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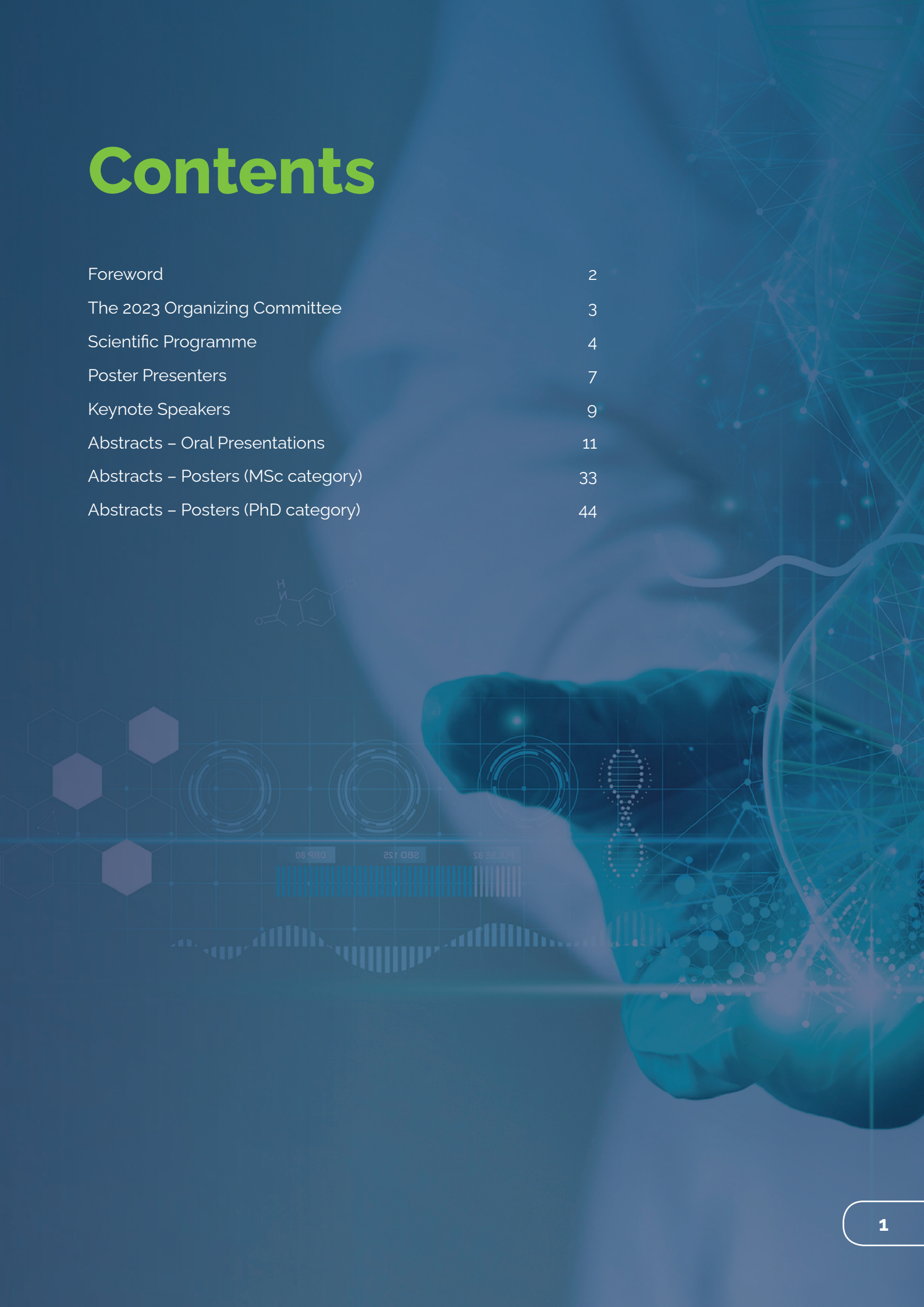
13TH ANNUAL BRIP SYMPOSIUM

16 & 17 October 2023

Scientific Programme & Abstract Book

Empowering Young Minds for a Transformative Future

Contents



Foreword

It is with immense pleasure and anticipation that we welcome you to the 13th Annual Biomedical Research and Innovation Platform (BRIP) Symposium. This year's theme will be "Empowering Young Minds for a Transformative Future."

In today's dynamic world of artificial intelligence, the role of young minds in shaping the future has never been more critical. It is our collective responsibility to inspire young minds to become innovative thinkers and challenge conventions. As leaders and mentors, we should encourage curiosity, promote critical thinking, and nurture independence. More importantly, failure and mistakes are undoubtedly part of the scientific journey and should be used as valuable steppingstones that will eventually lead to success.

Over the past 12 years, our annual BRIP Symposium has provided a platform for scholars, researchers, and visionaries from diverse fields to collaborate and share their insightful ideas. Throughout the Symposium, we will explore a wide array of topics, from cutting-edge research within the NCD space to innovative approaches, all aimed at fostering the growth and development of our young minds and future scientific leaders.

We have invited expert guest speakers that will allow for thought provoking discussion, which will serve as a source of inspiration with lasting impact on our collective journey toward a transformative future. We look forward to the enriching discussions, the exchange of ideas, and the friendships that will undoubtedly flourish during this conference.

We extend our heartfelt gratitude to all the participants, speakers, and the organizers who have made this conference possible. Your dedication to the cause of empowering young minds is a testament to the spirit of collaboration and shared vision. As we embark on this years' symposium, let us all be reminded that the power of knowledge and innovation knows no bounds.

With warm regards,
Rabia Johnson / Carmen Pheiffer
Co-Deputy Directors
Biomedical Research and Innovation Platform

THE 2023 ORGANIZING COMMITTEE

Prof Julia Goedecke

Dr Sylvia Riedel

Prof Carmen Pheiffer

Prof Rabia Johnson

Dr Kwazi Gabuza

Dr Sello Mikasi

Dr Tarryn Wilmer

Dr Jyoti Sharma

Dr Pritika Ramharack

Dr Ikanyeng Dolly Seipone

Dr Rianita van Onselen

DAY 1 MONDAY 16 OCTOBER

Venue – Auditorium (SAMRC Conference Centre, Cape Town) and MS Teams

8h15 – 8h45	Registration	
8h45 – 9h00	Welcome and opening by Professor Christo Muller, Chief Specialist Scientist, BRIP, SAMRC	
SESSION 1		
Session Chairs: Dr Pritika Ramharack & Dr Dolly Seipone		
9h00 – 9h45	**Keynote speaker:** Prof Vinesh Maharaj, Deputy Dean of Research and Postgraduate Education, University of Pretoria, *"African traditional medicine past, present, and future perspectives"*	
9h45 – 10h00	Phytochemical evaluation and the *in vitro* (antihyperglycaemic and antibacterial) activities of methanolic extracts from a *Cyclopia genistoides* Kombucha	Ewert Mthimunye (MSc), University of Zululand
10h00 – 10h15	Investigating the effects of chloroform and methanol extract of *Dicerocaryum senecioides* and *Flaveria trinervia* on metastatic breast cancer cells	Tubake Theona Sebei (MSc), University of Limpopo
10h15 – 10h30	*In vitro* evaluation of anticancer potential of *Cotyledon orbiculata* crude extracts in human cervical cancer cells	Thabang Marema (MSc), University of Limpopo
10h30 – 10h45	The *Momordica balsamina* methanol extract inhibits the interleukin-6-induced invasive, migratory, and adhesive effects of MDA-MB-231 breast cancer cells via the inhibition of the IL-6/JAK2/STAT3 pathway	Tshwarelo Mohale (MSc), University of Limpopo
10h45 – 11h00	Chemical and antioxidant characterization and chemopreventive properties of fermented and unfermented rooibos tea in a keratinocyte UVB exposure model	Danielle Davids (PhD), Cape Peninsula University of Technology
11h00 – 11h30	Tea/coffee	
SESSION 2		
Session Chairs: Prof Rabia Johnson & Dr Sello Mikasi		
11h30 – 12h15	**Keynote speaker:** Prof Ruan Kruger, North-West University, *"The Early Detection and Prevention of Cardiovascular Disease in Africa: focus on cardiovascular disease development in children and young adults"*	
12h15 – 12h30	Understanding the genetic basis of hypertension in a South African population	Hannah Fokkens (MSc), South African Medical Research Council
12h30 – 12h45	Dose-dependent effect of simvastatin on coenzyme $Q_{9/10}$ status in cultured cardiomyoblasts	Sinenhlanhla Xoliswa Happiness Mthembu (PhD), South African Medical Research Council
12h45 – 13h00	Risk factors and biomarkers of heart failure with a preserved ejection fraction in black South African patients	Marilet van Hoogland van Heerden (PhD), Sefako Makgatho Health Sciences University
13h00 – 13h15	Dapagliflozin reduced myocardial strain and diastolic dysfunction, and pro-hypertrophic biomarkers in diabetic patients with preserved ejection fraction	Sacramento Martinez Albaladejo (MSc), Instituto de Investigacion Sanitaria Fundacion Jimenez Diaz UAM
13h15 – 14h15	Lunch and Poster Session 1	

SESSION 3		
Session Chairs: Dr Rianita van Onselen & Dr Kwazi Gabuza		
14h15 – 15h00	**Keynote speaker:** Prof Olebogeng Harold Majane, Sefako Makgotho Health Sciences University, *"Synergistic effects of Hypertension, Obesity, and Diabetes on Cardiac structure and function"*	
15h00 – 15h15	Coenzyme Q_{10}, as an antioxidant prophylactic, attenuates doxorubicin-induced cardiotoxicity in an *in vitro* H9c2 cell model.	Sharnay Naidoo (MSc), South African Medical Research Council
15h15 – 15h30	Semaglutide attenuated cardiac hypertrophy and fibrosis in obese/type-II diabetic mice via AMPK/AKT/mTOR axis	Octavian Seriu Parascinet (MSc), Instituto de Investigacion Sanitaria Fundacion Jimenez Diaz
15h30 – 15h45	Expression of mammary developmental genes in dimethyl-benzanthracene (DMBA)-induced mammary tumours and role of maternal lipotropic nutrients	Anri Kotze (MSc), South African Medical Research Council
15h45 – 16h00	Chromomycin A5 is a novel inhibitor of the oncogenic TBX2 in breast cancer	Claire Bellis (PhD), University of Cape Town

DAY 2 TUESDAY 17 OCTOBER

Venue – Auditorium (SAMRC Conference Centre, Cape Town) and MS Teams

SESSION 1		
Session Chairs: Prof Carmen Pheiffer & Prof Julia Goedecke		
8h45 – 09h30	**Keynote speaker:** Prof Louise Groth Grunnet, Steno Diabetes Centre, Copenhagen, Denmark, *"The impact of an adverse fetal environment on offspring health – can we prevent the unhealthy consequences?"*	
9h30 – 09h45	Investigating neural tube development using a stem cell-based model of development	Alexa Rabeling (MSc), University of Cape Town
9h45 – 10h00	Evaluating the efficacy of curcumin derivatives on lipid metabolism in 3T3-L1 adipocytes	Marakiya Moetlediwa (MSc), South African Medical Research Council
10h00 – 10h15	Evaluating the effect of synthetic curcumin derivatives on skeletal muscle metabolism	Rudzani Ramashia (MSc), South African Medical Research Council
10h15 – 10h30	Longitudinal changes in sex hormone binding globulin and free testosterone in Black middle-aged African men living with and without HIV and their relationship with dysglycaemia, insulin secretion and sensitivity.	Ikanyeng Dolly Seipone (Postdoc), South African Medical Research Council
10h30 – 10h45	Exploring time-restricted eating as a strategy to prevent weight gain in South Africans living with HIV (TESSA)	Fatima Hoosen (Postdoc), University of Cape Town
10h45 – 11h45	Tea/coffee and Poster Session 2	

SESSION 2		
Session Chairs: Dr Tarryn Willmer & Dr Jyoti Sharma		
11h45 – 12h00	Design and synthesis of acyldepsipeptide-1 analogues: antibacterial activity and cytotoxicity screening	Sinazo Cobongela (PhD), Mintek
12h00 – 12h15	Integration of molecular, spatial, and clinical data to understand Mtb transmission among people with subclinical TB in a rural South African population	Yumna Moosa (Postdoc), Africa Health Research Institute
12h15 – 12h30	Investigating the co-operation between the human papillomavirus (HPV) oncoproteins E6/E7 with the oncogenic T-box transcription factor 3 (TBX3) to promote cervical cancer.	Carly Burmeister (PhD), University of Cape Town
12h30 – 12h45	The TBOX transcription factor-3 (TBX3) sensitizes pancreatic cancer cells to the antifungal drug, piroctone olamine	Karabo Serala (PhD), University of Cape Town
12h45 – 13h30	**Keynote speaker:** Prof Bey Schmidt, Health Systems Research Unit, South African Medical Research Council, *"Translating scientific research"*	
13h30 – 15h30	**Prize Giving, followed by a Closing Braai** Prizes presented by **Professor Johan Louw,** Senior Platform Director at the South African Medical Research Council	

POSTER PRESENTERS

Biomedical Research & Innovation Platform Symposium 2023

16 & 17 October 2023

Poster number	Name	Title	Degree	Institution
1	Didintle Tlhale	Gender specific lifestyle cardiovascular risk factors and co-morbidities in heart failure with a preserved ejection fraction patients living in South Africa	MSc	Sefako Makgatho Health Sciences University
2	Nompumelelo Malaza	Obesity and diabetes in pregnancy: association with maternal serum adiponectin	PhD	South African Medical Research Council
3	Teboho Yvette Satekge	Induction of apoptosis in cervical cancer cells using quinoxaline derivative LAM-21D.	MSc	University of Limpopo
4	Mabekane Rebecca Makgato	Development of an irritant-induced allergy model to characterise the anti-inflammatory properties of honeybush (*C. subternata*) in skin *in vitro*	MSc	Cape Peninsula University of Technology
5	Danelle Botha	Investigating the importance of ATM protein kinase in the ER stress response underlying metabolic disease: an *in vitro* study.	PhD	Stellenbosch University
6	Lerato Diseko	The relationship between host genetic make-up and human immunodeficiency virus in a South African population	PhD	University of the Free State
7	Nompilo Cele	*In vitro* antidiabetic and antihyperlipidemic properties of the extracts from *Cyclopia genistoides*	PhD	University of Zululand
8	Ayesha Shaik	Investigating DNA methylation of metabolic and inflammatory genes with therapeutic potential for obesity: a cohort study in South African women	MSc	Stellenbosch University
9	Jenske Didloff	Bioassay-guided isolation and identification of an antimycobacterial compound from *Gymnopilus junonius*	PhD	Nelson Mandela University
10	Leegan Govender	Determining the role of differential expression of candidate microRNAs in cardiometabolic diseases among HIV infected South Africans	MSc	South African Medical Research Council
11	Barend Jacobus Groenewald	Establishment of a novel insulin resistant cardiomyoblast spheroid model	MSc	Stellenbosch University

POSTER PRESENTERS

Poster number	Name	Title	Degree	Institution
12	Lilian Makgoo	The anticancer effect of HIV protease inhibitor on HPV-associated cervical cancer	PhD	University of Limpopo
13	Madikadike Moshape	The effects of a high fructose diet and glucocorticoid treatment on cardiac function in Sprague Dawley rats	MSc	Sefako Makgatho Health Science University
14	Cassidy O'Brien & Caitlin Odendaal	Chronic stress elicits distinct sex-specific responses in rat cardiac respiratory function and vascular reactivity	MSc	Stellenbosch University
15	Koketso Precious Maenetja	Investigating the cytotoxic effect of various anticancer agents in cervical cancer cell lines.	MSc	University of Limpopo
16	Donne Ashley Kritzinger	Exploring the cosmeceutical properties of Tanzanian seaweeds	PhD	Nelson Mandela University
17	Matladi Masete	Optimisation of pyrosequencing-based DNA methylation analysis for validation of biomarkers in gestational diabetes mellitus	PhD	South African Medical Research Council
18	Tanika Naidoo	The effect of *Senecio serratuloides* and *Sarcophyte sanguinea* on the hepatic metabolism of anti-diabetic and lipid lowering drugs	MSc	University of Zululand
19	Xolani Sibiya	The effect of *Aloe marlothii* and *Catharanthus roseus* on the hepatic metabolism of anti-diabetic and lipid lowering drugs	MSc	University of Zululand
20	Shana Edith De Bruyn Orr	Indigenous *Aspalathus linearis* extracts as a natural alternative to standard treatment of gut-related inflammatory conditions.	PhD	Cape Peninsula University of Technology
21	Johara Khan	Atypical masses in rat bone tissue: a green rooibos tomography study.	MSc	Stellenboscy University

INVITED SPEAKERS

Prof Vinesh Maharaj

Deputy Dean of Research and Postgraduate Education, University of Pretoria

Prof Vinesh Maharaj currently leads the Biodiscovery Centre in the Department of Chemistry and is the Deputy Dean of Research and Post Graduate Education, Faculty of Natural and Agricultural Sciences. Prof Maharaj is a natural product chemist and is trained in the discovery of new drug leads based on biodiversity samples. His main aim is to create a unique repository of natural products comprising 10 000 plant samples, which forms the basis for the library, the first of its kind in Africa. The samples are converted into high-throughput screening formats ready for biological testing for various diseases such as HIV, malaria, cancer and COVID-19. He obtained funding from the Department of Science and Innovation (DSI) to establish this platform to make the resources available to the national system of innovation. The infrastructure includes high-end hyphenated analytical equipment for the chemical characterisation of the library. He also serves as the M2Bio Research Chair for natural product research that is being conducted at the university on behalf of M2Bio.

Prof Ruan Kruger

Hypertension in Africa Research Team (HART), Faculty of Health Sciences of the North-West University

Professor Ruan Kruger is a Research Professor of Physiology in the Hypertension in Africa Research Team (HART) at the Faculty of Health Sciences of the North-West University. His research focuses on the early development of hypertension and cardiovascular disease in children and early adulthood. He is the President of the Childhood Hypertension Consortium in South Africa (CHCSA) and held the DSI-NRF South African Research Chair (SARChI) in the Early Detection and Prevention of Cardiovascular Disease in Africa. He is the Volunteer Coordinator in SA Heart®, the Chair of the Next Generation Network of the Southern African Hypertension Society (SAHS), holds fellowship (ISHF) status with the International Society of Hypertension (ISH) and leads sections of the international Youth Vascular Consortium. He serves on several other national and international organising committees including the International Congress on Hypertension in Children and Adolescents (ICHCA), International Society of Hypertension (ISH) and the International Pediatric Hypertension Association (IPHA). He has published over 100 research outputs in international peer reviewed journals and supervised more than 50 postgraduate students and postdoctoral fellows. He leads several research studies such as the Swiss-collaborative Exercise, Arterial Modulation and Nutrition in Youth South Africa (ExAMIN Youth SA) study, and the National Blood Pressure Screening in Children to Improve Paediatric Healthcare in South Africa.

INVITED SPEAKERS

Prof Olebogeng Harold I. Majane

Head of Department of Physiology (School of Medicine), Sefako Makgatho Health Science University

Professor Olebogeng Harold I. Majane is an Associate Professor, Head of Department of Physiology (School of Medicine) and the chairperson of the Postgraduate Committee of Senate at Sefako Makgatho Health Science University. He holds a PhD from the University of the Witwatersrand, which is complemented by a Post-Doctoral Fellowship from Ottawa Hospital, University of Ottawa, Canada, Ontario. He is the principal investigator of the Heart Failure Study at Dr George Mukhari Academic Hospital, Division of Cardiology at SMU. He has a wealth of knowledge and specializes in cardiovascular, respiratory and neurological pathophysiology. Throughout his illustrious career, Prof Majane has received numerous international accolades and recognitions, underscoring his dedication to excellence and his unwavering commitment to scientific wellness in the field of cardiovascular diseases. He supervised to completion 18 postgraduate students and published 54 research articles in international peer-reviewed journals with 903 citations.

Prof Louise Groth Grunnet

Health in Pregnancy and Childhood, Steno Diabetes Center Copenhagen, Denmark

Professor Louise Groth Grunnet is a Senior Researcher and Team Leader heading the Health in Pregnancy and Childhood team within Clinical Prevention Research at the Steno Diabetes Center Copenhagen. She has a Master's degree in Biology and obtained her PhD in Health Sciences from the University of Copenhagen in 2011. Her research focuses on fetal programming and the long-term consequences of fetal under- and over-nutrition, gestational diabetes, the pathophysiology of obesity, prediabetes, and type 2 diabetes. Furthermore, she focuses on the development of new interventions that can reduce the risk of prediabetes and obesity among women and children with an elevated risk.

Prof Bey Schmidt

Health Systems Research Unit, SAMRC

Professor Bey Schmidt is a public health researcher with an Honour's degree in Social and Medical Anthropology and a Master's and PhD degree in Public Health. Her expertise is in conducting qualitative and quantitative systematic reviews of public health and health system interventions. She is also interested in the implementation and evaluation of knowledge translation interventions that can enhance evidence-informed decision-making.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Phytochemical evaluation and the *in vitro* (antihyperglycaemic and antibacterial) activities of methanolic extracts from a *Cyclopia genistoides* kombucha

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Principal Investigator (AKB): BassonA@unizulu.ac.za

BACKGROUND

Kombucha tea is a functional fermented beverage resulting from the metabolic activity of *Medusomyces gisevii* on *Camellia sinensis* (L). The beverage is recognized for its copious presence of bioactive polyphenols derived from plants and microbes. The multi-target bioactivity of polyphenols suggests their potential as therapeutic agents for treating complex poly-phasic pathophysiologies, including diabetic foot ulcers (DFUs).

OBJECTIVES

In this study, a novel tisane substrate and alternative carbon source was used to evaluate *in vitro* the therapeutic potential of a *Cyclopia genistoides* (L) and raw honey Kombucha (*Cg-K*).

METHODOLOGY

Kombucha fermentation was done according to the traditional method and lyophilized. Methanol was used as a working solvent for subsequent analyses. The phytochemical characterization was conducted through the use of FT-IR and GC-MS analysis. Evaluation of *in vitro* antioxidant activity against synthetic and biological radicals was conducted through colorimetric means. C-glycosidase, β-lactamase and efflux-pump polypeptide in vitro inhibitory activities were assessed colourimetrically. Antimicrobial susceptibility was assessed using antibiotic resistant *Pseudomonas aeruginosa* (OK355350.1) and *Staphylococcus aureus* (AP025177.1) bacteria isolated from DFUs.

RESULTS

GC-MS analysis revealed α-linoleic acid derivatives, 5-hydroxymethylfurfural and 4H-pyran- 4-one as the major bioactive compounds. *Cg-K* crude extracts exhibited potent synthetic radical and appreciable biological radical scavenging capacities, IC_{50} values ranged between 3,84 and 23,68 $mg.mL^{-1}$. Significant inhibitory activity was observed for α-amylase and β-lactamase enzymes, IC_{50} values ranged between 3.75 to 4.13 $mg.mL^{-1}$ and 3,27 to 4,47 $mg.mL^{-1}$ respectively. *P. aeruginosa* (OK355350.1) and *S. aureus* (AP025177.1) showed appreciable susceptibility to Cg-K, each exhibiting an MIC-index of 0.50. In addition, the efflux pumps of both bacteria were inhibited to a degree comparable to that of reference standards.

CONCLUSION

The urgent need for the development of multi-target chemotherapies arises from the complexity of multi-factorial disorders with infection co-morbidities. Analogues of Kombucha, such as *Cg-K*, display possibilities for multi-target drug discovery opportunities.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Investigating the effects of chloroform and methanol extract of *Dicerocaryum senecioides* and *Flaveria trinervia* on metastatic breast cancer cells

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BACKGROUND

Plants have been used for centuries in various traditional healing practices worldwide. Research has revealed that some of these plants contain bioactive compounds with potential anticancer properties, not only inhibiting the growth of tumours but also mitigating metastasis. *Dicerocaryum senecioides* and *Flaveria trinervia* have both been reported to have anti-inflammatory and antioxidative effects, which can contribute to inhibiting metastatic processes such as migration of metastatic cells from their primary site and their subsequent adhesion at a secondary organ.

OBJECTIVES

Investigating the potential anti-invasive, anti-migrative, and anti-adhesive effects of *Dicerocaryum senecioides* and *Flaveria trinervia* chloroform and methanol extracts on MDA-MB-231 breast cancer cells.

METHODS

The effect of the extracts on the viability of MDA-MB-231 and HEK 293 human embryonic kidney cells was assessed using the cell counting kit-8 (CCK-8) kit. A transwell assay was used to microscopically assess the anti-migratory effects of the extracts on MDA-MB-231 cells as well as the ability of the cells to attach to a cell culture plate. Additionally, the effects of the extracts on the enzymatic activity of the matrix metalloproteinases (MMPs) was assessed using gelatin-zymography.

RESULTS

The findings revealed that there was no significant effect on cell viability at concentrations below 200 µg/ml ($p<0.05$). Moreover, the extracts suppressed cell invasion, migration, and adhesion. The *D. senecioides* chloroform extract inhibited up to 75% adhesion of the cells while its methanol extract inhibited 60%. The *F. trinervia* chloroform extract mitigated cell adhesion up to 60% and methanol inhibited 65%. Furthermore, both extracts inhibited MMP-2 and -9 activity in MDA-MB-231 by up to 40%.

CONCLUSION

Dicerocaryum senecioides and *Flaveria trinervia* showed potential as sources of compounds with anti-metastatic activity. Further studies are needed to isolate and characterise the active compounds responsible for these effects and to evaluate their activity in vivo and eventually clinical trials.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

In vitro evaluation of anticancer potential of *Cotyledon orbiculata* crude extracts in human cervical cancer cells

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BACKGROUND

Cervical cancer is rated the fourth most common cancer, and the leading cause of mortality in women, worldwide. This may be attributed to the lack of adequate healthcare facilities and late diagnosis, especially for underprivileged women; thus, novel, affordable and effective anticancer alternative strategies are needed. Medicinal plants are gaining a lot of interest as alternative source of drugs for various diseases, including cancer.

OBJECTIVES

The study was aimed at exploring the cytotoxicity and the potential anticancer activities of various *Cotyledon orbiculata* (*C. orbiculata*) crude extracts against cervical cancer cells.

METHODOLOGY

C. orbiculata leaves were collected, dried, and extracted using distilled water, methanol, acetone, and hexane. Cervical CaSki (ATCC®CRL-1550™) and HeLa (ATCC®CCL-2™) cancer cells; and non-cancer Hek-293 (ATCC®CRL-1573™) and Vero (ATCC®CRL-1587™) were cultured and maintained as described by the American Type Culture Collection, then the MTT assay was used to assess the cytotoxicity of the crude extracts. To determine whether *C. orbiculata* crude extracts regulates apoptosis or controls cell cycle arrest, a TACS™ Annexin V-FITC Apoptosis Detection and the Muse™Cell Cycle kits were utilized, following the manufacturer's instructions, respectively.

RESULTS

The acetone, methanol, and hexane crude extracts reduced the viability of both HeLa and CaSki cancer cells. The *C. orbiculata* crude extracts [hexane (IC_{50}=1000 µg/mL), methanol (IC_{50}=1000 µg/mL, water (IC_{50}=1000 µg/mL) and acetone (IC_{50}=500 µg/mL)] also induced late apoptosis on CaSki and HeLa cancer cells. The cell cycle results showed that IC_{50} crude extracts also induced S-phase cell cycle arrest of the CaSki and HeLa cancer cells while methanol crude extract induced G0/G1 phase cell cycle arrest on both tested cell lines.

CONCLUSION

This study showed that the *C. orbiculata* may contains therapeutic compounds with potential anticancer activities against cervical cancer and should be targeted for the development of novel anticancer drugs.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

The *Momordica balsamina* methanol extract inhibits the interleukin-6–induced invasive, migratory, and adhesive effects of MDA-MB-231 breast cancer cells via the inhibition of the IL-6/JAK2/STAT3 pathway

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BACKGROUND

The overexpression of IL-6 in triple-negative breast cancer (TNBC) cells and the tumour microenvironment drive inflammatory-mediated tumour cell survival, cancer progression, metastasis, and immune suppression through the activation of the IL-6/JAK2/STAT3 pathway.

OBJECTIVES

To investigate the anti-metastatic effects of *Momordica balsamina* methanol extract (MBME) in interleukin-6-activated MDA-MB-231 breast cancer cell line.

METHODS

The triple-negative breast cancer MDA-MB-231 and kidney HEK-293 cells were exogenously activated with IL-6 (50 ng/ml) during treatment. The MTT and annexin-V assays were used to determine the cytotoxicity of the MBME in MDA-MB-231 and HEK-293 cells. The transwell cell invasion, wound healing, gelatin-zymography, cell adhesion and extracellular matrix (ECM)-protein adhesion assays were performed to assess the potential anti-metastatic potential of the MBME. Real-time PCR and western blotting were used to investigate the mechanism of action of the MBME in IL-6-activated MDA-MB-231 cells.

RESULTS

The MBME (≤100 µg/ml) exhibited minimal toxicity on the viability of IL-6-activated MDA-MB-231 and HEK-293 cells. Annexin-V assay further confirmed the lack of significant toxicity of MBME (≤100 µg/ml) in IL-6-activated MDA-MB-231 and HEK-293, showing non-significant induction of apoptotic cell death. An increase in *Bax* and decrease in *Bcl-2, JAK2, STAT3, MMP-2 and MMP-9* mRNA expression, was observed in extract-treated IL-6-activated MDA-MB-231 cells. Western blot analysis showed that the extract decreased MMP-2, MMP-9, and vimentin and increased TIMP-3 protein expression in IL-6-activated MDA-MB-231 cells. Furthermore, a decrease in the activity of MMP-2 and MMP-9 in extract-treated IL-6-activated MDA-MB-231 cells was observed. Moreover, the MBME treatment significantly inhibited the invasive, migratory, adhesion, and attachment to ECM-proteins potential of IL-6-activated MDA-MB-231 cells.

CONCLUSION

The MBME exhibits the potential to inhibit the IL-6-induced metastatic effects of MDA-MB-231 cells through the modulation of the IL-6/JAK2/STAT3 pathway.

ABSTRACTS: PRESENTATIONS PhD CATEGORY

Chemical and antioxidant characterization and chemopreventive properties of fermented and unfermented rooibos tea in a keratinocyte UVB exposure model

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BACKGROUND

The use of *Aspalathus linearis* (rooibos) as a natural remedy has significantly increased due to its unique polyphenol composition and health-promoting properties including anti-mutagenic,anti-cancer and anti-inflammatory responses.

OBJECTIVES

This study aims to compare the chemical and antioxidant composition of ethanol and aqueous extracts from fermented and unfermented rooibos. Additionally, to identify specific cellular biomarkers involved in the chemopreventative effects of rooibos tea in a UVB irradiated keratinocyte pre-exposure model.

METHODS

Ethanol and aqueous rooibos extracts were prepared through a steeping method and further fractionated through reverse-phase column chromatography. The chemical and antioxidant characterization of the extracts was achieved by quantifying monomeric flavonoids by HPLC and determining total phenolic content and antioxidant activity (FRAP, ABTS, DPPH, ORAC) using photometric analyses. In the pre-exposure model, the activity of the teas was tracked by evaluating its impact on cell viability indices (ATP and Caspase-3), inflammatory responses (IL-1α, COX2, IL-8), and oxidative damage (GPX, SOD, CAT) using qPC.

RESULTS

A comparison of the teas indicated that ethanol extracts contained higher polyphenol content and antioxidant activity compared to aqueous extracts. The ethanol unfermented extract (EUF) presented the highest levels of aspalathin and antioxidant activity. The aqueous teas presented anti-apoptotic, anti-inflammatory responses and reduced oxidative damage against UVB irradiation.

CONCLUSION

The polyphenol composition of tea extracts concluded that ethanol teas presented higher content levels and antioxidant activity. Aqueous teas were found to have anti-inflammatory and anti-apoptotic effects against UVB damage. Ethanol teas are under investigation, and additional characterization of the proteome will be conducted for both types of tea extracts.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Understanding the genetic basis of hypertension in a South African population

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BACKGROUND

Hypertension (HTN) drives the global burden of cardiovascular disease and is a leading cause of cardiovascular-related mortality. Current evidence indicates that hypertension (HTN) is a multifactorial condition influenced by various risk factors, including genetics and environmental determinants. Furthermore, it is widely accepted that approximately 30-50% of hypertension cases may arise from genetic susceptibility, drastically impacting hypertension control.

OBJECTIVES

The primary objective of this study is to investigate genetic variations linked to the management of hypertension and examine how the guidelines provided by the American Heart Association (AHA) and the South African Hypertension Society (SAHS) affect the occurrence and risk factors related to hypertension in Mthatha, South Africa.

METHODS

In a cross-sectional study, individuals over 18 years of age were screened using the WHO Stepwise questionnaire and anthropometric measurements were taken. Univariate and multivariate analyses were performed to identify risk factors contributing to HTN. A candidate gene approach was adopted to explore the involvement of genetic variants in the regulation of HTN, by Whole Exome Sequencing (WES) of 5 normal control, 5 individuals with HTN and 5 treatment-resistant HTN.

RESULTS

In a total cohort of 1034 individuals, the prevalence of HTN drastically increased from 53.6% (SAHS) to 74.6% (AHA). Risk factors associated with both guidelines, including age, blood glucose, diabetic status, total cholesterol, triglycerides, waist-hip ratio, conicity index, are positively associated with the development of HTN ($p<0.05$). Of interest, two polymorphisms were identified that could possibly influence the drug pharmacodynamics in relation to the HTN drug response.

CONCLUSION

The prevalence of HTN was higher than previously reported (30-32%) with age, cholesterol, diabetes, and waist-hip ratio being significant predictors of HTN. Of interest were the identified variants linked to HTN drug response, however, a larger sample size is needed to validate the pharmacogenomic findings.

ABSTRACTS: PRESENTATIONS PhD CATEGORY

Dose-dependent effect of simvastatin on coenzyme $Q_{9/10}$ status in cultured cardiomyoblasts

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BACKGROUND

Coenzyme $Q_{9/10}$ (CoQ) is a critical component of the mitochondrial electron transport chain that is involved in cellular bioenergetics and is vital for protecting against oxidative stress. Although simvastatin is considered an important lipid-lowering drug with some cardioprotective effects, its long-term use has been associated with myocardial toxicity, which is in part facilitated by the detrimental effects of oxidative stress.

OBJECTIVES

To understand the implicated pathological mechanisms of long-term use of simvastatin in both normal and palmitic acid exposed H9c2 cardiomyoblasts.

METHODS

The current study explored the dose (0.3, 0,6, 1.25, 2.5, 5, 10, and 20 µM) and time (24 and 48 hours)-dependent effects of simvastatin on cultured cardiomyoblasts. Endpoint measurements included assessing CoQ content and oxidative status, production of cellular and mitochondrial reactive oxygen species (ROS), mitochondrial respiration, and viability of cells.

RESULTS

Results showed that low doses of simvastatin (≤0.6 µM) maintained cellular viability of cardiomyoblasts, in part by improving CoQ status, decreasing cellular ROS and enhancing mitochondrial respiration. Alternatively, exposure to higher simvastatin doses (between 1.25 and 5 µM) significantly increased ROS production and reduced CoQ content, albeit did not affect cell viability or mitochondrial respiration. However, exposure to simvastatin doses > 5 µM significantly reduced cell viability and altered CoQ status, while also accelerating ROS production. Notably, the detrimental effect of simvastatin on these cardiomyoblasts was worsened when exposed for 48 hours compared to 24 hours.

CONCLUSION

Our current findings suggests that optimal doses and exposure times are crucial aspect in prolong beneficial effects of simvastatin.

ABSTRACTS: PRESENTATIONS PhD CATEGORY

Risk factors and biomarkers of heart failure with a preserved ejection fraction in black South African patients

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BACKGROUND

Almost 50% of all heart failure (HF) cases have a preserved ejection fraction, which is often observed in the elderly (≥75 years). However, the mean age of HF presentation is considerably lower (40-55 years) in sub-Saharan Africa. Heart failure with a preserved ejection fraction (HFpEF) is therefore unlikely to be due to advanced age-related arterial stiffness. The risk factors and traditional biomarkers associated with HFpEF might also differ in a middle-age population group when compared to the elderly.

OBJECTIVES

This study investigated two biochemical markers, N-terminal pro b-type natriuretic peptide (NT-proBNP) and galectin-3, that predict HFpEF and specifically risk factors that predict or are associated with HFpEF in a black population in South Africa.

METHODS

This study was a case-control investigation. Sixty-six participants with HFpEF and 213 participants without HF from African descent, ≥18 years were enrolled. All participants gave informed consent and completed a standardised questionnaire. Echocardiographic, anthropometric, central haemodynamic measurements, pulse wave velocity (PWV) and biomarker analysis using commercially available enzyme-linked immunosorbent assay kits were done.

RESULTS

The mean age of HFpEF in black South African patients was 54.88±13.51 years. The prevalence of hypertension in HFpEF patients was 69% and 55% in the controls. PWV was significantly increased in participants with HFpEF (9.97±2.78 m/s) when compared to participants without this pathology (6.11±2.18 m/s) with a p-value of <0.0001, however there were no significant associations between central haemodynamic parameters, NT-proBNP (p=0.9746) and galectin-3 (p=0.2166). Lastly, NT-proBNP, but not galectin-3, was significantly associated with left ventricular hypertrophy (LVH) (p=0.0002) and left atrial (LA) diameter (p=0.0005).

CONCLUSION

HFpEF is more prevalent in a middle-aged black South African sample with increased arterial stiffness when compared to statistics from European and American populations. NT-proBNP, but not galectin-3, is independently associated with LVH and LA and hence could be used for the diagnosis of HFpEF in this community sample.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Dapagliflozin reduced myocardial strain and diastolic dysfunction, and pro-hypertrophic biomarkers in diabetic patients with preserved ejection fraction

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BACKGROUND

Type 2 Diabetes mellitus (T2DM) frequently coexists with cardiac failure and is a risk factor for its development and associated morbidity and mortality. However, sodium-glucose cotransporter 2 inhibitors (SGLT2i) are anti-diabetic drugs with potential cardioprotective actions.

OBJECTIVES

To analyze the effect of dapagliflozin in T2DM patients with preserved ejection fraction (EF) and evidence of incipient structural and/or functional damage.

METHODS

In this prospective pilot study, twenty-six patients with T2DM and preserved EF were treated with 10 mg/day of dapagliflozin for 6-9 months in the Hospital Fundación Jiménez Díaz. Before and after follow-up, anthropometric parameters and plasma samples were obtained. Biochemical factors and biomarkers of cardiac injury (inflammation, hypertrophy, fibrosis, steatosis) were detected by luminescence and ELISA. Also, standard, 3D and speckle tracking echocardiography were performed in all patients.

RESULTS

After a median follow-up of 6.6 months, dapagliflozin significantly reduced the left ventricle mass (LVM; -9.9 g/m^2) and the E/é ratio (-1.4), whereas it increased the absolute left ventricle global longitudinal strain (LVGLS; 0.74%), and the isovolumetric relaxation time (IVRT; 9.8 ms). There were not cardiovascular events during follow-up. Moreover, dapagliflozin induced a significant increase in HDL-cholesterol, hemoglobin, and hematocrit, and reduced body mass index (BMI) and hyperglycemia. Also, it ameliorated the ANP and CK-MB plasma levels. However, no associations were observed between these echocardiographic parameters and biomarkers.

CONCLUSION

In T2DM patients with preserved EF, dapagliflozin could induce early benefits in cardiac structure and function, and improvements on body weight, hyperglycemia, and lipid profile. However, the potential mediators and mechanisms of action are still undiscovered.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Coenzyme Q_{10}, as an antioxidant prophylactic, attenuates doxorubicin-induced cardiotoxicity in an *in vitro* h9c2 cell model

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BACKGROUND

Coenzyme Q_{10} (CoQ_{10}), an essential electron carrier in the mitochondrial respiratory chain, has been previously shown to alleviate cardiotoxic side-effects induced by doxorubicin (Dox). The premise is that Dox causes mitochondrial abnormalities, which lead to cardiac dysfunction, thus making CoQ_{10} an ideal prophylactic to mitigate DIC. However, the mechanism by which CoQ_{10} attenuates Dox-induced mitochondrial dysfunction is poorly understood.

OBJECTIVES

To determine whether CoQ_{10} supplementation can ameliorate DIC using an H9c2 cardiomyoblast model.

METHOD

H9c2 and MCF-7 cells were pre-treated with CoQ_{10} (2 or 3 µM), or 10 µM dexrazoxane (Dex, a cardioprotective drug) for 2 days, before being co-treated with 0.5 µM Dox for an additional 4 days. For the Dox-treated group, cells received media for 2 days before being treated with 0.5 µM Dox, to induce cardiotoxicity. Untreated cells served as the control. On day 7, oxidative stress (DCF and GSH), mitochondrial activity (Seahorse, JC-10 and MitoTracker), and apoptosis (Caspase 3/7 and Annexin V) were assessed. Results obtained were validated by gene expression (NRF2, NOX4 and caspase 9).

RESULTS

Pre-treatment with 2 µM and 3 µM CoQ_{10} attenuated DIC by decreasing ROS production ($p<0.01$) and improved mitochondrial activity ($p<0.05$). This was driven by an increase in total glutathione content ($p<0.05$), mitochondrial bioenergetics ($p<0.001$) and membrane potential ($p<0.05$). Subsequently, an improvement in mitochondrial mass ($p<0.05$) with a concomitant reduction in caspase 3/7 activity ($p<0.0001$), caspase 9 expression and cardiomyoblast death was observed in the CoQ_{10} treated cells versus those treated with Dox alone ($p<0.05$). Interestingly, pre-treating MCF-7 cells with CoQ_{10} significantly decreased Dox-induced caspase 3/7 activity.

CONCLUSION

This study demonstrated that CoQ_{10} enhanced antioxidant levels and mitochondrial activity, whilst decreasing dox-induced cardiac apoptosis. However, our findings also suggest that co-administering CoQ_{10} with Dox may reduce the efficacy of this chemotherapeutic drug.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Semaglutide attenuated cardiac hypertrophy and fibrosis in obese/type-II diabetic mice via AMPK/AKT/mTOR axis

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BACKGROUND

Obesity and type 2 diabetes mellitus (T2DM) frequently coexist and affect cardiac tissue. However, anti-diabetics such as glucagon-like peptide 1 receptor agonists (GLP-1RA) could also induce direct cardioprotective actions..

OBJECTIVES

Our main objectives were: (1) characterize the myocardium of BKS db/db mice treated with semaglutide and (2) analyze the hypertrophic and fibrotic signaling of these mice.

METHODS

Obese-T2DM BKS db/db mice were subcutaneously treated or not with semaglutide (25-100ug/kg/week for 12 weeks). Plasma and heart (left ventricle) were isolated and analyzed by biochemical analyses, histological (picrosirius red and hematoxilin/eosin), Western blot, and RT-qPCR.

RESULTS

BKS db/db mice developed obesity (1.59-fold vs. control, $p<0.05$), hyperglycemia (2.63-fold vs. control, $p<0.05$), and hyperlipidemia (1.28-fold vs. control, $p<0.05$), which were attenuated by semaglutide (0.84-, 0.71-, and 0.69-fold vs. BKS-db/db, respectively). Also, BKS db/db showed myocardial hypertrophy (1.40-fold vs. control) and fibrosis (2.01-fold vs. control) which was attenuated by semaglutide (0.87- and 0.62-fold vs. BKS db/db, respectively).

Finally, BKS-db/db mice exhibited an increase of AMPK phosphorylation while decreasing mTORC1 activation (0.22- and 4.04-fold vs. control, respectively). Semaglutide attenuated these effects in both AMPK and mTORC1 activation (1.24- and 0.53-fold vs. BKS db/db, respectively).

CONCLUSION

Obesity and T2DM may activate cardiac mTORC1 and related pro-hypertrophic and -fibrotic factors. However, semaglutide could activate GLP-1R and subsequent AMPK to decrease mTORC1 signaling and cardiac hypertrophy and fibrosis. Following *in vitro* assays will confirm the potential direct effects of semaglutide on the hypertrophic and fibrotic cardiac signalling.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Expression of mammary developmental genes in dimethyl-benzanthracene (DMBA)-induced mammary tumors and role of maternal lipotropic nutrients

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BACKGROUND

One of the emerging fields of interest in disease prevention is the role of fetal developmental genes on adulthood disease susceptibility. Of interest to this study is the role of fetal mammary developmental genes in breast cancer.

OBJECTIVE

The study aimed to identify fetal mammary developmental genes that are dysregulated in chemically-induced mammary tumors in Sprague-Dawley rats, and the role thereof maternal lipotropic (including methionine, vitamin B_{12}, folic acid and choline) nutrients.

METHODS

Pregnant Sprague-Dawley rats (n=7/group) were fed either the control, lipotrope-supplemented (LIP), or lipotrope plus vitamin B_6-supplemented (LIP+VitB6) diets during pregnancy and lactation. At weaning, female offspring were randomly selected from each group and designated the following groups (all fed the control diet hereon): non-cancer control (NCC), cancer control (CC), LIP, and LIP+VitB6. At 57 days of age, mammary tumors were chemically-induced in all offspring groups (except the NCC) by oral DMBA administration. At termination of the study, the animals were euthanized as approved by the relevant ethics committees [(SU: ACU-21932 and ECRA 01/21)] and normal mammary and tumor tissues excised for molecular studies, including assessment of mRNA expression by qRT-PCR.

RESULTS

Data showed that mammary developmental genes such as T box transcription factors, TBX2 and TBX3, are upregulated in DMBA-induced mammary tumors (CC) as compared with normal mammary tissues (NCC). However, tumor tissues of offspring exposed to LIP or LIP+VitB6 diets early in life, presented with significantly lower mRNA expression of TBX2 and TBX3 as compared with the CC tissues. Interestingly, the expression level of both genes in the treated groups was comparable to that of the NCC offspring.

CONCLUSION

Further studies will assess if this gene transcription outcome is driven by epigenetic changes and whether this provides a potential mechanism through which maternal methyl donor nutrients lower the susceptibility of offspring to chemically-induced mammary carcinogenesis.

ABSTRACTS: PRESENTATIONS PhD CATEGORY

Chromomycin A5 is a novel inhibitor of the oncogenic TBX2 in breast cancer

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BACKGROUND

Breast cancer (BC) is the most common cancer worldwide, with over 2 million new cases diagnosed per year. Current breast cancer treatments options are limited by both drug resistance and severe side effects. Therefore, targeted therapies have emerged as an attractive strategy for the treatment of BC. To this end, the transcription factor TBX2, which is commonly overexpressed in BC, has been identified as an attractive therapeutic target. Indeed, TBX2 acts as an oncogene in BC where it drives proliferation and promotes DNA damage repair to suppress cell death and confer drug resistance. We previously identified the marine-derived Chromomycin A5 (CA5), to have strong TBX2-binding affinity and here we show that CA5 exhibits anti-breast cancer through targeting TBX2 for degradation.

OBJECTIVES

Using a target-to-hit approach with the goal of inhibiting TBX2, we aim to characterise the *in vitro* and *in vivo* anti-cancer activity of CA5 in BC.

METHODS

MTT cell viability and clonogenic survival assays, 3D spheroid models, western blotting, immunofluorescence, qRT-PCR, flow cytometry, shRNA transfections, MG132 treatment, drug solubility testing and microsomal stability assays, murine breast cancer model.

RESULTS

CA5 exhibits potent and selective short- and long-term cytotoxicity in TBX2-driven BC in both 2D and 3D cell cultures with cytotoxicity dependent on the inhibition of TBX2. Mechanistically, CA5 induces DNA damage (γH2AX), cell cycle arrests and apoptosis (cleaved caspases 3, 7, 8 and 9; PARP) and targets TBX2 for proteasomal degradation leading to the de-repression of TBX2 tumour suppressor target genes (p21, PTEN, CST6 and NDRG1). CA5 was found to be moderately soluble and stable under physiological conditions, making it a promising drug candidate. Finally, in a C57/BL6 mouse model of BC, a single dose of 0.6mg/kg CA5 was found to be safe and efficacious when administered intravenously.

CONCLUSIONS

CA5 is promising for the treatment of TBX2-driven BC.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Investigating neural tube development using a stem cell-based model of development

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BACKGROUND

Neural tube defects (NTDs) arise from incomplete closure of the neural tube (NT). While folate supplementation has reduced NTD incidence, the mechanisms behind how NTDs arise are not known. Studying NTDs *in vivo* is complicated since the embryo is inaccessible from implantation. Researchers therefore developed in vitro models, one of which are trunk-like structures (TLSs) which model somitogenesis and NT development. In this model, aggregates of murine embryonic stem cells (mESCs) are grown, elongate and undergo a gastrulation-like process due to exposure to the Wnt agonist Chiron, and are embedded in Matrigel to drive NT and somite morphogenesis.

OBJECTIVES

This research aims to utilise a TLS-like model to investigate gastrulation and NT development by analysing the effects of two Wnt agonists, Chiron and BMP4, on these processes.

METHOD

500 mESCs/well were aggregated in U-bottomed 96-well plates in N2B27 medium and formed aggregates over 48 hours at which point 3µM Chiron or 1 ng/mL BMP4 was added for 24 hours, with medium changed back to N2B27 at 72 hours after aggregation. At 96 hours, aggregates were embedded in 5% Matrigel until 144 hours. Control aggregates were grown as above but received no signalling factors. Aggregates were collected at 96 and 144 hours for ICC and RT-qPCR, with growth analysed daily.

RESULTS

While aggregates grown without any signalling factors did not elongate over the culture period or express brachyury, a marker of gastrulation, at 96 or 144 hours, aggregates pulsed with Chiron or BMP4 did. Interestingly, aggregates pulsed with BMP4 showed higher expression of NT markers compared to Chiron pulsed aggregates.

CONCLUSION

The addition of Wnt agonists drove a gastrulation-like process, with Matrigel addition causing increased elongation. Expression of NT markers was higher in BMP4 aggregates compared to Chiron; indicating that BMP4 may be more crucial for NT development in this model.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Evaluating the efficacy of curcumin derivatives on lipid metabolism in 3T3-L1 adipocytes

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BACKGROUND

Curcumin has garnered attention due to its health benefits. Its anti-obesity therapeutic potential is hindered by its poor bioavailability, which necessitates alternative approaches to improve its biological efficacy, such as synthetic curcumin derivatives.

OBJECTIVES

To compare the efficacy of three curcumin derivatives to curcumin on lipid metabolism using *in silico* and *in vitro* approaches.

METHODS

Protox II, SwissADME, and SwissTargetPrediction were used to predict toxicity, pharmacokinetics and biological targets, while molecular docking was used to assess the binding affinities on predicted biological targets. 3T3-L1 adipocytes pre-stimulated with tumor necrosis factor alpha, lipopolysaccharides, and palmitate combination (model control) for 24 hours were co-treated with curcumin and the derivatives for 24 hours. Cell viability, lipolysis and lipid accumulation were assessed.

RESULTS

Computational predictions demonstrate that curcumin and the derivatives are potential drug candidates due to their high LD_{50} and adherence to Lipinski's rules. Based on ADME profile, the derivatives show improved bioavailability compared to curcumin. Compared to the derivatives, curcumin exhibited highest binding energy (kcal/mol) for fatty acid synthase (FAS), while 1B8 had low binding score for FAS. 1A6 had the lowest docking scores for peroxisome proliferator-activated receptor gamma (PPARγ), glycogen synthase kinase 3 beta (GSK3β), and acetyl-CoA carboxylase (ACC). 1B8 had the highest binding affinity for PPARγ and GSK3β, while 1A8 had the highest score for ACC. *In vitro*, results showed that cell viability was reduced in the model control ($p<0.05$) and cells treated with 1A8 at highest dose (40 µM, $p<0.01$). Lipolysis was increased in the model control ($p<0.0001$), while treatment with 1A8 at 10 µM significantly reduced lipolysis. Lipid content was reduced in model control cells, while treatment with curcumin and the derivatives had no observable effect.

CONCLUSION

Curcumin derivatives have potential anti-obesity effects mediated by reducing lipolysis in dysfunctional 3T3-L1 adipocytes and targeting key lipid metabolism genes.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Evaluating the effect of synthetic curcumin derivatives on skeletal muscle metabolism

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BACKGROUND

Curcumin, a polyphenolic compound from turmeric, has potential therapeutic benefits against metabolic diseases like skeletal muscle disorders. However, it's poor bioavailability prompts the development of synthetic curcumin derivatives.

OBJECTIVE

To compare the efficacy of three synthetic curcumin derivatives with curcumin on skeletal muscle metabolism using *in silico* and *in vitro* approaches.

METHOD

Chloro-curcumin derivatives (1A6 and 1A8) and an asymmetric curcumin derivative (1B8) were synthesized and characterized. Protox II, SwissADME, SwissTargetPrediction were used to predict toxicity, pharmacokinetics, and biological targets, while binding affinity of predicted biological targets was assessed using molecular docking. The effects of the compounds on cell viability were evaluated in differentiating C2C12 myoblasts using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide and adenosine triphosphate assays.

RESULTS

The synthesized curcumin derivatives had >99% purity and their structures were confirmed by fourier transform infrared (FTIR) and nuclear magnetic resonance (NMR) spectroscopy. Compared to curcumin, the predicted LD_{50} for the derivatives was higher, although 1B8 could potentially be hepatoxicity, immunotoxicity and cytotoxicity. Predicted ADME profiles were favorable for all compounds. Compared to the derivatives, curcumin exhibited lowest binding energy (kcal/mol) for the predicted biological targets, phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha (P110α) and myostatin and the highest score for c-Jun N-terminal protein kinase-1 (JNK1) and insulin-like growth factor-1 receptor (IGF1R). Besides JNK1 and IGF1R, 1A8 exhibited highest binding affinity for biological targets, while the binding energies of 1A6 were lowest for protein kinase B (AKT1), glycogen synthase kinase 3 beta (GSK3β), extracellular signal-regulated kinase 2 (ERK2), and JNK1, and lower for 1A8-IGF1R complex. High concentrations (10 and 20 μM) of curcumin and curcumin derivatives similarly reduced cell viability ($p<0.05$), whereas lower doses (1 and 5 μM) did not affect cell viability.

CONCLUSION

Curcumin derivatives present a potential to be further explored for their efficacy to improve skeletal muscle metabolism including myogenesis and insulin signaling.

Longitudinal changes in sex hormone binding globulin and free testosterone in Black middle-aged African men living with and without HIV and their relationship with dysglycaemia, insulin secretion and sensitivity

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BACKGROUND

Hypogonadism is one of the risk factors for type 2 diabetes (T2D) in men and is common among men living with HIV (MLWH). Sex hormone binding globulin (SHBG), a glycoprotein that transports and regulates testosterone bioavailability is higher in MLWH than men living without HIV (MWOH), but the pathophysiology and implications of this are unclear.

OBJECTIVES

To assess longitudinal changes of SHBG and free testosterone (Free-T) levels in Black African MLWH and MWOH and explore associations with incident dysglycaemia and measures of glucose metabolism.

METHODS

This longitudinal study included Black South African (SA) men (n=412) from the Middle-Aged Soweto Cohort, comprising 86 MLWH and 326 MWOH followed over 3.1±1.5-years. At baseline and follow-up body composition, SHBG, albumin and total testosterone were measured, and Free-T was calculated. At follow-up, an oral glucose tolerance test was carried out to assess glucose tolerance and determine insulin secretion and sensitivity. Associations between hormones and dysglycaemia and glucose metabolism parameters were explored using logistic and quantile regression models, all analyses were adjusted for age, total and central fat, smoking, and medication use.

RESULTS

Baseline SHBG concentrations were higher in MLWH than in MWOH ($p<0.001$) and increased more in MLWH than in MWOH (2.94 (-0.17 to 8.40) nmol/L vs.0.30 (-1.70 to 2.11) nmol/l), $p<0.001$ for interaction. Free-T did not differ by HIV status ($p=0.955$), decreased with time in both groups ($p=0.032$) and was not associated with dysglycaemia. Only baseline SHBG was associated with a lower risk of incident dysglycaemia [OR [95% CI] 0.966 [0.945-0.987] but this did not differ by HIV status. Baseline SHBG was associated with insulin sensitivity (0.15 [0.10-0.19], $p<0.001$) in MWOH only, whereas the change in SHBG was associated with β-cell function in MLWH only (0.35 [0.04-0.66], $p=0.026$)

CONCLUSION

SHBG levels predict the development of dysglycaemia and vary by HIV serotype and Free-T was not associated with dysglycaemia.

Exploring time-restricted eating as a strategy to prevent weight gain in South Africans living with HIV (TESSA)

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BACKGROUND

South Africa presents with a double burden of communicable and non-communicable diseases, with HIV and type 2 diabetes (T2D) amongst the leading causes of death. The preferred first-line anti-retroviral treatment (ART) contains dolutegravir (DTG), shown to increase body weight and compound the already high rates of obesity and associated T2D risk. South Africa has widespread food insecurity, making traditional dietary strategies difficult to implement. Time-restricted eating (TRE) may be an appropriate intervention in low-resourced communities.

OBJECTIVES

The aims were to explore the feasibility of TRE in patients living with HIV receiving DTG-based treatment, and refine the intervention before commencing a randomised controlled trial (RCT).

METHODS

Men and women (20-45 years old) living with overweight/obesity and HIV, receiving DTG-based treatment were recruited from a low-resourced community healthcare centre in Cape Town. Five focus groups and thirteen key informant semi-structured interviews were conducted. Interviews were analysed using NVivo.

RESULTS

Barriers to weight loss included the perception that others would associate excessive weight loss to defaulting ARTs or illness. A TRE-specific barrier included being unable to join in family meals that fall outside their eating window. Facilitators to weight loss included understanding the importance of a healthy lifestyle and improved functional-related outcomes associated with weight loss. Facilitators to TRE included the perception that TRE would be easy to follow as the eating window was considered similar to their current eating times, and that participants tended to be the one's responsible for meal preparation. Participants recommended the inclusion of dietary-based educational sessions.

CONCLUSION

These findings support feasibility of TRE as a weight maintenance intervention in women living with overweight/obesity and HIV, receiving DTG-based treatment in a low-resourced community. Modifications to the 1-year RCT will be made to ensure weekly participant interaction and support, and dietary-based information sessions every three months.

ABSTRACTS: PRESENTATIONS PhD CATEGORY

Design and synthesis of acyldepsipeptide-1 analogues: antibacterial activity and cytotoxicity screening

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BACKGROUND

Acyldepsipeptides (ADEPs) are regarded as potential antibiotics with a novel mechanism to combat bacterial resistance. However, ADEPs have limitations such as poor solubility and high cytotoxicity. Chemical modifications have been successful in improving the ADEPs limitations.

OBJECTIVES

In the current study, ADEP1 was modified by introducing a disulphide linkage, replacement of the octa-2,4,6-trienoic acid with either adamantane or palmitic acid, and lastly, comparing the use of D versus L amino acids.

RESULTS

The antibacterial effects of the ADEP1 analogues were investigated in Gram-positive and Gram-negative strains using agar well diffusion and microdilution assays. Cytotoxicity was evaluated in human embryonic kidney (HEK)-293 and colon cancer (Caco-2) cells by the MTS assay. Using solid phase peptide synthesis (SPPS), the percentage yield of the synthetic peptides was increased to >37% with >96% purity. These anionic ADEP1 analogues demonstrated a broad-spectrum antibacterial activity. Although the ADEP1 analogues did not display the expected antibacterial activity in relation to the parent structure, they were not cytotoxic against the tested cell lines.

CONCLUSION

This study proved that biocompatibility of natural ADEPs can be improved by modifying some of its chemical groups. Further studies are required to enhance the antibacterial activity of the ADEP1 analogues either by structural modifications or by using nanomaterial as nano-carriers.

Integration of molecular, spatial, and clinical data to understand Mtb transmission among people with subclinical TB in a rural South African population

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BACKGROUND

In high-burden settings, most TB disease derives from recent Mycobacterium tuberculosis (Mtb) transmission. Subclinical TB accounts for at least half of prevalent TB but its infectiousness is unknown.

METHODS

To better understand Mtb transmission in rural KwaZulu-Natal, South Africa, we integrated molecular, spatial and clinical data from a population-based multi-disease screening study conducted from 2018-2020. All participants over the age of 15 years were screened for TB. Participants with TB symptoms or radiological abnormality had sputum collected for liquid culture and whole genome sequencing. Genomes were assembled, annotated and clustered using published pipelines (TB profiler and MTBseq) and transmission investigations were done using TransPhylo.

RESULTS

Of 18,041 participants enrolled, 106 (0.6%) were liquid culture positive. 105/106 (99%) isolates were successfully whole genome sequenced and confirmed as Mtb (8/105 Lineage 1, 36/105 Lineage 2, 4/105 Lineage 3, 57/105 Lineage 4). 17/105 (16%) isolates grouped into 8 clusters (related closely to at least one other isolate by <12 single-nucleotide polymorphisms). 11/17 (65%) of clustered isolates were derived from individuals who were asymptomatic (defined as reporting none of the 4 WHO screening symptoms – cough of any duration, fever, night sweats or weight loss). 4/8 (50%) of clusters involved only people with asymptomatic TB. Geospatial analysis demonstrated that members of one cluster resided in the same household, members of three clusters resided in different households from the same neighborhood and members of four clusters had no discernable geospatial relationship.

CONCLUSION

One in six Mtb isolates from a cross-sectional population-based survey in rural KwaZulu-Natal clustered, consistent with high rates of recent transmission. A substantial proportion of people whose Mtb clustered were asymptomatic, suggesting that subclinical TB may contribute to transmission. To control ongoing transmission in high prevalence settings, more information about the infectiousness of subclinical TB and how it may contribute to transmission is urgently required.

ABSTRACTS: PRESENTATIONS PhD CATEGORY

Investigating the co-operation between the human papillomavirus (HPV) oncoproteins E6/E7 with the oncogenic T-box transcription factor 3 (TBX3) to promote cervical cancer

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BACKGROUND

Cervical cancer (CC) is a leading cause of cancer-related deaths in women in low- and middle-income countries. Persistent infection with high-risk strains of the Human Papillomavirus (HPV) is the causative agent of CC and its oncoproteins, E6/E7, cooperate with host factors to induce and maintain CC. Therefore, identifying these host factors may have important therapeutic benefits. We have previously reported that TBX3 is upregulated in CC tissues and cell lines where it co-operates with E6/E7 to promote CC proliferation and migration. The present study explores the E6/E7/TBX3 axis in CC.

OBJECTIVES

To assess the (1) mechanism(s) of TBX3 upregulation in CC, and (2) effect of E6/E7 expression on the TBX3-associated proteome.

METHODS

E6/E7 were either overexpressed or depleted in CC cells and the effect on TBX3 levels and promoter activity assessed by western blotting and luciferase reporter assays respectively. Co-immunoprecipitation and GST-pulldown assays were performed to determine if TBX3 interacts with E6/E7 and the region(s) of TBX3 involved. Mass spectrometry was performed to identify E6/E7/TBX3 interacting partners and co-immunoprecipitation assays were employed to validate those of interest.

RESULTS

This study reveals that E6/E7 activates TBX3 levels because overexpressing or depleting E6/E7 resulted in a corresponding change in TBX3 levels. We further show that, E6/E7 cooperate with c-Myc to activate the TBX3 promoter. Co-immunoprecipitation analysis revealed that TBX3 cooperates with E6/E7, and E6/E7 alter the TBX3-associated proteome. Indeed, we identified the serine/threonine phosphatase, PP2A, as an E6/E7/TBX3 cofactor, which plays a context-dependent tumour suppressor and tumour promoter role.

CONCLUSIONS

The E6/E7/TBX3 axis is important in driving CC progression. Understanding the molecular mechanisms underpinning CC is important in identifying potential therapeutic targets to treat this neoplasm.

ABSTRACTS: PRESENTATIONS PhD CATEGORY

The TBOX transcription factor-3 (TBX3) sensitizes pancreatic cancer cells to the antifungal drug, piroctone olamine

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BACKGROUND

Pancreatic cancer (PC) is a fatal disease with the worst prognosis of all cancers. In SA, 84% of patients diagnosed with PC die from the disease. Therefore, new therapeutic agents are urgently needed to reduce the burden associated with PC. Repurposing commercially available non-cancer drugs that inhibit key drivers of PC may facilitate the rapid identification of cost-effective drugs. In PC, the expression of the oncogenic transcription factor TBX3 correlates with distant metastasis and poor patient survival. Furthermore, ectopic expression of TBX3 in PC cells drives the oncogenic phenotypes including cell migration, invasion, and angiogenesis. Therefore, any drug that decreases the expression and/or activity of TBX3 may have major therapeutic benefits. In collaboration with the High Throughput Screening group at the Target Discovery Institute, University of Oxford, UK, we undertook a high-throughput drug-repurposing screen and identified Piroctone Olamine (PO) as a commercially available drug that can inhibit TBX3.

OBJECTIVES

To investigate the anti-cancer activities of PO in TBX3-driven PC.

METHODS

Human PC cell lines (BxPC-3, CFPAC-1, PANC-1, and SW1990) were used in this study. MTT, clonogenic assays, SA-β-gal assay, Annexin-V/PI staining, scratch motility, transwell invasion, 3D spheroid formation and invasion assays, immunocytochemistry, and western blotting were used to investigate the anti-cancer effects and mechanisms of action of PO.

RESULTS

PO showed IC_{50} values of <8 μM in PC cell lines, and compared to non-malignant cells, displayed selectivity (≥2) to PC cells. It also exhibited long-term cytotoxicity, induced DNA damage, apoptosis, and autophagy, and inhibited cell invasion, migration and 3D spheroid growth, viability, and invasion. Additionally, PO targeted TBX3 for proteasomal degradation and is less effective in TBX3-knocked-down PC cells.

CONCLUSION

Together, our data suggest that PO has great potential to be repurposed for the targeted treatment of TBX3-driven PC.

ABSTRACTS: POSTERS MSc CATEGORY

Gender specific lifestyle cardiovascular risk factors and co-morbidities in heart failure with a preserved ejection fraction patients living in South Africa

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BACKGROUND

Gender-specific characteristics of Heart Failure with Preserved Ejection Fraction (HFpEF) have been reported in western countries. However, limited data from Sub-Saharan Africa (SSA) show different onset and prevalence. Currently, no study has explored the sex-specific differences in HFpEF, in SSA.

OBJECTIVES

This cross-sectional study aimed to explore sex-specific disparities in lifestyle cardiovascular risk factors and co-morbidities related to HFpEF in South African individuals.

METHODS

339 participants were included, with 126 HFpEF patients (75 females) and 213 controls (123 females). All provided informed consent and completed a standardized questionnaire. Echocardiographic, anthropometric, and central hemodynamic measurements were assessed. Unpaired T-tests compared gender groups in HFpEF patients, while Pearson Correlation tests examined associations between HFpEF markers, co-morbidities, and risk factors with age adjustments.

RESULTS

Among HFpEF patients, males had higher alcohol consumption (Alc) and smoking rates than females ($p=0.028$ and $p=0.0008$, respectively). Conversely, females exhibited elevated C-reactive protein (CRP) levels and ejection fraction (EF) compared to males ($p=0.0015$ and $p=0.0201$, respectively). Gender-specific analyses in HFpEF patients and controls revealed that hypertension, waist circumference (WC), and body mass index (BMI) correlated with the E/A ratio (HFpEF marker) in males before age adjustments. After adjustments, Alc and WC still correlated with the E/A ratio. In females, diabetes, hypertension, WC, and BMI correlated with HFpEF before age adjustments. After adjustments, all correlations remained, except diabetes, while Alc correlated with the E/A ratio. Smoking and physical inactivity showed no correlation with the E/A ratio in gender-specific groups.

CONCLUSION

Males displayed higher smoking and Alc rates, while females showed elevated CRP levels and EF. With regards to correlations, HFpEF correlate with Alc and WC in males. In females, HFpEF correlate with Alc, hypertension, WC, and BMI. Understanding these disparities are crucial for exploring pathophysiological mechanisms of HFpEF patients in SA, prevention and the clinical management thereof.

Induction of apoptosis in cervical cancer cells using quinoxaline derivative LAM-21D

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BACKGROUND

Cervical cancer represents a major global health problem. It remains the cause of morbidity and mortality that burden mostly women in low- to middle-income countries.

OBJECTIVES

The aim of the study is to investigate the apoptosis-inducing effect of the quinoxaline derivative LAM-21D on cervical cancer cells (CaSki).

METHODS

MTT and KI67 proliferation assays were conducted to monitor the effect of the compound on cell viability and cell proliferation of CaSki and HEK-293 human embryonic kidney cells. Muse flow cytometry was used to determine the mode of cell death induced as well as assess the effect of the compound on oxidative stress and cell cycle progression.

RESULTS

The results have showed that LAM-21D negatively influenced the viability and proliferation of CaSki cells in a concentration-dependent fashion with an IC_{50} value of 250 µM. In addition, LAM-21D had minimal effect on HEK-293 cell viability and proliferation as compared to the CaSki cells. Furthermore, the compound was seen to induce oxidative stress as well as apoptotic cell death associated with cell cycle arrest in CaSki cells.

CONCLUSION

In conclusion, the findings of the study suggests that the quinoxaline derivative LAM-21D selectively inhibit cervical cancer (CaSki) cells proliferation by inducing apoptosis associated with S-phase cell division cycle arrest.

ABSTRACTS: POSTERS MSc CATEGORY

Development of an irritant-induced allergy model to characterise the anti-inflammatory properties of honeybush (*C. subternata*) in skin *in vitro*

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BACKGROUND

The prevalence of allergies associated with epithelial barrier dysfunction has increased at an alarming rate (2-3 fold) with skin allergies forming part of the major types of atopy in children and adults. Natural treatments, such as honeybush extracts, could be safer alternatives. The phenolic antioxidants in honeybush have a wide range of health benefits, including anti-oxidant and anti-inflammatory properties, however, their underlying mechanisms against epithelial barrier dysfunction and inflammation still need further characterisation. The major polyphenols present in *Cyclopia subternata* are xanthones, benzophenones, flavones, flavanones and dihydrochalcones. Therefore, we aim to outline the cytoprotective effects of *C. subternata* in DNCB-exposed keratinocytes (HaCaTs).

OBJECTIVES

Develop an irritant (2,4-Dinitrochlorobenzene)-induced allergy model, using HaCaTs to characterise the barrier restorative and anti-inflammatory properties of a hot water extract of green (unfermented) *C. subternata* plant material.

METHODS

A pre-exposure DNCB skin allergy model was optimised for seeding efficiency (6 hrs vs 24 hrs), DNCB concentration (80-10 µM) for cytokine production, cell viability (Caspase-3/7, ATP) and filaggrin expression. The *C. subternata* extract was screened for cytotoxicity (IC_{50} concentration) using cell viability. Anti-inflammatory and cyto-protective effects were determined by ELISA and gene expression (qPCR).

RESULTS

Optimum seeding efficiency for HaCaT cells in the pre-exposure model was after 24 hrs. DNCB induced minimal cytotoxic effect at 20µM. The extract reduced cell viability in a dose-dependent manner. It exhibited differential effects against IL-1α, IL-6, IL-8, TSLP, filaggrin and cytoprotective effect in DNCB-exposed HaCaTs.

CONCLUSION

In the pre-exposure irritant-induced allergy model, HaCaT cells require longer incubation periods for optimal seeding efficiency, because shorter periods render cells more sensitive to toxic effects of DNCB and *C. subternata* extract. This may distort the protective effects of the extract against inflammation and epithelial barrier dysfunction. The polyphenols present in *C. subternata* may be potential cytoprotective agents against inflammation caused by chemical irritants.

ABSTRACTS: POSTERS MSc CATEGORY

Investigating DNA methylation of metabolic and inflammatory genes with therapeutic potential for obesity: A cohort study in South African women

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BACKGROUND

Obesity and insulin resistance are modifiable risk factors that present opportunities for type 2 diabetes prevention and intervention.

OBJECTIVE

The current study aimed to (1) elucidate the epigenetic mechanisms underpinning obesity and insulin resistance in South African women, and (2) explore the potential of exercise intervention to reverse these pathogenic modifications.

METHODS

Obese (n=27) and normal-weight (n=27) South African women were recruited for the first arm of the study. Subcutaneous gluteal (GSAT) and abdominal (ASAT) adipose biopsies from study participants were subjected to targeted next-generation sequencing (tNGS), after which results were validated using bisulfite pyrosequencing. The second arm of this study investigated the impact of exercise on DNA methylation signatures identified in aim 1. To this end, pyrosequencing was employed to analyze DNA methylation in GSAT and ASAT biopsies from 19 South African women with obesity who underwent 12 weeks of aerobic and resistance training.

RESULTS

tNGS identified differential methylation of *Peroxisome Proliferator-Activated Receptor Gamma (PPARG), Macrophage Inhibitory Factor (MIF), Fatty Acid Synthase (FASN), Tumour Necrosis Factor Alpha (TNFA), FK506-binding protein (FKBP5), and Solute Carrier Family 6, Member 4 (SLC6A4)* in obese compared to normal weight women. Further investigation of these genes revealed hypermethylation within intron 5 of *FKBP5* in GSAT, and the promoter regions of *FASN* and *SLC6A4* in ASAT of obese compared to normal-weight women. Hypermethylated CpG sites within these genes correlated positively with markers of adiposity, insulin resistance, and inflammation. Importantly, compared to baseline, women who underwent 12 weeks of exercise training displayed a reversal of *SLC6A4* methylation in ASAT compared to the control group. These changes positively correlated with high-density lipoprotein levels and negatively correlated with Hemoglobin A1C (HbA1c).

CONCLUSION

This study provides novel evidence of adipose tissue-specific DNA methylation signatures that are associated with obesity and insulin resistance that can be modulated by exercise.

ABSTRACTS: POSTERS MSc CATEGORY

Determining the role of differential expression of candidate microRNAs in cardiometabolic diseases among HIV infected South Africans

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INTRODUCTION

The diagnostic/prognostic potential of microRNAs (miRNAs) in cardiometabolic diseases (CMDs) in general populations has gained prominence. However, its use in people living with human immunodeficiency virus (PLWH) has not been as extensively evaluated.

OBJECTIVES

We investigated the differential expression of miRNAs, miR-126-3p, -223-3p, and -320a in PLWH, with and without CMDs, in South Africa. MiRNAs were extracted from whole blood and its expression quantified by reverse transcription quantitative polymerase chain reaction.

METHODS

In this cross-sectional study, PLWH ≥18 years, were recruited from 17 randomly selected HIV clinics in the Western Cape between 2014-2015. Select anthropometric measurements and biochemical analyses were performed. CMDs and traits were defined as: obesity: body mass index ≥30 kg/m^2; raised waist circumference (WC): ≥94 cm men, ≥80 cm women; diabetes mellitus (DM): fasting glucose ≥7 mmol/L, or 2-hour glucose 7.8–11.1 mmol/L, or on DM medication; insulin resistance (IR): homeostatic model assessment of IR (HOMA-IR) >90th percentile; and elevated high-sensitivity C-reactive protein (hs-CRP) >3 mg/L. Differences in miRNAs expression were compared by Wilcoxon rank sum tests or Kruskal Wallis tests. Regression analysis assessed miRNAs associations with cardiometabolic variables and CMDs in separate models. A p-value <0.05 was considered significant.

RESULTS

Among 675 participants [128 men and 547 women (81%)], prevalence of CMDs were: 34.1% obesity, 63.3% raised WC, 8.6% DM, 9.9% IR, and 67.4% with elevated hs-CRP. No significant differences in miRNAs expression were determined between participants with and without individual CMDs. Also, no significant associations were determined between miRNAs and CMDs such as raised adiposity, DM, IR, or elevated hs-CRP. In robust linear regression, the association between miR-126-3p and HOMA-IR when adjusted for age, gender, and WC, was borderline significant (β-coefficient=0.016, p=0.056).

CONCLUSION

These miRNAs, unlike in general populations, were not significantly associated with select CMDs in PLWH. Further studies in larger samples are needed to examine these associations.

ABSTRACTS: POSTERS MSc CATEGORY

Establishment of a novel insulin resistant cardiomyoblast spheroid model

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BACKGROUND

Three-dimensional *in vitro* techniques, like spheroids, provide a better alternative to traditional monolayer cell cultures, as it can more accurately recapitulate in vivo conditions. However, very few spheroid models exist to study cardiometabolic pathologies like obesity and insulin resistance.

OBJECTIVES

This study aimed to 1) establish a novel insulin resistant cardiomyoblast spheroid model with the rat cardiomyoblast cell line, H9c2; 3) render this model insulin resistant (IR) with a hyper-insulinemic and high fatty acid media, and 3) further characterise the model under normoxic and IR conditions.

METHODS

Spheroids, seeded at 4×10^4 cells/spheroid, were grown for 96 hours on ultra-low attachment (ULA) plates and imaged using scanning electron microscopy (SEM) and transmission electron microscopy (TEM). Spheroids were rendered insulin resistant by adding 100 µM palmitic acid, 100 µM oleic acid, and 100 nM insulin to the media prior to seeding in ULA-plates. Insulin resistance was confirmed with Western blot analysis of the insulin-responsive proteins, PKB, mTOR and their phosphorylation levels.

RESULTS

Spheroids formed an organised and compact outer morphology with the presence of extra-cellular matrix. TEM images showed healthy cells with active mitochondria, formation of cell-to-cell junctions, and structural actin filaments. Western blot showed that spheroids grown in insulin resistant media, had decreased levels of phosphorylated PKB and mTOR compared to control spheroids in response to 30 minutes insulin stimulation, indicating that the spheroids are insulin resistant.

CONCLUSION

This study established a novel rat cardiomyoblast spheroid model using the H9c2 cell line and is also one of the first insulin resistant cardiac spheroid models to be characterised. This model can be used to determine the impact of potential pharmaceuticals on cardiac bioenergetics, and aid in the understanding of insulin resistant on the cardiovascular system.

ABSTRACTS: POSTERS MSc CATEGORY

The effects of a high fructose diet and glucocorticoid treatment on cardiac function in Sprague Dawley rats

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BACKGROUND

Metabolic syndrome (MetS) is linked to systemic inflammation and may contribute to left ventricular (LV) dysfunction. However, the effects of a high-fructose diet as a MetS model on LV function and the impact of glucocorticoids in MetS on LV function remain poorly understood.

OBJECTIVES

This experimental study aimed to investigate the effects of a high-fructose diet and glucocorticoid intervention on LV function in rats.

METHODS

Sprague Dawley rats were grouped into control, high-fructose (HF), and high-fructose + glucocorticoids (HFGC) groups (n=10 each). HF and HFGC rats consumed a 20% fructose solution, and HFGC rats received 10 mg/kg prednisolone daily for 10 weeks. Body mass, blood glucose, blood triglyceride concentrations, and visceral fat mass were measured.

Echocardiography assessed cardiac function, and enzyme-linked immunosorbent assays (ELISAs) determined circulating concentrations of insulin, and high sensitivity-C-reactive protein (hs-CRP). Differences were determined by a one-way ANOVA followed by Tukey post hoc tests.

RESULT

HF and HFGC groups displayed MetS features with increased visceral fat mass, circulating triglycerides, and insulin ($p=0.04$, $p=0.001$, $p=0.01$, respectively). The heart weight indexed to body mass, LV weight indexed to body mass and the relative wall thickness were greater in the GC+HF compared to the control ($p=0.04$; $p=0.009$; and $p=0.01$ respectively). Lateral e' was lower, and E/e' was higher in HF and HFGC groups compared to controls ($p=0.001$, $p=0.005$, $p<0.0001$, $p=0.004$, respectively). HF and HFGC groups showed higher cardiac collagen content than controls ($p=0.001$, $p<0.0001$).

CONCLUSION

A high-fructose diet, representing MetS, induces a state of low-grade inflammation, impaires LV relaxation, and increases LV diastolic filling pressures. Glucocorticoid treatment in MetS alleviates inflammation but worsens cardiac morphology by inducing concentric hypertrophy, without worsening LV diastolic dysfunction. Understanding the influence of dietary factors and pharmacological interventions on LV function in MetS can help develop targeted therapies for cardiovascular complications in at-risk patients.

ABSTRACTS: POSTERS MSc CATEGORY

Chronic stress elicits distinct sex-specific responses in rat cardiac respiratory function and vascular reactivity

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BACKGROUND

Although chronic psychosocial stress is linked to cardiovascular diseases, the underlying mechanisms remain elusive.

OBJECTIVES

We investigated the effects of chronic stress on endothelial function and cardiac mitochondrial respiration.

METHODS

A chronic restraint stress (CRS) model was applied to male and female Wistar rats (one-hour daily for 4 weeks, with an additional rest week) mimicking an anxious phenotype. Subsequently, circulating stress hormone levels were determined together with behavioural tests. After termination, *ex vivo* aortic vascular reactivity tests and high-resolution respirometry analysis (frozen hearts) were completed. Collected aortic and heart tissues were evaluated using molecular/biochemical analyses.

RESULTS

Behavioural tests and circulating stress hormones displayed little changes between control *versus* CRS groups. A modest decrease was observed in phenylephrine-mediated contractile responses in CRS males *versus* controls *($p<0.001$)*, with no changes for females. CRS female aortas displayed a greater acetylcholine-mediated relaxation versus controls *($p<0.01$)*. CRS males (unlike females) displayed altered mitochondrial functional versus control in various respiratory parameters i.e., routine respiration *($p<0.05$)*, electron transfer system capacity *($p<0.01$)*, leak respiratory phosphorylation *($p<0.01$)*, β-oxidation-linked oxidative phosphorylation *($p<0.05$)* and glucose-linked oxidation *($p<0.05$)* pathways. Unlike controls, protein levels for CRS animals increased in cardiac tissue for female complexes I *($p<0.05$)* and III *($p<0.05$)*, male *($p<0.05$)* and female ($p<0.05$) ATP synthase, but decreased for PGC-1α in males *($p<0.05$)*. Aortic tissue revealed increased *O*-GlcNAc levels in CRS females *versus* control ($p<0.01$), while elevated levels were present in CRS males versus CRS females *($p<0.01$)*. CRS males showed reduced aortic superoxide dismutase (SOD1) expression *versus* control males *($p<0.05$)*, whereas CRS females showed increased SOD 1 expression compared to CRS males *($p<0.01$)*.

CONCLUSION

Although the behavioural tests and stress hormone levels showed minimal changes, our data revealed that despite these limited whole-body changes, stress-related cellular perturbations manifested as the earliest alterations (in sex-dependent manner) in response to chronic stress.

ABSTRACTS: POSTERS MSc CATEGORY

Investigating the cytotoxic effect of various anticancer agents on cervical cancer cell lines

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BACKGROUND:
Cancer is one of the most common diseases that adversely affect human's, life worldwide. Cervical cancer being one of the various types of cancer that contribute to cancer-related death in women, it is the fourth most prevalent female malignancy, globally. Despite the advancement of the current treatments, cervical cancer incidences continue to rise due to late diagnosis and advanced stages of the disease, as well as resistance to current cancer drugs.

OBJECTIVES:
This study investigates the cytotoxic effect of various anticancer agents on cervical cancer cells. To achieve the aim of the study, the effect of various anticancer agents on cervical cancer cells were determined utilizing the MTT, viability, apoptosis, and cell cycle assay.

METHODS:
The effect of different anticancer agents (A2O3, CoCl2, NaB and Curcumin) were tested on cervical cancer cells (Ca-Ski and HeLa) and non-cancerous cells (Hek-293 and Vero) using the MTT assay. To fully assess the anticancer potential effect of the anticancer agents, viability assay, induction of cellular apoptosis and cell cycle progression were assessed utilizing the Muse® Cell Analyser.

RESULTS:
The anticancer agents induced a significant growth inhibition of the cervical cancer cells in a concentration-dependant manner. A change in morphology was detected, in contrast to the untreated cells, which displayed normal epithelial with elongated spindle shape, in both cell lines. The anticancer agents had little effect on inducing apoptosis, whereas the cell cycle analysis showed that anticancer agents had mostly arrested cervical cancer cells in the G0/G1 and S phases.

CONCLUSION:
Based on the apoptosis analysis, the anticancer agents may induce another mode of cell death, whereas the viability analysis indicates that the anticancer agents may be effective for therapeutic use against cervical cancer; thus, further studies should be conducted to fully understand the anticancer mechanisms of the selected anticancer agents.

ABSTRACTS: POSTERS MSc CATEGORY

The effect of *Senecio serratuloides* and *Sarcophyte sanguinea* on cytochrome P450 3A4-mediated metabolism of metformin, pioglitazone, rosiglitazone and glyburide

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BACKGROUND

Diabetes mellitus, a persistent metabolic condition, presents a significant global health threat. Existing treatments for diabetes have drawbacks and side effects. To address this, there is a need for diabetes management strategies that are safe and affordable. Studies have shown that *Senecio serratuloides* and *Sarcophyte sanguinea* can effectively regulate blood glucose levels, enhance insulin sensitivity, and protect pancreatic beta cells that produce insulin. It is important to assess the interaction of these plants with conventional diabetes medications, specifically by evaluating their effects on key cytochrome P450 enzymes. This evaluation will determine the efficacy, safety, and suitability of *Senecio serratuloides* and *Sarcophyte sanguinea* as potential treatments for this chronic metabolic condition.

METHODS

Plant material collected from Northern KwaZulu-Natal was processed in the Botany department. Following this, the extracts underwent characterization using LC-MS analysis. To evaluate their inhibitory effects on CYPA4, the Vivid™ assay was utilized for both the herbal extracts and individual drugs.

RESULTS

The LC-MS analysis was conducted to establish the fundamental fingerprint of *Senecio serratuloides* and *Sarcophyte sanguinea* extracts. The results indicated that the *Senecio serratuloides* extract exhibited weak inhibition of CYP3A4, whereas the *Sarcophyte sanguinea* extract demonstrated strong induction at a concentration of 0.1 µg/mL.

CONCLUSION

The preliminary results indicate that the extract of *Sarcophyte sanguinea* exhibits significant induction. This suggests the potential to increase the metabolism of diabetic drugs, which could potentially decrease their efficacy. However, conducting additional experiments to assess the effect of combination treatment on the xenobiotic genes involved in the metabolism of anti-diabetic drugs will provide clearer insights into the specific mechanism of interaction responsible for inducing herb-drug interactions.

Keywords: Diabetes, herb-drug interactions, hepatic metabolism, *Senecio serratuloides*, *Sarcophyte sanguinea*, metformin, Pioglitazone, Rosiglitazone, Glyburide, cytochrome P450, CYP3A4

ABSTRACTS: POSTERS MSc CATEGORY

The effect of *Aloe marlothii* and *Catharanthus roseus* on cytochrome P450 3A4 and 2C9 mediated metabolism of metformin, pioglitazone, rosiglitazone and glyburide

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BACKGROUND

Herb-drug interactions, particularly in the context of diabetes, pose a significant challenge in global healthcare. Current diabetes treatments come with notable limitations and adverse effects, underscoring the urgency for cost-effective and safe management strategies. Recent studies have unveiled the potential of Aloe *marlothii* and *Catharanthus roseus* as anti-diabetic herbal remedies, with demonstrated glucose-regulating properties. To ensure their safe and effective use with conventional diabetes medications, it is crucial to assess their interaction with pivotal cytochrome P450 enzymes.

METHODS

The plant material was collected in KwaZulu-Natal, which underwent processing within the Botany department. Subsequently, the extracts underwent characterization through LC-MS analysis. The Vivid™ assay was employed to assess the inhibitory impact of the herbal extracts.

RESULTS

The LC-MS analysis was conducted to establish the fundamental fingerprint of Aloe *marlothii* and *Catharanthus roseus* extracts. The results indicated that the Aloe *marlothii* extract exhibited weak inhibition of CYP3A4, whereas the *Catharanthus roseus* extract demonstrated strong induction at a concentration of 0.1,1 and 10 µg/mL. While induction was observed for both Aloe *marlothii* extract and *Catharanthus roseus* extract for CY2C9.

CONCLUSION

The preliminary results reveal that the extract of *Catharanthus roseus* extract exhibited significant induction. However, conducting additional experiments to assess the combination treatment will offer better insights into potential interactions.

Keywords: Diabetes, herb-drug interactions, hepatic metabolism, Aloe *marlothii* and *Catharanthus roseus*, metformin, Pioglitazone, Rosiglitazone, Glyburide, cytochrome P450, CYP3A4

Atypical masses in rat bone tissue: a green Rooibos tomography study

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BACKGROUND

High-fat (HF) and high-sugar (HS) diets impart complex diet-specific effects on bone metabolism and structural integrity. Natural products like Rooibos are commonly used to regulate metabolism.

OBJECTIVES

This study aimed to evaluate effects of obesogenic feeding and a green Rooibos extract (Afriplex GRT™, GRT) on femora of male Wistar rats using nano-computerized tomography (nano-CT) (ACU-2018-6786.

METHODS

Rats, sourced from Stellenbosch University's Animal Research Facility, were randomly assigned to one of three dietary groups (n=24 each), namely control (CON), high-sugar (OB1) or high-fat (OB2) for 17 weeks. Afriplex GRT™ supplementation occurred from weeks 11-17 for half the animals in each diet group (n=12 each). Soft tissue was removed from all femora prior to nano-CT scanning.

RESULTS

The nano-CT scans revealed atypical masses in the femoral shaft as well as the distal and proximal aspects (n=17, 25%). Thickening of both the distal and proximal growth plates were observed, which extended into the distal trochlear condylar junctions. Specifically, masses were observed in the CON-GRT group (n=9, 90%) while no masses were visible in the CON, OB2 or OB2-GRT groups. In addition, more masses were observed in the OB1-GRT group (n=5, 27%) compared to the OB1 group (n=3,28%).

CONCLUSION

These masses may be a result of osteoblastic (femoral shaft) or chondroblastic activity (growth plates). Reports of similar masses on nano-CT bone scans could not be found. Future studies will explore bone histomorphometry and immunohistochemistry to explore markers associated with osteo- and chondrogenesis.

ABSTRACTS: POSTERS PhD CATEGORY

Obesity and diabetes in pregnancy: association with maternal serum adiponectin

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BACKGROUND

Adiponectin is an insulin-sensitizing adipokine that is downregulated during obesity and insulin resistant states. Lower adiponectin levels have also been associated with pregnancy progression and adverse infant outcomes. This study investigated the effect of diabetes in pregnancy (DIP) on infant outcomes and the association between serum adiponectin levels, obesity and DIP.

METHODS

Pregnant women with type 1 (T1DM, n=26) and type 2 (T2DM, n=77) diabetes, gestational diabetes (GDM, n=58) and normoglycemia (n=69) were recruited at the Steve Biko Academic Hospital, Tshwane, South Africa between 2017 and 2022. Serum adiponectin concentrations were measured using an enzyme-linked immunoassay commercial kit. Body mass index (BMI) was categorized as normal weight (BMI = 18.5–24.9 kg/m^2), overweight (BMI = 25.0–29.9 kg/m^2), and obesity (BMI ≥30 kg/m^2).

RESULTS

Preterm birth was higher in women with T1DM and T2DM compared to women without diabetes (70.0% and 52.8% vs 19.3%; p<0.001). Lower levels of adiponectin were observed in pregnant women with T2DM diagnosed in pregnancy (2-fold; p<0.01) and GDM (2-fold; p<0.05) compared to T1DM. Serum adiponectin levels were negatively correlated with fasting (r= -0.244; p<0.05) and 1-h (r= -0.299; p<0.01) and 2-h (r= -0.246; p<0.05) oral glucose tolerance test glucose concentrations. BMI (r= -0.221; p<0.05) and body weight (r= -0.222; p<0.01) were negatively correlated with adiponectin concentrations, with lower levels observed in obese compared to normal-weight women (2-fold; p<0.05). The association between adiponectin and DIP remained significant after adjusting for age and GA but was lost when adjusting for weight or BMI.

CONCLUSION

Maternal serum adiponectin is associated with glucose concentrations and BMI; low levels were associated with obesity and diabetes in pregnancy. The correlation between adiponectin and hyperglycaemia was lost after adjusting for BMI, suggesting that adiponectin levels are primarily regulated by weight.

ABSTRACTS: POSTERS PhD CATEGORY

Investigating the importance of ATM protein kinase in the ER stress response underlying metabolic disease: an in vitro study

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BACKGROUND

Chronic endoplasmic reticulum (ER) stress underlies obesity and metabolic diseases, which remain a global health threat. Understanding the key role players of the ER stress response might aid in the development of novel drug targets. Ataxia-telangiectasia mutated protein kinase (ATM) participates in redox homeostasis and protein degradation (autophagy), which are pathways also regulated by the ER stress response. However, it remains unknown whether ATM plays a key role in the ER stress response.

OBJECTIVES

Investigate read-outs of the ER stress response in the presence and absence of ATM activation in vitro to assess the suitability of ATM as a potential drug target.

METHODS

HEK-293 cells (n=3-4) were treated with 3.75 µg/ml tunicamycin (ER stressor) with/without 1 µM KU-60019 (ATM inhibitor) for 9 hours. Protein and phosphorylated (activated) levels of ATM, IRE1 (ER stress), p62, LC3 (autophagy), and IκBα (inflammation) were measured (Western blotting). Oxidative stress (DCFH assay) and inflammation (flow cytometry) were also assessed.

RESULTS

IRE1 ($p<0.01$) and ATM ($p<0.001$) were activated by tunicamycin-induced ER stress, whereas the additional inhibition of ATM with KU-60019 further increased IRE1 activation ($p<0.001$). This was associated with increased inflammatory markers ($p<0.05$) and reactive oxygen species generation ($p<0.05$). KU-60019 alone increased p62 levels ($p<0.05$) and did not alter the LC3II/I-ratio. Neither tunicamycin alone nor the combination of tunicamycin and KU-60019 changed p62 levels and increased the LC3II/I-ratio ($p<0.01$).

CONCLUSION

Overall, the absence of ATM activation exacerbates the ER stress response and is associated with increased inflammation and oxidative stress, suggesting that ATM plays an important role in mitigating ER stress. Furthermore, this study shows that autophagy, which is an ATM-dependent process, may be initiated independently of ATM during ER stress.

ABSTRACTS: POSTERS PhD CATEGORY

The relationship between host genetic make-up and human immunodeficiency virus in a South African population

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BACKGROUND

The increasing prevalence of HIV has become one of the major public health challenges. The search for host factors and their genetic role to immune responses deduces essential understanding of pathogenesis. Recent research has indicated some blood groups to have a protective effect from HIV and the CCR5 delta-32 (CCR5Δ32) variant has been reported to account for protection against HIV in the European population.

OBJECTIVES

To elucidate the relationship between host blood groups and HIV in a central South African population.

METHODS

HRM-analysis was performed on 500 samples to detect the CCR5Δ32 variant. Furthermore, a case-control study was performed on 200 participants, 100 HIV-positive and 100 HIV-negative subjects, to establish if specific blood groups have a protective effect against HIV. Fisher Exact tests were used to compare frequencies on the antigens or phenotypes in the two groups. Exon 3 of A4GALT was screened for mutations using Sanger sequencing for 20 samples in the population group to determine the association of mutations with HIV and the P1/P2 status of the P1PK system.

RESULTS

The CCR5Δ32 variant was absent from our study population. All major blood groups were identified in the study population. None of the blood groups were associated with HIV susceptibility, however, a very rare Rhesus phenotype D,--E,e was found in one HIV positive individual. Several novel mutations were found in the A4GALT gene which were not associated with HIV and the P1/P2 status of the P1PK system.

CONCLUSION

The CCR5Δ32 variant was completely absent in our study population, therefore, we hypothesise that it has limited impact on the susceptibility of HIV in our region. The major blood groups were observed to be the same in the two studied groups. Blood groups were observed to have neither protective nor predisposing characteristics to HIV infection.

ABSTRACTS: POSTERS PhD CATEGORY

In vitro antidiabetic and antihyperlipidemic properties of the extracts from *Cyclopia genistoides*

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BACKGROUND

Diabetes mellitus and its associated complications including dyslipidaemia continues to pose a threat and health burden to human population worldwide. The use of natural products in the treatment of various diseases has a gain much interest in medicinal perspective. This study aims at investigating an *in vitro* antidiabetic and antihyperlipidemic properties of the sequential (n-hexane, dichloromethane, and 70% ethanol) extracted red honeybush (*Cyclopia genistoides*).

METHODS

The crude extracts were screened for its phytochemical constituents through GC-MS. Thereafter, the extract was screened for its antioxidant activity using ABTS, DPPH, hydroxyl radicals, metal chelating, and reducing power assays. The potential antidiabetic activity of the plant extract was evaluated against some carbohydrates (α-amylase and α-glucosidase), lipid (pancreatic lipase) digestive enzymes and glucose uptake stimulatory using C2C12 skeletal muscles and 3T3L-1 adipocytes. Moreover, extracts binding ability with bile acid was evaluated.

RESULTS

The crude extract exhibited the antidiabetic potential as it significantly ($P<0.05$) stimulated cellular glucose uptake on both C2C12 and 3T3L-1. The extracts further inhibited α-amylase and pancreatic lipase in a dose dependent concentration with DCM (0.018 µg/mL) and n-hexane (9.93 µg/mL) demonstrating highest activities, respectively. A strong antioxidant activity by efficiently scavenging ABTS, DPPH, $OH^{\bullet}$ radicals with IC_{50} values ranging from 0.014–0.048 mg/mL to 0.019–0.043 mg/mL. Furthermore, a strong affinity of the extracts to the cholic acid and deoxycholic acids with adsorption rate of 93.8% ethanolic extract and 91.1% n-hexane extract, respectively. The phytochemical screening revealed the presence two hundred and seventy-four chemical. Six compounds such as Decane (RT: 6.4), Undecane (RT: 7.7), Dodecane (RT: 9.00), Phytol (RT: 21.32), Heptadecanoic acid, 9-methyl, methyl ester (RT: 21.65), and 9-Octadecenamide (RT: 24.30) were detected to be present in all three extracts. It is apparent that honeybush extracts could serve as scaffold for diabetic therapy.

CONCLUSION

For future study, in vivo investigation of the antidiabetic activity of the crude extract are recommended.

Keywords: Antidiabetic, Antihyperlipidemic, Glucose uptake, C2C12, 3T3L-1, *Cyclopia genistoides*.

ABSTRACTS: POSTERS PhD CATEGORY

Bioassay-guided isolation and identification of an antimycobacterial compound from *Gymnopilus junonius*

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BACKGROUND

Tuberculosis continues to be a public health crisis, and it is imperative to search for new antimycobacterial drugs. Natural products have been used as primary sources for the discovery of pharmaceuticals. Medicinal macrofungi, have been exploited in traditional folk medicines for the treatment of several diseases; however, research on their antimycobacterial activity remains limited.

OBJECTIVES

The aim of this study was to isolate and characterise the antimycobacterial compound from an ethanol extract from the fruiting body of *Gymnopilus junonius*.

METHODS

Bioassay-guided fractionation was performed using column chromatography and preparative thin-layer chromatography to obtain fractions and isolate the active compound. A resazurin microplate assay was used to screen for antimycobacterial activity against *M. tuberculosis* H37Rv. The chemical structure was determined by ^{1}H nuclear magnetic resonance spectroscopy, heteronuclear single quantum coherence spectroscopy (HSQC), heteronuclear multiple bond correlation spectroscopy (HMBC), and high-resolution electrospray ionisation mass (HR-ESI-MS) spectrometry. Transmission electron microscopy (TEM) was used to observe the ultrastructural changes in *M. tuberculosis* induced by the compound. Cytotoxicity was evaluated in African green monkey kidney cells (Vero) and human liver cells (C3A) cells.

RESULTS

Bioassay-guided fractionation of *G. junonius* resulted in the isolation of an active compound exhibiting inhibitory activity against M. tuberculosis (MIC: 31.25 µg/mL). The active compound was identified as gymnopilene. Transmission electron microscopy showed that treatment with gymnopilene caused ultrastructural damage to *M. tuberculosis* cells, which was observed as the disruption and disintegration of the cell wall. Gymnopilene exhibited cytotoxicity in Vero and C3A cells.

CONCLUSION

This study showed that macrofungi could be considered a potential source of bioactive compounds. To the best of our knowledge, this study is the first to demonstrate that gymnopilene produced by *G. junonius* possesses inhibitory activity against *M. tuberculosis*.

The anticancer effect of HIV protease inhibitor on HPV-associated cervical cancer

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BACKGROUND

Cervical cancer is a Human Papilloma virus (HPV)-related disease, which is on the rise in a number of countries including South Africa. Human Immunodeficiency Virus Protease Inhibitors (HIV-PIs) have attracted a lot of attention for anticancer drug development. However, it remains unclear whether it worth the effort to repurpose HIV-PIs for the treatment of HPV-associated cervical cancer. This study was aimed at determining the anticancer mechanisms of lopinavir HIV protease inhibitor on HPV associated cervical cancer cell lines.

METHODS

MTT viability assay was used to evaluate the effect of lopinavir HIV protease inhibitor on the viability of cervical cancer cells (HeLa and CaSki) and non-cancerous cells (Hek-293). Further confirmation of the MTT assay was performed by analysing the effect of lopinavir IC_{50}s on cervical cancer cells (HeLa and CaSki) and non-cancerous cells (Hek-293) using the Muse™ Count & Viability assay. To confirm mode of death induced by lopinavir in HPV-associated cervical cancer cell lines, apoptosis was performed using Annexin V Assay. In addition, Muse™ Cell Cycle assay was used to check whether lopinavir promote or halt cell cycle progression in cervical cancer cell lines.

RESULTS AND DISCUSSION

Lopinavir did not affect the viability of non-cancerous cells (Hek-293) but it decreased the viability of the CaSki and HeLa cervical cancer cells in a dose-dependent manner. Lopinavir induced type I programmed cell death known as apoptosis in HPV related cervical cancer cells. Furthermore, it also induced cell cycle arrest thus halting cell cycle progression.

CONCLUSION

The use of HIV drugs as potential cancer therapeutics can be a promising strategy because these drugs especially lopinavir have shown anticancer properties notably in HPV related cervical cancer cells.

Keywords: Human Papilloma virus, cell cycle, apoptosis, HIV protease inhibitor.

ABSTRACTS: POSTERS PhD CATEGORY

Exploring the cosmeceutical properties of Tanzanian seaweeds

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BACKGROUND

Skin conditions are often neglected as they are mostly deemed as non-fatal. However, findings suggest that skin conditions can place a burden on health status and quality of life by having psychological and social consequences. For several decades, marine macroalgae have prospered at providing a source of bioactive compounds which demonstrate a diverse range of therapeutic activities.

OBJECTIVES

The objective was to compare the bioactivities of *Kappaphycus alvarezii*, *Eucheuma denticulatum*, *Sargassum oligocystum*, *Turbinaria conoides* and *Ulva fasciata* to deduce their suitability for cosmeceutical applications.

METHODS

The Hoechst 33342/propidium iodide dual staining method was used to assess cytotoxicity on keratinocytes (HaCaT) and fibroblasts (MRHF). The ability to combat oxidative stress was determined by the HaCaT resistance to oxidative stress assay and metal ion chelation. Inhibition of collagenase, elastase, protein glycation and NO production was used to determine Extracellular matrix (ECM) protection. Skin rejuvenation potential was investigated by assessing HaCaT and MRHF proliferation. Inhibition of tyrosinase and α-glucosidase was determined for dyspigmentation potential. Data was collected using cellomics-based assays and statistical significance was determined using the Student two tailed T-test.

RESULTS

S. oligocystum, *T. conoides* and *U. fasciata* demonstrated the most significant potential at combatting oxidative stress as assessed with metal ion chelation and in TBHP-induced HaCaTs. ECM protection was most prevalent with *T. conoides* due to decreased NO production in LPS-activated macrophages and an approximate inhibition of 20% of elastase activity. *U. fasciata* displayed the best potential for skin rejuvenation by stimulating proliferation of both keratinocytes and fibroblasts. Dyspigmentation potential as assessed by inhibition of tyrosinase and α-glucosidase was the most significant with *S. oligocystum*, *T. conoides* and *U. fasciata*.

CONCLUSION

The seaweed species proved to possess multiple beneficial activities suitable for cosmeceutical application, however, the use of a specified seaweed will depend on the target.

ABSTRACTS: POSTERS PhD CATEGORY

Optimisation of pyrosequencing-based DNA methylation analysis for validation of biomarkers in gestational diabetes mellitus

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BACKGROUND

Gestational diabetes mellitus (GDM) is associated with adverse short- and long-term effects for mothers and their offspring. DNA methylation is an epigenetic mechanism that plays an important role in the pathophysiology of GDM. Recently, our laboratory demonstrated altered genome-wide DNA methylation of genes key to metabolic regulation in women with GDM. The current study aims to expand on this and will optimise and validate altered DNA methylation in the complete sample set of South African women with/without GDM.

METHODS

Women with (n=43) and without (n=111) GDM were recruited at <28 weeks of pregnancy. DNA was isolated from whole blood and quantified using Qubit fluorometry. Three CpG sites corresponding to differentially methylated genes, peroxisome proliferator-activated receptor gamma coactivator 1-alpha (*PPARGC1A*), protein tyrosine phosphatase receptor type N2 (*PTPRN2*) and Insulin gene enhancer protein (*ISL1*), were selected based on the relevance to GDM pathophysiology. Primers were designed using Ensemble, UCSC Genome Browser, and PyroMark Assay Design Software. DNA methylation optimisation was performed by Quantitative Reverse Transcription PCR using methylation standards (0-100%). Agarose gel electrophoresis was used to assess amplicon size. DNA methylation was conducted using pyrosequencing. Validation analysis is currently in progress.

RESULTS

DNA concentrations ranged between 43.1 – 216 ng/µl and the 260/280 absorbance ratio indicated good DNA purity (~1.8). Gene sequences corresponding to CpG sites of interest were identified and confirmed to be in intron 1 of *PTPRN2*, intron 1 of *PPARGC1A* and exon 1 of *ISL1*. The amplicon product size of *PPARGC1A*, *PTPRN2* and *ISL1*, were successfully confirmed at 142 bp, 158 bp and 188 bp. The methylation levels correlated with the percentage of methylation for each standard, thereby confirming optimal conditions for methylation validations analysis.

CONCLUSION

This study will identify GDM-associated methylation changes that may offer potential as novel biomarkers for GDM. GDM prevention interventions may improve maternal and child health outcomes.

ABSTRACTS: POSTERS PhD CATEGORY

Indigenous *Aspalathus linearis* extracts as a natural alternative to standard treatment of gut-related inflammatory conditions

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BACKGROUND

Dysfunction of the intestinal epithelium can result in increased gut permeability causing deregulated transport across the cell membrane as well as cell-to-cell communication resulting in gastrointestinal (GI) disease. The precise regulation of the intestinal barrier allows the maintenance of mucosal immune homeostasis and prevents the onset of inflammation. *Aspalathus linearis* is known, to have health-promoting properties including anti-inflammatory effects.

OBJECTIVES

Analyse the cytotoxic, apoptotic and anti-inflammatory effects of aqueous unfermented (RgU) and fermented (RgF) rooibos extracts on porcine intestinal epithelial cells (IECs). Additionally, the study investigates the effects of the extracts on gene expression, specifically barrier integrity markers.

METHODS

Aqueous rooibos extracts were prepared by lyophilization and characterized by HPLC and antioxidant analysis. Lipopolysaccharide (LPS) was used to induce inflammation in the model with dexamethasone as a comparative anti-inflammatory control. The anti-inflammatory and protective effects of the rooibos extracts were determined by assessing cell viability (ATP), apoptosis (caspase assay), inflammation (enzyme-linked immunosorbent assay), gene expression (quantitative polymerase chain reaction).

RESULTS

HPLC analysis showed that unfermented extracts contained higher levels of total polyphenols (14.2 g/100 g). The optimal dexamethasone concentration of 0.15625 mM was selected for the model. The RgU and RgF extracts demonstrated anti-inflammatory properties ($p<0.05$) and RgU extracts had a significant anti-apoptotic effect ($p<0.05$). Both extracts were more effective in decreasing IL-8 concentrations compared to dexamethasone. Gene expression analysis showed the extracts significantly increased in barrier integrity.

CONCLUSION

The extracts demonstrated anti-inflammatory protection, thereby displaying the potential to restore and increase intestinal barrier integrity on IECs. When comparing the extracts to dexamethasone, tea extracts were significantly more effective in reducing IL-8 in LPS-induced inflammation conditions. High dexamethasone concentrations have damaging effects on IECs, demonstrating potential side effects of current treatment regimes. The current results show the potential of rooibos as a natural alternative supplement for preventing gut-related inflammatory conditions.

Keywords: *Aspalathus linearis*, Polyphenols, Gastrointestinal tract, Rooibos, Inflammation

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