an Associate Professor at the University of the Western Cape. Prof Shaw has authored numerous publications in the virology field, including the Orthomyxoviridae chapter in two editions of Fields Virology, and is co-inventor on 5 patent applications. She has served as PI and co-investigator on several grants from the National Institutes of Health in the USA and has been on the Editorial Board of the Journal of Virology since 2005.



## Guest Speaker: Prof Oscar Lorenzo,

**Universidad Autónoma, Madrid**  
**Email: [OLorenzo@fjd.es](mailto:OLorenzo@fjd.es)**

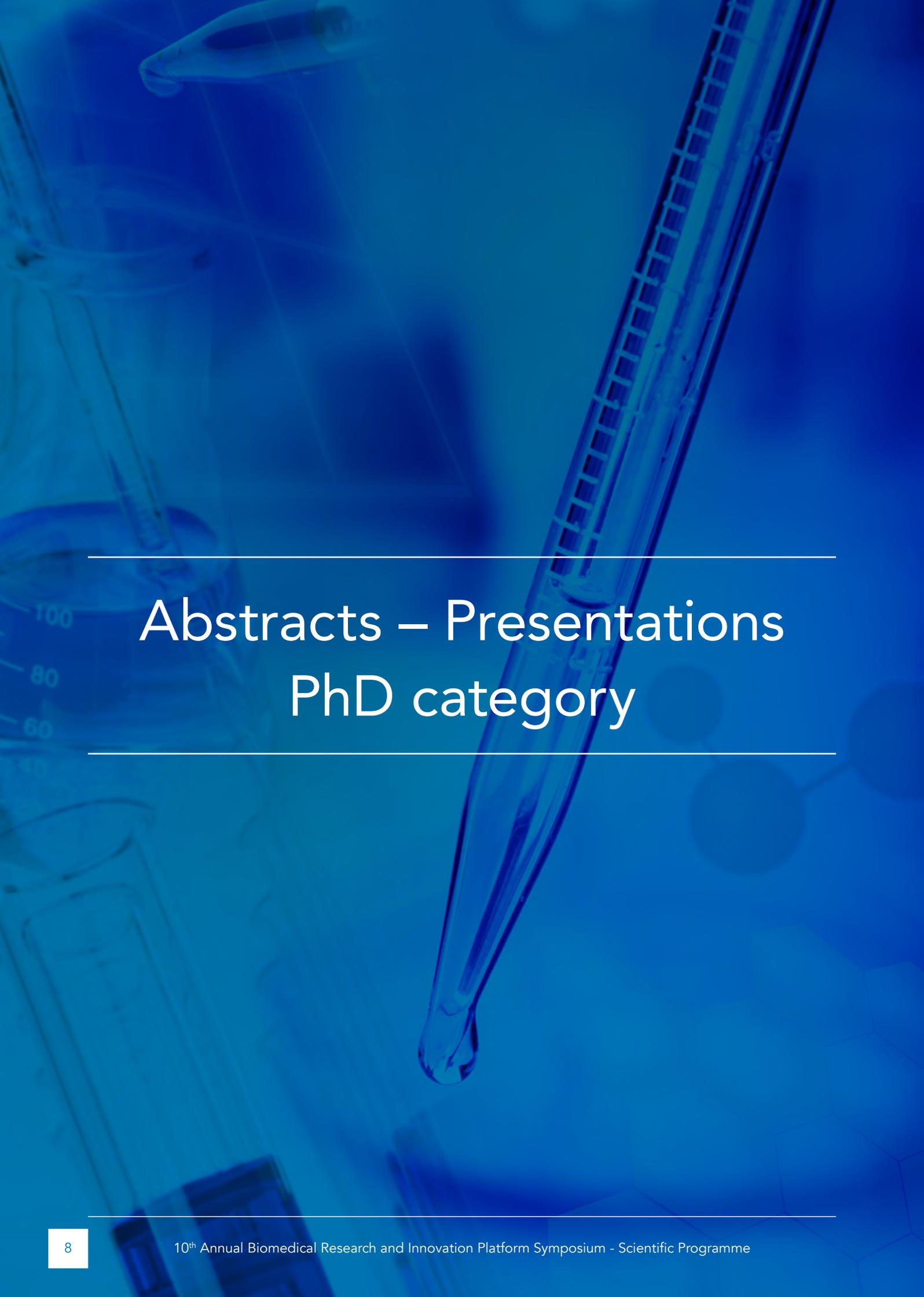
Prof. Oscar Lorenzo is a doctor in molecular biology at Universidad Autónoma, Madrid. His group is interested in studying cardiomyopathies either in human or in experimental models. In particular, they analyze the molecular mechanisms associated with diabetic cardiomyopathy (DCM) by studying different mediators of major pathways. Some of these mediators could work as potential targets against DCM either in type-I or type-II diabetes (e.g. incretin stimulators, SGLT2 inhibitors). In addition, they are interested in searching stable and soluble molecules in plasma able to predict or diagnose the cardiac damage associated to diabetes, acting as biomarkers.

# Biomedical Research & Innovation Platform Symposium 2020

19 & 20 October 2020

## Poster Presenters

Poster number	Name	Surname	Degree	Institution
1	Victoria	Damerell	PhD	UCT
2	Claire	Bellis	MSc	UCT
3	Thendo	Mabuda	MSc	BRIP/SU
4	Nonhlakanipho	Sangweni	PhD	BRIP/SU
5	Melisse	Erasmus	PhD	BRIP/SU
6	Sihle	Mabhida	PhD	BRIP/UWC
7	Yoonus	Abrahams	PhD	BRIP/SU
8	Asive	Myataza	PhD	BRIP/SU
9	Tesleem	Babalola	PhD	UKZN
10	Amberly	Oosthuizen	BSc Hons	SU/BRIP
11	Anri	Kotze	BSc Hons	SU/BRIP
12	Samukelisiwe	Shabalala	PhD	BRIP/UZ



---

# Abstracts – Presentations

## PhD category

---

# The expression and methylation of *Slc27a3* is altered in visceral adipose tissue of high fat, high sugar fed male Wistar rats

Amsha Viraragavan<sup>a,c</sup>, Tarryn Willmer<sup>a,b</sup>, Oelfah Patel<sup>a</sup>, Albertus Basson<sup>c</sup>, Rabia Johnson<sup>a,b</sup>  
and Carmen Pheiffer<sup>a,b</sup>

<sup>a</sup>Biomedical Research and Innovation Platform, South African Medical Research Council, Tygerberg, 7505, South Africa;

<sup>b</sup>Division of Medical Physiology, Faculty of Health Sciences, Stellenbosch University, Tygerberg, 7505, South Africa

<sup>c</sup>Department of Biochemistry and Microbiology, Faculty of Science and Agriculture, University of Zululand, Kwa-Dlangezwa 3886, South Africa

[amsha.viraragavan@mrc.ac.za](mailto:amsha.viraragavan@mrc.ac.za)

## BACKGROUND:

Accumulating evidence implicate fat distribution rather than fat mass in metabolic risk. Increased visceral adipose tissue (VAT) is associated with metabolic dysfunction, while subcutaneous adipose tissue (SAT) is considered protective. The molecular mechanisms that underlie these depot differences are not yet fully elucidated.

## OBJECTIVES:

To investigate gene expression and DNA methylation differences in VAT and SAT of male Wistar rats fed a high fat, high sugar (HFHS) or control diet.

## METHODS:

Male Wistar rats were fed a HFHS or a standard rodent diet (control) for three months, where after the expression of fatty acid metabolism genes in VAT and SAT was analysed by quantitative real time PCR using arrays and Taqman probes. Global and gene-specific DNA methylation was quantified using the Imprint® Methylated DNA Quantification Kit and pyrosequencing, respectively.

## RESULTS:

Body weight, retroperitoneal fat mass, insulin resistance, leptin and triglyceride concentrations and adipocyte hypertrophy were higher in rats fed the HFHS diet compared to control rats. The expression of solute carrier family 27 member 3 (*Slc27a3*), a long chain fatty acid transporter was 8.7-fold ( $p=0.02$ ) higher in VAT and 5.2-fold ( $p=0.04$ ) lower in SAT of HFHS-fed rats compared to controls. Taqman probes confirmed the increased expression of *Slc27a3*, while pyrosequencing showed 1.3-fold ( $p=0.04$ ) lower methylation in exon 1 of *Slc27a3* in VAT of HFHS-fed rats compared to controls. No differences were observed in SAT. The HFHS diet decreased global methylation in both VAT and SAT, although no depot differences observed.

## CONCLUSION:

Dysregulated fatty acid influx in VAT, in response to a HFHS diet, provides insight into the mechanisms that underlie depot-differences in adipose tissue expansion during obesity and metabolic disease. Therapeutic strategies toward reduction of capacity for fatty acid uptake in VAT, possibly through targeting *Slc27a3*, may have beneficial effects for the treatment of obesity and associated metabolic diseases.

# Oxidative stress in the male reproductive system and the proteins that may cause it: a proteomic investigation into oxidative damage in obesity-induced male fertility

Skosana, BT<sup>1</sup>, Tabb, D.<sup>2-6</sup>, Wang, X.<sup>7</sup>, Webster, I.<sup>1</sup>, Lochner, A.<sup>1</sup>, van der Horst, G.<sup>1,8</sup>, Aboua, Y.G.<sup>9</sup>, du Plessis, S.S.<sup>10</sup>

<sup>1</sup>Division of Medical Physiology, Department of Biomedical Sciences, Stellenbosch University, Cape Town, South Africa; <sup>2</sup>Division of Molecular Biology and Human Genetics, Department of Biomedical Sciences, Stellenbosch University, Cape Town, South Africa; <sup>3</sup>DST–NRF Centre of Excellence for Biomedical Tuberculosis Research, Stellenbosch University, Cape Town, South Africa; <sup>4</sup>South African Medical Research Council Centre for Tuberculosis Research, Stellenbosch University, Cape Town, South Africa; <sup>5</sup>Bioinformatics Unit, South African Tuberculosis Bioinformatics Initiative, Stellenbosch University, Cape Town, South Africa; <sup>6</sup>Centre for Bioinformatics and Computational Biology, Stellenbosch University, Stellenbosch, South Africa; <sup>7</sup>Division of Statistics and Data Science, Department of Mathematical Sciences, University of Cincinnati, Cincinnati, Ohio 45221, USA; <sup>8</sup>Department of Medical Bioscience, University of the Western Cape, Bellville, South Africa; <sup>9</sup>Faculty of Health and Applied Sciences, Department of Health Sciences, Namibia University of Science and Technology, Windhoek, Namibia; <sup>10</sup>College of Medicine, Mohammed Bin Rashid University of Medicine and Health Sciences, Dubai, UAE

[bts@sun.ac.za](mailto:bts@sun.ac.za)

## BACKGROUND:

Obesity is associated with oxidative stress (OS) as the expansion of adipocytes increases free radical production. OS has been implicated in male infertility by acting as a central mechanism through which many damage-inducing processes can occur. As many complexities regarding obesity-induced OS and its effects on male fertility are still unanswered, molecular analyses are required to allow further insights.

## OBJECTIVES:

To analyze the proteins involved in obesity-induced oxidative stress, an animal model of chronic diet-induced obesity was established, and antioxidant capacity and protein profiles were investigated.

## METHODS:

Forty male Wistar rats were randomly assigned to control (standard rat chow) or diet-induced obesity (DIO) (chow supplemented with saturated fat and sucrose) groups. At 60 weeks, animals were anesthetized and tissues were collected (testis, epididymis, sperm). The enzyme activity of catalase (CAT) and superoxide dismutase (SOD), and the quantitation of reduced glutathione (GSH) and lipid peroxidation (LPO) were carried out on testicular and epididymal tissues to determine antioxidant and OS status. Proteomic analysis of rat testis, epididymis and sperm was carried out using Liquid Chromatography Mass Spectrometry (LC-MS/MS) to assess changes in protein profiles between the control and DIO animals.

## RESULTS:

CAT activity was lower in the testes of DIO animals ( $p = 0.048$ ) but unchanged in the epididymis ( $p = 0.402$ ). SOD activity was significantly lower in the DIO testes ( $p = 0.014$ ) but not altered in the epididymides ( $p = 0.871$ ) compared to controls. LPO was not significantly altered in the testes ( $p = 0.8778$ ) and epididymides ( $p = 0.4743$ ). Total [GSH] in DIO testes was lower than in the controls ( $p = 0.009$ ). Epididymal (246) and sperm (61) proteins were identified; no testicular proteins were significantly expressed.

## CONCLUSION:

Proteomic analysis of the reproductive tissue has implicated cellular respiration, metabolism and inflammation as the primary sources of free radical production in obese males.

# Whole genome bisulfite sequencing in South Africa

Tracey Jooste<sup>a,b</sup>, Brigitte Glanzmann<sup>c,d</sup>, Erna Marais<sup>a</sup>, Lawrence Mabasa<sup>b</sup>, Rabia Johnson<sup>a,b</sup> and Craig Kinnear<sup>c,d</sup>

<sup>a</sup>Division of Medical Physiology, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg, Cape Town, South Africa.

<sup>b</sup>Biomedical Research and Innovation Platform (BRIP), South African Medical Research Council (SAMRC), Tygerberg, Cape Town, South Africa.

<sup>c</sup>Genomics Centre, South African Medical Research Council, Tygerberg, Cape Town, South Africa.

<sup>d</sup>DSI-NRF Centre of Excellence for Biomedical Tuberculosis Research, SAMRC Centre for Tuberculosis Research, Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa.

[tracey.jooste@mrc.ac.za](mailto:tracey.jooste@mrc.ac.za)

## BACKGROUND:

Cardiac dysfunction is the leading cause of death, claiming more lives annually than all the different forms of cancer combined. Several mechanisms have been implicated in the pathogenesis of diet-induced cardiovascular disease (CVD) and recently, increasing evidence suggests that dysregulation of the epigenome may play an important role. The advent and evolution of next generation sequencing has considerably impacted genomic research. However, until recently, researchers were unable to access platforms capable of massive parallel sequencing on a genome-wide scale, locally.

## OBJECTIVES:

In this study, we utilised a genome-wide sequencing approach to investigate DNA methylation associated with diet-induced CVD in rodents, for the first time in South Africa.

## METHODS:

To this end, male Wistar rats were maintained on either a standard maintenance, or a high fat, high sugar (HFHS) obesogenic diet for a period of 9 months. DNA methylation was evaluated by employing whole genome bisulfite sequencing (WGBS) of a total of 15 libraries, each pooled with two rats on the same diet.

## RESULTS:

Differences in physiological parameters as well as the biochemical assays performed coincided with the occurrence of a disease phenotype in the experimental group. Data sets obtained from WGBS demonstrated high fragment size distribution and efficient C to T conversion rates, reproducible between libraries generated from replicates within the same group. Furthermore, this study demonstrates that the data obtained is of high quality, with an average sequencing depth of > 10X per sample, and that the output is comparable to data generated internationally on a similar platform.

## CONCLUSION:

The reversible nature of epigenetic phenomenon's allows for the modification of the transcription of critical genes associated with the development of diet-induced CVD. Therefore, profiling DNA methylation on a genome wide scale, not only aids in the elucidation of the pathophysiology of CVD, but also the identification of promising new targets for epigenetic therapies.

# Repurposing drugs that target the interaction between HPV and TBX3 to treat cervical cancer

Khan, SF.<sup>a</sup>, Bleloch, J.<sup>a</sup>, Lu, S.<sup>b</sup>, Ramburan, A.<sup>c</sup>, Goding, G.<sup>b</sup>, Prince, S.<sup>a</sup>

<sup>a</sup>Division of Cell Biology, Department of Human Biology, University of Cape Town

<sup>b</sup>Ludwig Institute for Cancer Research, Nuffield Department of Medicine, University of Oxford

<sup>c</sup>Division of Anatomical Pathology, Faculty of Health Sciences, University of Cape Town

[khnsai002@myuct.ac.za](mailto:khnsai002@myuct.ac.za)

## BACKGROUND:

Cervical cancer (CC) is the leading cause of cancer related deaths amongst South African women and it is essential to identify effective and cheap therapies to treat it. Human Papillomavirus (HPV) is the causative agent of CC and its oncoproteins, E6/E7, cooperate with host factors to induce and maintain CC. A potential approach to facilitate rapid and cost-effective drug development is to identify and target these host factors with commercially available non-cancer drugs. In this regard, TBX3 is a key driver of several cancers and druggable target, but little is known about its status and role(s) in CC. Furthermore, we have identified commercially available drugs, niclosamide, piroctone olamine and pyrvinium pamoate (hit drugs) that target TBX3 and exhibit anti-cancer activity.

## OBJECTIVES:

Investigate (1) the status of TBX3 in CC; (2) the oncogenic role(s) of TBX3 in HPV+ and HPV- CC (3) if hit drugs target TBX3 and exhibit anti-CC activity.

## METHODS:

TBX3 status was determined in HPV+ CC patient tissues using immunohistochemistry. TBX3 was depleted by siRNA in HPV+ (HeLa and CaSki) and HPV- (C33A) CC cells and the impact on proliferation (growth curves) and migration (scratch assay) assessed. CC cells were treated with hit drugs and the impact on TBX3 levels (western blotting and immunofluorescence), CC cell survival (MTT and clonogenic assays), migration, cell cycle profile (FACS), senescence and spheroid formation were investigated.

## RESULTS:

This study reveals (1) TBX3 is upregulated and maintained in advanced stages of HPV+ CC; (2) TBX3 promotes HPV+ CC proliferation and migration and not in HPV- CC; (3) hit drugs reduced TBX3 levels, inhibited CC cell survival, migration and spheroid formation, induced cell cycle arrests and senescence.

## CONCLUSION:

Results from this study suggest that TBX3 cooperates with E6/E7 to promote HPV+ CC proliferation and migration and reveal 3 effective and cheap drugs to potentially treat CC.

# “It's only one tool, it's not the holy grail”: Stakeholder perspectives on food label health information

Melvi Todd<sup>a</sup>, Timothy Guetterman<sup>b</sup>, Elizabeth Joubert<sup>a,c</sup>

<sup>a</sup>Department of Food Science, Stellenbosch University, Stellenbosch, South Africa

<sup>b</sup>Department of Family Medicine, University of Michigan, Ann Arbor, Michigan, United States of America

<sup>c</sup>Plant Bioactives Group, Post-harvest and Agro-processing Technologies, Agricultural Research Council, Infruitec-Nietvoorbij, Stellenbosch, South Africa

[melvitodd19@gmail.com](mailto:melvitodd19@gmail.com)

## **BACKGROUND:**

Non-communicable diseases (NCDs) that account for 71% of deaths globally show little respect for gender, age or even income. Food labels are one tool that can assist consumers in making healthy food choices, potentially contributing to relief of the NCD burden.

## **OBJECTIVES:**

This article seeks to explore multi-stakeholder perspectives on the communication of health information on food labels, thereby providing insights for policymakers to consider.

## **METHODS:**

In-depth interviews were conducted with 31 expert and 12 consumer stakeholders in a diverse, developing country context on their views about the communication of health information on food product labels.

## **RESULTS:**

Five themes were identified based on inductive analysis: (i) physical barriers to label use, (ii) contextual and personal variables influencing engagement with label information (iii) messaging preferences (iv) stakeholder complexities and (v) ambassadors to change.

## **CONCLUSION:**

These findings provide practical insights for consideration by policymakers and shed new light on the need for a comprehensive approach to the reduction of NCDs. There is thus a call for cutting across different sectors and for support by a broad grouping of stakeholders to achieve sustainable change in public health outcomes. Ambassadors to change were shown to be a positive force for transformation that could be harnessed to support policymakers in the achievement of these positive health outcomes.

# Momordica balsamina induces pro-apoptotic activities associated with cell cycle arrest in HT-29 colon cancer cells

Kholofelo Malemela<sup>a,b</sup>, Sylvia Riedel-van Heerden<sup>b</sup>, Pieter Venter<sup>b</sup> and Vusi Mbazima<sup>a</sup>

<sup>a</sup>Department of Biochemistry, Microbiology and Biotechnology, Faculty of Science and Agriculture, University of Limpopo, Private Bag x 1106, Sovenga, 0727

<sup>b</sup>Biomedical Research and Innovation Platform, SAMRC, PO Box 19070, 7505, Tygerberg

[malemelakhlofelo@gmail.com](mailto:malemelakhlofelo@gmail.com)

## BACKGROUND:

*Momordica balsamina* is a plant rich in phytochemicals with a wide spectrum of medicinal values. *Momordica* species possess *in-vitro* antitumor activities and as such, could provide a promising alternative or adjuvant treatment option to chronic illnesses such as cancer for which conventional medicine does not yet provide a cure.

## OBJECTIVES:

To characterise the *M. balsamina* methanol extract (MBME) using reversed-phase liquid chromatography (RP-LC) coupled to ion mobility (IM) and high-resolution mass spectrometry (HRMS) and to investigate its potential anticancer activity *in-vitro* as well as its effect on selected major drug metabolising enzymes.

## METHODS:

RP-LC-IM-HRMS was used to characterise the chemical composition of the plant extract. The effect of MBME and 5-Fluorouracil, a well-established chemotherapeutic drug, on HT-29 colon cancer cell and normal C2C12 cell viability was assessed using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium-bromide (MTT) assay at 24 and 72 hours. Cell death was assessed by microscopy using the 5,5',6,6'-tetrachloro-1,1',3,3'-tetraethylbenzimidazolylcarbocyanine iodide (JC-1) dye and further quantified by flow cytometry using Annexin-V/PI in HT-29 cells. Cell cycle distribution was assessed by flow cytometry and the effect on drug metabolising enzymes, (CYP)1A2, 2A6, 2C8 and 2C9 assessed using CYP-P450 screening kits.

## RESULTS:

RP-LC-IM-HRMS analysis showed presence of eleven molecular species; three flavonol glycosides, five cucurbitane-type triterpenoid aglycones and three glycosidic cucurbitane-type triterpenoids. MBME significantly reduced viability of HT-29 cells (IC<sub>50</sub> 267 µg/ml) without significantly reducing C2C12 viability after 24 hours. 5-Fluorouracil induced cell death (IC<sub>50</sub> 3.2 µg/ml) at 72 hours of treatment. MBME and 5-Fluorouracil induced mitochondrial depolarisation of HT-29 cells and apoptosis as shown by JC-1 and Annexin-V/PI assays after 24 hours. MBME induced subG0/G1 cell cycle arrest and significantly inhibited activity of CYP2C8 and CYP2C9 with IC<sub>50</sub>s of 14 µg/ml and 26 µg/ml, respectively.

## CONCLUSION:

Due to its pro-apoptotic and cell cycle arrest activities, the MBME shows potential as a candidate for further drug development. However, its interaction with CYP-P450 enzymes requires further exploration.



---

# Abstracts – Presentations

## MSc category

---

# Connecting the dots: Investigating atm down-regulation as the potential link between adipose tissue and the heart in obesity and insulin resistance

Dan lle Botha<sup>a</sup>, Marguerite Blignaut<sup>a</sup>, Han l Sadie-van Gijzen<sup>a</sup>, Barbara Huisamen<sup>a</sup>

<sup>a</sup>Centre for Cardio-metabolic Research in Africa (CARMA), Division of Medical Physiology, Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Stellenbosch University, South Africa

[19198639@sun.ac.za](mailto:19198639@sun.ac.za)

## BACKGROUND:

Adipose tissue communicates with peripheral organs through endocrine secretions. Ataxia-telangiectasia mutated protein kinase (ATM) participates in insulin-mediated signalling: decreased ATM functionality is associated with insulin resistance, diabetes and cardiovascular disease. Obesity reduces cardiac ATM, however the link between adiposity and peripheral ATM regulation remains unclear. MicroRNA-421 and microRNA-18a pathologically down-regulate ATM in cancer, making this a promising mechanism for regulating ATM in obesity. Aim: To determine the effect of obesity on ATM in the heart and adipose tissues and the expression levels of microRNA-421 and microRNA-18a in the heart.

## OBJECTIVES:

Using H9c2 cardiomyoblasts, this study will evaluate i) whether they are metabolically sensitive to obese-simulating treatments, ii) whether microRNA-421 and microRNA-18a levels are influenced by obese-simulating treatments, and iii) the activity of ATM and other metabolic proteins in subcutaneous and visceral adipose-derived stem cells (ASCs) and their differentiated adipocyte counterparts originating from lean (n=4) and high-fat diet (n=4) rats.

## METHODS:

Quantification of proteins through Western blotting and microRNAs through qRT-PCR.

## RESULTS:

24 hours of insulin stimulation caused insulin resistance in H9c2 cells (decreased phospho-PKB versus 15 minutes,  $p < 0.01$ ). ATM activity (phospho/total-ratio) was decreased in H9c2 cells co-treated with insulin and fatty acids (palmitic- and oleic acid) versus insulin ( $p < 0.05$ ) and fatty acids only ( $p < 0.05$ ) treatments. No significant changes in microRNA levels were observed. Total ATM levels were lower in visceral adipocytes versus subcutaneous adipocytes ( $p < 0.05$ ) originating from lean rats, but not high-fat diet rats. ATM activity was lower in the subcutaneous adipocytes versus subcutaneous ASCs ( $p < 0.05$ ) originating from lean and high-fat diet rats.

## CONCLUSION:

H9c2 cells develop insulin resistance, and obese-simulating conditions influence ATM activity. Results suggest depot- and differentiation-dependent roles for ATM in adipocyte metabolism, which may be affected by diet. Studies to determine whether adipocyte secretions influence ATM levels through specific microRNAs in H9c2 cells are ongoing.

# 10-Year Audit of Pregnancies Affected by Diabetic Ketoacidosis at the Pretoria Academic Complex

Ncamsile F. Maseko<sup>a</sup>, Sumaiya Adam<sup>a</sup>, Danie Van Zyl<sup>b</sup>

<sup>a</sup>Department of Obstetrics and Gynaecology, Faculty of Health Science, University of Pretoria, South Africa

<sup>b</sup>Department of Internal Medicine, Faculty of Health Science, University of Pretoria, South Africa

## BACKGROUND:

Diabetic ketoacidosis (DKA) during pregnancy is one of the most serious hyperglycaemic emergencies. Standard DKA management guidelines are designed to ensure optimal management and minimise adverse outcomes.

## OBJECTIVES:

To determine the level of adherence to DKA management guidelines in the Pretoria Academic Complex (PAC) and to determine maternal and perinatal outcomes of pregnancies complicated by DKA.

## METHODS:

This was a retrospective clinical record audit using the Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) guidelines, 2017, against information documented in patient's clinical records. Adherence to three cornerstones of therapy: intravenous fluids, insulin therapy and management of electrolytes was measured. A descriptive analysis were conducted and data were presented in frequencies and percentages.

## RESULTS:

A total of 56 records of pregnancies that were complicated with DKA over a 10 year period were reviewed. Median age was 29 years and 64.3% (n=36) patients had Type 1 Diabetes Mellitus. DKA was categorised into mild (46.4%, n= 26), moderate (37.5%, n=21) and severe (14.3%, n= 8). Majority (94.1%, n=48) of DKA resolution was > 24 hours from time of admission, demonstrating substandard use of guidelines. Of the 48 recorded pregnancies with perinatal outcomes, 19 had adverse outcomes; 4.2% (n=2) had second trimester miscarriage, 31.2% (n=15) were stillbirths, 4.2% (n=2) early neonatal deaths. There was no recorded maternal deaths.

## CONCLUSION:

This review demonstrated lower adherence to guidelines and higher adverse perinatal outcomes. The management of DKA in pregnancy involves prompt diagnosis and initiation of acute care. Effective management of DKA will reduce both maternal and perinatal morbidity and mortality.

# Mitochondrial function affects insulin signalling in skeletal muscle cells

Sinenhlanhla X.H. Mthembu<sup>a,b</sup>, Christo J.F. Muller<sup>a,b,c</sup>, Evelyn Madoroba<sup>b</sup>, Johan Louw<sup>a,b</sup>, Abidemi P. Kappo<sup>d</sup>, Sithandiwe E. Mazibuko-Mbeje<sup>a,e</sup>

<sup>a</sup>Biomedical Research and Innovation Platform, South African Medical Research Council, Tygerberg 7505, South Africa. <sup>b</sup>Department of Biochemistry and Microbiology, University of Zululand, KwaDlangezwa 3886, South Africa.

<sup>c</sup>Division of Medical Physiology, Faculty of Health Sciences, Stellenbosch University, Tygerberg 7505, South Africa.

<sup>d</sup>Department of Biochemistry, Faculty of Science, University of Johannesburg, Kingsway Campus, Auckland Park 2006, South Africa. <sup>e</sup>Department of Biochemistry, Faculty of Natural and Agricultural Sciences, North West University, Mafikeng Campus, Private Bag X 2046, Mmabatho, 2735, South Africa.

[Sinenhlanhla.Mthembu@mrc.ac.za](mailto:Sinenhlanhla.Mthembu@mrc.ac.za)

## BACKGROUND:

Insulin resistance (IR) and mitochondrial dysfunction are characteristic features of type 2 diabetes mellitus (T2DM). Identification of cellular processes and gene networks contributing to impaired insulin action and mitochondrial dysfunction, might offer new drug targets or therapeutic strategies for T2DM. However, a causal relationship between mitochondrial dysfunction and insulin resistance has not been established in skeletal muscle. Accordingly, we have evaluated the effect of antimycin A (AA), a mitochondrial electron transport chain complex III inhibitor, on mitochondrial bioenergetics and insulin signalling in C2C12 skeletal muscle cells.

## METHODS:

Mitochondrial dysfunction was induced in C2C12 myotubes by treating cells with different concentrations of AA (3.125, 6.25, 12.5, 25, and 50  $\mu$ M) for 12 hours. Thereafter, mitochondrial activity, ROS production, glucose uptake, Seahorse XF Real-time ATP and Mito Stress assays were performed. Gene and protein expression were assessed using the real-time polymerase chain reaction (RT-PCR) and Western blot analysis.

## RESULTS:

This study confirmed that AA induces mitochondrial dysfunction in C2C12 myotubes, culminating in a significant decrease in mitochondrial respiration and downregulation of genes involved in mitochondrial bioenergetics (TFAM, UCP2, PGC1 $\alpha$ ). Increased AMPK phosphorylation and extracellular acidification rates (ECAR) confirmed a compensatory increase in glycolysis. However, the myotubules were insulin resistant as confirmed by a significant decrease in protein kinase B/ AKT expression and insulin stimulated glucose uptake.

## CONCLUSION:

This study confirmed that an adaptive relationship exists between mitochondrial functionality and insulin responsiveness in skeletal muscle, and that therapeutics or interventions improving mitochondrial function could ameliorate insulin resistance as well.

# Development of an Individualized Genetic Drug Therapy for Diabetic and Hypertensive Patients in Cape Admixed Population

Z. Brophy<sup>a</sup>, B. Pearce<sup>a</sup>, M. Benjeddou<sup>a</sup>

<sup>a</sup>Department of Biotechnology, Faculty of Natural Science, University of the Western Cape, South Africa

[3337960@myuwc.ac.za](mailto:3337960@myuwc.ac.za)

## BACKGROUND:

Type 2 diabetes Mellitus (T2DM) and hypertension (HTN) has become a significant public health concern, due to its association with modifiable and non-modifiable factors. The potential of discovering single nucleotide polymorphisms (SNPs) as a non-modifiable factors to serve as molecular biomarkers to elucidate disease pathophysiology is receiving increasing interest globally.

## OBJECTIVES:

To investigate the association between pharmacogenetic biomarkers and response to antidiabetic and antihypertensive treatment.

## METHODS:

MassARRAY panels were designed and optimized by Inqaba Biotechnical Industries, to genotype 27 biomarkers for 99 type 2 diabetic and 162 hypertensive outpatients.

## RESULTS:

Preliminary results shows that the CT genotype of the rs2282143 polymorphism was significantly associated with increased response to antidiabetic therapy after correction (OR= 0.24, 95% CI [0.43-0.73], p-value= <0.001). An association was also found between the AG genotype of rs4648287 a decreased response to antihypertensive therapy after correction (OR= 1.81, 95% CI [0.89-8.25], p-value=0.03).

## CONCLUSION:

This is the first study investigating the association between genetic variants and responsiveness to medication for diabetic and hypertensive patients. Further work to explore the potential of more pharmacogenetic biomarkers for the Cape Admixed population is warranted. It is recommended that proposed results be included in pharmacogenomics profiling systems to individualize drug therapy for diabetic and hypertensive patients from the Cape Admixed population.

# Effect of LPS-induced inflammation on skeletal muscle differentiation and function

Nnini Obonye<sup>a,b</sup>, Sithandiwe E. Mazibuko-Mbeje<sup>d</sup>, Johan Louw<sup>a,c</sup>, Hans Strijdom<sup>b</sup> and Christo J.F. Muller<sup>a,b,c</sup>

<sup>a</sup>Biomedical Research and Innovation Platform, South African Medical Research Council, Tygerberg, 7505, South Africa. <sup>b</sup>Division of Medical Physiology, Faculty of Health Sciences, Stellenbosch University, Tygerberg, 7505, South Africa. <sup>c</sup>Department of Biochemistry and Microbiology, University of Zululand, KwaDlangezwa, 3886, South Africa.

<sup>d</sup>Department of Biochemistry, North-West University, Mmabatho, 2745, South Africa

[Nnini.Obonye@mrc.ac.za](mailto:Nnini.Obonye@mrc.ac.za)

## BACKGROUND:

High-fat diets alter the intestinal wall permeability, allowing inflammatory substances such as endobacterial endotoxin – lipopolysaccharide (LPS) - into circulation. The presence of endotoxin in circulation (metabolic endotoxemia), has been reported in obese and type 2 diabetes mellitus (T2DM) patients. Metabolic endotoxemia is proposed to be one of the contributing factors to low-grade systemic inflammation seen in obese and T2DM patients. Evidence has also shown that inflammatory responses are involved in the inhibition of myogenic differentiation by upregulating negative regulatory factors of myogenesis and protein degradation pathways, contributing to skeletal muscle wasting. As skeletal muscle accounts for 70–90% of insulin stimulated blood glucose uptake, progressive loss of skeletal muscle mass is an adverse confounding factor in T2D.

## OBJECTIVES:

This study aimed to investigate the effects of LPS-induced inflammation on muscle function and metabolism.

## METHODS:

To mimic the effect of metabolic endotoxemia on myogenesis, C2C12 mouse myoblasts were cultured in high glucose media treated with LPS (0.1 µg/mL or 1 µg/mL) for 24 hours. Thereafter glucose uptake and IL-6 secretion, was assessed. Quantitative Polymerase Chain Reaction (qPCR) and Western blot analysis were performed on genes involved with insulin signalling (AKT, IRS-1), and muscle cell growth and differentiation (myogenin, MyoD and mTOR).

## RESULTS:

Our results showed that LPS treatment had no cytotoxic effects on cultured myoblasts. Furthermore, LPS- induced inflammation was confirmed by increased IL-6 secretion and a reduction of glucose utilization. At a molecular level, LPS reduced expression of myogenic genes (MyoD and myogenin) and mTOR. Interestingly, activation of AKT was inhibited by LPS treatment; however, this inhibition was rescued by insulin in a dose-dependent manner.

## CONCLUSION:

Our data suggests that LPS-induced inflammation inhibits myogenesis by downregulating MyoD and myogenin, as well as mTOR, a key regulator of cell growth and protein synthesis. Establishing a link between inflammation, insulin resistance and skeletal muscle wasting.

# An evaluation of the role of platelet activation in HIV-related cardiovascular diseases onset

Leanne Dominick, Eman Teer, Festus Kamau, Ingrid Webster, Hans Strijdom and M. Faadiel Essop

Centre for Cardio-metabolic Research in Africa (CARMA), Departments of Physiological Sciences and Medical Physiology, Stellenbosch University

[17788471@sun.ac.za](mailto:17788471@sun.ac.za)

## BACKGROUND:

Although roll-out of combined anti-retroviral treatment (cART) lowered HIV-AIDS onset, HIV-positive individuals display increased cardiovascular diseases (CVD) onset. As enhanced myocardial fibrosis is emerging as a crucial mediator of HIV-induced CVD, for this cross-sectional study we hypothesized that persistent platelet activation results in increased release of pro-fibrotic mediators (i.e. transforming growth factor- $\beta$  [TGF- $\beta$ ]) and myocardial fibrosis.

## OBJECTIVES:

- 1) Evaluate platelet activation marker expression and indices.
- 2) Correlate platelet activation with TGF- $\beta$ , blood pressure (BP) and electrocardiogram (ECG) measurements.
- 3) Determine the relationship between platelet activation and markers of HIV disease progression (viral load, CD4 count).

## METHODS:

Thirty-six aged-matched male and female participants were recruited in Worcester (Western Cape): n=13 HIV-negative, n=23 HIV-positive on cART (18-55 years old), while those with tuberculosis co-infection and pregnancy were excluded. BP and ECG recordings were completed, while fasted blood samples were collected. Flow cytometric analyses were employed to evaluate platelet activation markers (CD62P, latent associating protein [LAP], glycoprotein A-repetitions predominant [GARP]) and a pro-fibrotic marker (TGF- $\beta$ 1).

## RESULTS:

Our data reveal significant heart rate variations in HIV-positive participants vs. controls ( $P<0.05$ ). Although only 14% of HIV-positive individuals presented with an irregular sinus rhythm, there was a significant, positive correlation between diastolic BP and T wave duration ( $P<0.05$ ). Moreover, platelet activation markers (CD62P, LAP) displayed a significant, negative correlation with BP (systolic and diastolic) ( $P<0.05$ ). GARP exhibited significant, positive correlations with diastolic BP ( $P<0.05$ ), TGF- $\beta$ 1 ( $P<0.0001$ ) and viral load ( $P<0.05$ ).

## CONCLUSION:

Our data reveals that platelet activation is associated with altered BPs that, in turn, are linked to heart rate variability. The TGF- $\beta$ -docking receptor GARP emerges as a key role player as it was associated with a pro-fibrotic milieu and higher viral loads. Thus, GARP may lead to platelet-mediated TGF- $\beta$  release that may result in BP and heart rate alterations in HIV-positive individuals.

# Potential anti-cancer activity of the chloroform fraction of *Bidens pilosa* in MCF-7 breast cancer cell line

Olga Raboshakga, Kgomotso Poopedi, Vusi Mbazima, Leseilane Mampuru

Department of Biochemistry, Microbiology & Biotechnology, University of Limpopo, Private Bagx1106, SOVENGA, 0727

[Olga.raboshakga@ul.ac.za](mailto:Olga.raboshakga@ul.ac.za)

## BACKGROUND:

Breast cancer remains a health burden worldwide. GLOBOCAN has reported a continuous rise in breast cancer incidence rates, ranking it as the second most prevalent cancer in South African black women. It accounts for a significant increase in mortalities. Conventional therapies have posed shortcomings. An idyllic anti-cancer therapeutic agent should selectively destroy cancerous cells, preferably by inducing apoptosis. Plant-derived bioactive agents have become ideal treatment options as they display less cytotoxic effects in comparison to the use of synthetic chemicals.

## OBJECTIVES:

The study was aimed at assessing the potential anti-cancer molecular mechanism(s) of *Bidens pilosa* by determining the signalling mode of cell death exerted on MCF-7 breast cancer cell line.

## METHODS:

Cytotoxicity and anti-proliferative effects of the extract was analysed using the Muse® Count and Viability and Ki-67 Proliferation assays. Muse® Cell Cycle and Multi-color DNA Damage assays were utilised to analyse cell division cycle progression and genotoxic effects, respectively. Apoptosis was assessed using Muse® Annexin-V, acridine orange and ethidium bromide staining assays and Human apoptosis RT<sup>2</sup> Profiler™ PCR Array.

## RESULTS:

Chloroform fraction exerted the most toxic effects and 70% proliferation inhibition. Genotoxic effects and G<sub>2</sub>/M cell division cycle arrest were observed, and were repairable. Upregulation of *caspases -7, -8, -9, -10 and -14, cytochrome c, DFFA, AIF, CIDEB, FADD, Fas, FasLG, GADD45A, AIP, TNF-α and X-IAP* were observed. *Caspases -2, -3 and -6, Smac/Diablo, Bcl-2, Bad, Bax, Bak, Apaf1, Bid, CIDEA, RIP and p53* were found to be downregulated. Biochemical features such as chromatin condensation and DNA fragmentation indicative of the advent of apoptotic process were observed.

## CONCLUSION:

*Bidens pilosa* chloroform fraction possesses proliferation inhibitory properties and induces caspase-mediated extrinsic apoptosis process. The fraction has a potential for further development as a potent anti-cancer therapeutic agent.

# Investigating high-density lipoprotein (HDL) functionality, composition and subclass in HIV patients

Peter Hudson<sup>a</sup>, Nicholas J. Woudberg<sup>a</sup>, Carmelita Abrahams<sup>a</sup>, Festus Kamau<sup>b</sup>, Nicolas Vuileumier<sup>c</sup>,  
Hans Stijdom<sup>b</sup>, Miguel A. Frias<sup>c</sup>, and Sandrine Lecour<sup>a</sup>

<sup>a</sup>Hatter Institute for Cardiovascular Research in Africa, Department of Medicine, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa; <sup>b</sup>Centre for Cardio-metabolic Research in Africa, Division of Medical Physiology, Faculty of Medicine and Health Sciences, Stellenbosch University, South Africa; <sup>c</sup>Division of Laboratory Medicine, Department of Diagnostics, Geneva University Hospitals, Switzerland.

[hdsfet003@myuct.ac.za](mailto:hdsfet003@myuct.ac.za)

## BACKGROUND:

While antiretroviral therapy (ART) has increased the life expectancy of individuals with human immunodeficiency virus (HIV), this population faces an increased risk for cardiovascular disease (CVD). High-density lipoprotein-cholesterol (HDL-C) levels traditionally serve as an inverse marker of risk, however, new research suggests that HDL function and subclass may be more accurate predictors.

## OBJECTIVES:

To explore whether HIV and/or ART modulates HDL subclass and function in an HIV-infected population.

## METHODS:

The study consisted of 50 healthy HIV-negative controls, 50 HIV-infected ART-treated patients and 44 HIV-infected ART-untreated patients (HIV naïve). The levels of ten HDL subclasses (grouped into large, intermediate and small) were measured using the Lipoprint® system. Antioxidative and antithrombotic functions of HDL were assessed by measuring paraoxonase-1 (PON1) activity and platelet activating factor acetylhydrolase (PAF-AH) activity, respectively.

## RESULTS:

HIV naïve patients had lower HDL-C than HIV-negative *and* ART-treated patients ( $1.05 \pm 0.5$  vs  $1.33 \pm 0.4$  vs  $1.31 \pm 0.7$  mmol/L, respectively,  $p < 0.05$ ). The percentage of the largest subclass of HDL, HDL-1, was higher in HIV naïve patients compared to HIV-negative patients ( $12.46 \pm 6.33$  vs  $9.43 \pm 4.41\%$ ,  $p < 0.05$ ). The larger subclasses (HDL-1, HDL-2, HDL-3) were inversely correlated with CD4 count in all HIV infected patients ( $r = -0.21$ ,  $r = -0.26$  and  $r = -0.28$ ,  $p < 0.05$ ). Similarly, smaller HDL subclasses (HDL-7 and HDL-8) were inversely correlated with viral load ( $r = -0.24$  and  $r = -0.24$ ,  $p < 0.05$ ). There were no changes in PON1 activity or PAF-AH activity, however an increase in PON1 activity was associated with an increase in small HDL ( $r = 0.19$ ,  $p < 0.05$ ).

## CONCLUSION:

This study suggests that HIV and/or ART leads to a shift in HDL subclass distribution, favoring lower larger HDL subclasses. More in-depth studies should be conducted to better understand the exact role of HIV and/or ART on the modification of HDL.



---

# Abstracts - Posters

## PhD category

---

# The role of the oncogenic TBX3 in the transformation of mesenchymal stem cells into a subset of sarcomas

Victoria Damerell<sup>a</sup>, Tarryn Willmer<sup>b</sup>, Michelle du Toit<sup>a</sup>, Shanel Swartz<sup>a</sup>, Katie Lennard<sup>c</sup>, Nicola Mulder<sup>c</sup>,  
Dhirendra Govender<sup>d</sup>, Michael Pepper<sup>e</sup> and Sharon Prince<sup>a</sup>

<sup>a</sup>Division of Cell Biology, Nutritional Sciences and Physiology, Department of Human Biology, <sup>c</sup>Division of Computational Biology, Department of Integrative Biomedical Sciences, Institute of Infectious Disease and Molecular Medicine, <sup>d</sup>Division of Anatomical Pathology, Department of Pathology, Faculty of Health Sciences, University of Cape Town, South Africa, <sup>e</sup>Institute for Cellular and Molecular Medicine, Department of Immunology, SAMRC Extramural Unit for Stem Research and Therapy, Faculty of Health Sciences, University of Pretoria, South Africa, <sup>b</sup>Biomedical Research and Innovation Platform, South African Medical Research Council, Tygerberg 7505, South Africa

[dmrvic001@myuct.ac.za](mailto:dmrvic001@myuct.ac.za)

## BACKGROUND:

Sarcomas, diverse malignancies of mesenchymal origin, are frequently misdiagnosed and their clinical management is severely challenged. This is in part due to a lack of understanding of the molecular mechanisms underpinning the transformation of mesenchymal stem cells (MSCs), the cells of origin of sarcomas. We have shown that TBX3 is upregulated by c-Myc in several sarcoma subtypes and that it partners with nucleolin to promote the formation of these sarcoma subtypes.

## OBJECTIVES:

This study aims to determine whether (1) TBX3 in combination with c-Myc and nucleolin may be important biomarkers for the reliable diagnosis of sarcomas and (2) TBX3 can drive the transformation of MSCs into sarcomas.

## METHODS:

C-Myc, TBX3 and nucleolin mRNA and protein levels of patient-derived sarcoma tissues were determined using a PCR array and immunohistochemistry. FLAG-TBX3 overexpressing MSCs were generated using lentiviral gene transfer. The proliferative and migratory ability of TBX3-MSCs were measured by MTT and scratch motility assays. Markers of cell cycle progression, migration, invasion as well as levels of target genes repressed by TBX3 were assessed using qRT-PCR and western blotting. The trilineage differentiation potential of MSCs was assessed by inducing adipogenic, chondrogenic and osteogenic differentiation.

## RESULTS:

The overexpression of c-Myc, TBX3 and nucleolin protein and mRNA levels were observed in patient-derived sarcoma tissues and were associated with advanced sarcoma stages. Overexpression of TBX3 in MSCs enhanced their proliferative and migratory ability which corresponded with increased levels of markers of cell cycle progression, migration and invasion and downregulation of TBX3 target gene expression. It enhanced osteogenic and chondrogenic differentiation whereas adipogenic differentiation was blocked.

## CONCLUSION:

Our study provides evidence that (1) the co-expression of c-Myc, TBX3 and nucleolin may be used as biomarkers for the reliable diagnosis of specific sarcoma subtypes; and (2) TBX3 alone may be enough to drive MSCs into a transformed phenotype.

# The effect of Pinocembrin on impaired mitochondrial bioenergetics associated with Doxorubicin administration in an MCF-7 cell model

Nonhlakanipho F. Sangweni<sup>a,b</sup>, Lawrence Mabasa<sup>a</sup>, Barbara Huisamen<sup>b</sup>, Derick van Vuuren<sup>b</sup>, Reenen Barry<sup>c</sup>,  
Rabia Johnson<sup>a,b</sup>

<sup>a</sup>Biomedical Research and Innovation Platform (BRIP), South African Medical Research Council, Tygerberg 7505, South Africa. <sup>b</sup>Division of Medical Physiology, Faculty of Health Sciences, Stellenbosch University, Tygerberg 7505, South Africa <sup>c</sup>Research and Development Department, Biopharm, Hamilton, New Zealand

[Nonhlakanipho.Sangweni@mrc.ac.za](mailto:Nonhlakanipho.Sangweni@mrc.ac.za)

## BACKGROUND:

In a recent study, we demonstrated the prophylactic effect of Pinocembrin (Pin) against Doxorubicin (Dox)-induced cardiotoxicity. However, literature indicates that during chemotherapy, distinct bioenergetics dysfunction in cancer mitochondrial subpopulations may be reversed by the co-administrative use of cardioprotective agents.

## OBJECTIVES:

To address this, the degree of impaired mitochondrial function associated with the combined use of Dox plus Pin, using an MCF-7 breast cancer cell model was studied.

## METHODS:

To mimic a clinical setting of chronic Dox administration, MCF-7 cells were treated with 0.5 $\mu$ M of Dox for 6 days. The effect of Pin on Dox-induced mitochondrial damage was assessed by co-treating the cancer cells with Dox (0.5 $\mu$ M) plus Pin (1 $\mu$ M) for the same treatment duration. Untreated cells served as the vehicle control and cells treated with Pin (1 $\mu$ M) alone were used to establish the compounds anti-cancer properties. On day 7 mitochondrial bioenergetics was quantified using the Seahorse XF Cell Mito Stress Test Kit.

## RESULTS:

Co-treatment with Dox plus Pin enhanced the basal and spare respiratory capacity of the MCF-7 cells, suggesting the compounds' ability to compensate the cells energy demands. However, no significant difference in the cells maximal respiratory capacity or rate of ATP turnover was observed. Furthermore, the cancer cells co-treated with Pin presented with impaired coupling efficiency, respiratory control ratio and state apparent which were comparable with that detected in cells treated with Dox alone. Despite previous reports, Pin displayed no anti-cancer properties, at the tested concentration, as demonstrated by the preserved bioenergetics of the MCF-7 cells.

## CONCLUSION:

Although Pin, as an adjunct to Dox, influenced the respiratory parameters of the cancer cells, this effect was not sufficient to ameliorate the cells mitochondrial function as determined by the reduced mitochondrial flux ratios.

# Diet influences risk factors for diabetes-induced cardiac dysfunction

Melisse Erasmus<sup>a,b</sup>, Ebrahim Samodien<sup>b</sup>, Carmen Pheiffer<sup>a,b</sup>, Rabia Johnson<sup>a,b</sup>

<sup>a</sup>Biomedical Research and Innovation Platform, South African Medical Research Council. Francie van Zijl drive, Parow Valley, Cape Town, South Africa.

<sup>b</sup>Department of Medical Physiology, Stellenbosch University, Tygerberg campus. Francie van Zijl drive, Tygerberg, Cape Town, South Africa.

[Melisse.Scheepers@mrc.ac.za](mailto:Melisse.Scheepers@mrc.ac.za)

## INTRODUCTION:

Unhealthy diets is associated with an increased risk of cardiovascular disease (CVD). Conversely, polyphenols are known to reduce cardiovascular risk. Fibrosis, which results in stiffening of the heart muscle, is positively associated with cardiac dysfunction.

## OBJECTIVES:

To determine whether different diets increase the expression of genes and proteins associated with cardiac fibrosis, and whether AfriplexGRT™ supplementation can attenuate the expression of these genes in a high-sucrose/medium fat (OB1) or high fat/fructose/cholesterol (OB2) diet-induced Wistar rat model.

## METHODS:

Male Wistar rats were divided into 3 groups, being fed: a control diet (n=12), a diet high sucrose/moderate fat (OB1) (n=24) or a diet high in fat/fructose/cholesterol (n=24) for 10 weeks. The OB1 and OB2 groups were then each split into 2 groups (n=12) with or without diet supplemented with AfriplexGRT™ for a further 7 weeks. At termination, blood was collected for serum analysis and heart tissue collected for RNA and protein analysis.

## RESULTS:

OB2 diet increased the CVD risk factors (cholesterol, LDL and triglycerides), which were marginally reduced by AfriplexGRT™. OB2 diet decreased the AST/ALT ratio, however, AfriplexGRT™ was unable to reverse this. Gene expression regulation was not significant, however *COL1A*, *LOXL2* and *TGF-β2* were moderately increased by the OB2 diet but this was not observed at the protein level.

## CONCLUSION:

The known risk factors for CVD were increased by a diet high in fat/fructose/cholesterol and decreased the serum AST/ALT ratio to <1, indicative of NAFLD. This was not translated to the fibrotic gene and protein expression. In conclusion, the OB2 diet increased non-modifiable risk factors of CVD, which is important for the implementation of mitigation strategies in patients, prior to overt symptoms.

# Prevalence of Hypertension and associated risk factors in a rural black population of Mthatha town, South Africa

\*Sihle E. Mabhida<sup>a,b</sup>, \*Jyoti Shama<sup>a</sup>, Brownyn Myers<sup>c</sup>, Teke Apalata<sup>d</sup> Mongi Benjeddou<sup>b</sup> and Rabia Johnson<sup>a,e</sup>

<sup>a</sup>Biomedical Research and Innovation Platform, South African Medical Research Council, Tygerberg 7505, South Africa. <sup>b</sup>Department of Biotechnology, Faculty of Natural Science, University of the Western Cape, Private Bag X17, Bellville, Cape Town 7535, South Africa,

<sup>c</sup>Division of Alcohol Tobacco and other research unit, South African Medical Research Council, Tygerberg, 7505.

<sup>d</sup>Division of Medical Microbiology, Department of Laboratory-Medicine and Pathology, Faculty of Health Sciences, Walter Sisulu University and National Health Laboratory Services, Mthatha, South Africa. <sup>e</sup>Division of Medical Physiology, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg 7505, South Africa.

*\*Authors contributed to the work equally*

[sihle.mabhida@mrc.ac.za](mailto:sihle.mabhida@mrc.ac.za), [Jyoti.Sharma@mrc.ac.za](mailto:Jyoti.Sharma@mrc.ac.za)

## BACKGROUND:

Hypertension (HTN) is a persistent global health problem affecting approximately 1.3 billion individuals globally. The prevalence of HTN has been increasing alarmingly in low- and middle-income countries including South Africa having the heaviest burden of disease with the prevalence of hypertension between 27-58%. However, a paucity of data exists pertaining to hypertension prevalence in the rural parts of South Africa. This study aims to assess the prevalence and associated risk factors of hypertension amongst rural black population of Mthatha town, Eastern Cape.

## METHODS:

The present cross-sectional study included black African individuals aged  $\geq 18$  years (576 subjects). Sociodemographic information, anthropometric measurements, such as body weight, height and three independent blood pressure measurements were taken using World Health Organization STEPwise questionnaire. Diagnosis of high blood pressure (BP)/hypertension was done in accordance with guidelines provided by American Heart Association (2018). Overweight and obesity was assessed using body mass index (Body weight (kg)/Height (cm)<sup>2</sup>). Statistical package for social sciences (SPSS) windows version 16.0 (SPSS, Inc., Chicago, IL., USA) was used to analyse the data. Univariate and multivariate logistic regression analysis was utilized to investigate the associated factors with hypertension.

## RESULTS:

The mean age of the participants was  $46.8 \pm 14.5$  years. The results demonstrated that 73.4% of subjects had BP in high BP/hypertensive range. In a univariate analysis, of all the participants, male gender, age, western diet, education as well as income status, and overweight/obese status were associated with the BP scores in hypertensive range. However, in the multivariate regression analysis, the only variables that remained significantly associated with hypertensive status were age, BMI, and westernized diet.

## CONCLUSION:

There is a high prevalence of hypertension among the study participants and age, BMI, westernized diet were the most important determinants of hypertension among black African population of Mthatha, South Africa.

# High fat, high sugar diet induces hepatic steatosis and decreased PGC1 $\alpha$ expression and hypermethylation in male Wistar rats

Yoonus Abrahams<sup>a,b</sup>, Ebrahim Samodien<sup>a</sup>, Shantal Windvogel<sup>b</sup>, Oelfah Patel<sup>a</sup>, Rabia Johnson<sup>a,b</sup>  
& Carmen Pfeiffer<sup>a,b</sup>

<sup>a</sup>Biomedical Research and Innovation Platform, South African Medical Research Council, Cape Town, South Africa

<sup>b</sup>Division of Medical Physiology, Stellenbosch University, Cape Town, South Africa

[Yoonus.Abrahams@mrc.ac.za](mailto:Yoonus.Abrahams@mrc.ac.za)

## BACKGROUND:

Obesity and its co-morbidities represent one of the greatest health challenges of the modern era. The pathophysiological changes that occur during the development of obesity are generally well described, although the epigenetic mechanisms that link obesity with metabolic disease are not yet fully elucidated.

## OBJECTIVES:

To investigate hepatic DNA methylation of key genes in high fat, high sugar-fed Wistar rats.

## METHODS:

Male Wistar rats (n=20) were fed a chow diet or a high fat, high sugar (HFHS) diet for 12 weeks. Bodyweights were measured weekly. Retroperitoneal fat and liver weights, and glucose, insulin and triglyceride concentrations were assessed at termination. Hepatic steatosis was assessed using histology and quantifying triglyceride content. Gene expression and DNA methylation was measured using quantitative real time PCR and pyrosequencing, respectively.

## RESULTS:

Twelve weeks of HFHS feeding induced obesity ( $567.0 \pm 8.8$  g vs.  $474.0 \pm 10.5$  g,  $p < 0.001$ ) and hyperinsulinemia ( $6.14 \pm 2.79$  ng/ml vs.  $3.78 \pm 1.97$  ng/ml,  $p = 0.042$ ). The livers from HFHS-fed rats contained more triglycerides ( $2.05 \pm 0.56$  mg/g vs.  $1.13 \pm 0.16$  mg/g,  $p < 0.001$ ) and had higher messenger RNA expression of Sterol regulatory element-binding transcription factor 1 (2.04-fold,  $p < 0.001$ ) and Peroxisome proliferator-activated receptor alpha (1.35-fold,  $p < 0.05$ ) compared to chow fed rats. The expression of the mitochondrial biogenesis gene, Peroxisome proliferator-activated receptor gamma coactivator 1-alpha (*Pgc1 $\alpha$* ) was significantly repressed, while a DNA methylation site within its promoter was significantly hypermethylated by HFHS feeding.

## CONCLUSION:

The HFHS diet induced obesity, hepatic steatosis and increased the expression of lipogenesis genes in Wistar rats. These changes were accompanied by decreased expression and hypermethylation of *Pgc1 $\alpha$* , and identifies DNA methylation as an epigenetic mechanism that links obesity and hepatic mitochondrial dysfunction. Additional studies are required to fully elucidate the causal role of HFHS diet-feeding on hepatic DNA methylation and mitochondrial dysfunction.

# Gender differences in the development of obesity and metabolic disease

Asive Myataza<sup>a,b</sup>, Tarryn Willmer<sup>a,b</sup>, Shantal Windvogel<sup>a</sup>, Rabia Johnson<sup>a,b</sup> and Carmen Pfeiffer<sup>a,b</sup>

<sup>a</sup>Division of Medical Physiology, Stellenbosch University, Tygerberg, South Africa

<sup>b</sup>Biomedical Research and Innovation Platform, South African Medical Research Council, Tygerberg, South Africa

[asive.myataza@mrc.ac.za](mailto:asive.myataza@mrc.ac.za)

## BACKGROUND:

Gender differences in the development of obesity are widely reported. Females appear to have later onset of obesity-related metabolic disorders compared to males. The mechanisms that underlie these differences remain largely unknown.

## OBJECTIVES:

To determine whether the expression of key metabolic genes in skeletal muscle differ in female and male Wistar rats in response to high fat, high sugar feeding.

## METHODS:

Female and male Wistar rats (n=40) were fed a control or high fat, high sugar (HFHS) diet for 9 months. Bodyweights were measured weekly, while glucose, insulin, triglyceride and cholesterol concentrations, and liver weights were assessed at termination. Gene expression was measured using quantitative real time PCR.

## RESULTS:

Male rats gained more weight than controls after three months of HFHS feeding (362.4 vs. 333.1, g p=0.002), whereas weight gain in females was induced after seven months (268.5 vs. 247.0 g, p=0.005). HFHS feeding increased glucose intolerance and glucose (5.1 vs. 4.8 mmol/L, p≤0.001) and insulin (6.6 vs. 3.1 ng/ml, p<0.05) concentrations in males only. Triglycerides were increased in both HFHS-fed females (1.81 vs. 0.76 mmol/L, p=0.005) and males (3.10 vs. 1.23 mmol/L, p<0.001), while a trend towards increased cholesterol concentrations was observed in females only (1.90 vs. 1.57 mmol/L, p=0.08). Male rats fed the HFHS diet had 25-fold higher expression of Insulin-like growth factor-2 (*IGF2*) and 5-fold lower expression of Sterol regulatory element-binding transcription factor 1 (*SREBF1*), while no differences were observed in females.

## CONCLUSION:

This study demonstrates differences in the response of female and male Wistar rats to HFHS feeding and highlights the importance of gender as a biological variable in obesity research. Skeletal muscle expression of *IGF2* and *SREBF1* may partly underlie gender differences in obesity and metabolic disease. Additional studies are required to further elucidate the gender-specific role of skeletal muscle.

# Determinants of technical efficiency of public district hospitals in KwaZulu-Natal Province

Tesleem K Babalola; Indres Moodley

Department of Public Health, University of KwaZulu-Natal, Durban South

[kydbabalola@gmail.com](mailto:kydbabalola@gmail.com)

## **BACKGROUND:**

The district hospitals play a crucial role in supporting primary health care and serve as a gateway to more specialist care through a referral system. The majority of South Africans access health care services through the public sector district health system.

## **OBJECTIVES:**

Given the enormous task assigned to the public district hospital within the country, this study was aimed at examining factors influencing their technical efficiency.

## **METHODS:**

Data were collected for thirty-eight public district hospitals in KwaZulu-Natal province from 2014/15 to 2016/17. Data envelopment analysis (DEA) technique was used to determine the technical efficiency of the hospitals, adopting both the constant return to scale (CRS) and variable return to scale (VRS) models. Tobit regression model was used to determine factors related to the technical efficiency of the district hospitals.

## **RESULTS:**

This study showed that a significant proportion of the district hospitals was technically inefficient. The Tobit regression model identified catchment population, the proportion of inpatients treated per medical personnel, the proportion of inpatients treated per nursing personnel and expenditure per patient day equivalent as factors influencing technical efficiency of the district hospitals

## **CONCLUSION:**

Findings from this study suggest that the technical efficiency of the district hospitals can be enhanced through an effective referral system and improved peoples' health-seeking behaviour. Also, a standard mix of clinical staff towards efficient service delivery and periodic cost analysis of health services with the view of saving cost as well as maintaining the quality of health care should be considered.

# Up-regulated expression of chemokines contributing to the development of NAFLD in Wistar rats fed a high fat diet

Samukelisiwe Shabalala<sup>a,c</sup>, Pritika Ramharack<sup>a</sup>, Hanél Sadie<sup>b</sup>, Liske Kotzé-Hörstmann<sup>b</sup>, Lawrence Mabasa<sup>a</sup>, Abidemi Kappo<sup>e</sup>, Carmen Pheiffer<sup>a,b</sup>, Albertus Basson<sup>c</sup>, Corina Walsh<sup>d</sup>, and Rabia Johnson<sup>a,b</sup>

<sup>a</sup>Biomedical Research and Innovation Platform (BRIP), South African Medical Research Council (SAMRC), Tygerberg 7505, South Africa. <sup>b</sup>Division of Medical Physiology, Faculty of Health Sciences, Stellenbosch University, Tygerberg, South Africa. <sup>c</sup>Department of Biochemistry and Microbiology, University of Zululand, KwaDlangezwa 3886, South Africa. <sup>d</sup>Voeding en Dieetkunde, Faculty of Health Sciences, University of Free State. <sup>e</sup>Department of Biochemistry, Faculty of Science, University of Johannesburg, Auckland Park 2006, South Africa.

[samukelisiwe.shabalala@mrc.ac.za](mailto:samukelisiwe.shabalala@mrc.ac.za)

## BACKGROUND:

Non-alcoholic fatty liver diseases is the most common chronic liver diseases and has become a public health concern. Increased consumption of sugar sweetened beverages has been linked to the development of NAFLD and subsequent hepatic inflammation. This study investigated the molecular mechanisms of hepatic lipid accumulation in the onset of steatosis to understand whether its impairment could be an early event of liver inflammatory injury.

## OBJECTIVES:

The main objective of this study was to determine the effect of a High-Fat-Diet (HFD) on hepatic fat deposition and inflammation in Wistar rats.

## METHODS:

To establish a model of NAFLD, wistar rats were fed either a normal diet (control, n=12), OB1 (low-fat-diet, 14% fat, 32% protein, and 54% carbohydrate, n=12) or an OB2 (HFD, 60% fat, 20% protein, and 20% carbohydrate, n=12) for 10 weeks. Metabolic parameters such as body weight and blood glucose were measured. At termination, blood was collected for serum lipid profiles and liver enzyme analysis. Further, liver tissues were collected for assessment of morphology using hematoxylin and eosin stain. The role of OB2 diet on inflammation and fatty liver markers was evaluated using a cytokines and chemokines PCR array.

## RESULTS:

The results obtained showed that feeding with either OB1 or OB2 diet for a period of 10 weeks significantly increased body weight when compared to normal diet. Histological analysis demonstrated that OB2 diet induced macrovascular steatosis, portal and lobular inflammation, while OB1 showed no steatosis and hepatic inflammation when compared to the control. Also, OB2 diet showed an aggravated inflammatory response with increased expression of IL1B (6.4-fold), IL12B (10.2-fold), TNF- $\alpha$  (9.82-fold), CCL2 (9.2-fold) and CXCL10 (13-fold) relative to the control diet.

## CONCLUSION:

Taken together, the results obtained confirm that HFD alters lipid and glucose metabolism resulting in an acute inflammatory response that further exacerbated the hepatic phenotype of NAFLD.



---

# Abstracts - Posters

## MSc/BSc Hons category

---

# The marine-derived antibiotic chromomycin A5 targets the oncogenic TBX2: a new strategy to treat breast cancer

C. Bellis<sup>a</sup>, S. Chakraborty<sup>a</sup>, M. Mlaza<sup>a</sup>, B. Del Bianco Sahm<sup>b</sup>, P. Rezende Teixeira<sup>b</sup>, L. Costa-Lotufo<sup>b</sup>,  
and S. Prince<sup>a,b</sup>

<sup>a</sup>Faculty of Health Sciences, Department of Human Biology, University of Cape Town, Observatory, Cape Town, South Africa

<sup>b</sup>Department of Pharmacology, Institute of Biomedical Sciences, University of São Paulo, Brazil

[blclla010@myuct.ac.za](mailto:blclla010@myuct.ac.za)

## BACKGROUND:

Breast cancer (BC) is the leading cause of cancer-related mortality in women worldwide and current treatments often fail due to drug resistance. TBX2 transcription factor is commonly overexpressed in BC tumours where it functions as a powerful pro-proliferative factor and confers drug resistance by inducing an S-phase arrest to allow for DNA damage repair and tumour cell survival. Targeting TBX2 may thus be a promising anti-breast cancer strategy. We therefore performed a reverse-affinity chromatography screen to search for compounds with binding affinity for TBX2 and chromomycin A5 (CMA5), a marine-derived antibiotic, was identified.

## OBJECTIVES:

This study aimed to investigate the anti-cancer effect of chromomycin A5 (CMA5), a marine antibiotic and TBX2-binding compound, in estrogen-receptor positive, TBX2-driven MCF-7 and T47D BC cells.

## METHODS:

Short-term cytotoxicity and long-term cell viability were assessed using MTT and clonogenic assays. The mechanism of action of CMA5 was assessed by analysing key morphological and molecular markers of DNA damage, apoptosis, the cell cycle and senescence by microscopy, immunocytochemistry and western blotting. TBX2 levels were similarly measured by immunocytochemistry and western blotting. TBX2 was knocked down using an shRNA transfection.

## RESULTS:

CMA5 had potent anti-cancer activity with IC50 values of  $\leq 6.5$  nM and a selectivity index of  $>5$ . Colony formation ability was significantly reduced with CMA5 treatment. Mechanistically, CMA5 induced double-stranded DNA damage (increased  $\gamma$ H2AX levels and p53 induction), apoptosis (induction of caspase activity and cleaved PARP) and importantly reduced TBX2 levels. Moreover, the efficacy of CMA5 appeared to be contingent on TBX2 levels as target depletion lead to a reduction in the efficacy of CMA5.

## CONCLUSION:

Together results from this study show that CMA5 is a potent novel compound with a selective inhibition of TBX2-driven BC.

# Effect of green rooibos tea extract (Afriplex GRT™) on inflammatory and oxidative stress genes in an *in vitro* and *in vivo* model of NAFLD.

Thendo Innocent Mabuda<sup>a,b</sup>; S. Windvogel<sup>b</sup>; R. Johnson<sup>a,b</sup>; C. Muller<sup>a,b,c</sup>; K. Gabuza<sup>a</sup>.

<sup>a</sup>Biomedical Research and Innovation Platform, South African Medical Research Council, Cape Town.

<sup>b</sup>Centre for Cardio-metabolic Research in Africa (CARMA), Division of Medical Physiology, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa

<sup>c</sup>Department of Biochemistry and Microbiology, University of Zululand, eMpangeni.

[Thendo.Mabuda@mrc.ac.za](mailto:Thendo.Mabuda@mrc.ac.za)

## BACKGROUND:

Non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) have been associated with the rise in liver dysfunction. Inflammation and oxidative stress are key mediators in NAFLD development. Current therapeutics used to treat NAFLD include insulin sensitizers and vitamin E. Afriplex GRT™ previously showed to decrease inflammation and oxidative stress in cardiac cells.

## OBJECTIVES:

To investigate if the Afriplex GRT™ extract and pioglitazone protects against hepatic oxidative stress, apoptosis and inflammation in both NAFLD models.

## METHODS:

Oleic acid [1 mM] was used to induce hepatic steatosis *in vitro*, whereafter the effects of mono- or co-treatment with Afriplex GRT™ and pioglitazone were quantified by the 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium (MTT) assay for metabolic activity/viability and Oil red O staining for lipid accumulation. In addition, the expression of genes and proteins associated with the development of NAFLD *in vitro* and *in vivo* (AKT, AMPK- $\alpha$ , TNF- $\alpha$ , SOD2, IRS1, PPAR- $\alpha$ , SREBF1, ChREBP and FASN) were analyzed by quantitative real-time polymerase chain reaction and Western blot.

## RESULTS:

Afriplex GRT™ reduced lipid accumulation in a dose-dependent manner *in vitro*, whereas co-treatment with pioglitazone was effective at the lowest Afriplex GRT™ concentration ( $p < 0,05$ ). Cell viability was maintained across all treatments. Genes involved in carbohydrate and lipid metabolism (*SREBF1*, *ChREBP* and *FASN*) were differentially expressed in both models, contributing to reduced lipid content by Afriplex GRT™. Improved insulin signaling was also identified as a mechanism of action whereby Afriplex GRT™ ameliorated hepatic steatosis. Afriplex GRT™ action also showed to reduce oxidative stress (*SOD2*) and inflammatory cytokine (TNF- $\alpha$ ) by gene and protein expression, respectively.

## CONCLUSION:

Afriplex GRT™ reduces hepatic steatosis in both models by modulating *SREBF1*, *ChREBP* and *FASN* gene expression. The extract also protects against oxidative stress and inflammation, by reduced expression of *SOD2* and TNF- $\alpha$ , suggesting that Afriplex GRT™ has potential as a therapeutic for NAFLD.

# The effect of *Sclerocarya birrea* (marula) leaf extract on hepatic lipid accumulation in mice

Anri Kotze<sup>a,b</sup>, Samukelisiwe Shabalala<sup>b,c</sup>, Rabia Johnson<sup>a,b</sup>, Clare Kimani<sup>a,b</sup>, Christo J.F. Muller<sup>a,b,c</sup> and Lawrence Mabasa<sup>b</sup>

<sup>a</sup>Division of Medical Physiology, Faculty of Health Sciences, Stellenbosch University, Tygerberg, South Africa

<sup>b</sup>Biomedical Research and Innovation Platform, South African Medical Research Council, Tygerberg 7505, South Africa

<sup>c</sup>Department of Biochemistry and Microbiology, University of Zululand, KwaDlangezwa 3886, Richard's Bay, South Africa

[anri.kotze@mrc.ac.za](mailto:anri.kotze@mrc.ac.za)

## BACKGROUND:

Non-alcoholic fatty liver disease (NAFLD) is an umbrella term used to refer to various stages of liver disease, all of which are characterized by hepatic lipid accumulation. Currently, the only recommended intervention for NAFLD is lifestyle changes. Of interest to this study, is the health beneficial effect of *Sclerocarya birrea*, a plant commonly known as marula tree.

## OBJECTIVES:

Specifically, the study aimed to assess whether a marula leaf extract is able to ameliorate obesity-induced hepatic lipid accumulation.

## METHODS:

Obese db/db mice (OB) and their lean littermate control (CON) were treated with or without (n=6/group) a marula leaf extract (MLE at 600 mg/kg body weight) as follows: CON, CON plus MLE, OB, OB plus Met (Metformin at 500 mg/kg body weight), or OB plus MLE. Mice were exposed to their respective treatments for a period of 29 days, upon which all animals were euthanized and liver tissues collected and stored in RNALater or snapfrozen for assays. Hematoxylin and Eosin staining was performed to assess the extent to which MLE reduced hepatic lipid accumulation. Further, quantitative real-time polymerase chain reaction was used to determine the expression of lipogenic genes such as fatty acid synthase (FASN) and carnitine palmitoyltransferase I (CPT1). The activity of these genes was further assessed by Western blot to confirm the protein expression.

## RESULTS:

Preliminary data showed that the OB plus MLE mice presented with reduced hepatic lipid accumulation when compared to OB mice. This was further supported by the downregulation of FASN mRNA levels, which contrasted with an increase in CPT1 expression, a gene involved in beta oxidation.

## CONCLUSION:

The study showed that marula leaf extract may be able to ameliorate hepatic lipid accumulation in part via modulation of beta oxidation. Nonetheless, further studies are required to validate the findings as well as establish the detailed mechanism of action.

# Impact of exercise intervention on DNA methylation of *FKBP5* in obese, insulin resistant South African women

Amberly Oosthuizen<sup>a</sup>, Tarryn Willmer<sup>a,b</sup>, Stephanie Dias<sup>a,c</sup>, Julia Goedecke<sup>b,d</sup> and Carmen Pfeiffer<sup>a,b</sup>

<sup>a</sup>Division of Medical Physiology, Stellenbosch University, Tygerberg, South Africa

<sup>b</sup>Biomedical Research and Innovation Platform, South African Medical Research Council, Tygerberg, South Africa

<sup>c</sup>Department of Obstetrics and Gynecology, University of Pretoria, South Africa

<sup>d</sup>Division of Exercise Science and Sports Medicine, University of Cape Town, South Africa.

[Amberly.Oosthuizen@mrc.ac.za](mailto:Amberly.Oosthuizen@mrc.ac.za)

## BACKGROUND:

Obesity and insulin resistance are modifiable risk factors which present opportunities for type 2 diabetes prevention and intervention. We previously showed that DNA methylation of *FK506-binding protein (FKBP5)* is altered in subcutaneous adipose tissue (SAT) from obese compared to normal-weight South African women, and significantly associated with adiposity and insulin resistance. The aim of this study was to explore the effect of a 12-week exercise intervention on *FKBP5* methylation in obese, insulin resistant (OBIR) South African women.

## METHODS:

OBIR South African women (n=35) were randomized into an exercise (n=20) or control (n=15) group. The exercise group underwent aerobic and resistance training for 12-weeks, while participants from the control group continued their normal daily activities. DNA methylation of two CpG dinucleotides within *FKBP5* intron 7 was measured in gluteal SAT (GSAT) using pyrosequencing. The presence of the *FKBP5* rs1360780 polymorphism was evaluated using quantitative real-time PCR.

## RESULTS:

No significant changes in *FKBP5* methylation were observed in GSAT in response to exercise training. However, when stratified based on genotype, carriers of the T allele presented higher *FKBP5* methylation after exercise training when compared to baseline (CpG542, 29% vs 37%, p=0.033; CpG543, 31% vs 38%, p=0.028), while no DNA methylation differences were observed in individuals with the C/C genotype.

## CONCLUSION:

Exercise training induces *FKBP5* hypermethylation in OBIR South African women, which occurs in a genotype-specific manner. These findings highlight epigenetic changes that can be modulated by exercise during obesity and may aid in appropriate interventions to reduce the surging impact of this disease.







---

## Contact

Tel: +27 21 938 0911  
Fax: +27 21 938 0200  
Email: [info@mrc.ac.za](mailto:info@mrc.ac.za)