11th ANNUAL

Showcasing the scientific resilience of our next generation scientists amidst the COVID pandemic.

BRIP

BIOMEDICAL RESEARCH AND INNOVATION PLATFORM

SYMPOSIUM

SCIENTIFIC PROGRAMME

18 & 19 OCTOBER 2021

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Showcasing the scientific resilience of our next generation scientists amidst the COVID pandemic.

11th Annual Biomedical Research and Innovation Platform Symposium

Scientific Programme

18 & 19 October 2021

Foreword

It is my honor to welcome delegates and participants to the 11th Biomedical Research and Innovation Platform (BRIP) Symposium to be held 18 – 19 October 2021. Following the very successful virtual 10th Symposium, it was hoped that we could welcome our friends and colleagues to a face-to-face meeting, however, with the safety of our delegates foremost the 11th Symposium is to be hosted as a hybrid event.

On behalf of the organizing committee, I would like to thank the invited speakers, oral and poster presenters, chairpersons and delegates for their participation. We hope that this symposium offers an exhilarating atmosphere to our young emerging scientists to showcase their work in the field of health and medical sciences. We would like to encourage established researchers and academics to use this opportunity to encourage joint research participation, strengthen networks and promote scientific publication.

I would like to thank the Symposium organizing and program committee members for all their hard work. I hope you enjoy participating in the 11th BRIP Symposium and that the sessions are interesting and informative. We look forward to seeing all of you next year at the BRIP Symposium.

Johan Louw
Interim Director
Biomedical Research and Innovation Platform

Organising committee

Dr Babalwa Jack

Dr Pritika Ramharack

Dr Nireshni Chellan

Dr Oelfah Patel

Dr Lawrence Mabasa

Ms Noluxabiso Mangwana

Dr Sylvia Riedel-van Heerden

Prof Rabia Johnson

11th Annual Biomedical Research and Innovation Platform Symposium

18-19 October, 20201

Scientific Programme

Day 1

13h00 – 13h15	**Registration/log-in**	
13h15 – 13h30	**Welcome and Opening:** Dr Mongezi Mdhluli (Chief Research Operation Officer in the office of the SAMRC President)	

Session 1

Session Chairs: Drs Tarryn Willmer & Samukelisiwe Shabalala

13h30 – 14h00	**Key note speaker:** Dr David Martínez Selva, Diabetes and Metabolism Department Vall d'Hebron Research Institute (VHIR), Barcelona, Spain "Sex hormone binding globulin regulation by nutritional factors and its role in human disease development (Obesity and/or FLD)"	
14h00 – 14h15	Beta cell regenerative potential of *Zanthoxylum chalybeum* aqueous stem bark extract	Clare Kimani (PhD)
14h15 – 14h30	Doxorubicin-induced cardiotoxicity is associated with a change in high-density lipoprotein subclass in a mouse breast cancer model	Carmelita Abrahams (PhD)
14h30 – 14h45	An investigation into the role of adiposity and progestins used in menopausal hormone therapy on hallmarks of breast cancer	Hayley Jackson (PhD)
14h45 – 15h00	Anti-metaflammatory effect of the acetone extract of *Commelina benghalensis* on 3T3-L1 adipocytes and Raw 264.7 macrophages	Ontefetse N Plaatjie (MSc)
15h00 – 15h15	Tea break	

Session 2

Session Chairs: Drs Yonela Ntamo & Lawrence Mabasa

15h15 – 15h45	**Key note speaker:** Prof Aruni Bhatnagar, Professor of Medicine at University of Louisville, USA: "Monitoring COVID-19 using randomized testing and wastewater analysis"	
15h45 – 16h00	Detection of SARS-CoV-2 viral RNA in Stellenbosch University student residences using a wastewater-based epidemiology approach	Noluxabiso Mangwana (PhD)
16h00 – 16h15	Inter-individual genetic variation and the development of hypertension in a Xhosa African population of Eastern Cape, South Africa	Sihle Mabhida (PhD)
16h15 – 16h30	Impact of lifestyle on cytochrome P450 monooxygenase repertoire is clear in the bacterial phylum *Firmicutes*	Tiara Padayachee (MSc)
16h30 – 16h45	Pinocembrin attenuates doxorubicin-induced cardiotoxicity by regulating autophagy and apoptosis	Nonhlakanipho Sangweni (PhD)
16h45 – 17h00	**Discussion and closing for the day**	

Day 2

8h40 – 8h50	**Registration/log-in**	
8h50 – 9h00	**Welcome and Opening:** Prof Christo Muller, Chief Specialist Scientist, BRIP	

Session 3

Session Chairs: Drs Pieter Venter & Oelfah Patel

9h00 – 9h30	**Key note speaker:** Dr Matthys Potgieter, Epcon "Modelling the evolution of the COVID-19 pandemic using artificial intelligence"	
9h30 – 9h45	Morphological and gene expression differences in cardiac, retroperitoneal, and inguinal fat in an experimental model of obesity and type 2 diabetes	Thembeka Nyawo (PhD)
9h45 – 10h00	ATM as a novel key player in oxidative stress induced senescence in the cardiomyocyte	Sarah Harries (MSc)
10h00 – 10h15	The genetic architecture of amygdala nuclei	Mary Mufford (PhD)
10h15 – 10h30	The antimicrobial and anti-inflammatory effects of silver nanoparticles synthesized from *Cotyledon orbiculata*	Caroline Tyavambiza (PhD)
10h30 – 10h45	Tea break	

Session 4

Session Chairs: Drs Kwazi Gabuza & Stephanie Dias

10h45 – 11h15	**Key note speaker:** Prof M Razeen Davids, Division of Nephrology, Stellenbosch University and Tygerberg Hospital, Cape Town, South Africa "Treating kidney failure in South Africa – the role of a renal registry"	
11h15 – 11h30	Distinct differences in P-selectin in Parkinson's disease and healthy control groups: a case for a potential biomarker for Parkinson's disease	MJ van Vuuren (PhD)
11h30 – 11h45	Investigation of the intestinal immune status in diabetic C57BLKS *db/db* mice	Kauthar Parker (MSc)
11h45 – 12h00	A TBX3 oncogenic signalling axis important in breast cancer	Stephanie Ncube (PhD)
12h00 – 12h30	**Discussion**	
12h30 – 12h45	**Prize giving and closing: Prof Johan Louw, Senior Director – Centre and Platforms Office**	

Venue: Microsoft Teams

Guest speaker: Dr David Martínez Selva,

Diabetes and Metabolism Department Vall d'Hebron Research Institute (VHIR), Barcelona, Spain

My name is David Martínez Selva and I got my Bachelor's Degree in Biology in 1996 at the University of Barcelona. I obtained my PhD in Biochemistry and Molecular Biology at the Autonomous University of Barcelona in 2001. After my PhD I accepted a postdoctoral position for 7 years in Professor Hammond laboratory first at the London Regional Cancer Center, University of Western Ontario, Ontario, Canada and later on at the Child and Family Research Institute (CFRI) in the University of British Columbia (UBC), Vancouver, British Columbia, Canada where I worked on the molecular mechanisms regulating hepatic sex hormone binding globulin (SHBG) production in several human SHBG transgenic mice and HepG2 cells.

Ten years ago I obtained a principal investigator position through the Miguel Servet Program in the Diabetes and Metabolism Department at the Vall d'Hebron Research Institute in Barcelona, Spain. I have two main research lines: (i) Study the molecular mechanisms regulating SHBG expression in human disease (mainly in obesity, type 2 diabetes and NAFLD). The results have been published in high impact journals (Simo et al. Diabetes 2012, Simo et al. Mol Endocrinol 2012a, Simo et al. Mol Endocrinol 2012; Sáez et al. Mol Nutr Food Res 2014; Simo et al. Endocrinology 2015; Simo et al. Trends Endocrinol Metab. 2015; Sáez et al. Sci Rep 2017; Sáez et al. JCEM 2018; Brianso-Llort et al. Mol Nutr Food Res 2020). (ii) Study the role of SHBG in human disease development. The results have been published in high impact journals (Sáez et al. Endocrinology 2015; Sáez et al. Endocrinology 2017; Sáez et al. J Nutr Biochem 2020).

Guest Speaker: Prof Aruni Bhatnagar,

PH.D., FAHA

Dr. Bhatnagar is Professor of Medicine and Distinguished University Scholar at the University of Louisville. He is the Director of the Christina Lee Brown Envirome Institute and Co-Director of the American Heart Association Tobacco Regulation Center. He is a leading expert on the mechanisms by which environmental exposures such as air pollution affect cardiovascular disease risk. Dr. Bhatnagar's initial work involved the purification and characterization of aldose reductase and its role in diabetic complications. To this end, he established the identity of this enzyme in several tissues and investigated its structural, kinetic, and inhibitory properties. His work has shown that increasing NO availability prevents aldose reductase activation and sorbitol accumulation in diabetic tissues. Additionally, his recent studies show that glucose activates multiple protein kinases and that the activation of these kinases is required for the inflammatory effects of glucose in vascular tissues. At UofL, Dr. Bhatnagar's work also led to elucidation of the mechanisms by which free radicals and lipid peroxidation products affect the function of individual ion channels. He was the leader of a Program Project Grant from the NIEHS to study the cardiovascular toxicity of environmental aldehydes. In this program-project he directed a large multi-disciplinary team of investigators studying the molecular and cellular mechanisms of aldehyde toxicity. His studies at UofL have led to the development of the new field of Environmental Cardiology. He was the Deputy Editor of *Circulation Research* for 10 years. He has participated in over 50 NIH review panels and chaired several review panels. He was the recipient of the President's Award for Outstanding Scholarship, Research and Creative Activity, University of Louisville, and Partner in Healthcare Award – Contributing to Greater Louisville Healthcare Community, in 2007. In 2007, he also received the first Outstanding Faculty Mentor of Graduate Students, and the Outstanding Mentor Award from the Conference of Southern Graduate Schools. In 2017, he was designated Research Exemplar by Washington University. Dr. Bhatnagar has published 381 peer-reviewed manuscripts, 25 book chapters and reviews and over 200 abstracts. He has mentored 61 graduate students and post-doctoral fellows in his laboratory and has served on the dissertation committee of 18 Ph.D. students.

Guest Speaker: Dr Matthys Potgieter,

Epcon

Matthys Potgieter is a South African medical doctor pursuing a PhD in the field of *Mycobacterium tuberculosis* proteogenomics and metaproteomics focusing on the development of software to identify determinants of pathogen virulence at the molecular level. As Science Lead and co-founder at EPCON, Matthys specializes in the use of biologically inspired computing approaches to help solve real-world health problems, including deep learning approaches for computer-assisted diagnostics, and bayesian approaches to epidemic mapping and hotspot detections, to optimize the yield and efficiency of public health interventions. During the Covid-19 epidemic, Matthys and the team at EPCON developed an integrative tool for Covid-19 burden estimation using temporal and spatial modelling, providing the ability to interrogate the potential effects of any interventions on the spread and management of pandemics and their burden on the health care system. Matthys is passionate about bridging the gap between machine learning insights with human understanding and scientific investigation, and optimizing health systems using the assistance of automated and validated technologies.

Guest Speaker: Prof Razeen Davids,

Professor Razeen Davids is Head of the Division of Nephrology at Stellenbosch University and Tygerberg Hospital. In 2000-2001 he spent a year at the University of Toronto as an International Society of Nephrology (ISN) Fellow with Professor Mitch Halperin studying electrolyte and acid-base disorders. He has since been a host mentor to ISN Fellows from several African countries and from Nepal. His interests include electrolyte and acid-base disorders, medical education - especially e-learning - and the epidemiology of chronic kidney disease.

With Professor Halperin, he wrote a series of "Masterclasses in Medicine" articles in the QJM in the form of "clinical detective stories" to engage the reader in solving challenging electrolyte and acid-base cases. He also completed a PhD on the development and usability evaluation of an e-learning resource on electrolyte and acid-base disorders. Prof Davids is an ISN Educational Ambassador.

He was involved in establishing a national renal registry for South Africa and later also the African Renal Registry, with Ghana, Burundi, Zambia, Kenya, Botswana and Nigeria as the first countries to join the project.

Prof Davids is Deputy Editor of the African Journal of Nephrology and has overseen the migration of the Journal from a traditional paper journal to an online, open access publication.

Biomedical Research & Innovation Platform Symposium 2021

18 & 19 October 2021

Poster Presenters

Poster number	Name	Surname	Degree	Institution
1	Melvi	Todd	PhD	ARC/SU
2	Carol	Mahachi	PhD	SU
3	Matladi Innocent	Masete	MSc	BRIP/UP
4	Amanda	Menzele	MSc	UCT
5	Dintle	Molopi	MSc	CARMA/SU
6	Sharnay	Naidoo	MSc	BRIP/CARMA/SU
7	Frans	Everson	PostDoc	CARMA/SU
8	Boipelo	Kgokane	MSc	CARMA/SU
9	Mante	Kgakishe	MSc	UL
10	Nnini	Obonye	MSc	BRIP/CARMA/SU

Abstracts – Presentations PhD category

Beta cell regenerative potential of *Zanthoxylum chalybeum* aqueous stem bark extract

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[2]Division of Clinical Anatomy, Stellenbosch University
[3]Biomedical Research and Innovation Platform, South African Medical Research Council
[4]Institute of Primate Research, Nairobi, Kenya
[5]Department of Biomedical Sciences, Ross University School of Veterinary Medicine, PO Box 334, Basseterre, St Kitts and Nevis, West Indies

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BACKGROUND:
Diabetes is characterized by pancreatic beta cell dysfunction and loss of beta cell mass even with pharmaceutical intervention. Despite this, the pancreas harbours an inherent regenerative capacity that may be enhanced by targeting molecular pathways that regulate apoptosis, neogenesis, transdifferentiation and proliferation. *Z. chalybeum* extracts are used traditionally to treat diabetes mellitus in Africa with pharmacological efficacy having been confirmed experimentally using *in vitro* and *in vivo* models of diabetes. However, effects on beta cell regeneration remain to be established.

OBJECTIVES:
This study evaluated the effects of a chemically characterised *Z. chalybeum* aqueous stem bark extract on beta cell regeneration.

METHODS:
RIN-5F pancreatic beta cells were cultured under normal conditions or in the presence of diabetogenic stressors (palmitate or streptozotocin) before treating with varying concentrations the extract and assessing cell viability, proliferation, apoptosis and oxidative status. *In vivo*, pancreas tissue from streptozotocin-induced diabetic male Wistar rats, treated with *Z. chalybeum* were examined for the expression of beta cell proliferation and differentiation markers. LC-MS/MS analysis was conducted to elucidate the chemical profile of the *Z. chalybeum* extract.

RESULTS:
In normal cells, *Z. chalybeum* increased cell viability and cell numbers, without altering the cell cycle. In palmitate or streptozotocin-pre-treated cells, *Z. chalybeum* did not mitigate ROS generation or apoptosis. *In vivo*, preliminary analysis showed beta cell hyperplasia in extract-treated islets. However, the average beta cell size was smaller than that in the normal and diabetic control groups. Further, although not statistically significant, Pdx-1 expression was higher in extract-treated islets. LC-MS/MS analysis of *Z. chalybeum* identified several bioactive phenolic compounds that could account for the observed activity.

CONCLUSION:
Z. chalybeum extract has mitogenic effects in RIN-5F pancreatic beta cells, and the findings were corroborated *in vivo* in diabetic Wistar rats. However, further studies are still needed to elucidate the molecular mechanisms involved.

Doxorubicin-induced cardiotoxicity is associated with a change in high-density lipoprotein subclass in a mouse breast cancer model

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BACKGROUND:
Doxorubicin (DOX) is an effective and frequently used chemotherapy. Unfortunately, many cancer patients suffer from cardiotoxic side effects of this drug. DOX treatment is also associated with dyslipidemia which may contribute to cardiovascular damage. We aimed to establish an *in vivo* breast cancer mouse model to investigate the association between DOX-induced cardiac toxicity and a change in high-density lipoprotein (HDL) subclass.

METHODS:
Breast cancer was induced in female C57/Bl6 mice (7-8 weeks old) by subcutaneous injection of the E0771 cell line. Once tumours were palpable, DOX (5 mg/kg, i.p.) was given weekly for 5 consecutive weeks. The following groups were considered: Control (C, n=11), Tumour control (T, n=14), DOX (D, n=11) and DOX+Tumour (DT, n=12). Cardiac function was monitored with echocardiography and HDL subclass distribution was measured in serum using the Lipoprint® system.

RESULTS:
A 5-week treatment with DOX reduced tumour volume (5512±1223 mm^3 for T vs 3229±699mm^3 for DT, p=0.02). DOX treatment also reduced cardiac radial strain of the anterior wall (30.04±4.24Pk% for D vs 46.41±5.21Pk% for C, $p<0.05$) and tend to reduce the ejection fraction. In mice with the tumour, a shift in HDL classes from intermediate to large HDL subclasses was observed 64.8±3.5% (T) vs 74.8±2.0% (C) for intermediate HDL subclasses and 34.6±3.6% (T) vs 25.7±2.0% (C) for large HDL subclasses. This effect was lost in the presence of DOX in breast cancer mice.

CONCLUSION:
In this preclinical mouse breast cancer model, DOX treatment reduced tumour growth, a benefit that was unfortunately associated with early cardiac damage and a shift in HDL subclasses from intermediate to large. Further analysis of HDL functionality and composition is in progress to assess whether this shift in HDL subclass effectively contributes to cardiac damage.

An investigation into the role of adiposity and progestins used in menopausal hormone therapy on hallmarks of breast cancer

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BACKGROUND:
Breast cancer prevalence is disproportionately higher in postmenopausal compared to premenopausal women. This may be partly attributed to the use of menopausal hormone therapy (MHT), containing a progestin in combination with estrogen, with the progestin component considered the culprit for the increased risk of breast cancer incidence. Additionally, obesity increases the risk of breast cancer in postmenopausal women, but whether obesity exacerbates breast cancer in women using progestin-containing MHT is not clear.

OBJECTIVES:
This study evaluated whether adiposity exacerbates the effects of progestins, medroxyprogesterone acetate (MPA), norethisterone (NET) and drospirenone (DRSP) on specific hallmarks of breast cancer.

METHODS:
3T3-L1 murine adipocytes were used as a cell line model mimicking adiposity. The T47D ERα+ and MDA-MB-231 ERα- breast cancer cell lines were treated with adipocyte conditioned medium (ACM) that had been pre-treated with a specific progestin. Cell proliferation, migration, and invasion were investigated using a 3-(4,5-dimethylthiazol-2-yl)-2,5diphenyltetrazolium bromide (MTT) cell viability assay, a wound-healing migration assay, and a transwell invasion assay, respectively.

RESULTS:
Treatment with ACM did not affect MPA-, NET- and DRSP-induced proliferation and migration in T47D cells. In contrast, treatment with ACM increased MPA-induced proliferation and migration in MDA-MB-231 cells. While NET and DRSP had no effect on MDA-MB-231 proliferation in the absence and presence of ACM, ACM increased NET- and DRSP-induced migration. Preliminary results showed that while neither MPA- nor NET-treated ACM affected cell invasion in T47D cells, it was increased by DRSP-treated ACM.

CONCLUSION:
Adiposity did not affect progestin-induced proliferation and migration in T47D cells, whereas in MDA-MB-231 cells, adiposity exacerbated MPA-induced proliferation, as well as MPA- NET- and DRSP-induced migration. These results suggest that adiposity may exacerbate progestin-induced responses in ERα-, but not ERα+ breast cancer *in vivo*.

Detection of SARS-CoV-2 viral RNA in Stellenbosch University student residences using a wastewater-based epidemiology approach

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BACKGROUND:
Wastewater-based epidemiology is a cost-effective, complementary surveillance system that can be used to monitor the prevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in communities through the shedding of SARS-CoV-2 in faeces. Due to a proportion of coronavirus disease 2019 cases being asymptomatic, the current SARS-CoV-2 diagnostic capacity is limited, posing a challenge in tracking and tracing new infections especially in defined communities. Targeted surveillance is essential in settings such as student residences, which are considered infection hotspots.

OBJECTIVES:
This study evaluated the efficacy of SARS-CoV-2 targeted wastewater surveillance for outbreak mitigation at Stellenbosch University's student residences.

METHODOLOGY:
Wastewater samples (n=195) were collected bi-weekly from manholes at Tygerberg Campus (TC) and Stellenbosch Campus (SC) using passive sampling devices. Total RNA was extracted from 25 mL of wastewater using a Qiagen RNeasy® PowerSoil® Total RNA kit. SARS-CoV-2 quantitative reverse transcriptase PCR was performed using the Bio-Rad iTaq™ Universal Probes One-Step Kit targeting the Nucleocapsid proteins. Quantitative analysis was performed using an Applied Biosystems™ QuantStudio™ 7 Flex Real-Time PCR instrument.

RESULTS:
SARS-CoV-2 RNA was detected in all samples collected during the peak of the third wave. Before onset of the third wave, SARS-CoV-2 viral loads on both campuses averaged 550 gc/mL. The SARS-CoV-2 virus loads on both campuses rapidly increased on 09-Jun-2021 (the start of the third wave in Western Cape), with one of the SC residences (SC 4) reaching at 30000 gc/mL and one of the TC residences (TC 4) peaking at 35000 gc/mL. These results preceded an increase in verified diagnostic cases, prompting a decision to cease campus activities and transition to online learning from June to August 2021.

CONCLUSION:
The outcomes of this study suggest that wastewater surveillance can be utilized as a non-invasive method to monitor high-risk university student residences, generating an alarm for informed decision-making to minimizing transmission.

Inter-individual genetic variation and the development of hypertension in a Xhosa African population of Eastern Cape, South Africa

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BACKGROUND:
Accumulative evidence shows that hypertension (HTN) has now become a leading cardiovascular disease risk factor, with 1.13 billion individuals affected globally. While data exist on individuals of European descent, currently, there is a scarcity of data on the African population, particularly the role inter-individual genetic variation plays in HTN. Thus, the study sought to investigate the influence of inter-individual genetic variation on HTN prevalence in a South African population.

METHODS:
To accomplish these aims, *in silico* identification of genetic variants potentially associated with HTN was performed. This approach allows for identification of single nucleotide polymorphisms (SNPs) associated with the development of HTN using publicly available databases. A total of 84 SNPs linked to 53 prioritized genes related to HTN were identified and used to perform co-expression analysis. Subsequently, with the use of MassArray analysis, the presence of 13 selected SNPs identified in the *in-silico* method (co-expression clusters) were evaluated using DNA from 265 HTN patients and their age-matched controls (n = 154).

RESULTS:
Of the three clusters identified, *AGT, AGTR1, AGTR2* and *ACE* were co-expressed, and as such, identified as potential multiple drug targets. Genotyping results showed that most SNPs identified in clusters didn't deviate from the Hardy Weinberg equilibrium. We also observed that SNPs linked to *AGT* (rs2004776, p = 0.043; rs3789678, p = 0.020; and rs4762, p = 0.046) were significantly associated with HTN in the Xhosa African population of Eastern Cape.

CONCLUSION:
This study demonstrated that the prevalence of HTN was high among the Xhosa African population of Eastern Cape and that rs2004776, rs3789678, rs4762 located within the AGT gene might be a strong predictor of HTN. As such, a follow up study with a greater sample size will be interrogated to confirm this association.

Pinocembrin attenuates doxorubicin-induced cardiotoxicity by regulating autophagy and apoptosis

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BACKGROUND:
In a recent study we demonstrated the cardioprotective effect of pinocembrin (Pin), a potent flavonoid, against doxorubicin (Dox)-induced cardiotoxicity. However, the mechanism by which Pin offers its prophylactic benefits remains unclear. Moreover, given the concerns surrounding the co-administrative use of chemotherapy with novel cardioprotectants, it remains equally important to study the efficacy of Dox when used with Pin.

OBJECTIVES:
Thus, the aims of this study were two-fold. The first was to study the prophylactic effect of Pin against Dox-induced autophagy and apoptosis in an H9c2 cardiomyoblast model. Then, to determine the efficacy of Dox when co-administered with Pin using an MCF-7 breast cancer model.

METHODS:
To establish proof of concept, H9c2 cells were treated with Dox (0.5uM) for 6 days. Thereafter, the prophylactic effect of Pin against Dox-induced cardiotoxicity was determined by treating the cells with Dox + Pin (1 μM) for the same duration. Hereafter, western blot analysis was used to quantify the expression of mitochondrial function, autophagy, and apoptosis markers. Subsequently, the effect of Pin on the chemotherapeutic potential of Dox was studied by exposing the MCF-7 cells to the same treatment conditions as described above.

RESULTS:
As an adjunct to Dox, Pin ameliorated cardiac mitochondrial function by enhancing the expression of pAMPK, PG1-α, UCP2 and PPARγ. We further observed a noticeable improvement in the regulation of autophagy markers; pMTOR, p53, LC3B, ATG5 and PINK1. As a result, Pin significantly attenuated Dox-induced apoptosis by increasing pAkt expression and decreasing caspase 3/7activity. More importantly, the efficacy of Dox was preserved following co-treatment with Pin, as could be seen by the continued cancer cell death.

CONCLUSION:
The data presented in this study demonstrates that Pin might be a suitable candidate that can be safely administered with Dox to alleviate the risk of developing cardiomyopathy without potentiating cancer.

Morphological and gene expression differences in cardiac, retroperitoneal, and inguinal fat in an experimental model of obesity and type 2 diabetes

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BACKGROUND:
Adipose depots contribute differently to the pathogenesis of metabolic diseases that increase cardiovascular disease risk. Cardiac fat (CF), a unique visceral fat depot, has emerged as an important player in cardiovascular health. Accumulating evidence suggests that adipose tissue expansion and metabolic derangements within CF are linked with deteriorating cardiovascular health.

OBJECTIVES:
This study compares morphological and gene expression differences in CF, visceral and subcutaneous adipose depots, using *db/db* mice, an established experimental model of obesity and type 2 diabetes (T2D).

METHODS:
CF, retroperitoneal (RF) and inguinal (IF) fat, representing visceral and subcutaneous fat, respectively, were collected from 18-week-old male *db/db* mice and non-diabetic littermates. Morphological differences between fat depots were assessed using haematoxylin & eosin staining and image analysis. Gene expression differences were evaluated using quantitative real-time PCR, targeting genes involved in oxidative stress, thermogenesis, inflammation, and substrate metabolism.

RESULTS:
Adipocyte hypertrophy was evident in all adipose depots of *db/db* mice, although smaller, multilocular adipocytes were observed in CF compared to RF and IF. The expression of uncoupling protein 1 (*UCP1*) was higher in CF compared to RF and IF, independent of diabetes status. Uncoupling protein 2 (*UCP2*) was increased in IF and RF of *db/db* mice compared to non-diabetic mice. The expression of adenosine 5' monophosphate-activated protein kinase (*AMPK*), nuclear factor erythroid 2-related factor (*NRF2*), fatty-acid-binding protein (*FABP4*) and glucose transporter type 4 (*GLUT4*) was increased, while glutathione S-transferases (*GST*) was decreased in IF of *db/db* mice compared to non-diabetic mice. Tumour necrosis factor alpha (*TNFα*) expression was increased in the RF of *db/db* mice compared to non-diabetic mice.

SUMMARY:
Adipocyte morphology and gene expression differed according to adipose depot and diabetes status. The increased expression of *UCP1* in CF highlights its unique thermogenic characteristics and potential as a therapeutic target in cardiovascular disease.

The genetic architecture of amygdala nuclei

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BACKGROUND:
A number of genetic variants influencing total amygdala volume have been identified in previous research. However, the genetic architecture of its distinct nuclei have yet to be thoroughly explored.

OBJECTIVES:
We aimed to investigate whether increased phenotypic specificity through segmentation of the nuclei aids genetic discoverability and sheds light on the extent of shared genetic architecture and biological pathways between the nuclei and disorders associated with the amygdala.

METHODS:
T1-weighted brain MRI scans (n=36,352, mean age= 64.26 years, 52% female) of trans-ancestry individuals from the UK Biobank were segmented into nine amygdala nuclei with FreeSurfer v6.1, and genome-wide association analyses were performed on the full sample and a European-only subset (n=31,690). We estimated heritability using Genome-wide Complex Trait Analysis, derived estimates of polygenicity, discoverability and power using MiXeR, and determined genetic correlations and shared loci between the nuclei using Linkage Disequilibrium Score Regression, followed by functional annotation using FUMA.

RESULTS:
The SNP-based heritability of the nuclei ranged between 0.17-0.33, and the central nucleus had the greatest statistical power for discovery. Across the whole amygdala and the nuclei volumes, 38 novel significant ($p < 5x10^{-9}$) loci were identified, with most loci mapped to the central nucleus. The mapped genes and associated pathways revealed both unique and shared effects across the nuclei, and immune-related pathways were particularly enriched across several nuclei.

CONCLUSION:
These findings indicate that the amygdala nuclei volumes have significant genetic heritability, increased power for discovery compared to whole amygdala volume, may have unique and shared genetic architectures, and a significant immune component to their aetiology.

The antimicrobial and anti-inflammatory effects of silver nanoparticles synthesized from *Cotyledon orbiculata*

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BACKGROUND:
Cotyledon orbiculata, commonly known as pig's ear, is an important medicinal plant of South Africa. It is used in traditional medicine to treat many ailments, including skin eruptions, abscesses, inflammation, boils and acne. Several therapeutic drugs have been sourced from medicinal plants. Medicinal plants have also been used in the synthesis of nanomaterials, especially metallic nanoparticles. Nanomaterials produced in this way produce are more biocompatible and thus more suitable for biomedical applications.

OBJECTIVES:
This study aimed to synthesize silver nanoparticles using *C. orbiculata* aqueous extract and to investigate the antimicrobial, anti-inflammatory and wound healing properties of the synthesized nanoparticles as well as the plant extract.

METHODS:
The *C. orbiculata* extract was used to synthesize silver nanoparticles which were then characterized. The antimicrobial activity of the extract and nanoparticles were evaluated against skin pathogens (*Staphylococcus aureus, Staphylococcus epidermidis*, Methicillin resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa* and *Candida albicans*). The immunomodulatory activity of the extract and nanoparticles were evaluated by determining their effects on cytokine production in THP-1 macrophages. The cytokine levels (TNF-alpha, IL-1 beta, and IL-6) were measured using the enzyme linked immunoassay. The wound healing activity was assessed using the scratch assay on cell cultures.

RESULTS:
C. orbiculata aqueous extracts were able to successfully synthesize spherical silver nanoparticles, which are 20-40nm in size. Antimicrobial activity of silver nanoparticles was higher than that of the extracts. The nanoparticles exhibited good antimicrobial activity, with the highest activity observed against *P. aeruginosa* (5 µg/mL). The nanoparticles also showed anti-inflammatory activity by inhibiting cytokine secretion in lipopolysaccharide-treated macrophages. Both the nanoparticles and the extract showed good wound healing activities.

CONCLUSION:
It can be concluded that *C. orbiculata* synthesized nanoparticles possess antimicrobial and anti-inflammatory properties. These nanoparticles can therefore be of importance in the development of new antimicrobial and anti-inflammatory drugs.

Distinct differences in P-selectin in Parkinson's disease and healthy control groups: a case for a potential biomarker for Parkinson's disease

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BACKGROUND:
Parkinson's disease (PD) is characterised by progressive loss of dopaminergic neurons in the substantia nigra (SN) and the presence of intracellular α-synuclein aggregates, known as Lewy bodies. More than half of neurons in the substantia nigra are already lost at the time of the onset of symptoms, the focus of research has shifted to early detection rather than treatment. The aetiology of PD includes various interlinking pathological pathways, such as impaired protein clearance, inflammation and hypercoagulation. With no cure available it becomes vital to identify biomarkers for the early detection of PD. This study identifies P-selectin, a major activator of both immune cell recruitment and the coagulation cascade, as a potential biomarker for PD.

OBJECTIVES:
To identify key biomarkers functioning at various underlying pathological pathways for the early detection and diagnosis of PD. We investigated the presence of biomarkers, including protein clearance / aggregation (α-syn and mitochondrial chaperone protein), mortalin, markers of inflammation / coagulation (C-reactive protein, serum amyloid A, soluble intercellular cell adhesion molecule-1, soluble vascular cell adhesion molecule-1, and P-selectin).

METHODS:
Plasma samples from PD patients and healthy controls were analysed for potential biomarkers using ELISA techniques. Selected analytes (P-selectin and mortalin) were visualised by fluorescence microscopy and analysed using ImageJ. Thromboelastography formed part of coagulation parameters.

RESULTS:
Contrary to what we expected, circulating mortalin levels was significantly higher in PD patients, compared to healthy controls ($p < 0.01$). Analysis of mean fluorescent area indicated a significantly higher P-selectin levels in PD patients compared to controls ($p < 0.0001$).

CONCLUSION:
Our results identify P-selectin as a potential biomarker for PD. Further investigation is necessary in a different study design to confirm these results that may contribute to the development of an early PD diagnostic panel.

A TBX3 oncogenic signalling axis important in breast cancer

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BACKGROUND:
Breast cancer is the leading cause of cancer-related deaths in women globally with 58% occurring in low-middle-income countries. There is therefore a need to identify more effective breast cancer therapies. The transcription factor TBX3 is critical for breast development and when expressed in postnatal mammary tissues it contributes to breast cancer. Importantly, TBX3 has been validated as a novel therapeutic target and identifying breast cancer oncogenic factors that co-operate with TBX3 may represent important anti-cancer drug targets.

OBJECTIVES:
To identify and characterise (1) signalling molecules that upregulate TBX3 and (2) protein partners that cooperate with TBX3 to promote breast cancer.

METHODS:
To determine if c-Myc regulates TBX3 expression, luciferase reporter and qRT-PCR assays were performed. Nucleolin and Hsc70 were identified and validated as TBX3 co-factors by affinity purification coupled with mass spectrometry, immunoprecipitation assays and confocal microscopy/co-localisation analysis. The functional significance of (1) TBX3-Hsc70 was investigated by siHsc70, MG132 (proteasomal inhibitor) and western blotting and (2) TBX3-nucleolin by RNAi/overexpression in rescue experiments coupled with scratch motility assays. The effect of the nucleolin targeting aptamer, AS1411, on TBX3/nucleolin levels, subcellular localisation, ability to regulate target genes and as a therapy for breast cancer was tested in western blotting, immunofluorescence, qRT-PCR and MTT assays. All experiments were carried out in two breast cancer cell lines.

RESULTS:
We show that c-Myc upregulates TBX3 transcriptionally. Hsc70 enhances TBX3 stability and nucleolin cooperates with TBX3 to promote breast cancer cell migration. The nucleolin targeting aptamer, AS1411, inhibits breast cancer cell viability and migration with no effect on normal breast epithelial cells and mislocalizes TBX3 and nucleolin to the cytoplasm blocking their ability to activate the breast cancer oncogene, ID1.

CONCLUSION:
c-Myc/TBX3/Hsc70/nucleolin is an important oncogenic pathway in breast cancer and AS1411 disrupts this pathway making it a promising therapeutic agent for treating breast cancer.

Abstracts – Presentations MSc category

Anti-metaflammatory effect of the acetone extract of *Commelina benghalensis* on 3T3-L1 adipocytes and Raw 264.7 macrophages

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BACKGROUND:
Obesity is characterised by chronic low-grade inflammation termed metaflammation, which is often accompanied by insulin resistance (IR) and type 2 diabetes mellitus (T2DM). Metformin and non-steroidal anti-inflammatory (NSAID) drugs are commonly used in the treatment of metaflammation. However, data from clinical studies regarding the anti-inflammatory properties of metformin is inconsistent and the use of NSAIDs is costly. *Commelina benghalensis* (CB) is a natural herb that exhibits anti-oxidant, anti-inflammatory, and analgesic activities. As such it is explored as an alternative agent to metformin and NSAIDs in preventing the development of T2DM via inhibition of metaflammation.

OBJECTIVES:
The objective was to explore whether CB could reduce obesity-induced metaflammation in Raw 264.7 macrophages.

METHODS:
The leaves of CB were collected at Bushbuckridge, Mpumalanga Province in South Africa. Ground leaves of CB were exhaustively extracted by maceration in acetone. The presence of secondary metabolites in the extract was determined using various chemical tests. Adipocyte-conditioned medium (Ad-CM) was generated by growing mature 3T3-L1 adipocytes in 1% foetal bovine serum-supplemented media. To mimic the environment of macrophages near adipocytes, Raw 264.7 macrophages were cultured in Ad-CM. The secreted adipokines were assessed using a mouse adipokine proteome profiler. The expressed pro-inflammatory cytokines and chemokines were determined using a mouse cytokine protein profiler.

RESULTS:
The extract tested positive for tested secondary metabolites.The Ad-CM contained adipokines (MCP-1, VEGF, Lipocalin-2, IGFBP-6, TIMP-1, pentraxin 3 and Pref-1). The data showed that CB reduced the expression of MCP-1, CD45, IL-1Ra, and MIP-1α in Ad CM activated Raw 264.7 macrophages. In addition, the acetone extract decreased the expression of pro-inflammatory cytokines (IL-1β, IL-1Ra, IP10, IL-1α, and IL-1β) in lipopolysaccharide-activated Raw 264.7 macrophages.

CONCLUSION:
Commelina benghalensis contains compounds with potential anti-metaflammatory activity. It inhibited pro-inflammatory cytokines and chemokines and could potentially lead to a reduced susceptibility of developing T2DM in obesity-induced metaflammation.

Impact of lifestyle on cytochrome P450 monooxygenase repertoire is clear in the bacterial phylum *Firmicutes*

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BACKGROUND:
P450s enzymes play a key role in organisms primary and secondary metabolism. The impact of lifestyle on P450 profiling in bacteria is scarcely reported. Thus, impact of lifestyle on P450 profiles in the bacterial phylum *Firmicutes* is analyzed as it contains bacteria that are adapted to diverse lifestyles.

OBJECTIVES:
Assessing the impact of lifestyle on P450 profiling in *Firmicutes* species. Genome data-mining, annotation and phylogenetic analysis of P450s and their association with secondary metabolism in *Firmicutes* species was carried out.

METHODS:
Species and database: 972 *Firmicutes* species genome available at Kyoto Encyclopedia of Genes and Genomes were used in this study.

Genome data mining and annotation of P450s: The whole proteome of each *Firmicutes* species was analyzed for protein family assignment using NCBI Batch Web CD-Search Tool. Then, P450 hit proteins were annotated following the International P450 Nomenclature Committee rules.

Phylogenetic analysis: P450 protein sequences were aligned using MAFFT. Trex Web server and iTOL was used to infer, visualize, and colour the tree.

Generation of P450 profile heat maps: MeV (Multi-experiment viewer) program used for generation of heat-maps to check presence and absence of family in *Firmicutes* species.

Secondary metabolite cluster analysis and P450s identification: Using Anti-SMASH programme, secondary metabolite clusters and P450s part of the clusters were identified.

Comparative analysis: P450s and clusters data for other bacterial species, from published articles were retrieved and used for comparative analysis.

RESULTS:
712 P450s found in 229 species were grouped into 14 and 53 P450 families and subfamilies. *Firmicutes* species have the lowest number of P450s and the lowest P450 diversity compared to bacterial species belonging to the genera *Streptomyces* and *Mycobacterium* and from the phylum *Cyanobacteria*.

CONCLUSION:
Firmicutes species that are pathogens and adapted to simple lifestyles lost P450s in their genomes indicating lifestyle impacted P450 profiles in *Firmicutes* species.

ATM as a novel key player in oxidative stress induced senescence in the cardiomyocyte

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BACKGROUND:
The heart is comprised of terminally differentiated cardiomyocytes that cannot divide postnatally, creating a unique context for cellular senescence. Reactive oxygen species (ROS) can damage the protective telomeres of cardiomyocyte DNA to induce senescence. Ataxia Telangiectasia Mutated (ATM), a DNA repair protein, is essential for redox homeostasis in the cytosol when activated by ROS. The loss of ATM could therefore be a novel driver of senescence due to its role in DNA repair and redox homeostasis.

OBJECTIVES:
To i) determine if ATM levels decrease with age in hearts of male Wistar rats and ii) establish an *in vitro* oxidative stress-induced senescence model to investigate ATM's role in senescence using H9c2 cardiomyoblasts.

METHODS:
Hearts of Wistar rats were fractionated by differential centrifugation into nuclear, cytosolic and mitochondrial fractions. Western Blotting was performed to determine ATM and H2AX protein levels. The *in vitro* model was established by treating H9c2 cells with various doses of H_2O_2 for 24 hours. Treatment was removed and cells were maintained for 3, 5 and 10 days. Cell viability, apoptosis and mitochondrial oxidative stress were determined after 24 hours and 3 days post-treatment. Beta-galactosidase, p16 and p21 expression levels (markers of senescence) were investigated at 3, 5 and 10 days.

RESULTS:
ATM and H2AX levels significantly decreased ($p<0.05$) with age. In the *in vitro* model, cell viability and apoptosis were not significantly influenced when treated with 5-15μM H_2O_2. Mitochondrial oxidative stress was evident after 3 days post-treatment but did not induce senescence. Senescence markers are currently being assessed at 5 and 10 days after oxidative stress induction.

CONCLUSION:
Cardiac ATM and DNA repair decrease in aged male Wistar rats. Preliminary data suggests that the *in vitro* model of oxidative stress-induced senescence in H9c2 cells is a promising model for investigating the role of ATM in senescence.

Investigation of the intestinal immune status in diabetic C57BLKS *db/db* mice

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BACKGROUND:
The prevalence of obesity is increasing worldwide and drives the type 2 diabetes (T2D) pandemic. Anti-inflammatory and anti-diabetic properties of green rooibos extracts (GRE) suggested it has potential for therapeutic strategies. Emerging evidence suggests that low-grade systemic inflammation and altered immune homeostasis in the gut could be underlying factors in the pathogenesis of T2D.

OBJECTIVES:
The aim of this study was to investigate the intestinal immune status in a diabetic C57BLKS *db/db* mouse model and to elucidate whether GRE treatment exerts beneficial effects. Immune status was determined by using Immunoglobulin A (IgA) as the main mucosal protecting antibody, regulatory T cells (Tregs) expressing forkhead domain-containing protein (Foxp3) due to their tolerogenic functions and transforming growth factor-β (TGF-β), which induces the expression of Foxp3 in Tregs.

METHODS:
Lean non-diabetic (*db/+*) and obese diabetic (*db/db*) mice were treated with (i) vehicle control, (ii) pioglitazone, as a positive control (15 mg/kg), (iii) GRE low dose (74 mg/kg), and (iv) GRE high dose (740 mg/kg) for 16 weeks. IgA+ areas and Foxp3+ cells in small intestinal tissues were assessed using immunohistochemistry. In colon tissue, IgA expression was analysed using western blot and TGF-β expression was determined using ELISA.

RESULTS:
A two-way ANOVA showed increased levels ($p=0.0004$) of IgA in the small intestines of pioglitazone treated *db/db* mice compared to control *db/+* mice. Foxp3+ cells in the small intestine were significantly decreased ($p=0.0005$) in *db/db* mice compared to *db/+* mice regardless of treatments (diabetes effect). In the colon, TGF-β ($p=0.002$) and IgA ($p=0.0004$) expression were also significantly decreased in the *db/db* mice regardless of treatment. GRE treatment of diabetic mice showed no significant effects.

CONCLUSION:
The data suggests a disruption in gut homeostasis and immune defence in diabetic animals. Further investigation of the underlying mechanisms of action are required.

Abstracts - Posters PostDoc

A first-line fixed-dose combination ART regimen containing Efavirenz/Emtricitabine/Tenofovir exhibit beneficial effects on retinal microvascular calibre in a South African HIV-infected study population.

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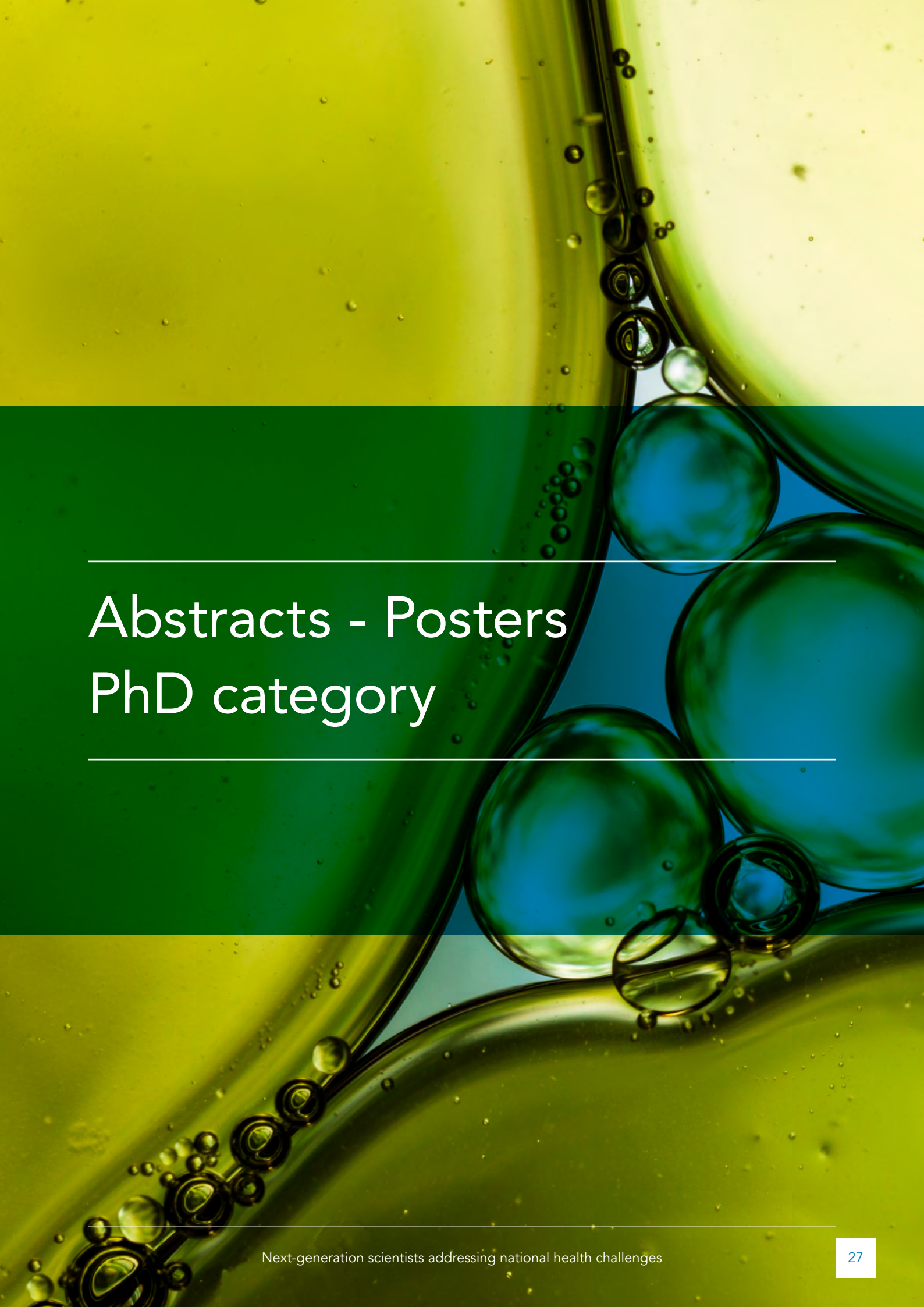
BACKGROUND:
The retinal microvasculature is known to be a surrogate marker of vascular endothelial function and atherosclerosis (arteriolar/venular widening or narrowing); however, the pro-atherosclerotic effects of HIV and antiretroviral therapy (ART) in terms in retinal vessel calibre remain unclear in the South African population.

OBJECTIVES:
This study aimed to investigate the effects of a fixed-dose combination ART regimen containing Efavirenz/Emtricitabine/Tenofovir on retinal microvascular calibres in a South African HIV-infected study population.

METHODS:
HIV-free and HIV-infected participants receiving ART (Efavirenz 600mg, Emtricitabine 200mg, and Tenofovir 300mg) were recruited from health clinics in Cape Town. Data were collected via health questionnaires (Demographic and lifestyle characteristics) and anthropometric (BMI and waist-to-hip ratio) and blood pressure measurements (systolic and diastolic blood pressure) were taken. Biochemical analyses (lipogram, fasting glucose and liver enzymes) were performed by the national health laboratories. Retinal images were captured, and microvascular calibres (central retinal arteriolar equivalent (CRAE) and central retinal venular equivalent (CRVE)) determined. Linear stepwise regression analyses were performed to determine independent associations. Statistical significance was set at $p < 0.05$.

RESULTS:
The total study population (n = 295: HIV-free: n = 143; HIV+ART: n = 152) had a mean age of 39.7±10.3 years. CRVE negatively correlated with ART (r = -0.130; p = 0.030), and positively correlated with viral load (r = 0.279; $p < 0.001$). CRAE/CRVE ratio negatively correlated with viral load (r = -0.183; p = 0.029). Stepwise regression analysis (controlling for age, gender BMI and blood pressure), HIV+ART negatively predicted CRVE (standardised β-coefficient: -0.123, p = 0.037).

CONCLUSION:
HIV-infected participants receiving a fixed-dose combination ART containing Efavirenz/Emtricitabine/Tenofovir was associated with reduced CRVE (characteristic of an inti-inflammatory effect) and increased CRAE/CRVE ratios (previously associated with a reduced risk for mortality in HIV/AIDS).



Abstracts - Posters
PhD category

Consumers' understanding of front-of-pack labels on food packages: A mixed methods study in South Africa

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BACKGROUND:
Food labels, and mainly the nutritional information, are difficult to decipher by many consumers. Formats used to improve consumer understanding of labels include a range of nutrient summaries and warning labels.

OBJECTIVES:
To increase the value created by food labels in South Africa by providing policymakers with insights on the best way to communicate health information on the front of food packages.

METHODS:
The exploratory mixed-method design used interviews (n = 49) to explore stakeholders' suggestions for the improvement of food labels, followed by an online consumer survey (n = 1261) where six front-of-pack (FOP) labels, applied to a fictitious cereal product, were compared to a control (no FOP label). A mixed model ANOVA (Analysis of Variance) was used to compare differences in perceived healthiness between different front-of pack labels.

RESULTS:
Participants perceived the cereal with the health warning (stop sign) as less healthy compared to the control ($p<0.01$). The product with the low health star rating (1.5/5) was also perceived to be less healthy than the control ($p<0.01$), whilst the "unhealthy" Guideline Daily Amount (GDA) label was not perceived to be less healthy ($p=0.06$). The cereal bearing a health claim (low GI) was rated healthier than the control ($p<0.01$), as was the cereal with the high health star rating (4.5/5; $p<0.01$). The "healthy" GDA was not perceived to be healthier than the control ($p=0.12$).

CONCLUSION:
The label depicting a warning performed best to indicate less healthy nutritional profile, with the low health star rating also being effective. The use of health star ratings as part of FOP labelling hold promise to both discourage consumers from less healthy food purchases as well as to guide towards healthier choices.

Proteolytic markers associated with kidney disease in HIV positive individuals before initiation of anti-retroviral therapy (ART)

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INTRODUCTION:
Tissue destruction contributes to chronic kidney disease progression with proteolytic enzymes, neutrophil gelatinase (NGAL) and matrix metalloproteinase-9 (MMP-9), playing individual and interactive roles. When complexed, NGAL and MMP-9 become inactive.

OBJECTIVES:
To determine if NGAL and MMP-9 in urine or plasma differentiate between different forms of kidney diseases in patients with treatment naïve human immunodeficiency virus (HIV) infection (HIV+) to those with focal segmental glomerulosclerosis and no HIV infection and if the complex fails to differentiate whether measured in urine or plasma.

METHODS:
36 patients participated, 25% were male: 10 HIV+ controls, no kidney disease (HIV-NKD), 10 HIV-associated nephropathy (HIVAN), 6 HIV focal segmental glomerulosclerosis (HIV-FSGS) and 10 FSGS no HIV (KD-FSGS). HIVAN and FSGS features were established on histology of biopsied renal tissue. Urine and plasma free NGAL, free MMP-9 and MMP-9/NGAL-complex were analysed using enzyme-linked immunosorbent assay and normalized to urine creatinine and expressed as ng/mg.

RESULTS:
NGAL: Urine NGAL (ng/mg) was significant different in group HIVAN compared to HIV-NKD at $p<0.01$; and HIVAN and HIV-FSGS at $p<0.05$. Plasma NGAL was significantly higher in HIVAN compared to other groups at $p<0.05$.

MMP-9: Urine MMP-9 (ng/mg) differed significantly between HIVAN and HIV-NKD at $p<0.05$.

MMP-9/NGAL-complex: Urine MMP-9/NGAL-complex (ng.mg) was significantly higher in HIVAN compared to HIV-NKD at $p<0.05$.

CONCLUSION:
Urine and plasma NGAL differentiated and distinguished between HIVAN, HIV-NKD and HIV-FSGS. Urine and plasma MMP-9 did not differentiate between the different types of kidney diseases. MMP-9/NGAL complex varied in HIVAN and did not separate the groups when measured in either urine or plasma samples.

Abstracts - Posters
MSc

Metabolic and microRNA expression differences in pregnancies complicated by diabetes mellitus

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BACKGROUND:
Diabetes during pregnancy poses a serious threat to the health of mother and child. All types of diabetes, type 1 diabetes (T1D), type 2 diabetes (T2D) and gestational diabetes (GDM) are associated with adverse pregnancy outcomes. The severity of adverse effects is related to the type of diabetes, which may be attributable to different pathophysiologies. The mechanisms that underlie the different types of diabetes during pregnancy has not yet been fully elucidated.

OBJECTIVES:
The aim of this study was to investigate metabolic and microRNA (miRNA) expression differences in pregnant women with T1D, T2D, GDM and normoglycemia.

METHODS:
Serum was collected from pregnant women with T1D (n=8), T2D (n=38), GDM (n=33) and normoglycaemia (n=39) at 16-27 weeks of gestation. Differences in insulin, C-peptide, total and high molecular weight (HMW) adiponectin and C-reactive protein (CRP) was assessed using enzyme-linked immunosorbent assays. MiRNAs were isolated from serum and expression levels assessed using miScript miRNA PCR arrays, followed by validation with individual SYBR Green PCR assays.

RESULTS:
Insulin and C-peptide concentrations were higher in pregnant women with GDM and T2D compared to normoglycemia. Lower concentrations of total and HMW adiponectin were observed in pregnant women with T2D and GDM compared to T1D and normoglycemia, while higher CRP levels were observed in pregnant women with T2D and GDM compared to T1D and normoglycemia. The expression of miR-19a-3p was lower in GDM, miR-20a-5p was lower in T1D and miR-29a-3p was higher in T2D of pregnant women compared to normoglycemia. Several other miRNAs were differentially expressed between the diabetes groups; however, these were not statistically significant.

CONCLUSION:
Metabolic parameters and miRNA levels differed according to the type of diabetes in pregnancy. These findings highlight the different pathophysiological mechanisms that underlie diabetes during pregnancy and may offer opportunities for risk stratification and intervention to mitigate adverse effects.

Hyperglycaemia-induced impairment of the autorrhythmicity of mouse embryonic stem cell derived cardiomyocytes

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BACKGROUND:
Diabetes mellitus with uncontrolled hyperglycaemia is a leading cause of cardiovascular disease. Diabetic hearts are particularly vulnerable to rhythm disturbances, but the underlying aetiology remains unknown.

OBJECTIVES:
The aim of this study was to explore the effects of hyperglycaemia on the autorrhythmicity of a cardiac developmental model of mouse embryonic stem cell (mESC)-derived cardiomyocytes

METHODS:
Pluripotent mESCs were differentiated into cardiomyocytes through embryoid body (EB) formation, and cultured in culture medium containing either baseline (25mM) or high (50mM) glucose concentration. Time-lapse images of beating EBs were captured on an EVOS™ imaging system and analysed using the ImageJ software coupled with a motion-detecting macro to detect the beating rate and variations in beat-to-beat intervals. The episodes of ectopic beats and onset of asystole were recorded before and after the application of the arrhythmogenic drug quinidine. Action potentials (AP) were measured using fluorescence microscopy and the voltage-sensitive dye di-4-ANEPPS.

RESULTS:
The proportion of beating EBs in high glucose was significantly lower compared to baseline ($p<0.05$; n>14 EBs). In addition, the beating rate in high glucose was reduced compared to that in baseline condition [bpm, mean (SD): 35(13) vs 49(20), $p=0.005$]. However, there was no significant difference between the standard deviation of the beat-to-beat intervals ($p=0.25$). The onset of quinidine-induced asystole in beating EBs occurred earlier in the high glucose (% asystolic EBs at 3 minutes: 75% in high glucose vs 25% in baseline glucose), however the frequency of drug-induced ectopic beats was similar between the two glucose groups ($p=0.6$, n=8 EBs). There were also no significant differences in the AP amplitude and AP duration ($p>0.05$ for both parameters, n=6 EBs).

CONCLUSION:
Hyperglycaemia suppressed the autorrhythmicity of mESC-derived cardiomyocytes and increased the cellular sensitivity to pro-arrhythmic stimulation, with possible clinical implications in diabetic cardiac arrhythmogenesis. The underlying mechanisms were unrelated to electrical changes in the baseline AP profile and will require further molecular studies on the cardiomyocyte pacemaker tissue modulation.

The vascular and endothelial effects of HIV, antiretroviral therapy, and rooibos – Functional effects and mechanism

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BACKGROUND:
Both human immunodeficiency virus-1 (HIV-1) infection and antiretroviral therapy, increase the risk of cardiovascular disease. Rooibos (RB) has been shown to exert potential ameliorative effects against cardiovascular risk factors. A gap however remains in the mechanisms involved. Endothelial dysfunction is characterized by an imbalance in endothelial-derived vasodilatory and vasoconstrictor factors, subsequently reduced nitric oxide bioavailability. The aim of this study was to investigate the functional and mechanistic effects of HIV-1 protein, ART and RB and combination thereof on the endothelium of isolated Wistar rat aorta, by using the aortic ring system.

OBJECTIVES:
To measure vascular reactivity of isolated aortic rings pre-incubated with a cocktail of HIV-1 proteins. To determine the effects of first line ART cocktail (ART1), Second-line ART cocktail (ART2), RB and a combination thereof on endothelial-dependent vasodilation and vasoconstriction.

METHODS:
Stellenbosch University Committee for Animal Care and Use granted ethical approval (ACU-2019 8936). Wistar rats, (+/-250 grams) were obtained from the Animal Care Facility, Tygerberg and euthanised with an intraperitoneal overdose (160mg/kg body weight) of sodium pentobarbital. Thereafter, thoracic aorta were immediately excised, cleaned and washed in Krebs-Henseleit buffer.

Isolated 3 mm-sized aortic rings were incubated for 24 hours with either of the following to establish 8 groups: Control (vehicle control), HIV-1 (25ng/ml), ART1 (efavirenz = 2.8nM, tenofovir = 250nM and emtricitabine = 0.65μM), ART2 (lopinavir = 5μM and ritonavir = 1μM), RB (2%) and a combination thereof. Thereafter, aortic rings were mounted, and contraction/relaxation reactivity was determined in an organ bath perfusion system (AD Instruments, Australia).

RESULTS:
HIV-1 and 2% RB groups significantly reduced contractility, compared to Controls. ART1 and ART2 significantly decreased relaxation, compared to the Control group.

CONCLUSION:
Endothelial dysfunction is the underlying mechanism involved in cardiovascular risk factor susceptibility. ART impairs endothelium-dependent nitric oxide vasorelaxation, while HIV-1 and RB independently impairs vasoconstriction.

Coenzyme Q_{10} attenuates doxorubicin-induced cardiotoxicity in an *in vitro* H9c2 cell model.

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BACKGROUND:
The efficacy of the chemotherapeutic drug, doxorubicin (Dox), is driven by its pro-apoptotic nature. However, accumulative research demonstrates that the clinical significance of Dox is limited by its cardiotoxic side-effects. Currently, coenzyme Q10 (CoQ_{10}), an endogenous antioxidant that exists in its oxidized (ubiquinone- CoQ) or reduced (ubiquinol- $CoQH_2$) form, is suggested to alleviate Dox-induced cardiotoxicity. However, limited *in vitro* studies have investigated the precise role of CoQ_{10} on Dox-induced cardiotoxicity.

OBJECTIVES:
To investigate the cardioprotective effect of CoQ_{10} supplementation against Dox-induced cardiac apoptosis.

METHODS:
To attain the most effective cardioprotective dose, H9c2 cells were co-treated with Dox (0.5 µM) plus varying concentrations (3,6,12,23 and 46 µM) of either CoQ or $CoQH_2$ for 6 days. To determine the efficacy of CoQ_{10} to offer protection against Dox, cells were treated with Dox alone and co-treated with either Dox + CoQ, Dox + $CoQH_2$ or Dox + Dexrazoxane (positive control) for 6 days. Untreated cells served as the control. On day 7, the cardiomyoblasts metabolic activity and rate of early and late apoptosis were quantified by an ATP assay and staining the cells with annexin-V and propidium iodide.

RESULTS:
The results demonstrated that CoQ at 3µM improved ATP activity, whereas $CoQH_2$ did not. A significant decrease in apoptosis (15% viability) was observed in cells treated with Dox when compared to control (90.1%). Co-treatment of Dox + CoQ provided significant cardiac protection (40% viability). Contrary to previous reports, co-treatment with $CoQH_2$, at all concentrations, was unable to mitigate Dox-induced apoptosis but, rather enhanced cytotoxicity by inhibiting ATP activity and accelerating apoptosis.

CONCLUSION:
The findings presented in this study show that a low dose of CoQ (3 µM) offers cardiac protection, whilst co-administration of Dox + $CoQH_2$ led to aggravated apoptosis and a complete inhibition of the cardiomyoblasts metabolic capacity.

Cardiovascular risk in people living with HIV/AIDS on antiretroviral therapy (ART): Does endothelial function play a possible role?

Results from the EndoAfrica study.

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BACKGROUND:
Cardiovascular disease (CVD) burden is on the rise in HIV-infected patients. However, factors contributing to these trends remain inadequately explored in sub-Saharan Africa.

OBJECTIVES:
We aimed to investigate whether HIV infection, with/without antiretroviral therapy (ART) is associated with altered endothelial function in a Western Cape cohort. We achieved this by determining endothelial function which was assessed clinically via flow mediated dilation (FMD) and biochemically via biomarker analysis. Multiple linear regression analyses were applied to elucidate independent association while correcting for possible confounders.

METHODS:
We recruited and categorized participants from Western Cape province as: (HIV-negative (Control), n=50; HIV-positive ART-naïve (HIV/noART), n=41; HIV-positive on ART (HIV+ART), n=50). Interviews were conducted using comprehensive questionnaires where lifestyle, family and medical history were recorded. Body mass index (BMI) and blood pressure (BP) were measured and levels of circulating biomarkers such as high-sensitivity C-reactive protein (hs-CRP), tumor necrosis factor-alpha (TNF-α) and intercellular adhesion molecule-1 (ICAM-1) were analysed using the Luminex technique. Percentage flow-mediated dilation (%FMD) was determined using a non-invasive ultrasound system.

RESULTS:
Following stepwise linear regression analysis (confounders: age, gender, ethnicity, smoking, alcohol consumption, employment status, BMI and BP), viral load was inversely associated with %FMD (-0.101, (95%CI: -0.191 to -0.010); p = 0.029), and CD4 cell count was inversely associated with hsCRP (-0.568, (95%CI: 1.086 to -0.051); p = 0.032) and TNF-α (-5.587, (95%CI: -10.46 to -0.910); p = 0.020). ART was inversely associated with ICAM-1 (-0.222, (95%CI: -0.445 to -0.0003); p = 0.049).

CONCLUSION:
High viral load and low CD4 cell counts were associated with endothelial dysfunction as evidenced by impaired %FMD and elevated levels of inflammatory markers (hs-CRP and TNF-□) in the HIV cohort. Conversely, ART may confer vasoprotection through a reduction in ICAM-1 levels. Endothelial function appears to be an intersection between HIV/AIDS, ART and cardiovascular risk.

Momordica cardiospermoides crude methanolic leaf extract downregulates MMP-2, MMP-9 and serpin E1 and upregulates TIMP-1 protein expression in MDA-MB-231 breast cancer cells.

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BACKGROUND:
Medicinal plants continue to play a role in anticancer drug development as they are reservoirs of bioactive compounds that exert a plethora of pharmacological effects.

OBJECTIVES:
Investigate the *in vitro* anti-metastatic effects of *Momordica cardiospermoides* methanolic extract on MDA-MB-231 breast cancer cells.

METHODS:
The cytotoxic effects of the methanolic extract on MDA-MB-231 breast cancer and HEK-293 kidney cells was assessed using the muse count and viability assay. The mode of cell death induced by the extract was assessed using the annexin V and dead cell kit assay. The methanolic extract was evaluated for its anti-migrative and anti-adhesive effects using the wound healing and cell adhesion assays, respectively. The effect of the methanolic extract on matrix metalloproteinase-2 and -9 protein expression was assessed using western blot analysis. The human angiogenesis antibody array kit was used to determine the effect of the methanolic extract on the expression of tissue inhibitor of metalloproteinase-1 (TIMP-1), serpin E1, urokinase (uPA) and vascular epithelial growth factor (VEGF).

RESULTS:
A concentration-dependent decrease in MDA-MB-231 viability resulted from treatment with the methanolic extract. Comparatively, the extract maintained HEK-293 viability at 85–98%. Additionally, the methanolic extract proved to be selectively cytotoxic to MDA-MB-231 cells. The methanolic extract induced apoptotic cell death in a concentration-dependent manner, although insignificant. Treatment with the methanolic extract suppressed MDA-MB-231 cell migration and inhibited cell adhesion in a concentration-dependent manner. Furthermore, the extract was seen modulate the expression of MMP-2 and MMP-9, serpin E1, uPA and VEGF proteins.

CONCLUSION:
The study demonstrated the potential of *M. cardiospermoides* crude methanolic extract as an anti-metastatic agent.

The effect of an aspalathin-rich rooibos extract on lipopolysaccharide-induced inflammation in myoblasts

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BACKGROUND:
Skeletal muscle plays a central role in maintaining normoglycemia. Chronic inflammation is implicated in the development of insulin resistance, metabolic dysfunction and loss of skeletal muscle mass. *Aspalathus linearis* (rooibos) polyphenols such as aspalathin improve insulin sensitivity in muscle and fat cells and protect against the development of metabolic dysfunction and could thereby alleviate accelerated muscle loss, as seen in type 2 diabetic individuals.

OBJECTIVES:
The aim of this study was to assess the effect of an aspalathin-rich green rooibos extract (Afriplex GRT™) on myoblast inflammation, metabolism and myogenesis in an adipocyte and myoblast co-culture model.

METHODS:
To establish the skeletal muscle model of inflammation, C2C12 myoblasts were exposed to lipopolysaccharides (LPS) (0.1 µg/mL and 1 µg/mL) for 24 hours and treated with Afriplex GRT™ (GRT) (1 µg/mL and 10 µg/mL) for a further 24 hours. Inflammation (IL-6 secretion), glucose uptake, and expression of myogenic genes and proteins were assessed. A co-culture system using C2C12 myoblasts and 3T3-L1 pre-adipocytes and mature adipocytes were used to study the interplay between the secretion of IL-6 and adiponectin.

RESULTS:
The metabolic endotoxemia caused by LPS adversely affected muscle mass and skeletal muscle energy metabolism. The myogenic regulatory factors (MyoD and myogenin) were downregulated by LPS before and during myoblast differentiation. In co-culture, LPS significantly increased IL-6 secretion in both myoblasts and 3T3-L1 pre-adipocytes, whereas differentiated 3T3-L1 adipocytes modulated IL-6 secretion in co-culture. Afriplex GRT™ was unable to ameliorate these effects of LPS-induced inflammation.

CONCLUSION:
The study confirms that in co-culture, adipocytes can modulate the effects of LPS-induced inflammation on myoblast function and myogenesis, Afriplex GRT™ however did not enhance these effects.

Notes

Notes

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