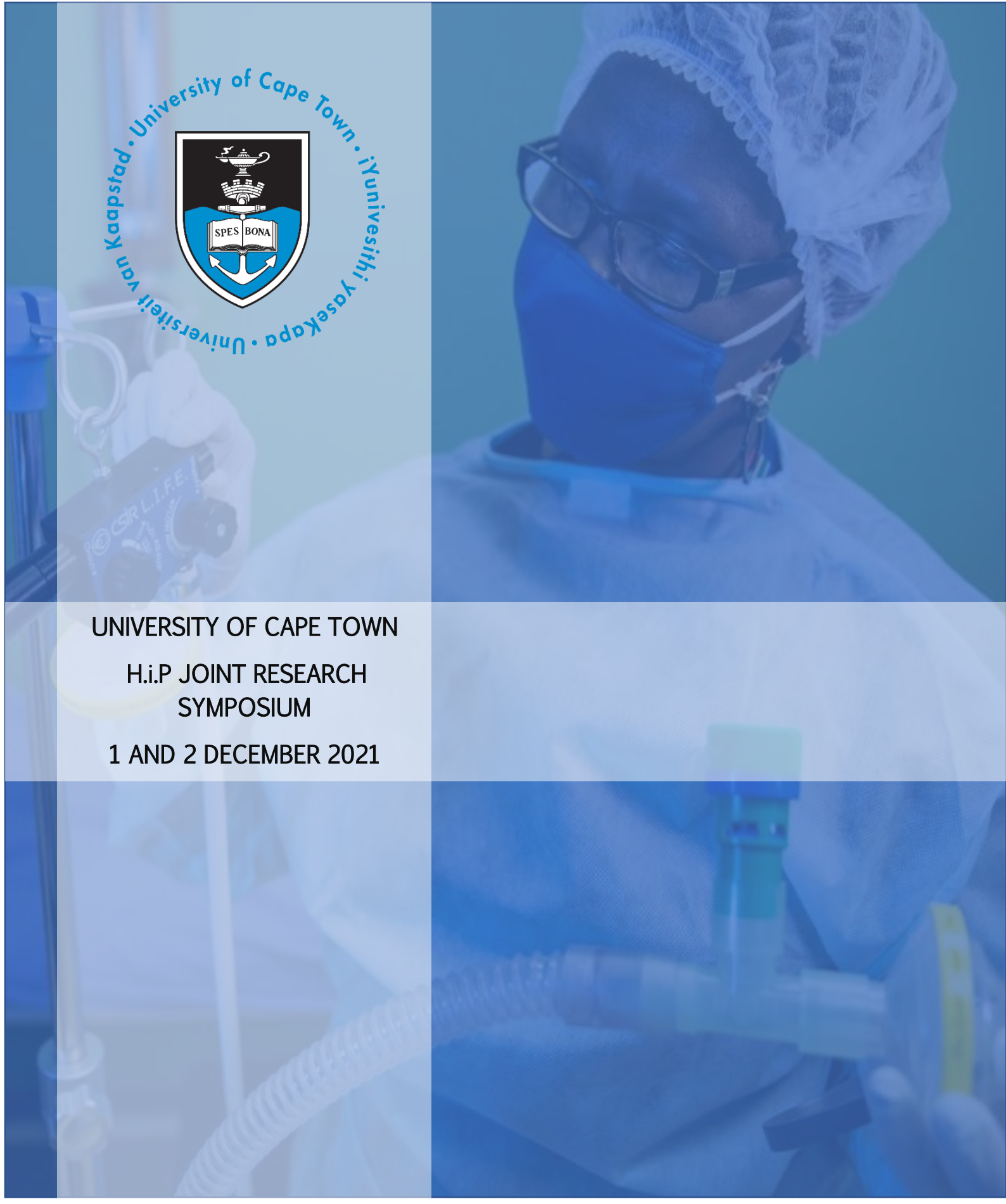

UNIVERSITY OF CAPE TOWN

H.i.P JOINT RESEARCH SYMPOSIUM

1 AND 2 DECEMBER 2021

HUB Department of Human Biology

iBMS Integrative Biomedical Sciences
Computational • Molecular • Systems

Department of PATHOLOGY University of Cape Town

The H.i.P. Departments are thankful for the generous support from our Sponsors

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Welcome!

Vho tanganedzwa! Welcome! Namukelekile! Baie Welkom! Karibu! Akwaaba! Sannu! Namaste! Mauya! Titambire! It gives us great pleasure to welcome you to the Joint Human Biology (HUB)-integrated Biomedical Medical Sciences (iBMS)-Pathology (PTY)-[H.i.P] Biennial Research Symposium 2021. The three departments are among the biggest in the faculty in terms of research activities, postgraduate students, and research staff. The H.i.P Symposium is a continuation of previous Research Days the three Departments have held over the years. What is special about this year's event is the agreement among the three departments that from 2021, the event will be held every 2 years coordinated by the respective Departmental Research Committees working together during each event. The theme of the 2021 Symposium is **"Igniting urgency in catalysing transformative and impactful health research"**. The theme is borrowed from our Dean, Professor Lionel Green Thompson's reflections on the activities of our faculty. The conference hopefully showcases some of the solutions on how we can contribute to making the world population healthier through our interrogation of health science research that is critical in reducing the burden of diseases among our populations and responsive to the United Nations Sustainable Development Goals (SDGs).

H.i.P, organised in the Faculty of Health Sciences (FHS), provides a platform for more than 1000 postgraduate students, postdoctoral fellows, and emerging researchers to showcase their ground-breaking research. The papers that are presented here were carefully selected for their scientific excellence by the Scientific Committee Chaired by Dr Hlumani Ndlovu, thank you and your team for such an excellent job. We are excited that we were able to attract six keynote speakers, leading experts in their fields globally, including eminent speakers from South Africa Medical Research Council (SAMRC) and the National Research Foundation (NRF).

This joint symposium comes at a time the world is dealing with the devastating effects of the SARS-Cov-2 virus which cause COVID-19. The last 21 months has not been easy making for researchers, and it was also challenging for the organising committee to plan without knowing what the few months ahead were going to be like, thus, the hybrid model of this meeting. Moreso, with COVID-19, the global economic situation has been hit-hard particularly with "lockdowns", thus, we would really want to thank our sponsors, Inqaba Biotec and Whitehead Scientific (Pty) Ltd, who stood by us during such difficult times and pledged financial support. In addition, we would like to thank the Heads (HODs) of the three Departments, who have supported us financially as well as seconding personnel to assist. Thank you, Professors Hendricks, Prince and Ramesar. Without all the support from our sponsors, we would not have been able to hold this Symposium.

We are particularly grateful to our invited speakers who believed in us and supported us by their presence. It is our sincere hope that their presence will be beneficial to the attendees to this Symposium particularly to young researchers who are taking part in this conference, some of whom it's their first time. We are excited inform you that we have set aside funds to give prizes to best presenters.

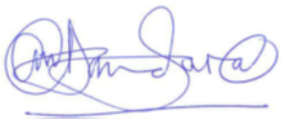
We would like to thank the Symposium Organising Committee for the dedication to this task which seemed impossible in the beginning but now is reality. Deputy Chair, Professor Sudesh Sivarasu (you were the bedrock for organising this Symposium), Dr Hlumani Ndlovu, Chair Scientific Committee (for the endless meetings), Dr Akhona Vava, Dr Joseph Raimundo, Dr Calvin Mole, Professor Jessica Opie, Dr Jacolene Kroft. Finally, we want to thank the administrative engine for the Symposium, Coleen Fredericks and Adielah Van Der Schyff. We salute you!

To our keynote speakers and presenters, if it was not because of COVID-19, it was the wish of the organising committee to bring you physically to the Faculty of Health Sciences in Cape Town for networking.

With this, we would like to invite you to sit back, and enjoy the two days showcasing scientific excellence.

Ke a leboga! Thank you! Ndatenda! Ndiyabulela! Ndo livhuwa!

Sincerely,



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Chair, H.i.P Joint Research Symposium 2021
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Organizing Committee

Ms. Adielah van der Schyff

Dr Akhona Vava

Mr Calvin Mole

Ms Colleen Fredericks (Conference Secretary)

Prof Collet Dandara (Conference Chair)

Dr Jacolene Kroft

Prof Jessica Opie

Dr Joseph Raimando

A/Prof Sudesh Sivarasu (Deputy Chair)

Scientific Committee

Dr Hlumani Ndlovu (Chair)

A/Prof Delva Shamley

Ms Bianca Southon

Dr Sonwabile Dzanibe

Dr Fezile Khumalo

Dr Shaeen Mowla

Dr Akhona Vava

Mr Calvin Mole

Prof Vicki Lambert

Dr Victoria Nembaware

Dr Nayari Soko

Messages from the Heads of Department

Department of Human Biology: Prof Sharon Prince

It is my Joint Research Symposium 2021 which will be held on a hybrid platform (both virtual and in person) on the 1st and 2nd of December 2021. The joint symposium is hosted by three of the largest research Departments within the Faculty of Health Sciences, namely, Human Biology (HUB), Integrative Biomedical Sciences (iBMS) and Pathology (PTY), in short, called the H.i.P Joint Research Symposium.

The event will showcase the outstanding and diverse research being done by postgraduate students (Honours, Masters and Doctoral) and postdoctoral fellows within the four Divisions in HUB viz, the Divisions of Biomedical Engineering (BME), Clinical Anatomy and Biological Anthropology (CABA), Cell Biology (CB) and Physiological Sciences (PHYS), as well as research from the other two partnering Departments.

We are grateful for the many abstracts which were submitted. Each abstract was reviewed by at least three independent members of the scientific and technical committee and the top 80 abstracts have been selected for either oral or poster presentations. Independent national and international experts will judge the presentations and the top presenters will receive the best presentation awards.

I am excited about the inclusion of several national and international keynote speakers in this research symposium which includes the President of the South African Medical Research Council (SAMRC) and the CEO of the National Research Foundation (NRF). I am sure that these talks will inspire and reaffirm our commitment to contributing to scientific research and training in Africa.

I wish to take this opportunity to thank the Organizing Committee for arranging an outstanding programme, the Chairs, Judges, our Participants as well as our Sponsors for their continued support and for their generous contributions towards the awards.

Please join us online and in person to enjoy and celebrate the diverse and fascinating research activities happening across the Departments of Human Biology, Integrative Biomedical Sciences and Pathology. Let us use this opportunity to establish inter-disciplinary, cross-disciplinary and trans-disciplinary research across our Departments.

Head of Department of Integrative Biomedical Sciences: Prof Denver Hendricks

Dear Research Day participants,

I am so pleased that we've decided to host the Joint Post Graduate Research Day this year, despite the very difficult circumstances we've experienced during the past two years. This is a wonderful opportunity for us to share and celebrate our successes of this period.

The Research Day celebrates two of the cornerstones of a university – creating knowledge and sharing knowledge. However, during the past two years, the COVID pandemic has wreaked an unprecedented impact on our postgraduate students who play a key role in creating knowledge and sharing that knowledge. The laboratories were closed for close to nine months last year, and we also changed the way research was done thereafter. This has retarded project progress in many cases and impacted on the availability of funds for students to continue their research with extended timelines.

To our postgraduate students, I would say, don't despair - we will find a way forward! You represent the future scientists who will grapple with the problems which your era will unleash on you, and the tenacity and creativity you develop now will provide a solid foundation for your future. Remember the important role that science has played in creating solutions for the COVID pandemic, but don't forget that these scientific solutions may mean little if we are unable to address the many social problems which confront us, particularly the lack of equity.

In conclusion, I look forward to a very successful Joint PG Research Day, I thank the conference organising committee for all their hard work and their efficiency in arranging this conference, and I also thank the presenters who volunteered to participate.

Best wishes

Denver Hendricks

Head of Department of Pathology: Prof Raj Ramesar

It is my pleasure to welcome all of you, speakers and attendees to this joint Research Symposium of the Departments of Human Biology (H), Integrated biomedical Sciences (I) and Pathology (P) (HIPS). I want, upfront, to acknowledge all of the staff (including Academic and PASS) and students (undergrad and postgrad), as well as Postdoctoral Fellows who are engaged in each of our Departments, and who contribute to the academic project. Research is but one, but very important arm of the academic project, which if designed and carried out appropriately has the potential of constantly improving everything we do, including the target aspect of our work: improving the lives of the communities we serve. It is quite remarkable when interviewing a young candidate for the intercalated MBChB/BSc programme, when one hears about the true place of research i.e., *'in my clinic I will be seeing one patient at a time, genuinely intending to make their lives better, however, if I do targeted research on locally prevalent problems, there is the possibility of me contributing to breakthroughs that will impact the lives of whole communities'*. We are fortunate to attract some of the brightest young minds into our various undergraduate and postgraduate programmes…it is imperative that we use every opportunity to highlight to students how research has led to the current remarkable and revolutionary treatments available to our patients. Although we have a tightly packed MBChB curriculum, we have purposely designed the Short Study Module (SSM), which is perhaps not optimally utilised; however, it has the potential of '*turning on the lights'* of our remarkable undergraduate cadre of students, encouraging continued research throughout their further 3 years in the undergraduate programme. This inculcating of a research culture that firmly embedded in our community, constantly questioning processes, curricula and current interventions towards improvement is what we should be aspirant of at UCT. This serves as a call to action, for us to work across boundaries, (as is evident in this Symposium), igniting the agency of our students and staff, towards an improved society.

H.i.P Biennial Research Symposium 2021 Agenda

1st & 2nd December 2021

Physical Sessions:

Technical Session Venue: New Learning Centre Lecture Theatre, UCT Medical Campus

Exhibitors & Refreshments: Frances Ames, Bernard Fuller Building, UCT Medical Campus

Virtual Sessions: Microsoft Teams

Day 1 Live Stream : https://bit.ly/H_i_P_Research_Day_1

Day 2 Live Stream: https://bit.ly/H_i_P_Research_Day_2

2 Days Agenda Summary

Day 1 [1st Dec 2021]	Plenary Session 1	***08h00 to 10h30***
	Technical Session 1	**10h45 to 13h00**
	Technical Session 2	**13h45 to 16h00**
	Plenary Session 2	**16h15 to 17h00**
Day 2 [2nd Dec 2021]	Plenary Session 3	**08h30 to 10h30**
	Technical Session3	**10h45 to 13h00**
	Technical Session 3	**13h45 to 16h00**
	Plenary Session 4 & Awards	**16h15 to 17h30**
	Cocktail and Snacks	**17h30 to 18h30**

Agenda: Day 1 : 1st December 2021 [08h00 to 17h00]

Plenary Session 1 : 08h00 to 10h30 (NLC)

Session	Activity	Time Slot	Speaker	Title	Session Chair
Registration	Symposium Registration	08h00 to 08h15			
Plenary Session 1	Conference Welcome	08h15 to 08h45	Prof. Collet Dandara - Conference Chair Prof. Sharon Prince HOD – HUB Prof. Denver Hendricks HOD - iBMS Prof. Raj Ramesar HOD-Pathology Prof. Liesl Zuhlke Dy. Dean Research, FHS A/Prof. Lionel Green Thompson – Dean, FHS		Prof. Collet Dandara
	Keynote Lecture 1	08h45 to 09h15	Prof. Bryan Bryson Biological Engineering at MIT Member of the Ragon Institute of MGH, MIT, and Harvard	Engineering the host-pathogen interface	
	Keynote Lecture 2	09h15 to 09h45	Prof. Kelly Chibale Director of H3D research center, UCT	*Kissing Many Frogs Before Meeting The Prince: Drug*	

				Discovery & Development	
	Emerging Research Session (ERS)				Prof. Liesl Zuhlke Dy. Dean Research, FHS
	ERS01	09h45 to 10h00	Dr Adhil Bhagwandin, Department of Human Biology	Sleep and glymphatics: Notes from nature	
	ERS02	10h00 to 10h15	Dr. Tariq Ganief Department of integrative Biomedical Sciences	Neuro Proteomics / Stem Cell Differentiation	
	ERS03	10h15 to 10h30	Dr. Lerato Majara Department of Pathology	A genome-wide association study of schizophrenia in the South African Xhosa	
Tea / Exhibitor Showcase/ Online Exhibition (10h30 to 10h45) : Frances Ames					

Technical Session 1: 10h45 to 13h00 (NLC)

Technical Session 1	Abstract ID	10h45 to 12h00	Speaker	Title	Session Chair
Oral Presentation 1	ORL01	10h45 to 11h00	Ditshego Ralefeta	Investigating the impact of mycobacterial cell-cell heterogeneity on susceptibility to anti-tuberculosis (TB) chemotherapy.	Prof. Thomas Franz
	ORL02	11h00 to 11h15	Claire Bellis	The marine-derived antibiotic chromomycin A5 targets the oncogenic TBX2: a new strategy to treat breast cancer	
	ORL03	11h15 to 11h30	Musalula Sinkala	Leveraging Big Data Resources and Data Integration in Biology: Applying Bioinformatics and Data Mining to Gain Insights into the Biology of Cancer	
	ORL04	11h30 to 11h45	Ryan Dinkele	Cough-independent aerosolization of Mycobacterium tuberculosis suggests a role for tidal breathing in tuberculosis transmission	
	ORL05	11h45 to 12h00	Roxanne Megan Hattingh	Investigating the impact of postnatal development on human pyramidal neuron signal processing	

Technical Session 1	Abstract ID	12h00 to 13h00	Speaker	Title	Session Chair
Poster Presentation 1	POS01	12h00 to 12h30	Aaliyah Saferdien	Anti-cancer effects of Dodonaea viscosa, a herbal medicine used by traditional healers.	Prof. Thomas Franz
	POS02		Tatenda Lovemore Bvudzijena	Developing novel antibodies (scFv)-SNAP-based fluorophores for Acute Leukemia's immunophenotyping	
	POS03		Saif Feroz Khan	Repurposing drugs that target the interaction between HPV and TBX3 to treat cervical cancer	
	POS04		Ursula Claire Andong Koung Edzidzi	Recombinant SNAP tag-based antibody-drug conjugates targeting Triple-negative breast cancer	
	POS05		Amalia Naita Awala	An investigation of neuroglial cell activation in neurocysticercosis	
	Q&A		Q&A		
	POS06	12h30 to 13h00	Avril Walters	Investigating Neuronal Immune Responses To Early Central Nervous System Mycobacterium Tuberculosis Infection In Mice	
	POS07		Maryam Karaan	Antibody engineering to evaluate binding, internalisation, and intracellular routing of tumour-targeting fusion proteins.	
	POS08		Teresa Steyn	Investigating cestode modulation of host neuronal excitability and cell-type-specific gene expression in neurocysticercosis.	
	POS09		Vinasha Ramasamy	Novel proteins and pathways associated with the antifibrotic peptide Ac-SDKP	
	POS10		Cenza Rhoda	A study of the expression and cellular function of the human FAM111B gene	
	Q&A		Q&A		
Lunch / Exhibitor Showcase/ Online Exhibition (13h00 to 13h45) : Frances Ames					

Technical Session 2: 13h45 to 16h00 (NLC)

Technical Session 2	Abstract ID	13h45 to 15h00	Speaker	Title	Session Chair
Oral Presentation 2	ORL06	13h45 to 14h00	Firzana Firfirey	ABCB1 and OPRM1 polymorphisms collectively modulate chronic shoulder pain and dysfunction in a South African breast cancer survivor's population	Dr Fezile Khumalo
	ORL07	14h00 to 14h15	Roopam Dey	Effects of genetic variations in knee ligament length change during external to internal rotation	
	ORL08	14h15 to 14h30	Safiye Yildiz	Population Based Next Generation Sequencing (NGS) Multigene Panel Analysis of Germline Mutations Predisposing to Colorectal Cancer in South African Populations	
	ORL09	14h30 to 14h45	Victoria Patten	The identification of somatic mutations in oesophageal squamous cell carcinoma (OSCC) patients by whole genome sequence analysis.	
	ORL10	14h45 to 15h00	Sarah McCarley	Effects of Polymorphisms in Proprotein Convertase Subtilisin/Kexin Type 6 (PCSK6) and Protein C, Inactivator of Coagulation Factors Va and VIIIa (PROC) Genes on Warfarin Dose Variability among Southern Africans.	

Technical Session 2	Abstract ID	15h00 to 16h00	Speaker	Title	Session Chair
Poster Presentation 2	POS11	15h00 to 15h30	Anathi Asanda Nkayi	Evaluating plants as transient expression systems of recombinant immunodiagnostics/-therapeutics and conserving their integrity by compatible solutes	Dr Fezile Khumalo
	POS12		Dennis Makafui Dogbey	Modulation of engineered targeted viral vectors for cancer immunotherapy	
	POS13		Kristy Winkler	Application of CRISPR interference to identify	

				conditional gene essentialities in mycobacterial DNA repair	
	POS14		Josh Selfe	Investigating baseline and activity-dependent chloride ion dynamics in human brain cell types.	
	POS15		Beatrice Relebogile Ramorola	Molecular Characterisation of Diffuse Large B-Cell Lymphoma (DLBCL) in South Africa – defining biomarkers in an HIV positive context.	
	Q&A				
	POS16	15h30 to 16h00	Lillian Freda Andera	Temporal Trends in HIV-associated Lymphoma in Cape Town, South Africa	
	POS17		Temhlanga Mndzebele	Neutralizing antibody sensitivity of replication-competent HIV-1 from the latent reservoir of ART-treated individuals	
	POS18		Zahra Latib	Programmed cell death ligand-1 (PD-L1) expression in HIV-associated Diffuse Large B-cell Lymphoma – role and regulation	
	POS19		Humaira Lambarey	Characterisation of SARS-CoV2 seroprevalence in non-hospitalised HIV-infected patients from Gugulethu, South Africa	
	POS20		Melissa J Blumenthal	KSHV, but not EBV, co-infection associates with COVID-19 severity and outcome in South African patients	
	Q&A		Q&A		
Tea / Exhibitor Showcase/ Online Exhibition (16h00 to 16h15): Frances Ames					

Plenary Session 2 : 16h15 to 17h00 (NLC)

Session	Activity	Time Slot	Speaker	Title	Session Chair
Plenary Session 2	Keynote Lecture 3	16h15 to 16h45	Prof. John Rinn University of Colorado	Engineering the host-pathogen interface	Dr. Hlumani Ndlovu
	Closing of Day 1	16h45 to 17h00	Prof. Collet Dandara		
Close of Day 1					

Day 2 Agenda: 2nd December 2021 [08h30 to 18h30] (NLC)

Session	Activity	Time Slot	Speaker	Title	Session Chair
Plenary Session 3	Keynote Lecture 4	08h30 to 09h00	Prof Christa Janse van Rensburg, President of SASMA	Taking the fatigue out of travel and synchronising the body clock	A/Prof Sudesh Sivarasu
	Keynote Lecture 5	09h00 to 09h30	Prof. Glenda Gray, President SAMRC	SAMRC's responses to health challenges	
	Mental Health Workshop				Professor Jackie Hoare
Tea / Exhibitor Showcase/ Online Exhibition (10h30 to 10h45): Frances Ames					

Technical Session 3: 10h45 to 13h00 (NLC)

Technical Session 3	Abstract ID	10h45 to 12h00	Speaker	Title	Session Chair
Oral Presentation 3	ORL11	10h45 to 11h00	Takunda L. Ngwenya	Ex vivo labelling of BCC using SNAP tag-based antibody fusion proteins	A/Prof. Delva Shamley
	ORL12	11h00 to 11h15	Leonardo Alves de Souza Rios	HIV-1 protein Tat co-operates with JunB in enhancing MYC expression in HIV-associated Burkitt lymphoma	
	ORL13	11h15 to 11h30	Maximilian J. Spies	"The effect of clothing on decomposition and scavenging in Cape Town, South Africa.	
	ORL14	11h30 to 11h45	Wilmari Uys	Age-related changes in morphology of the forensically relevant blowfly, Chrysomya chloropyga (Diptera: Calliphoridae), during the intra-puparial period	
	ORL15	11h45 to 12h00	Abid Ali	Molecular mechanisms regulating oncogenic functions of TBX2 in breast cancer	

Technical Session 3	Abstract ID	12h00 to 13h00	Speaker	Title	Session Chair
	POS21	12h00 to 12h30	Rofhiwa Nesamari	TB immunity in people living with HIV starting	

Poster Presentation 3				treatment early or during chronic infection	A/Prof. Delva Shamley
	POS22		Lynthia Paul	Molecular characterisation of Clostridium perfringens isolates from patients at Groote Schuur Hospital	
	POS23		Cosnet Lerato Rametse	Barrier Integrity & understanding HIV Susceptibility in the penis: A Mechanistic search for Medical Male Circumcision	
	POS24		Hundaol Hordofa	Comparison Of Profiles Of Pharmacogene Variants In Populations In Malaria Endemic And None-endemic Geographical Areas	
	POS25		Sadiyah Malek	Assessing morphological mandibular traits for sex estimation in Holocene San and Khoekhoe populations	
	POS26		Jia Fan	Magnetic resonance imaging characterisation of heap hydrolysis	
	Q&A		Q&A		
	POS27	12h30 to 13h00	Grace Mayuni	Generation of anti-FAPα(scFv)-SNAP-based antibody fusion protein for in vivo radioimaging/-immunotherapy application	
	POS28		Jess Bourn	Creating and analysing an African pan-genome	
	POS29		Elizabeth Sarah Dinkele	Intersection of traditional African medicine and Western biomedicine in patient-held explanatory models of Mseleni Joint Disease.	
	POS30		Nicole Midgley	Implementation, evaluation and refinement of a targeted gene panel for inherited retinal diseases in Africa	
	POS31		Maureen Etuket	Design and Development of an Open-Source ADL-Compliant Prosthetic Arm for Trans-radial Amputees.	
	Q&A		Q&A		
Lunch / Exhibitor Showcase/ Online Exhibition (13h00 to 13h45): Frances Ames					

Technical Session 4: 13h45 to 16h00 (NLC)

Technical Session 4	Abstract ID	13h45 to 15h00	Speaker	Title	Session Chair
Oral Presentation 4	ORL16	13h45 to 14h00	Jia Fan	Resting-state functional connectivity reductions in the cingulate gyrus in HIV exposed uninfected neonates	Dr Nyarai Soko
	ORL17	14h00 to 14h15	Alexandra Lancaster	Effect of 3 different subscapularis attachment positions on tendon length, post-RTSA in two different designs: An OpenSim modelling study	
	ORL18	14h15 to 14h30	Omotola Abdulmalik	PD-L1 protein expression profiling in a cohort of HIV positive and negative cervical cancer	
	ORL19	14h30 to 14h45	Lwando Mampunye	Pioneering BRCA1/2 point-of-care testing for integration of germline and tumor genetics in breast cancer risk management	
	ORL20	14h45 to 15h00	Stephanie Maria Ncube	A TBX3 oncogenic signalling axis important in breast cancer	

Technical Session 4	Abstract ID	15h00 to 16h00	Speaker	Title	Session Chair
Poster Presentation 4	POS32	15h00 to 15h30	Edmund Wessels	FlexiGyn – A Flexible Mobile Office Hysteroscopy System	Dr Nyarai Soko
	POS33		Habtamu Yimam	Design and development of novel anatomical scapular fracture fixation plates: population-based and fracture-focused design	
	POS34		Lorraine R. Chonyera	A retrospective analysis of fatal ground level falls and falls from a height: A 5 year review	
	POS35		Adeyemi Daniel Adetimehin	Caught in the act: impact of Crematogaster spp. (Hymenoptera: Formicidae) necrophagous behavior on neonate pigs (Sus scrofa domesticus L.) in the Western Cape Province of South Africa	

	POS36		Leanne Haworth	Motion of the glenoid edge under load in 3 degrees of freedom: Development of an augmented ASTM F2028 Test Rig and Preliminary Results	
	POS37		Sarah Grace Lampert	Development and validation of a quantitative method to measure retinol and retinyl palmitate using high performance liquid chromatography	
	Q&A		Q&A		
	POS38	15h30 to 16h00	Ashraf Ebrahim Vahed	Design, development and validation of a system for the prediction of adrenaline concentration in solution containing degradation by-products	
	POS39		Nyamwezi Parfaite Ndarhwa	Security for networked smart healthcare systems: A systematic review	
	POS40		Isaac Lebogang Khobo	Predicting Cognitive Performance Using Multimodal MR Neuroimaging—comparing classification performance of decision trees, SVM, and generalized linear models in children with perinatally-acquired HIV	
	POS41		Lara Paul	A systematic review of research on coaches in rugby union and rugby league	
	POS42		Trevor Shepherd Mafu	A pathway-based analysis of polymorphisms within angiogenesis-related genes and shoulder pain and disability in breast cancer survivors	
	Q&A		Q&A		
Tea / Exhibitor Showcase/ Online Exhibition (16h00 to 16h15): Frances Ames					

Plenary Session 4: 16h15 to 17h30 (NLC)

Session	Activity	Time Slot	Speaker	Title	Session Chairs
Plenary Session 4	Keynote Lecture 6	16h15 to 16h45	Professor Fulufhelo Nelwamondo, Chief Executive Officer	Impact of the new student funding model	Prof. Sharon Prince

			National Research Foundation		HOD – HUB Prof. Denver Hendricks HOD – iBMS Prof. Raj Ramesar HOD – Pathology
	Summary of the Conference	16h45 to 17h00	Prof. Collet Dandara Conference Chair		
	Best Presentation Awards	17h00 to 17h25	Professor Fulufhelo Nelwamondo, CEO, NRF (Special Guest) Prof. Collet Dandara - Conference Chair Prof. Sharon Prince HOD – HUB Prof. Denver Hendricks HOD - iBMS Prof. Raj Ramesar HOD-Pathology Prof. Liesl Zuhlke Dy. Dean Research, FHS A/Prof. Lionel Green Thompson – Dean, FHS		
	Vote of Thanks	17h25 to 17h30	Prof. Collet Dandara - Conference Chair		
Cocktail and Snacks (17h30 to 19h00) Drinks / Exhibitor Showcase Venue: Frances Ames / Bernard Fuller Cafeteria					

Keynote Speaker's Profiles

Professor Glenda Gray: President & CEO of the SAMRC

An NRF A1 rated scientist, CEO and President of the South African Medical Research Council (SAMRC), Professor Glenda Gray is a qualified paediatrician and co-founder of the internationally recognised Perinatal HIV Research Unit in Soweto, South Africa. Prior to her appointment at the SAMRC, she was the Executive Director of the Perinatal HIV Research Unit, an affiliate of Wits University.

Glenda's global profile includes a role as Co-PI of the HIV Vaccine Trials Network (HVTN), a transnational collaboration for the development of HIV/AIDS prevention vaccines. She is also Director of International Programmes for HVTN and Chairperson of the Board of the Global Alliance for Chronic Diseases, and a member of the Institute of Medicine of the National Academies, USA.

She received South Africa's highest honour - the Order of Mapungubwe - for her pioneering research in PMTCT. Other prestigious accolades include the Nelson Mandela Health and Human Rights Award for significant contributions in the field of mother-to-child transmission of HIV. Selected as one of Time's 100 Most Influential People in the World, Glenda is a recognised leader in her field. Her qualifications include an MBBCH, FCPaeds (SA), DSc (honoris causa SFU), DSc (honoris causa SUN), LL.D (Rhodes).

Professor Fulufhelo Nelwamondo: CEO of the National Research Foundation

Fulufhelo Nelwamondo is the CEO of the National Research Foundation of South Africa. He holds a PhD in Electrical Engineering, with specialisation in Computational Intelligence from the University of the Witwatersrand. He was a Postdoctoral Fellow at the Graduate School of Arts and Sciences at Harvard University and was the youngest South African to receive the prestigious Harvard-South Africa Fellowship. Fulufhelo is a registered Professional Engineer, a Senior Member of the Institute of Electronic and Electrical Engineers (IEEE), a senior member of the Association of Computing Machinery (ACM), amongst others.

Prior to his current role, he held executive positions at the Council for Scientific and Industrial Research, and has served in several Boards, Councils, Ministerial Task Teams and Advisory committees. Fulufhelo is passionate about the Fourth Industrial Revolution, particularly in the potential impact its research and technologies can bring in the advancement of humankind, thereby addressing the social ills of poverty, unemployment and inequality.

He has been a recipient of many awards, for his contribution to Science, Engineering and Technology. In 2017, he was awarded the Order of Mapungubwe in Silver, the highest civilian honour bestowed by the President of the Republic of South Africa. Fulufhelo has worked in areas of advanced modelling, information security, data science, and artificial intelligence, and is a Visiting Professor at the University of Johannesburg's Institute of Intelligent Systems.

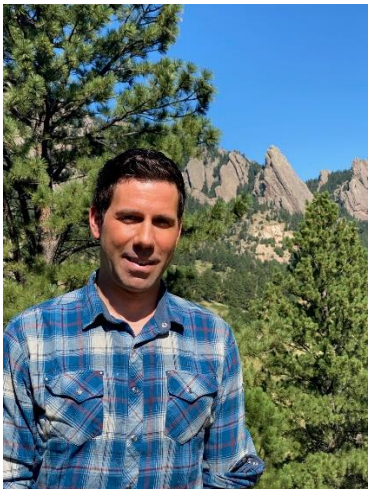
Professor Kelly Chibale: Director of H3D Research Centre

Kelly Chibale is a full Professor of Organic Chemistry at the University of Cape Town (UCT) where he holds the Neville Isdell Chair in African-centric Drug Discovery & Development. He is also a Full Member of the UCT Institute of Infectious Disease & Molecular Medicine, a Tier 1 South Africa Research Chair in Drug Discovery, founding Director of the South African Medical Research Council (SAMRC) Drug Discovery & Development Research Unit at UCT and the Founder and Director of the UCT Drug Discovery and Development Centre (H3D).

Kelly obtained his PhD in Synthetic Organic Chemistry from the University of Cambridge in the UK (1989-1992). This was followed by postdoctoral stints at the University of Liverpool in the UK (1992-94) and at the Scripps Research Institute in the USA (1994-96). He was a Sandler Sabbatical Fellow at the University of California San Francisco (2002), a US Fulbright Senior Research Scholar at the University of Pennsylvania School of Medicine (2008) and a Visiting Professor at Pfizer in the UK (2008).

In 2018 Kelly was recognized by Fortune magazine as one of the World's 50 Greatest Leaders and in 2019 he was named as one of the 100 Most Influential Africans by New African magazine.

Professor John Rinn: University of Colorado



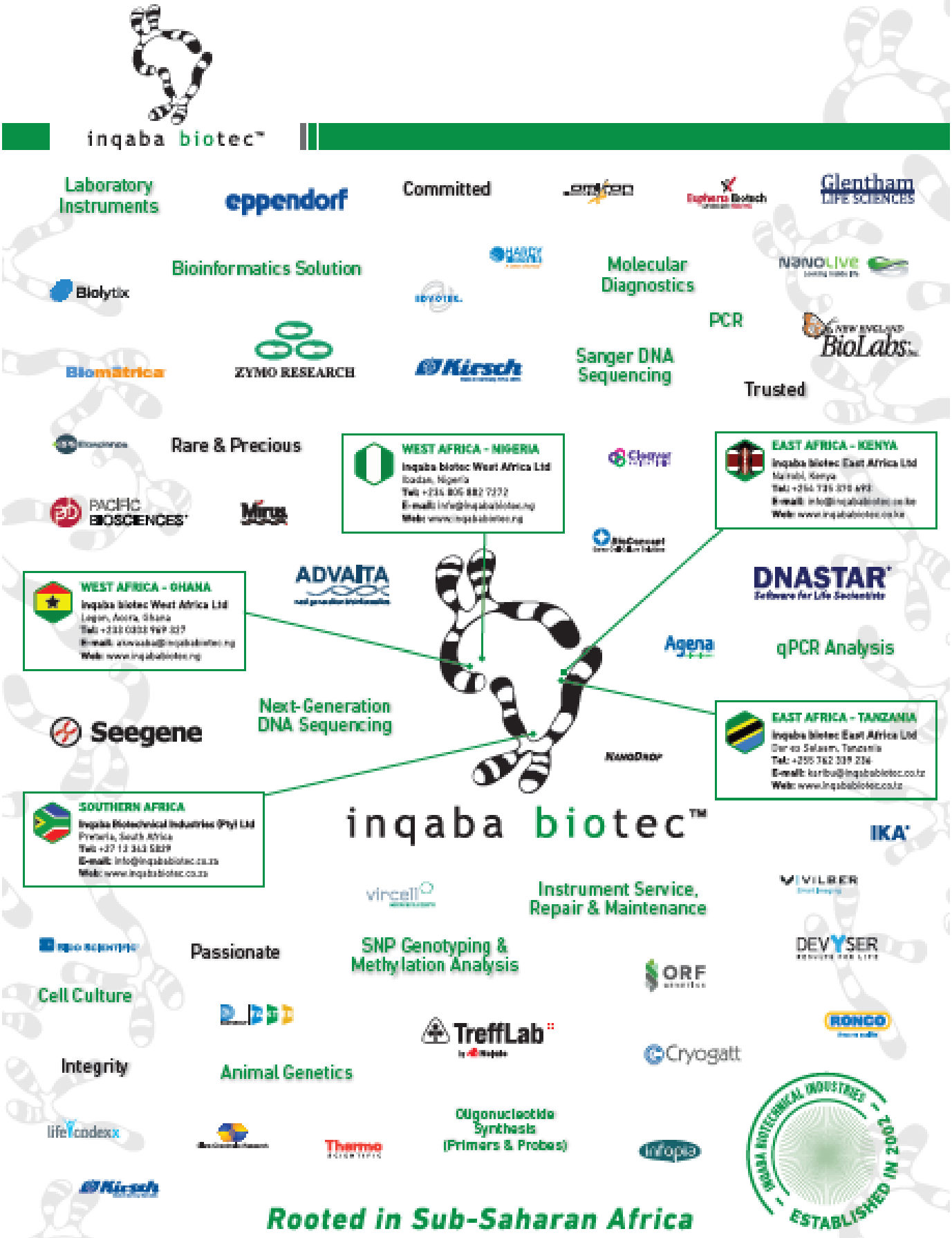
Dr. Rinn obtained his PhD in Molecular Biophysics and Biochemistry from Yale University. His thesis research in Michael Snyder's lab was one of the first to discover thousands of lncRNAs encoded in the human genome. Dr. Rinn continued to work on lncRNA regulation as a Damon Runyon Postdoctoral Fellow with Howard Chang at Stanford. He started his independent research program at Harvard University in the Department of Stem Cell and Regenerative Biology and the Broad Institute. After receiving tenure, Dr. Rinn moved his research program to focus more on RNA biochemistry at the University of Colorado Boulder BioFrontier's Institute. Collectively, the Rinn lab's research has been recognized by several national and international awards, including NIH Directors Innovator Award and Howard Hughes Medical Institute Faculty scholars' program. Dr. Rinn was recently considered one of the top 1% influential scientists of the decade by the Web of Science in Genetics and Molecular biology.

Professor Bryan Bryson: MIT, USA

Bryan Bryson is the Esther and Harold Edgerton Assistant Professor of Biological Engineering at MIT and a member of the Ragon Institute of MGH, MIT, and Harvard. Bryan completed his undergraduate studies at MIT in mechanical engineering before obtaining a PhD in biological engineering also at MIT. After graduate school, Bryan went to the Harvard TH Chan School of Public Health where he trained with Sarah Fortune and became interested in new approaches to examine host pathogen interactions in TB infection. Bryan started his lab a little over three years ago where his lab focuses on bridging quantitative approaches to understand how the immune system eliminates deadly pathogens.

Professor Christa Janse Van Rensburg: President of SASMA

Professor Janse van Rensburg is a Sports Physician and Rheumatologist and the Head of Section Sports Medicine at the University of Pretoria. She trained more than 80 post-graduate doctors to become sports physicians since 2000. She is the current President of the South African Sports Medicine Association (SASMA). She is a Fellow of the American College of Sports Medicine (ACSM) and was selected as Member of the Scientific Committee of the International Olympic Committee (IOC) World Conference on Prevention of Injury and Illness in Sport (Monaco, 2020). She is also a board member of the medical committee of World Netball. She regularly presents at national and international conferences, including several of the IOC Advanced Team Physician Courses, and various ACSM annual meetings. She was also a keynote speaker at several conferences and has been invited to lecture for the Royal Society of Medicine. She is a National Research Foundation (NRF) rated researcher with an excess of 100 articles in peer-reviewed journals. Her MD proved that exercise is beneficial in patients suffering from rheumatoid arthritis. Her current research focus encompasses effects of travel on athletes, epidemiology of injuries and illness in different sporting disciplines such as trail running and netball, and the effect of exercise in patients suffering from arthritic diseases. She is collaborating internationally with colleagues from across the world on the effect of lockdown and COVID-19 on athlete wellness and performance, challenges faced by Paralympic tennis players and post-career health of rugby- and football players. She also serves on the editorial board of the British Journal of Sports Medicine (BJSM) and the American Journal of Physical Medicine and Rehabilitation (AJPMR) and further contributes to education by writing blogs and participating in webinars and podcasts. A blog that she co-authored on “Should people wear face masks during exercise” was the most downloaded blog on the BJSM platform in 2020. She accompanied many sports teams as a sports physician, including the SA Olympic team to Athens as well as the SA Commonwealth team to Manchester and the SA team to the All African Games in Abuja. She was also a Venue Medical Officer for the 2010 FIFA World Cup. In her private capacity she is an animal lover and an avid sports fan, both as spectator and participant. She played national level netball and completed Comrades and 10 Argus Cycle Tours.



WHAT WE STAND FOR

PLATINUM SPONSOR

Emerging Researcher Profiles

Dr Adhil Bhagwandin: Department of Human Biology

Sleep and glymphatics: Notes from nature

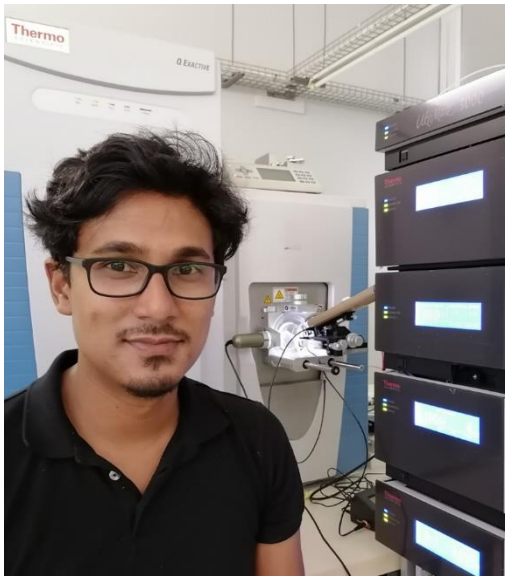
Sleep is a behaviour common to all organisms, though its exact function remains a mystery. It is postulated that sleep facilitates memory consolidation, metabolic maintenance, free-radical removal, and a host of other crucial functions. At its basic level, sleep is comprised of non-rapid eye movement (NREM or deep sleep), and rapid eye movement (REM) phases. In humans, it is suggested that an individual obtains roughly 7-8 hours of sleep per night. Comparatively, a wide array of sleep durations and sleep phenomenology exists amongst other mammals and vertebrates. Some notable examples include: the African elephant (2hrs of sleep per day and the lowest for all terrestrial mammals recorded so far); cetaceans (whom sleep with half their brain while the other half is awake, however; still obtain 8 hrs of sleep; and Arabian Oryx (whom sleep 4-6 hrs per day). Briefly though, sleep is crucial and varies enormously amongst organisms. The brain, much like every other vertebrate organ system, produces a vast array of metabolic waste. It had been suggested, many centuries ago, that brain tissue possesses a unique analogy of the lymphatic system. It is only recently that this mechanism has been understood and named the glymphatic system. Importantly, the glymphatic system appears to be most active during NREM sleep. Given the variance of sleep and the timing of glymphatic activity, it is necessary to investigate the comparative relationship of these variables; the results of which could broaden the understanding of human sleep and associated sleep pathologies.

Lerato Meraja: Department of Pathology

A genome-wide association study of schizophrenia in the South African Xhosa

Genome-wide association studies (GWAS) have been used to identify the common genetic variants that are associated with schizophrenia, predominantly in populations of European ancestry. There is a paucity of data on the genetic and environmental factors that contribute to the risk of schizophrenia in populations of African ancestry. The aim of this study was to investigate common variants and environmental factors that contribute to schizophrenia risk in the South African Xhosa (SAX) population through a GWAS approach. A GWAS was conducted in 2,086 Xhosa individuals with and without schizophrenia (n_{cases} = 1,038; $n_{controls}$ = 1,048) using a custom-designed Affymetrix Axiom^{TM} GWAS array designed to capture common genetic variation in SAX. Further, the impact of childhood trauma and biological sex on the genetic aetiology of schizophrenia outcome were investigated. The GWAS yielded one SNP (rs35172303, *P* = 4.74e-08, OR = 0.6004, 95% CI:[0.499,0.721]) in the gene *ZFP3* that met the genome-wide significance threshold. After controlling for childhood trauma, four additional SNPs in *ZFP3,* that were in linkage disequilibrium ($r^2 > 0.6$) with rs35172303, were significantly associated with schizophrenia. No conclusive results were obtained from the sex-stratified GWAS as the female strata was significantly underpowered. *ZFP3* — although not previously associated with schizophrenia in large-scale GWAS — may be important for disease risk in African populations, and childhood trauma is likely an important contributor to this risk. It is therefore imperative that genomics studies are conducted in African populations at large scale to uncover previously-unidentified variants that may have biological relevance.

Dr Tariq Ganief: Department of Integrative Biomedical Sciences



Identifying host signaling pathways regulated by gut microbial metabolites

The gut microbiome influences host metabolism, metabolite levels and is associated with many diseases. Levels of the GM derived metabolite trimethylamine (TMA) is known to correlate with atherosclerosis and was recently shown to inhibit the inflammatory mediator kinase, IRAK4. Here, we profiled the TMA mediated changes in the proteome and phosphoproteome of LPS stimulated microglia using triple SILAC based high-resolution mass spectrometry. In total, we quantified 8710 proteins and 13450 phosphosites after LPS and TMA treatment for 10 and 180 minutes. Using GO-BP enrichment analysis, we show that TMA suppresses LPS signaling after 10 minutes while a mixture of both pro- and anti- inflammatory signaling is evident at 180 minutes. To understand the signaling mechanisms inhibited by TMA, we generated a literature curated network detailing the signaling path following LPS stimulation to target protein translation. Using this network, we show that TMA inhibits LPS induced activation of MAPK 1/3 and downstream transcription factors Jun and STAT which leads to modulation in target inflammatory protein production. In conclusion, deep proteome and phosphoproteome analysis reveals both detailed and global mechanisms involved in microbiome mediated host inflammatory modulation.

GOLD SPONSOR

ORAL PRESENTATIONS

ORL01	Investigating the impact of mycobacterial cell-cell heterogeneity on susceptibility to anti-tuberculosis (TB) chemotherapy.
Full names of Authors *Presenting Author	**Ditshego Ralefeta*,** Valerie Mizrahi, Digby Warner
Department	Pathology

ABSTRACT:

As agent of tuberculosis (TB), Mycobacterium tuberculosis is a leading infectious cause of death globally, surpassing HIV and malaria. The success of M. tuberculosis as human pathogen derives in part from its ability to survive host-mediated antibacterial defences, as well as clinical interventions including extended duration combination chemotherapy. Understanding the molecular mechanisms underpinning these characteristics is essential to the development of novel approaches to improved anti-TB interventions. The mycobacterial mutasome is a DNA damage-inducible complex that has been implicated in SOS-induced mutagenesis and the emergence of drug-resistance during antibiotic therapy. In prior work, we observed that mutasome induction is not uniform in a population of clonal bacilli exposed to the same exogenous genotoxic stress. By elucidating a mechanism for generating heterogeneity under applied stress, our goal is to identify targets for novel interventions aimed at curbing the evolution of drug resistance.

MATERIALS AND METHODS:

By applying a panel of transcriptional reporter mutants in combination with single-cell time-lapse fluorescence microscopy, fluorescence-activated cell sorting (FACS), transcriptomics and proteomics, this study is investigating the possibility that a sub-population of “SOS-active” cells might give rise to drug resistance.

RESULTS:

Flow cytometry data and microscopic analysis of antibiotic stressed transcriptional reporter mutants revealed that mutasome induction is heterogenous, wherein four distinct sub-populations were observed: SOS positive, unresponsive, recA and dnaE2 positive. Single cells were obtained by FACS for SOS post-antibiotic recovery characterization in antibiotic-free media. Bacterial cell size increased gradually for the first 3-4 generation times after which cells assumed a normal cell size comparable to that of the untreated control. Single-cell fluorescence intensities also increased in the first 3-4 generations and were moderately proportional to bacterial cell size. The SOS unresponsive sub-population displayed a delayed lag-phase following antibiotic removal.

DISCUSSION:

Collectively, these data point to the importance of heterogeneity in the mycobacterial response to antibiotic therapy and post-antibiotic recovery, supporting the need for further research to elucidate the mechanisms driving non-homogenous responses in clonal (micro)populations.

ORL02	The marine-derived antibiotic chromomycin A5 targets the oncogenic TBX2: a new strategy to treat breast cancer.
Full names of Authors *Presenting Author	**C. Bellis***, S. Chakraborty, M. Mlaza, B. Del Bianco Sahm, P. Rezende Teixeira, L. Costa-Lotufo, and S. Prince
Department	Human Biology

ABSTRACT:
Breast cancer (BC) is the most common cancer and the leading cause of cancer-related death in women globally. The transcription factor, TBX2, is commonly over-expressed in BC where it drives proliferation, suppresses cell death, and plays a role in DNA damage repair and drug resistance. Although important during embryogenesis, TBX2 plays no known function in adult tissues and is therefore an attractive anti-cancer target. We therefore screened marine natural compounds for TBX2-binding affinity and identified a compound called Chromomycin A5 (C-A5). This project investigates C-A5 as a TBX2-targeting anti-cancer compound in BC.

MATERIALS AND METHODS:
All experiments were performed in the MCF7 and T47D breast cancer cells. Short and long-term cytotoxicity were assessed by MTT and clonogenic assays, and spheroid analyses. The ability of C-A5 to target TBX2 through the proteosome 26S pathway and to induce DNA damage, cell cycle arrests and apoptosis were determined by treatment with a proteosome 26S inhibitor (MG132), western blotting, immunofluorescence, and flow cytometry. TBX2 target genes were assessed by qRT-PCR analyses.

RESULTS:
C-A5 selectively induces cytotoxicity in BC cells, targets TBX2 for degradation in a time-dependent manner through the proteasomal pathway which results in the re-expression of tumour suppressor genes repressed by TBX2. C-A5 induces DNA damage, cell cycle arrests, and apoptosis which is TBX2-dependent because TBX2 knockdown decreased the sensitivity of BC cells to C-A5, while over-expressing TBX2 sensitized them to the drug.

DISCUSSION:
Here we demonstrate that C-A5 is a promising drug to treat TBX2-driven BC and potentially other TBX2-driven cancers.

ORL03	Leveraging Big Data Resources and Data Integration in Biology: Applying Data Mining to Gain Insights into the Biology of Cancers.
Full names of Authors *Presenting Author	**Musalula Sinkala***
Department	Integrative Biomedical Sciences

ABSTRACT:

Over the last few years, large-scale "molecular profiling" projects applying these technologies have yielded vast amounts of genetic, epigenetic, transcription, protein expression, metabolic and drug response data for cancerous tumours, diseased tissues, and cell lines. Furthermore, comprehensive information has been gathered on the properties of thousands of cellular proteins, their functions, their interaction partners and the signalling or metabolic pathways within which they function.

MATERIALS AND METHODS:

Here, we extract meaningful information on cellular processes and phenotypes of cancer by applying data mining and integration approaches on datasets from over 20 publicly available resources. Instead of testing a few hypotheses that are defined well before data is collected, we show how data from these resources can be applied to develop testable hypotheses based on observed connections between potential causes and effects that we never thought existed.

RESULTS:

Using the data mining and integration approaches, we have defined the foundational metabolic features of different cancer supertypes and subtypes upon which discriminatory strategies for treating tumours could be constructed. Furthermore, we discovered vulnerabilities in specific pathway genes that are reflected in the responses of cancer cells to MAPK targeting drugs: a revelation with great potential for guiding the development of innovative therapies.

DISCUSSION:

The overarching message here is that the time has already arrived where we can leverage available data resources that now provide modern medicine with powerful tools for devising novel strategies to treat some of the world's most burdensome diseases.

ORL04	Cough-independent aerosolization of Mycobacterium tuberculosis suggests a role for tidal breathing in tuberculosis transmission.
Full names of Authors *Presenting Author	**Ryan Dinkele***, Sophia Gessner, Andrea McKerry, Bryan Leonard, Juan Leukes, Ronnett Seldon, Digby F. Warner*, and Robin Wood*
Department	Pathology

ABSTRACT:
Interrupting tuberculosis (TB) transmission requires an improved understanding of how (and when) the causative organism, Mycobacterium tuberculosis (Mtb), is aerosolized. Although cough has commonly been assumed to be the dominant source of Mtb aerosols, recent evidence of cough-independent Mtb release suggests the additional contribution of alternative mechanisms.

MATERIALS AND METHODS:
Here, we combined aerosol sampling with real-time assessment of CO2 concentration and particle count data to investigate the aerosolization of Mtb and particulate matter from GeneXpert-positive patients during three separate, five-minute respiratory manoeuvres: Tidal Breathing (TiBr), Forced Vital Capacity (FVC), and Cough.

RESULTS:
On average, TiBr produced 7- to 22- fold fewer particles than FVC and Cough, respectively. For all manoeuvres, the proportions of particles detected across size categories from 0.5 – 5 µm were similar, with minor variation only observed in particles between 1.5 – 2 µm ($p = 0.014$). and >5 µm ($p = 0.020$). Viable Mtb bacilli were detected in 66%, 70%, and 61% of TiBr, FVC, and Cough samples, respectively. Notably, while Cough produce threefold more Mtb than TiBr, the relative infrequency of coughing compared to breathing imply that TiBr likely contributes >90 % of the daily aerosolised Mtb across a range of cough frequencies.

DISCUSSION:
Our results suggest that while Cough increases particle aerosolization compared to TiBr, this is not associated with increased Mtb aerosolization. Instead, TiBr produces more Mtb per particle than Cough. Assuming the number of viable Mtb organisms detected provides a proxy measure of patient infectiousness, these observations imply a significant contribution of TiBr to TB transmission.

ORL05	Investigating the impact of postnatal development on human pyramidal neuron signal processing.
Full names of Authors *Presenting Author	**Roxanne M***. Hattingh, Matthijs B. Verhoog, Joseph V. Raimondo
Department	Human Biology

ABSTRACT:
The primary excitatory neurons of the neocortex, pyramidal neurons, are known to undergo considerable maturation after birth. Postnatal changes have been observed in neuronal morphology, including dendritic spine density, which peaks during mid-childhood to about twice that observed in adults. Here, we make use of a rare opportunity to obtain live brain tissue resected during epilepsy surgery from patients in all stages of childhood, to study the physiological effects of these changes.

MATERIALS AND METHODS:
A pipeline involving the preparation of acute cortical brain slices, patch-clamp electrophysiology, confocal microscopy and 3D digital reconstructions was performed on human L2/3 pyramidal neurons. This data was used to construct morphologically-detailed computational models of paediatric neurons.

RESULTS:
To investigate the effects of developmental changes in spine density, we simulated a synaptic activation in a spine, and measured the degree of voltage attenuation that occurred during passive propagation. Spine density was changed by scaling the models' surface area by a factor (F). We observe greater attenuation of synaptic potentials for higher values of F. The relationship between spine density and signal attenuation varies alongside changes in position of the activated spine.

DISCUSSION:
These results suggest that changes in spine density significantly impact passive signal processing in human pyramidal neurons. Higher spine densities in paediatric neurons may mean that synaptic inputs decay quicker, especially in distal apical dendrites. This would impact the function of individual neurons and networks in the paediatric brain.

ORL06	ABCB1 and OPRM1 polymorphisms collectively modulate chronic shoulder pain and dysfunction in a South African breast cancer survivor's population.
Full names of Authors *Presenting Author	**Firzana Firfirey*,** Alison September, Delva Shamley
Department	Human Biology

ABSTRACT:

Chronic shoulder pain and disability afflicts ~60% of breast cancer survivors (BCS) and has become a major concern. Treatment includes opioids, however, chronic use without adequate pain relief has serious health consequences and may increase the risk of mortality. Genes functioning in the metabolism, distribution and signalling of opioids have been investigated towards elucidating the mechanisms of pain relief and transition of acute to chronic pain. This study aimed to investigate the association between polymorphisms of the opioid transporter (ABCB1) and opioid receptor (OPRM1) gene and chronic shoulder pain and disability in BCS.

MATERIALS AND METHODS:

ABCB1(rs1045642 G>A, rs1128503 G>A) and OPRM1(rs1799971 A>G, rs540825 T>A) polymorphisms were genotyped in cohort of n=272 BCS using TaqMan® SNP genotyping assays. The SPADI tool was used to evaluate shoulder 1) Pain, 2) Disability, and 3) Pain and Disability. Statistical analysis was applied to measure significant differences in the distribution of the genotypes, alleles haplotypes and inferred alleles (gene-gene interactions) between groups with significance accepted at $P<0.05$.

RESULTS:

The ABCB1 rs1045642 G>A (A/A) genotype was independently associated with a reduced likelihood of reporting moderate-high disability (P=0.015) and SPADI (P=0.004). The inferred ABCB1(rs1045642G>A-rs1128503G>A) A-G/A-A and OPRM1(rs1799971 A>G-rs540825T>A) G-T haplotypes, were associated with a reduced likelihood of reporting moderate-high disability/SPADI and pain, respectively ($P<0.05$). The ABCB1 (rs1045642 G>A)-OPRM1 (rs540825 T>A) A-T (P=0.019, OR:0.62, 95% CI 0.33-1.16) and G-A (P=0.021, OR:1.57, 95% CI:0.30-3.10) allele-allele combinations were associated with a reduced and increased likelihood of reporting moderate-high disability. The same trend was observed for the SPADI phenotype.

DISCUSSION:

This study provides initial evidence for an association between polymorphisms in ABCB1 and OPRM1 and the prevalence of chronic shoulder pain and disability in BCS.

ORL07	Effect of COL1A1 rs1107946 genotypes and its inferred haplotypes on knee ligament length change during tibiofemoral rotation.
Full names of Authors *Presenting Author	**Roopam Dey***, Samantha Beckley, Shaun Stinton, Willem van der Merwe, Thomas Branch, Alison V. September, Mike Posthumus, Malcom Collins
Department	Human Biology

ABSTRACT:

Knee laxity has been reported to depend on the genetic profile of an individual. Hypermobility of the knee joint, which can lead to anterior cruciate ligament (ACL) tears, has been associated with mutations within COL1A1 and/or COL3A1 genes. Variants of these genotypes, especially COL1A1 rs1107946, COL1A1 rs1800012, and COL3A1 rs1800255 have been characterised as factors that can moderate the risk of ACL ruptures. Currently, there are no studies in the literature that have studied the effect of these genetic variations on the behaviour of knee ligaments during rotational motion. The aim of this study is to examine the effect of COL1A1 rs1107946 GG and GT genotypes and the effect of low and high COL1A1 rs1107947-rs1800012 inferred haplotypes on the knee ligament length change and its kinematics.

MATERIALS AND METHODS:

A validated open-source bilateral knee musculoskeletal model was adapted to perform tibiofemoral rotation in OpenSim. The model consisted of anterior cruciate ligament (ACL), posterior cruciate ligament (PCL), lateral collateral ligament (LCL), medial collateral ligament (MCL), and deep medical collateral ligament (DMCL). Quasi-static external to internal rotation joint angles were used as kinematic input for the OpenSim model. These joint angles were collected, as a part of a previous doctoral study, from 106 moderately active subjects using the Robotic Knee Testing (RKT) device. Ligament length change was tracked throughout the motion and plotted. The ligament length changes for each group were statistically compared using statistical parametric mapping.

RESULTS:

The internal ligament bundles (ACL and PCL) did not display any significant difference in length change between the low and high COL1A1 rs1107947-rs1800012 inferred haplotypes and COL1A1 rs1107946 GG and GT genotypes. Among external knee ligament bundles (LCL, MCL, and DMCL) all the ligament bundles, except the LCL, displayed significant difference in ligament length change. This difference was most prominent from the point of maximum external rotation to the point of neutral rotation for all the groups compared.

DISCUSSION:

This study was able to highlight significant phenotypic changes in ligament length changes in cohorts belonging to different genotype. External medial knee ligaments behave differently during initial stages external to internal rotation depending on the subject's genetic profile.

ORL08	Population Based Next Generation Sequencing (NGS) Multigene Panel Analysis of Germline Mutations Predisposing to Colorectal Cancer in South African Populations.
Full names of Authors *Presenting Author	**Safiye Yildiz***, George Rebello, Raj Ramesar
Department	Pathology

ABSTRACT:

Multigene panels are commonly used in hereditary colorectal cancer (CRC) mutation detection and these help resolve subjects with unknown germline mutations associated with Lynch syndrome (LS). A limited number of published reports of multigene panel testing for hereditary CRC in indigenous Africans are available yet. This study aimed to determine the proportion of indigenous Africans with a germline mutation in the known CRC genes using a multigene panel.

MATERIALS AND METHODS:

Study cohort selected based on pathology reports of patients from Groote Schuur Hospital (GSH) and from the National Cancer Registry (NCR) (n=83). 14-gene NGS panel screening was performed. NGS data were analysed using Ion Reporter and variants were prioritised following the selected pathogenicity criteria. Observed variants were validated by Sanger sequencing. Long-range PCR (LR-PCR) was implemented for the validation of PMS2 variants due to pseudogene interference.

RESULTS:

Fourteen patients from the GSH (~21%) presented with a pathogenic germline variant; of which nine (~13%) variants occurred in one of the mismatch repair (MMR) genes associated with LS. In two patients from the NCR (~13%) two germline mutations in MSH2; and an additional pathogenic variant in PMS2 were identified in one of the two individuals. Two patients from the GSH carried a pathogenic variant in PMS2. LR-PCR was successful in confirming the true variants in PMS2.

DISCUSSION:

Multigene panel screening yielded a satisfactory positivity rate and helped identify sixteen germline variants. The unresolved cases will undergo further screening and the remainder of patients from the GSH of indigenous Africans are subjected to NGS panel screening.

ORL09	The identification of somatic mutations in oesophageal squamous cell carcinoma (OSCC) patients by whole genome sequence analysis.
Full names of Authors *Presenting Author	**Victoria Patten***, Denver Hendricks, Hocine Bendou, Iqbal Parker
Department	Integrative Biomedical Sciences

ABSTRACT:

MUC3A is a membrane-bound glycoprotein component of mucous gels whose aberrant expression has been correlated with invasion and metastasis in a variety of cancers. Objectives for the study are to identify the location of MUC3A mutations in our OSCC sample cohort through bioinformatics analysis, with laboratory confirmation of mutations through PCR and expression analysis through qPCR in order to identify the effect of MUC3A mutations on the development and progression of OSCC.

MATERIALS AND METHODS:

30 tumour-blood pairs were subjected to Whole Genome Sequencing (WGS) and bioinformatics analysis to investigate somatic mutations. PCR analysis of cell line and patient DNA was performed to confirm the bioinformatics results. Investigations of expression profiles will follow using rt-PCR to elucidate any correlation that might exist linking these mutations to the development and progression of OSCC.

RESULTS:

Bioinformatics analysis identified 73% of the patient cohort with mutations in MUC3A, a gene with no previous associations with OSCC. This opens the question of how and why these mutations are present in the tumour samples of these patients. While we were not able to confirm the bioinformatics mutations, other interesting heterozygous mutations have been observed through DNA sequencing. Further screening and investigations into the effect on protein function are underway.

DISCUSSION:

These mutations can potentially shed light on and broaden our understanding of the mechanisms involved in the development and progression of OSCC and may lead to possible drug-able targets for patient therapy allowing for the development of better diagnostic or therapeutic approaches.

ORL10	Effects of Polymorphisms in Proprotein Convertase Subtilisin/Kexin Type 6 (PCSK6) and Protein C, Inactivator of Coagulation Factors Va and VIIIa (PROC) Genes on Warfarin Dose Variability among Southern Africans.
Full names of Authors *Presenting Author	Arinao Ndadza, Nyarai Soko, Emile Chimusa, Mpiko Ntsekhe, and Collet Dandara **(Sarah McCarley*)**
Department	Pathology

ABSTRACT:

Warfarin is one of the most prescribed drugs and used for treatment and prevention of thromboembolic disorders. There is wide interindividual variability in the doses required for patients to reach the international normalised ratio (INR). The inter-individual variability in warfarin doses is due to genetic and non-genetic factors. In this study, we seek to understand the contribution on two genes that are not traditionally considered in understanding the pharmacogenetics of warfarin, and these are, proprotein convertase subtilisin/kexin type 6 (PCSK6) and protein C, inactivator of coagulation factors Va and VIIIa (PROC).

MATERIALS AND METHODS:

A total of 154 black African participants on warfarin treatment were recruited. Blood samples were withdrawn for DNA extraction and medical records were used to get clinical information. Extracted DNA was used to genetically characterise six single nucleotide polymorphism in PCSK6 (rs1058291G>A, rs3743190C>T, & rs3825896G>T) and PROC (rs5936T>C, rs5937T>C, & rs2854696T>C), using restriction fragment length polymorphism (RFLP), TaqManSNP genotyping and Sanger sequencing assays. Statistical analyses were performed using STATA and Graphpad Prism, taking a 5% significance level.

RESULTS:

We report for the first time the variant allele frequencies of the six SNPs, PCSK6 rs1058291A (0.12), rs3743190T (0.14), rs3825896T (0.36), PROC rs5936C (0.65), rs5937C (0.26), and rs2854696C (0.11), respectively. There were some quantitative and qualitative differences in the distribution of the variant alleles when compared to other world populations. The PROC rs5936 T/T genotype was associated with significantly increased ($p = 0.029$) mean warfarin maintenance dosage (39.74 ± 12.43) compared with the G/G (34.37 ± 11.42; $P = 0.02$) and G/T (34.51 ± 11.91; $P = 0.05$) genotypes, respectively, and explained 4.5% in warfarin variability.

DISCUSSION:

The findings in this study are important because they reveal that, to fully understand the genetic determinants of warfarin dose requirements, there is a need to not only focus on the traditional genes such as VKORC1 and CYP2C9, but to also consider the contribution of genetic variation in genes contributing to minor pathways. In addition, the study calls for the inclusion of African participants in identifying clinically relevant genetic variants impacting on optimal warfarin dose for successful precision medicine guidelines.

ORL11	Ex vivo labelling of BCC using SNAP tag-based antibody fusion proteins.
Full names of Authors *Presenting Author	Stefan Barth, Marc Henry, Suresh Madheswaran (Takunda L Mgwenya*)
Department	Integrative Biomedical Sciences

ABSTRACT:

Skin cancer refers to the abnormal growth of skin cells. Basal Cell Carcinoma (BCC) is the most common skin cancer type in the world. In South Africa, it claims about 700 lives per year and approximately 20,000 cases are reported each year. South Africans are more susceptible to skin cancer as the country has high ultra violet radiation (UVR), with a high average daily temperature of 22°C. This project will aim at preparing a diagnostic procedure allowing to differentiate BCC from other types of skin cancers and to support complete excision of BCC without leaving any trace of residual abnormal cells leftover after surgery. This can be achieved by use of the advanced SNAP-tag antibody labelling technology. The tumour will be diagnosed based on differentially overexpressed tumour-associated cell surface antigens (TAAs) that are reported to be present and absent in BCC. If a patient has BCC, the patient might be asked to undergo Moh's surgery and the tumour is removed by excision. The use of labelled scFv-SNAP-tag will allow precise detection of the tumour boundaries and result in a once off excision surgery to avoid multiple excision. The project may also allow the replacement of the fluorophore with toxic molecules for treatment of the BCC, where surgical excision is impossible/impeded. The TAAs under investigation are also reported to possess internalisation properties. This technology can also allow the use of these anti scFv-SNAP tag markers as toxin trafficking molecules to deliver the drug conjugates or toxic into the cells to induce apoptosis of the cancerous cells. This technology cannot only be restricted to BCC, but can also be investigated on other cancers.

MATERIALS AND METHODS:

The study will involve the in-silico cloning of the different antibody (scFv)-SNAP fusion constructs (99EpCAM, 19EpCAM AND LGR5), followed by molecular cloning generated constructs, protein expression in mammalian cells and bacterial cells, protein purification by IMAC, conjugation of SNAP fusion proteins to Benzyl-guanine (BG)-modified fluorophores, flow cytometric analyses of BCC cell lines and confirmation of targets on selected FFPE sections of South African BCC patients by immunofluorescence imaging. Anticipatorily, taking the research further to PhD, the replacement of fluorophores with chromophores/drugs/toxic substances to target patients' BCC samples may be investigated.

RESULTS:

I have currently generated the In-silico plasmids to be studied and molecular cloning and protein expression experiments are currently underway.

DISCUSSION:

The molecular dynamics (MD) simulation methods used and current biological results will be briefly discussed.

ORL12	HIV-1 protein Tat co-operates with JunB in enhancing MYC expression in HIV-associated Burkitt lymphoma.
Full names of Authors *Presenting Author	**Alves de Souza Rios L***, Mapekula L, Mowla S
Department	Pathology

ABSTRACT:

Burkitt lymphoma (BL) is one of the most over-represented non-Hodgkin lymphomas among HIV-infected individuals, and displays complex karyotypes, with generally poor outcomes in this population group. Accumulating evidence indicates that the molecular pathogenesis of HIV-associated malignancies is unique, with components of the virus playing an active and direct role in driving oncogenic pathways. Further studies to understand this complex pathobiology is needed and could lead to therapeutic advances in this patient group.

MATERIALS AND METHODS:

Immunohistochemistry was used to detect Tat protein in BL patient tumour samples; transfection of BL cell lines, followed by western blotting was used to study changes in oncogenic factors; luciferase reporter assays and site-directed mutagenesis was used to study the regulation of oncogenic c-MYC by Tat; immunoprecipitation assays and chromatin immunoprecipitation assays were used to study the collaboration between Tat and AP-1 factors.

RESULTS:

HIV-1 Tat protein was detected within the tumours of HIV-positive BL patients, and ectopic expression of this viral protein led to enhanced expression of oncogenic c-MYC in BL cells. Using a reporter assay, the activity of the c-MYC gene promoter was shown to be enhanced in the presence of Tat, and this was partially mediated via two AP-1 binding elements located at positions -1128 bp and -1375 bp. We further show that Tat can exist within a protein complex with the AP-1 factor JunB, and that this complex can bind these AP-1 recognition sites within the c-MYC promoter.

DISCUSSION:

These findings therefore indicate that in HIV-infected individuals, HIV-1 Tat potentially infiltrates B-cells where it can directly enhance the expression of oncogenic factors, contributing towards the more aggressive disease phenotype observed in these patients.

ORL13	The effect of clothing on decomposition and scavenging in Cape Town, South Africa.
Full names of Authors *Presenting Author	Devin A. Finaughty, Louise J. Friedling, Victoria E. Gibbon **(Maximilian J Spies*)**
Department	Human Biology

ABSTRACT:
Limited taphonomic research has been conducted in the Western Cape, South Africa where most forensic cases involve clothed individuals. We assessed the influence of common seasonally appropriate clothing on decomposition in a forensically significant habitat in Cape Town.

MATERIALS AND METHODS:
Deployed over two consecutive summers and winters, ten ~60 kg domestic pig carcasses (6 clothed, 4 unclothed), were used as proxies for human decomposition. Clothing was chosen based on local forensic case files and tailored to fit the pigs, preventing unrealistic scavenger access. Daily weight loss was used to quantitatively track decomposition progression.

RESULTS:
Clothed carcasses took on average 22 days longer (475.92 more ADD) than unclothed carcasses to reach 68% mass loss. Double-layer clothing notably inhibited decay during the colder, wetter winters with a mean of 108 vs 71 days (1921.94 vs 1099.64 ADD) for clothed and unclothed carcasses, respectively, to reach 68% loss. Thinner clothing appeared comparatively negligible during the hotter, drier summers with a clothed mean of 19 vs 14 days for unclothed carcasses (424.93 vs 295.38 ADD) to reach 68% mass loss. Weight loss was closely linked with scavenging activity by the Cape grey mongoose (Galerella pulverulenta) which displaced clothing to feed on the abdomen. Scavenging was hindered by denim trousers, causing altered feeding patterns and preferential scavenging on unclothed carcasses.

DISCUSSION:
This research suggests forensically realistic season-specific appropriately tailored clothing is required in taphonomic research. We show it can delay decomposition affecting ADD and postmortem interval estimations substantially by modulating the effect of weather, season, and vertebrate scavenging behaviour.

ORL14	Age-related changes in morphology of the forensically relevant blowfly, Chrysomya chloropyga (Diptera: Calliphoridae), during the intra-puparial period.
Full names of Authors *Presenting Author	**Wilmari Uys***, Calvin Gerald Mole, Marise Heyns
Department	Pathology

ABSTRACT:

Minimum post-mortem intervals (minPMI) can be determined by utilising insects found on or near deceased individuals. Typically, blowfly larvae are examined morphologically to determine their age and subsequently, estimate PMI. However, little research has considered pupae for estimating PMI in a South African context. Therefore, the current study investigated morphological changes in Chrysomya chloropyga pupae over time with the aim of establishing developmental timelines and PMI estimation.

MATERIALS AND METHODS:

Ch. chloropyga were reared under controlled conditions (25°C, 65% RH, 14:10 L:D cycle). Upon initiation of the pupal stage, specimens were collected, hot-water-killed at specific time points, and subsequently stored in 70% ethanol. Prior to morphological examinations, the puparium was removed, and the pupae photographed using a stereomicroscope. Changes in morphological features over time were identified and categorised using descriptive and numerical scales.

RESULTS:

Morphological features corresponding to age were clearly observed. Legs and wings were visible 12 hours post-pupariation, fully developed by 18 hours, but continued to change in structure and colour throughout the puparial stage. The mouthparts became noticeable by 18 hours but continuously changed in structure and colour until adult emergence. The eyes and body parts start pigmentation after 60 hours and gradually darken until the end of the pupal stage.

DISCUSSION:

This study demonstrates clear associations between changes in morphological features and distinct time points during pupal development. These changes are of such nature that they can be utilised to determine the puparial age and subsequently estimate minimum PMI.

ORL15	Molecular mechanisms regulating oncogenic functions of TBX2 in breast cancer.
Full names of Authors *Presenting Author	**Abid Ali***, Jade Peres, Alexis Joy Mufweba, Sharon Prince
Department	Human Biology

ABSTRACT:
In 2020, breast cancer (BC), was responsible for the death of approximately 0.65 million women. TBX2 is an early driver of BC and has been identified as a potential drug target to treat BC. This study Aims to determine whether TBX2 (1) is phosphorylated and stabilized by Akt1, (2) interacts with PELP1 and HNRNPC to carry out its oncogenic functions and (3) TBX2 regulating TBX2 target genes and proliferation of breast cancer cells (3) upregulates ID1 to promote proliferation.

MATERIALS AND METHODS:
To address Aim 1, western blotting was performed after the inhibition of AKT with chemical inhibitors and siRNA and site-directed mutagenesis. Aim 2 was addressed by co-immunoprecipitation assays and confocal microscopy. Chromatin immunoprecipitation and luciferase reporter assays were preformed to investigate if TBX2 transcriptionally activates ID1. The functional significance of TBX2, HNRNPC and PELP1 was investigated using qRT-PCR, western blotting, reporter and proliferation assays.

RESULTS:
AKT1 phosphorylates TBX2 at S623 and this results in increased levels of TBX2 in BC cells. TBX2 interacts and co-localizes with HNRNPC and PELP1 and knocking down either HNRNPC or PELP1 decreases TBX2 levels and proliferation and increases the expression of tumour suppressor genes (CST6, NDRG1, Cdkn1a, PTEN, and FOXI1) repressed by TBX2. TBX2 directly bound and activated ID1 expression in BC cells.

DISCUSSION:
Our results show that the AKT1/TBX2/HNRNPC/PELP1/ID1 axis plays an important role in promoting BC cell proliferation and that targeting this axis may have therapeutic benefit.

ORL16	Resting-state functional connectivity reductions in the cingulate gyrus in HIV exposed uninfected neonates.
Full names of Authors *Presenting Author	**Jia Fan***, Fleur L. Warton, Samantha Fry, Mark F. Cotton, Sandra W. Jacobson, Joseph L. Jacobson, Christopher D. Molteno, Francesca Little, Andre J.W. van der Kouwe, Barbara Laughton, Ernesta M. Meintjes
Department	Human Biology

ABSTRACT:

Resting state fMRI (rs-fMRI) is used to identify brain regions that are temporally correlated when the subject is not performing any explicit task. Aggressive promotion of combination antiretroviral treatment (ART) in pregnancy has significantly reduced new perinatal HIV infections giving rise to a growing population of HIV exposed uninfected (HEU) children. While children who are HEU perform better than their HIV-infected counterparts, they continue to demonstrate greater neurodevelopmental delay than children who are HIV-unexposed uninfected (HUU), especially in resource-poor settings. Here we examine resting state functional connectivity (RSFC) in neonates exposed to HIV and ART in utero.

MATERIALS AND METHODS:

Mothers with and without HIV were recruited at <31 weeks gestation from an antenatal clinic at the Michael Mapongwana Community Health Centre (MMCHC) in Khayelitsha, Cape Town, South Africa. Rs-fMRI data were acquired in 106 neonates born to these women at mean gestational age (GA) 41.4±1.0 weeks. Of these, 42 infants were born to mothers with HIV who had started ART pre conception (HEU pre), 29 to mothers with HIV who started ART post conception (HEU post), and 35 to mothers who were HIV uninfected.

RESULTS:

Ten resting-state networks were generated by independent component analysis (ICA). Notably, connectivity within the default mode network (DMN) was not fully integrated as often seen in young individuals, and the somatosensory network was split into left, right, and medial parts. Voxelwise group comparison between a combined HEU group and HUU revealed localized RSFC reductions in the cingulate gyrus (CG) within 3 networks: medial somatosensory, anterior and posterior DMN.

DISCUSSION:

Connectivity deficits in the CG in neonates who are HEU suggest that the maternal immune response may indirectly impact fetal brain development. The CG, which is a component of the limbic system lying on the medial aspect of the cerebral hemisphere, may be particularly vulnerable due to its proximity to perivascular spaces through which pro-inflammatory cytokines from the mother's immune response may penetrate the fetal brain.

ORL17	Effect of 3 different subscapularis attachment positions on tendon length, post-RTSA in two different designs: An OpenSim modelling study.
Full names of Authors *Presenting Author	**Alexandra Lancaster***, Stephen Roche, Sudesh Sivarasu
Department	Human Biology

ABSTRACT:

The role of subscapularis (SSc) tendon repair in reverse total shoulder arthroplasty (RTSA) remains uncertain, studies have linked SSc repair to improved stability and decreased rates of dislocation. The aim of this study was to investigate the effect of attaching the SSc in different locations on the proximal humerus in two different RTSA implants with different neck shaft angles.

MATERIALS AND METHODS:

The RTSA joint was modelled in OpenSim using both a Biomet and a Delta RTSA implant. The Biomet has a neck shaft angle of 135° and the Delta an angle of 155°. The SSc tendon length was measured for abduction, flexion and internal/external glenohumeral (GH) rotation at three attachment positions on the proximal humeral head. Results were compared between the attachment positions and between the RTSA Biomet, RTSA Delta, Total Shoulder Arthroplasty (TSA) and anatomical shoulder.

RESULTS:

Results show that the SSc tendon length between the different attachment positions was <0.05mm for GH rotation at 20° of abduction, <0.03mm for GH rotation at 90° of abduction and <0.03mm for both GH abduction and GH flexion. Comparing the healthy shoulder, TSA, RTSA Delta and RTSA Biomet shows a difference in tendon length of <0.03 for GH rotation at 20°, <0.02mm for GH rotation at 90°, <0.02mm for GH abduction and <0.04mm for GH flexion.

DISCUSSION:

These results indicate that the minimal change in tendon length achieved by changing the attachment position of the SSc tendon or using different RTSA implants is unlikely to alter clinical range of motion and strength in the RTSA shoulder.

ORL18	PD-L1 protein expression profiling in a cohort of HIV positive and negative cervical cancer.
Full names of Authors *Presenting Author	**Omotola Abdulmalik***, Padmini Govender, Nomonde Mbatani, Hue-Tsi Wu, Richard Naidoo
Department	Pathology

ABSTRACT:

Cervical cancer is a major disease burden in women globally. Despite advances in management, mortality still remains high particularly in developing countries. HIV is associated with worse outcomes in cervical cancer. PD-L1 plays a significant role in the pathology of several cancers. Furthermore, therapies directed towards this pathway has shown promising results. This investigates the differences in PDL1 expression in both HIV positive and negative cervical carcinoma using immuno-histo-chemical methods. The PDL1 data was correlated with clinical-pathological parameters.

MATERIALS AND METHODS:

Eighty FFPE tissue samples blocks were used in our study The H&E slides were reviewed by a pathologist and the selected tissue blocks were cut and stained using immuno-histo-chemical methods with the DAKO clone 22C3.

RESULTS:

The PDL1 expression was done using the Combined Positive Score which was > 1, in 51.3% of cases and, HIV status was not significantly correlated with the expression of PDL1. In addition, the distribution of PD-L1 expression was heterogenous in the 80% of samples with homogenous distribution in 2.5%. Survival analysis showed that different expression levels did not significantly affect survival in this cohort.

DISCUSSION:

We successfully demonstrated PDL1 expression in our study cohort. The PDLI expression was similar in both our study cohorts, with no significant difference in the two groups and the expression of PDL1 was not prognostic in our study. Furthermore, the pattern of PD-L1 expression was heterogenous in most of our cases.

ORL19	Pioneering BRCA1/2 point-of-care testing for integration of germline and tumor genetics in breast cancer risk management.
Full names of Authors *Presenting Author	**Lwando Mampunye***, Nerina C. van der Merwe, Kathleen A. Grant, Armand V. Peeters, David J. French, Martin Kidd, Kelebogile E. Moremi, Maritha J. Kotze,
Department	Pathology

ABSTRACT:
Research performed in South African (SA) breast, ovarian and prostate cancer patients resulted in the development of a rapid BRCA point-of-care (POC) assay designed as a time- and cost-effective alternative to laboratory-based technologies currently used for first-tier genetic testing. In this study the performance of the new assay was evaluated for the first time using a portable screening device (ParaDNA).

MATERIALS AND METHODS:
DNA samples for germline testing were obtained retrospectively from 50 patients with early-stage hormone receptor-positive breast cancer previously referred for pharmaco-genomic tumor profiling using the RNA-based Mamma Print test. Currently, SA patients with hormone-receptor-positive breast cancer are not routinely selected for BRCA1/2 testing as is the case for triple-negative disease. An initial evaluation involved the use of multiple control samples representing each of the pathogenic founder/recurrent variants included in the BRCA 1.0 POC Research Assay.

RESULTS:
Comparison with a standard laboratory-based first-tier real-time polymerase chain reaction (PCR) assay demonstrated 100% concordance. Clinical utility was evident in five patients with the founder BRCA2 c.7934delG variant, identified at the 10% (5/50) threshold considered cost-effective for BRCA1/2 testing. BRCA2 c.7934delG carrier status in these cases was associated with a significantly younger age ($p=0.03$) at diagnosis compared to non-carriers. In three of the BRCA2 c.7934delG carriers a high-risk 70-gene Mamma Print profile indicated a significantly increased risk for both distant/metastatic and local recurrence of their cancer.

DISCUSSION:
Initiating germline DNA testing at the POC early in the treatment planning process, irrespective of family history and tumor subtype, will increase access to the most common pathogenic BRCA1/2 variants identified in SA and may reduce loss to follow-up. The ease of using cheek swabs/saliva in future for result generation within one hour assay time, potentially combined with genetic counselling, will enable the application of translational pharmacogenomics across ethnic groups in SA.

ORL20	A TBX3 oncogenic signalling axis important in breast cancer.
Full names of Authors *Presenting Author	**Stephanie Maria Ncube*,** Arul-Jothi Nagarajan, Jonathan Blackburn, Sharon Prince
Department	Human Biology

ABSTRACT:

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

MATERIALS AND METHODS:

To determine if c-Myc regulates TBX3 expression qRT-PCR assays were performed after ectopic c-Myc overexpression in MCF-7 BC cells in the presence or absence of Actinomycin D (de novo transcription inhibitor). Nucleolin and Hsc70 were identified and validated as TBX3 co-factors by affinity purification coupled with mass spectrometry, immunoprecipitation assays and confocal microscopy/co-localisation analysis. The functional significance of (1) TBX3-Hsc70 was investigated by siHsc70, MG132 (proteasomal inhibitor) treatment and western blotting and (2) TBX3-nucleolin by RNAi/overexpression rescue experiments coupled with scratch motility assays. The effect of the nucleolin targeting aptamer, AS1411, on TBX3/nucleolin levels and subcellular-localisation was tested by western blotting, immunofluorescence and MTT assays.

RESULTS:

We show that c-Myc upregulates TBX3 transcriptionally, Hsc70 enhances TBX3 stability and nucleolin cooperates with TBX3 to promote BC migration. AS1411, inhibits BC cell viability and migration with no effect on normal breast epithelial cells and mislocalizes TBX3 and nucleolin to the cytoplasm blocking their ability to activate target genes.

DISCUSSION:

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

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POSTER PRESENTATIONS

POS01	Anti-cancer effects of Dodonaea viscosa, a herbal medicine used by traditional healers.
Full names of Authors *Presenting Author	Shaheen Mowla, **Aaliyah Saferdien***
Department	Pathology

ABSTRACT:

Cancer is a leading public health problem worldwide, and while modern treatments have undeniably improved the outcome of patients, many cancers remain refractory or untreatable. More effective treatment is clearly needed, and the use of natural phytochemical compounds is an emerging strategy to prevent, delay, or cure cancer. In South Africa, high HIV prevalence is a compounding factor to the development of cancer, with the incidence of certain cancers being disproportionately high among HIV positive individuals. One such cancer is Burkitt lymphoma (BL), a highly aggressive B-cell derived malignancy. Increasingly, cancer patients are making use of traditional medicine (TM), as an alternative to chemotherapy. Extracts from the plant Dodonaea viscosa (DV) is used by traditional healers in the Western Cape and holds promise as a chemo-preventative agent. This project aims to explore this.

MATERIALS AND METHODS:

BL cell lines were exposed to aqueous DV extracts (DVE), and its effect on specific cancer hallmarks were assessed. This included proliferation, colony formation and apoptosis.

RESULTS:

DVE was found to potently and preferentially inhibit the proliferation of BL cells. This was shown by cell viability and BrDU incorporation assays showing reduced proliferation of cancer cells. Using a caspase3/7 activity assay, DVE was shown to enhance apoptosis, which was corroborated using western blotting and Annexin V assays. Additionally, treated cancer cells displayed morphological characteristics typical of those undergoing apoptosis.

DISCUSSION:

Aqueous extracts from the Dodonaea viscosa plant have potent and specific anti-cancer properties against BL cells, as shown in in vitro assays. Future work will focus on identifying the mechanism of action of DVE and using an in vivo mouse model to confirm anti-tumour effects.

POS02	Developing novel antibodies (scFv)-SNAP-based fluorophores for Acute Leukemia's immunophenotyping
Full names of Authors *Presenting Author	**Tatenda Lovemore Bvudzijena*,** Bernard Murithi Mirianga, Stefan Barth
Department	Integrative Biomedical Sciences

ABSTRACT:

In Africa, most countries lack up to date statistics of different leukemia sub-types prevalence's, as a result of poor registry and limited diagnostics tools. Blast morphology is mostly utilized in diagnosis of Leukemia in many parts of Africa, and this has serious limitations in making accurate and timely diagnoses. Timely diagnosis has great influences on overall treatment outcomes and prognosis monitoring, using advanced technologies like flow-cytometric immunophenotyping would allow to clearly define each subtype of acute leukemia and reveal rare biphenotypic and bilineage acute leukemia. Flow-cytometric analysis utilize monoclonal antibodies targeting unique overexpressed markers on leukemic blast. However, current costs of antibodies are likely to limit their availability in already strained developing countries' economies. An alternative approach would be use of an easy to tailor fashion of smaller antibody fragments coupled with a SNAP tag, which can be readily produced recombinantly under cost-controlling conditions. The scFv-SNAP fusion protein undergoes a self-labeling reaction forming a covalent bond with O6-benzylguanine (BG) derivatives. BG can be chemically attached to a variety of synthetic labels such as fluorophores and small molecule toxins. This study aims to explore SNAP tag-based antibody fusion proteins as a supplementary diagnostics tool for Acute Leukemia and the targets of interest include the following antigens overexpressed on leukemic cells: CD11c, CD14, MPO, TdT, and HLA-DR. Exposure to recombinant antibody technologies, protein engineering and expression will promote local development of next generation immunodiagnostics and therapeutics in Africa, and this could be considered as a cost-containment strategy for cancer remedies which are being priced for the first-world markets.

MATERIALS AND METHODS:

The study will involve the in-silico engineering and design of the different antibody (scFv)-SNAP fusion constructs using publicly available sequences, followed by molecular cloning, protein expression in mammalian, protein purification by IMAC, conjugation of SNAP fusion proteins to Benzyl guanine (BG)-modified fluorophores and flow cytometric analyses of leukemic cell lines.

RESULTS:

We have properly assembled sequences for scFv-SNAP fusion constructs and used a plasmid vector backbone which comprises all the unique features for protein expression in mammalian systems. Synthesis of Fusion Protein Encoding ORFs, generation of the specific (scFv)-SNAP fusion proteins, in vitro proof of binding on leukemic cell lines, and establishment of a method for multiparameter flow cytometry are the next steps to be followed.

DISCUSSION:

The molecular dynamics simulation methods used, and current biological results will be briefly discussed.

POS03	Repurposing drugs that target the interaction between HPV and TBX3 to treat cervical cancer
Full names of Authors *Presenting Author	**Saif Feroz Khan*,** Jenna Bleloch, Sizhu Lu, Amsha Ramburan, Colin Goding, sharon Prince
Department	Human Biology

ABSTRACT:

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

MATERIALS AND METHODS:

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

RESULTS:

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

DISCUSSION:

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

POS04	Recombinant SNAP tag-based antibody-drug conjugates targeting Triple-negative breast cancer
Full names of Authors *Presenting Author	**Ursula-Claire Andong-Koung-Edzidzi*,** Liyabona Mponda, Chardae Friedberg, Olusiji Alex Akinrinmade, Ramamurthy Dharanidharan, Stefan Barth
Department	Integrative Biomedical Sciences

ABSTRACT:

Triple-negative breast cancer (TNBC) is the most aggressive and highly heterogeneous subtype of breast cancer. Surgery and chemotherapy are often associated with recurrence, multi-drug resistances and high costs. The aim of this project is the generation of recombinant antibody fragments fused to SNAP-tag to target TNBC. SNAP-tag is a self-labeling protein-tag, which allows a rapid and simple labelling reaction with a variety of benzylguanine (BG)-modified substrates. This provides a 1:1 stoichiometry between the recombinant SNAP-tag fusion protein and BG-modified substrates such as photosensitizers or small molecule toxin to induce apoptosis. SNAP-tag antibody drug conjugates are elegant solutions to overcome the challenges associated with conventional therapies.

MATERIALS AND METHODS:

Recombinant SNAP-tag based antibody-drug conjugates will be generated using SNAPGene software followed by molecular cloning. The plasmids DNA will be transfected in HEK293T cells for protein expression. The supernatant will be purified using IMAC. Protein expression and integrity will be validated using SDS-PAGE and western blot before assessing the binding potential of the recombinant fusion proteins after conjugation to BG-Alexa488 (flow cytometry and confocal microscopy) as well as the cytotoxic potency after conjugation to the synthetic toxin BG-AURIF in EpCAM and ASPH positive TNBC cells.

RESULTS:

Anti-ASPH constructs: pCB-ASPH-EMC-SNAP; pCB-ASPH-TLD-SNAP and pCB-ASPH-Furin-PFO-Furin-SNAP Anti-99EpCAM constructs: pCB-99EpCAM-EMC-SNAP; pCB-99EpCAM-TLD-SNAP and pCB-99EpCAM-Furin-PFO-Furin-SNAP

DISCUSSION AND CONCLUSION:

Human antibodies are promising therapeutic tools and SNAP tag-based antibody fusion protein are representing derivatives for easy and stoichiometric conjugation to synthetic labels with high homogeneity at hopefully affordable productions costs. Such recombinant biopharmaceuticals will be further refined to provide next generation immunodiagnostics and therapeutics for TNBC.

POS05	An investigation of neuroglial cell activation in neurocysticercosis
Full names of Authors *Presenting Author	**Amalia Naita Awala*,** Rachael Dangerambizi, Joseph V. Raimondo
Department	Human Biology

ABSTRACT:

Neurocysticercosis (NCC) a parasitic infection of the central nervous system (CNS) caused by the larvae of the cestode Taenia solium, is the leading cause of adult acquired epilepsy in the developing world. The hallmark for symptomatic NCC is neuroinflammation, however, the neuroinflammatory mechanisms underlying this disease are grossly understudied, especially the role that microglial cells play during the neuroimmune response to T. solium infection.

MATERIALS AND METHODS:

To investigate the neuroinflammatory effects of the parasite, we stimulated cultured mouse organotypic brain slices (OBSs) with taenia larvae homogenate for 24 hours. These were compared with untreated control slices, and slices stimulated with lipopolysaccharide (LPS), an established neuroimmune activator. The potential immunosuppressive effects of the Taenia larvae on microglial activation was assessed by concurrently treating OBSs with LPS and Taenia larvae homogenate. Inflammatory activation of microglial cells was measured by immunostaining for the inflammatory transcription factor NFIL6, a robust marker for cell activation.

RESULTS:

We found that the co-application of LPS and Taenia larvae homogenate suppresses the microglial activation and pro-inflammatory cytokines release that we observed in the LPS only treatment group, constituting an anti-inflammatory effect. Microglial activation was not observed in untreated slices or in slices treated with Taenia larvae homogenate only, a cytokine response was also not observed.

DISCUSSION:

This data makes valuable contributions towards understanding the neuroinflammatory mechanisms underlying this debilitating disease. It also gives valuable insights that parallel the clinical manifestations of the disease and has implications for potential treatments for NCC.

POS06	Investigating Neuronal Immune Responses To Early Central Nervous System Mycobacterium Tuberculosis Infection In Mice
Full names of Authors *Presenting Author	**Avril Walters*,** Sohair Geyer, Nai-Jen Hsu, Roanne Keeton, Muazzam Jacobs
Department	Pathology

ABSTRACT:

Central nervous system tuberculosis (CNS-TB) is one of the most severe forms of extra-pulmonary tuberculosis and is most prevalent in children and immunocompromised individuals. The CNS has always been regarded as immune-privileged. However, studies have shown that Mycobacterium tuberculosis (M.tb) can infect various cell types in the brain including neurons and activate an immune response in the CNS. The contribution of neurons to the immune regulation in CNS-TB is not known therefore warrants further investigating.

MATERIALS AND METHODS:

The immune properties of neurons will be investigated using in vitro and in vivo models. RNA extraction, microarray analysis, flow cytometry and luminex will be performed in primary neuronal cultures. The in vivo component will comprise of intracerebral infection and flow cytometry analysis in the mouse brains.

RESULTS:

Intracerebral infections showed a significant increase in MHC-I presentation, IL1B and TNF-a pro-inflammatory cytokines in the neurons of infected mice by 14 days post infection. Peripheral cellular recruitment did not reveal any significant differences in the recruitment of neutrophils, monocytes/macrophages and dendritic cells, but MHC-II presentation was significantly upregulated in all these innate immune cells. The percentage of CD4+ and CD8+ lymphocytes recruited to the brain were not significantly different at these early time points but there was however a significant increase in TBet expression in both CD4+ and CD8+ T cells.

DISCUSSION:

Our data suggests neurons are capable of initiating an immune response against M.tb infection. For future study we will be assessing the neuronal transcriptome for molecular changes during M.tb infection. Furthermore, we will set up co-cultures to investigate the immune regulatory role of neurons. A better understanding of neuronal immunity will improve therapeutic strategy in CNS-TB.

POS07	Antibody engineering to evaluate binding, internalisation, and intracellular routing of tumour-targeting fusion proteins.
Full names of Authors *Presenting Author	**Maryam Karaan*,** Dharanidharan Ramamurthy, Stefan Barth
Department	Integrative Biomedical Sciences

ABSTRACT:

Recombinant immunotherapeutic fusion proteins (rIFPs) were designed to target triple-negative breast cancer (TNBC). This is a heterogeneous and aggressive subset of breast cancer accounting for 15-20% of all diagnosed breast cancer cases, with women of premenopausal age and African descent inordinately predisposed. Based on previous studies, we hypothesised that the ability to bind to two identical antigens through a bivalent antibody increases the total strength of the reaction and that increasing the affinity and valency of tumour-targeting antibodies results in improved tumour uptake. Furthermore, the rate of internalization and intracellular routing of rIFPs, may be significant for their therapeutic efficacy. Understanding these factors could impact the use of such biopharmaceuticals for targeted treatment with relevant cell surface biomarkers.

MATERIALS AND METHODS:

The rIFPs were transiently expressed in mammalian cell culture and purified using IMAC. Following SDS-PAGE and Western Blot protein analysis, the proteins were fluorescently labelled and the differences between the mono- and bivalent antibody formats were evaluated in vitro using confocal imaging. The efficacy in binding to targeted cell surface receptors, rate of internalisation, and intracellular routing of internalised rIFPs were evaluated to determine such differences. Differences in rIFP-mediated cytotoxicity were evaluated in vitro using XTT-based cell viability assays.

RESULTS:

The rIFPs were successfully expressed, purified, and characterised. Preliminary imaging results indicate that the bivalent rIFPs display increased binding affinity and faster internalisation rate compared to the monovalent counterpart when applied to a confirmed CSPG4+ TNBC cell line.

DISCUSSION:

Protein characterisation, confocal imaging and XTT-based cytotoxicity assay data will be discussed.

POS08	Investigating cestode modulation of host neuronal excitability and cell-type-specific gene expression in neurocysticercosis.
Full names of Authors *Presenting Author	**Teresa Steyn***
Department	Human Biology

ABSTRACT:

Neurocysticercosis is the leading helminthic brain infection in humans, caused by larvae of the pork tapeworm Taenia solium (T. solium). The most common and severe clinical manifestation of the disease is epilepsy, with seizures occurring in 70 to 90% of neurocysticercosis cases. Interestingly, patients with neurocysticercosis generally experience few or no seizures during the early, viable cyst stages of the disease when T. solium larvae actively suppress the host inflammatory response. Furthermore, seizures usually occur when cestode larvae begin to die and are no longer able to suppress the host immune response. This raises an intriguing question as to whether the anti-inflammatory effect of viable cestode larvae could in fact suppress seizures activity in the brain.

MATERIALS AND METHODS:

To better understand what effect viable cestode larvae are having in the brain, this project will use whole-cell patch clamping and single nucleus RNA sequencing to investigate how in vitro exposure to viable cestode larvae modulates host neuronal excitability and cell-type-specific gene expression in mouse brain tissue. Additionally, I will be comparing other treatment conditions including Lipopolysaccaride as well as Lipopolysaccaride together with Taenia larvae as a means of further exploring the neuromodulatory effects of cestodes.

RESULTS:

At present, I am still in the process of collecting and analysing data. However, my preliminary analysis of the data has suggested that there are no significant differences in the intrinsic properties of neurons that were exposed to either Lipopolysaccaride, Lipopolysaccaride and Taenia crassiceps, or just regular growth media (control). I am still processing the single nucleus RNA sequencing data, but thus far I have seen all of the major cell-types that I would have expected to be in the mouse brain.

DISCUSSION:

This research will improve our understanding of how viable cestode larvae, as well as inflammatory challenges, alter neuronal excitability and gene expression in the brain. My goal is to also use the findings from the snRNAseq results to identify possible therapeutic targets that can be tested in future functional studies for the prevention or treatment of seizures in neurocysticercosis and other seizure conditions.

POS09	Novel proteins and pathways associated with the antifibrotic peptide Ac-SDKP
Full names of Authors *Presenting Author	**Vinasha Ramasamy*,** Siyavuya Fikamva, Mpiko Ntsekhe, Edward Sturrock
Department	Integrative Biomedical Sciences

ABSTRACT:

Ac-SDKP is a physiological tetrapeptide synthesised from thymosin β4 and cleaved by angiotensin-1 converting enzyme (ACE). A role for Ac-SDKP in inflammation and fibrosis in various pathologies, including tuberculous (TB) pericarditis, has been described (Cavasin et al., 2007; Ntsekhe et al., 2012). We investigated the molecular mechanisms of the antifibrotic effects of Ac-SDKP in the development of fibrosis and its deregulation in TB pericarditis.

MATERIALS AND METHODS:

A mass spectrometry approach was employed to study changes in the proteome of Ac-SDKP treated fibroblasts and macrophages. To identify pathways regulated by Ac-SDKP, western blotting for TGF-β/Smad and a phospho tyrosine kinase array were employed. Further, deregulation of Ac-SDKP metabolism in pericardial fluid from patients with TB pericarditis was investigated using ELISAs and enzymatic activity assays for ACE and prolyl oligopeptidase.

RESULTS:

An array of proteins and pathways were identified to be significantly regulated by Ac-SDKP including extracellular matrix proteins- collagens I and VI, fibrillin and laminin as well as transforming growth factor β and fibroblast growth factor signalling. Further, reactome analysis showed neutrophil degranulation to be significantly enriched in Ac-SDKP treated macrophages. Last, Ac-SDKP levels were significantly decreased in TB pericardial fluid; a reduction accompanied by a local 28% increase ACE enzymatic activity.

DISCUSSION:

Our results confirm previous observations of extracellular matrix constituent reduction by Ac-SDKP, but also identified various matrisome components and biological processes not previously associated with Ac-SDKP. Further, a mechanism of altered Ac-SDKP levels in the pericardium through increased ACE enzymatic action is described. These data provide further insight into the molecular actions of Ac-SDKP and potential therapeutic avenues for fibrosis management.

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POS10	A study of the expression and cellular function of the human FAM111B gene
Full names of Authors *Presenting Author	**Cenza Rhoda*,** Nonhlanha Khumalo, Afolake Arowolo
Department	Medicine

ABSTRACT:

POIKTMP, a multi-system fibrosing disease, results from mutations in the human FAM111B gene. Despite rising interest in the role of FAM111B mutations, knowledge of this gene remains limited. Therefore, this study provides insight into the cellular function of FAM111B, which is also overexpressed in some cancers, and investigates the pathological effect of the FAM111B Y621D POIKTMP-associated mutation.

MATERIALS AND METHODS:

Bioinformatics studies coupled with quantitative PCR and Western blots analysis were employed to assess FAM111B gene and protein expression. Subsequently, RNA-interference mediated gene silencing, and recombinant gene expression technologies were used to dysregulate FAM111B gene expression in HT1080 cells. Downstream cell-based functional assays were performed to determine the effects of down-and up-regulation of FAM111B, respectively, and to determine FAM111B interacting proteins using mass spectroscopy proteomics (MSP). FAM111B expression in POIKTMP patient-derived and healthy skin fibroblasts were also evaluated.

RESULTS:

The knockdown of FAM111B in HT1080 suggests reduced cell proliferation and migration and increased apoptosis. Conversely, the overexpression of FAM111B increased apoptosis and cell migration. Furthermore, Y621D FAM111B mutant cells showed reduced expression of FAM111B, decreased apoptosis, invasion, and an increase in proliferation and migration. Furthermore, our MSP results show that wildtype and mutant FAM111B may interact with proteins HSP7C and G3V3W4, respectively, to minimize apoptosis and accelerate proteolytic cleavage of damaged proteins, including the mutant protein Y621D.

DISCUSSION:

Altogether, our data suggest that FAM111B promotes cells viability, and FAM111B Y621D mutation may contribute to the rapid proteolytic clearance of FAM111B, thereby leading to reduced cellular fitness.

POS11	Evaluating plants as transient expression systems of recombinant immunodiagnostics/-therapeutics and conserving their integrity by compatible solutes
Full names of Authors *Presenting Author	**Anathi Nkayi*,** Krupa Naran, Ann Meyers, Stefan Barth
Department	Integrative Biomedical Sciences

ABSTRACT:

Development of recombinant immunotherapeutic and immunodiagnostic proteins aimed at targeting overexpressed tumour cell-specific cell surface antigens is fast growing. These proteins have properties which are interdependent and can be manipulated to improve their immunotherapeutic potential. They provide a more precise and specific immunodiagnostic/-therapeutic approach for cancer treatment. It is pivotal that these proteins are produced in large quantities. Once available they might need to be stored for longer periods while maintaining their functionality and stability. Given the limitations of the commonly used expression systems, this contribution proposes the use of plants as transient expression of immunotherapeutics/diagnostics for the expression of an exemplified triple negative breast cancer specific biopharmaceutical. During and after production proteins usually require periods of storage, thus it is critical that protein functionality is maintained during the whole time.

MATERIALS AND METHODS:

Chondroitin sulphate proteoglycan 4 (CSPG4) single-chain variable fragment (scFv)-SNAP was in silico designed. Successfully cloned plasmids containing the corresponding open reading frame were expressed in Nicotiana benthamiana plants. The secreted protein was purified by IMAC purification and analysed by immunoblotting. Furthermore, purified SNAP-tag based fusion proteins already analysed for binding with a benzyl-guanine (BG) modified fluorophore were subjected to various freeze-thaw experiments before and after supplementing with compatible solutes and were assessed for protein stability.

RESULTS:

CSPG4(scFv)-SNAP tag fusion protein could be generated in plants and enriched by IMAC. Melting curves were generated from freeze-thaw experiments and have been validated as potential procedure to ascertain protein integrity.

DISCUSSION:

Yield in plants was not sufficient to proceed with downstream experiments, suggestions to improve yield will be discussed. Supplementation with selected compatible solutes is improving protein stability.

POS12	Modulation of engineered targeted viral vectors for cancer immunotherapy
Full names of Authors *Presenting Author	Alex Olusiji Akinrinmade, Stefan Barth, **Dennis Makafui Dogbey***
Department	Integrative Biomedical Sciences

ABSTRACT:

Gene delivery systems are mechanistic constructs that deliver therapeutics to diseased cells. These technological systems either by viral or non-viral platforms make up an integral part of emerging cancer gene therapy and immunotherapy therapeutics. Though several viral vectors have been utilised for the above-mentioned purpose, adeno-associated viruses (AAV) have dominated and are largely preferred due to its small and easy to manipulate genome size, less immunogenicity as well as poor disease-causing abilities. However, challenges of non-specificity, off-target organ transduction, packaging and purification of viral particles have bedevilled approval of AAV-based therapies currently in clinical trials

MATERIALS AND METHODS:

Recombinant AAV plasmids will be cloned using molecular techniques of polymerase chain reaction splicing by overlap extension to introduce and amplify gene segments displaying the molecules for site-directed bioconjugation. rAAVs plasmid will be transfected in HEK 293 T cells, packaged, harvested, and purified. Purified rAAV particles will be modified by EGFR- and EpCAM-targeting recombinant antibody fragments. Targeted binding to EGFR and EpCAM surface antigens on tumour cell lines will be determined by eGFP encoded AAV cassette and visualized under confocal microscopy.

RESULTS:

This project aims to establish and evaluate a targeted viral vector delivery system which can readily to EGFR- and EpCAM-positive cells by antibody engineering. Preliminary data from our lab and elsewhere have demonstrated the efficacy of this promising approach to cancer therapy.

DISCUSSION:

Challenges affecting gene delivery platforms is predominantly marked by non-specificity, poor production yield and immunogenicity of viral vectors. Though, non-viral gene delivery platforms are preferred due non-immunogenicity, however, are poor transducers of target cells. Here, the focus is to develop a targeted viral gene delivery system based on protein and antibody engineering technology already existing in the MB&I lab

POS13	Application of CRISPR interference to identify conditional gene essentialities in mycobacterial DNA repair
Full names of Authors *Presenting Author	**Kristy Winkler*,** Timothy de Wet, Mandy Mason, Digby Warner
Department	Pathology

ABSTRACT:

Despite the availability of an effective frontline chemotherapy, tuberculosis causes 1.5 million deaths globally each year. The prolonged duration of the standard combination regimen and the spread of drug-resistant Mycobacterium tuberculosis (Mtb) strains have demonstrated the urgent need for treatment-shortening antibiotics. Improving throughput in the drug discovery pipeline demands a deeper understanding of Mtb metabolism. Mycobacterial DNA replication and repair are metabolic processes for which the bacterium possesses a complex repertoire of functionally overlapping genes. Both processes have been implicated in both the long-term persistence of Mtb and the emergence of drug resistance.

MATERIALS AND METHODS:

We constructed a pooled CRISPR interference (CRISPRi) knockdown library in the fast growing, non-pathogenic model, M. smegmatis, targeting ~140 essential and non-essential genes involved in mycobacterial DNA metabolism. This library was screened against the key second-line anti-TB drug, moxifloxacin, which targets DNA gyrase, to identify conditional gene essentialities and potential redundancies within mycobacterial DNA replication and repair.

RESULTS:

The chemical-genetic interactions identified using the CRISPRi library were compared to previous results from a transposon knockout library screened under the same conditions. In addition to confirming the utility of CRISPRi in enabling induced depletion of essential genes, this analysis identified individual genes that sensitise or desensitise the mutant strains to moxifloxacin for downstream characterisation.

DISCUSSION:

Future work will focus on the construction of a dual-knockdown library, comprising every combination of the ~140 genes assayed in this work. The longer-term aim is to apply these mutants in screens designed to identify vulnerabilities that might be exploited for future combination drug development.

POS14	Investigating baseline and activity-dependent chloride ion dynamics in human brain cell types.
Full names of Authors *Presenting Author	**Josh Selfe***, Joseph Raimondo
Department	Human Biology

ABSTRACT:

Epilepsy is a severe neurological disorder characterised by recurrent seizures. Seizures occur when inhibitory systems in the brain cannot constrain the generation and spread of excess excitation. These inhibitory systems rely on cellular transmembrane chloride ion gradients to function. Current methods used to study chloride dynamics are difficult to use and have a low throughput. The aim of this project is to develop the first optical tool for the investigation of chloride ion drive in brain cell types.

MATERIALS AND METHODS:

This tool uses a genetically encoded voltage indicator (GEVI). This fluorescent reporter is expressed by biolistic transfection in mouse organotypic hippocampal brain slices and imaged to record membrane potential changes. Chloride currents are generated, and the GEVI is used to record resultant changes in membrane potential, which are classified as either hyperpolarising, shunting, or depolarising. The chloride currents will be generated by applying GABA to the cell, or by activating an optogenetic chloride channel.

RESULTS:

The GEVI can detect membrane potential changes caused by application of GABA, and changes in the chloride driving force. Both supra- and sub-threshold events are detected. This has been used to characterise the responses to GABA of different brain cell types. Additionally, we have successfully co-expressed the GEVI and the chloride channel to create the first all optical reporter of chloride ion drive.

DISCUSSION:

This optical tool will allow for the rapid determination of chloride ion drive in many cells concurrently, without altering the drive in doing so. This will greatly assist the study of inhibition in the brain.

POS15	Molecular Characterisation of Diffuse Large B-Cell Lymphoma (DLBCL) in South Africa – defining biomarkers in an HIV positive context.
Full names of Authors *Presenting Author	Katherine Antel, Dharshnee Chetty and Shaheen Mowla, **Beatrice Relebogile Ramorola***
Department	Pathology

ABSTRACT:

Diffuse large B-cell lymphoma (DLBCL) is the most common non-Hodgkin lymphoma (NHL) diagnosed in people infected with HIV. Despite the increased access to antiretroviral therapy (ART), the prevalence of this high-grade lymphoma in HIV-positive individuals remains high. Molecular and genetic studies have revealed that HIV-associated DLBCL has unique and distinct pathogenic features. The aim of this research project is to identify biomarkers that are characteristic of the pathogenesis of DLBCL in the context of HIV infection.

MATERIALS AND METHODS:

Peripheral blood samples were collected from newly diagnosed (both HIV-positive and HIV-negative), chemotherapy naïve DLBCL patients. Recruitment sites were at GSH, Haematology E5 and Radiation Oncology LE32. Whole blood was stained with specific antibodies and analysed by flow cytometry to evaluate lymphocyte populations. For each sample, the remaining blood was processed, and the plasma was stored.

RESULTS:

Twenty-one patients recruited between 1 September 2020 and 30 September 2021. Of those parents, 38% (n=8) were HIV-positive. The median age in the HIV-positive group was 47, compared to 58 in the HIV-negative group. As expected, the mean CD4/CD8 ratio in the HIV-positive group was lower. Interestingly, this group displayed a higher proportion of activated cytotoxic T-cells. Additionally, it appears that infection with HIV promoted B-cell maturation, reflected by higher populations of mature and memory B-cells and there were less cytotoxic Natural killer cells in this group.

DISCUSSION:

In the context of HIV, DLBCL patients are often diagnosed younger (<50 years) compared to the general population. Observations of this study indicate that there are distinct differences in immune cell populations between HIV infected and uninfected DLBCL patients, indicating a difference in pathobiology between the two groups. Recruitment will continue so that this data can be consolidated. In addition, secreted activation markers will be measured in the stored plasma. Our data supports the possibility of a differential and personalised approach to the management of the disease in the context of HIV.

POS16	Temporal Trends in HIV-associated Lymphoma in Cape Town, South Africa
Full names of Authors *Presenting Author	**Lillian F. Andera*,** Dharshnee R. Chetty, Zainab Mohamed, Jenna Oosthuizen, Karryn Brown, Girisha Panchoo, Kudakwashe Simba, Gerdien Kritzinger, Sumaya Cassim, Katherine R. Antel, Amsha Ramburan, Jessica Opie, Vernon J. Louw, Estelle R. Verburgh
Department	Medicine

ABSTRACT:

The 2016 World Health Organisation (WHO) classification of lymphoid malignancies aimed to refine diagnoses to improve patient management. In the resource constrained and HIV burdened setting of Sub-Saharan Africa, lymphoma diagnoses show a unique pattern compared to developed countries. We studied the baseline characteristics of aggressive lymphoma diagnosed and treated at a public referral academic treatment centre.

MATERIALS AND METHODS:

Division of Clinical Haematology and Department of Radiation Oncology, Groote Schuur Hospital and the University of Cape Town. This descriptive retrospective study included HIV positive and HIV negative adolescents and adults diagnosed with aggressive lymphoma over 16 consecutive years from 2005 to 2020. Trends of incidence, lymphoma subtypes, fluorescence in-situ hybridisation (FISH) molecular diagnoses and HIV status in aggressive lymphoma patients.

RESULTS:

Out of 1804 aggressive lymphoma patients diagnosed, 42.6% were HIV positive with 53.7% males. HIV status did not differ by sex (51.6% males vs 48.4% females). The proportion of HIV positive aggressive lymphoma patients increased from 27.2% in 2005 to 44.3% in 2020. Age at the time of aggressive lymphoma diagnoses ranged from 13.3-92.8 years old for the total population with a median age of 42.7 years (IQR 32.7-56.8). HIV positive patients were diagnosed with aggressive lymphoma at a significantly younger age (median 38.1 years) than HIV negative patients (median 50.8 years); p-value <0.001. The three most commonly diagnosed aggressive lymphomas were diffuse large B-cell lymphoma (n=642, 35.6%), Hodgkin's lymphoma (n=462, 18.1%) and Burkitt's lymphoma (n=195, 10.9%). A predominance of >87% HIV positivity was found in subjects with Burkitt's lymphoma, Plasmablastic lymphoma, as well as the related lymphoproliferative disorder, Multicentric Castleman's Disease. Thus, the number of annually diagnosed aggressive lymphoma cases increased from 81 cases in 2005 to 131 cases in 2020. In 122 of all lymphoma cases, FISH probes for MYC, BCL2, BCL6 gene rearrangements were used in the diagnostic algorithm, and since 2018, clarified diagnoses of 20/157 diffuse large B-cell lymphoma and 1/2 high-grade B-cell lymphoma cases.

DISCUSSION:

We show that both the proportion of HIV-associated lymphoma, and the overall incidence of aggressive lymphoma, are increasing. The anti-retroviral treatment (ART) national program since 2004 has not had an impact on HIV-associated lymphoma. The upward diagnostic trend in all lymphomas may be explained by population growth and recent improvements in referral and diagnostic pathways. This work is contributing towards developing a more focused algorithm incorporating FISH and other molecular tests in the diagnostic workup of lymphoma based on the WHO 2016 classification of lymphoid malignancies.

POS17	Neutralizing antibody sensitivity of replication competent HIV-1 from the latent reservoir of ART-treated individuals
Full names of Authors *Presenting Author	**Temhlanga Mndzebele*,** Haajira Kaldine, Penny Moore, Carolyn Williamson, Melissa-Rose Abrahams
Department	Institute of Infectious Disease and Molecular Medicine

ABSTRACT:

HIV-1 remains incurable due to a persistent reservoir unaffected by antiretroviral therapy (ART). Neutralizing antibodies (nAbs), recognize and kill diverse strains of HIV-1 yet viral escape is an ongoing challenge. The frequency of nAb escape in the reservoir is unclear. The aim of this study is to investigate the neutralization sensitivity of the latent reservoir to longitudinal autologous plasma/monoclonal antibodies (mAbs) and known broadly neutralizing antibodies (bNAbs).

MATERIALS AND METHODS:

Reservoir viruses were selected from women from the CAPRISA 002 cohort, CAP188 (n=9), CAP256 (n=2) and CAP287 (n=2), based on timing of reservoir entry and representation of unique evolutionary lineages. Envelope PCR and TOPO cloning was carried out. Env-pseudoviruses were generated by HEK293T transfection. Antibody sensitivity was tested in TZM-bl neutralization assays. Approximate-maximum-likelihood trees were plotted using FigTree.

RESULTS:

For CAP256, one virus demonstrated sensitivity to 67% (18/27) of autologous mAbs, while the other showed 100% resistance. In phylogenetic analyses, the resistant virus clustered with pre-ART viruses from later in infection and exhibited a K169E escape mutation. All four tested CAP188 viruses resisted neutralization by autologous nAbs in plasma from later than 93 weeks post-infection, with one becoming sensitive to late time-point nAbs. Known bNAb escape mutations were identified in reservoir viruses. V3-glycan bNAbs showed the greatest potency (average 0.0625 ug/ml) and breadth (100%) against our panel.

DISCUSSION:

HIV-1 reservoir virus sensitivity to an autologous mAb lineage agreed with phylogenetic timing of reservoir establishment. However, there was greater complexity in interpreting nAb escape using plasma. The presence of escape mutations in the reservoir may limit sensitivity to bNAbs.

POS18	Programmed cell death ligand-1 (PD-L1) expression in HIV-associated Diffuse Large B-cell Lymphoma – role and regulation
Full names of Authors *Presenting Author	**Zahra Latib*,** Shaheen Mowla
Department	Pathology

ABSTRACT:

The programmed death ligand-1 (PD-L1) is an essential protein involved in the modulation of immune responses. In the tumour microenvironment (TME), the PD-1/PD-L1 axis is hijacked by cancer cells to escape immune surveillance, where cancer cells overexpress PD-L1 to evade cell death. Diffuse Large B Cell Lymphoma (DLBCL), a highly aggressive cancer, is over-represented among HIV-infected individuals. Studies have shown that PD-L1 is overexpressed in DLBCL, and even more so in HIV-associated DLBCL. Currently, the role and regulation of PD-L1 in DLBCL remains unclear, and defining this role is the focus of this study.

MATERIALS AND METHODS:

An overview of this study involves (a) measuring the population of Bregs, PD-L1-positivity, and soluble PD-L1 levels, in the blood of HIV-positive and -negative newly diagnosed DLBCL patients; (b) analysing the tumour microenvironment (TME) to determine the effect of HIV-infection on PD-L1 and immune cells; and (c) exploring the relationship between HIV-1, the EBV nuclear antigen 2 (EBNA2), PD-L1 and c-MYC

RESULTS:

We have successfully recruited four newly diagnosed DLBCL patients and analysed their peripheral immune cells which indicates presence of a Breg population. Recruitment is ongoing. Additionally, we have received an EBNA2-expressing DLBCL cell model from a collaborator which was expanded, and then exposed to HIV. Total protein has been harvested and is currently being analysed for changes in PD-L1 and c-MYC protein levels.

DISCUSSION:

The results of this early study is promising and the goal is that the findings will provide insight into the pathobiology of HIV-associated DLBCL.

POS19	Characterisation of SARS-CoV2 seroprevalence in non-hospitalised HIV-infected patients from Gugulethu, South Africa
Full names of Authors *Presenting Author	**Humaira Lambarey*,** Abeen Chetram, Melissa Blumenthal, Georgia Schafer
Department	Integrative Biomedical Sciences

ABSTRACT:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), causing the current Covid-19 global pandemic, has been rapidly spreading since being first detected in December 2019. At present, due to the broad range of symptoms, the physiological basis of SARS-CoV2 infection is not known but an individual's immune system response is sure to play a pivotal role. A serological assay in the form of an ELISA may provide information that may aid in understanding infection as well as immunity to the virus. Recent studies have evaluated the IgG, IgM and IgA antibodies in patient serum.

MATERIALS AND METHODS:

In our study, a cohort of 150 HIV-infected patients from Gugulethu, Western Cape were tested by ELISA to determine the presence of SARS-CoV2 antibodies in the plasma (pre-pandemic plasma served as control (n=29)). ELISAs were performed using the S1 and RBD portions of the Spike protein from SARS-CoV2, together with detection of IgG, IgM and IgA to determine optimal conditions.

RESULTS:

SARS-CoV2 IgG antibody screening of HIV- infected patients (n=150) from the time of recruitment in October 2020 to July 2021 indicated over 70% of the cohort (107/150) showed the presence of SARS-CoV2 specific IgG antibody present in the plasma.

DISCUSSION:

Recruitment of patients started at the end of the first Covid-19 wave in the Western Cape. Our results confirm data established by researchers from the UCT School of Public Health, in that poorer communities were particularly hard hit by the first Covid-19 wave in South Africa. However, the same communities showed a much more moderate second and third wave, probably due to an extremely high Covid seroprevalence (possibly indicating cross-protectivity).

POS20	KSHV, but not EBV, co-infection associates with COVID-19 severity and outcome in South African patients
Full names of Authors *Presenting Author	**Melissa J Blumenthal*,** Humaira Lambarey, Abeen Chetram, Catherine Riou, Robert J. Wilkinson, Georgia Schäfer and the HIATUS consortium
Department	Integrative Biomedical Sciences

ABSTRACT:

In South Africa, the COVID-19 pandemic is occurring against the backdrop of high HIV, tuberculosis and non-communicable disease burdens as well as prevalent herpesviruses infections such as Epstein-Barr virus (EBV) and Kaposi's sarcoma-associated herpesvirus (KSHV).

MATERIALS AND METHODS:

As part of an observational study of adults admitted to Groote Schuur Hospital, Cape Town, during the period June – August 2020 and assessed for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection, we measured KSHV serology and KSHV and EBV viral load (VL) in peripheral blood in relation to Coronavirus disease 2019 (COVID-19) severity and outcome.

RESULTS:

104 patients with PCR-confirmed SARS-CoV-2 infection were included. 29.8% of the cohort was HIV-positive and 41.1% were KSHV seropositive. EBV and KSHV VL were detectable in 84.4% and 20.6% of the cohort, respectively. Thirty (28.8%) patients died and detectable KSHV VL was associated with death adjusting for age, sex, HIV status and EBV (p=0.036, adjusted OR=3.17 [95% CI: 1.08–9.32]). Furthermore, in HIV negative COVID-19 patients, there was a trend indicating that KSHV VL may be related to COVID-19 disease severity (p=0.054, unstandardized co-efficient 0.86 [95% CI: -0.015–1.74]) in addition to death (p=0.008, adjusted OR=7.34 [95% CI: 1.69–31.49]).

DISCUSSION:

While the design of our study cannot distinguish if disease synergy exists between COVID-19 and KSHV nor if either viral infection is indeed fuelling the other, these data point to a potential contribution of KSHV infection to COVID-19 outcome, or SARS-CoV-2 infection to KSHV reactivation, particularly in the South African context of high disease burden, that warrants further investigation.

POS21	TB immunity in people living with HIV starting treatment early or during chronic infection
Full names of Authors *Presenting Author	**Rofhiwa Nesamari*,** Catherine Riou, Roanne Keeton, Nigel Garrett, Kogieleum Naidoo, Nesri Padayatchi, Quarraisha Abdool Karim, Salim Abdool Karim, Wendy A. Burgers
Department	Pathology

ABSTRACT:

Antiretroviral therapy (ART) is associated with a 65% reduction in TB risk and mortality. When initiated early, ART results in a 2.5-fold decrease in TB incidence, making it a crucial step in TB protection for PLWH. In this study, we characterised TB immunity in individuals who initiated ART early compared to those who initiated during chronic HIV infection.

MATERIALS AND METHODS:

Participants were selected from the CAPRISA 002 study, a longitudinal cohort of PLWH who were followed from HIV seroconversion to HIV treatment. We studied 16 PLWH who initiated ART early (median 7.5 [IQR 3-9] months) and 22 who initiated late (66 [46-77] months). Cells were stimulated with M.tb antigens followed by intracellular cytokine staining and flow cytometry. M.tb-specific responses were determined before initiation and 2 years after ART (24 [22-28] months).

RESULTS:

Comparison of the early and late ART groups demonstrated that the median CD4/CD8 ratio after ART was significantly higher in the early ART group compared to the late ART group (p=0.0023; 1.24 vs. 0.82), while other clinical parameters were similar. While the median frequency of M.tb-specific CD4 responses was lower in those starting treatment late, both before (0.32% and 0.19%) and after ART (0.35% and 0.24%), these were not significantly different. Furthermore, no phenotypic differences were detected between groups.

DISCUSSION:

In our preliminary analyses, we have not identified any differences in the magnitude, function or phenotype of M.tb-specific CD4 cells between early or late ART starters. Further work is needed to elucidate the mechanisms of protection from TB after early ART initiation.

POS22	Molecular characterisation of Clostridium perfringens isolates from patients at Groote Schuur Hospital
Full names of Authors *Presenting Author	Thembisa Monki, Amanda Khumalo,Brian Kullin, **Lynthia Paul***
Department	Pathology

ABSTRACT:

C. perfringens is the causative agent of diseases ranging from diarrhoea to necrotising gastrointestinal disease and gas gangrene. Typing of the organism is based on carriage of one or more toxins with toxin types associated with specific hosts. Human disease is caused by type A (Alpha toxin only) or F (Alpha and Cpe toxins), although occasional disease with other toxin types has been described. Information on isolates causing disease in Africa is mostly absent, as routine diagnostic tests only screen for the Cpe toxin when foodborne outbreaks occur. However, the continuous threat the organism poses to human and livestock health and the growing awareness of 'One-Health' principles warrant more in-depth studies.

MATERIALS AND METHODS:

Clinical isolates (n=19) of C. perfringens were identified by 16S rRNA gene sequencing and further characterised by antimicrobial susceptibility testing, PCR-based toxin screening and whole genome sequencing (WGS).

RESULTS:

Isolates were identified as toxin type A (16/19) and type F(3/19). WGS identified further identified the beta2 toxin (3/16 isolates). All isolates were susceptible to piperacillin/tazobactam and imipenem. Resistance against clindamycin, metronidazole, amoxicillin/clavulanic acid, and/or penicillin G were observed. WGS analysis of one MDR isolate revealed the presence of genes encoding resistance to beta lactams and lincosamides, as well as the virulence factors associated with this organism.

DISCUSSION:

This is the first study describing molecular traits for local C. perfringens isolates, notably reporting invasive isolates usually associated with non-lethal diarrhoea, the presence of a toxin of potential avian origin in human strains and drug resistance markers associated with antimicrobial resistance.

POS23	Barrier Integrity & understanding HIV Susceptibility in the penis: A Mechanistic search for Medical Male Circumcision
Full names of Authors *Presenting Author	Micheal Mzwiwoxolo, Clive M. Gray, **Cosnet Lerato Rametse*)**
Department	Pathology

ABSTRACT:

The biological mechanisms underlying HIV risk reduction following medical male circumcision (MCC) remains ill-defined. Our research question: does skin barrier integrity change around the penis after MMC to lower HIV susceptibility? This study aims to show changes to penile skin barrier integrity in vivo before and after MMC and in the presence of an asymptomatic sexually transmitted infection (aSTI) by measuring penile skin transepithelial water loss (TEWL) and hydration.

MATERIALS AND METHODS:

Vapometers and moisture meters SC and D were used to measure TEWL and dermal surface hydration as measures of barrier integrity. TEWL (n=56 adult males) and moisture SC and D measurements (n=38 adult males) were measured on the glans, inner foreskin and penile shaft before MMC in each participant. Follow-up measurements were made at 2, 12 and 24 weeks after MMC in the glans and shaft (n=16).

RESULTS:

Ongoing data show in aSTI negative men before MMC, the inner foreskin and glans had higher TEWL versus the shaft: median=30.6 & 29.8 vs 13.7 g/hr/m2 respectively. Six months after MMC, TEWL in the glans significantly decreased (p=0.011) to match that of the shaft. In aSTI positive men (n=10), TEWL in the glans was lower before MMC compared with men who were STI negative: median of 12.7 vs 29.7 g/hr/m2, p= 0.043).

DISCUSSION:

One mechanism for how MMC lowers HIV susceptibility is possibly by improving skin barrier integrity of the penis, as shown by lower TEWL and increased hydration around the glans after circumcision. This may not be the case for aSTI positive males.

POS24	Comparison Of Profiles Of Pharmacogene Variants In Populations In Malaria Endemic And None-Endemic Geographical Areas
Full names of Authors *Presenting Author	**Hundaol Hordofa***, Emile Chimusa, Delesa Damene, Collet Dandara
Department	Pathology

ABSTRACT:

Inter-ethnic differences in response to medication can be explained through population structure determined from genetic variants affecting drug metabolism. Antimalarial drugs are used in populations carrying different patterns of genetic variability. However, there is limited information on the distribution of genetic variants of pharmacogenomics importance in African populations.

MATERIALS AND METHODS:

We obtained genome-wide genotype datasets of four malaria endemic African populations including Mali, Kenya, Gambia and Malawi (N~11,000 from MalariaGEN consortium). In addition to this, we accessed reference datasets of global populations composed of 20 ethnic groups from African Genome Variation Project (AGVP) and 1000 Genome consortium Project. We obtained all pharmacogenes from databases such as PharmVar and PharmGKB. We further obtained antimalarial pharmacogenes reported thus far from published literatures. We retrieved SNPs that map to these genes from dbSNP databases, and we used this dataset to compare the population structure of the pharmacogenes in malaria endemic and global population. We also genotyped one of the genes (CYP2C8) that code for enzymes that metabolise some of the most common antimalarial drugs, using Sanger sequencing.

RESULTS:

The analysis of MAF proportion of all pharmacogenes variants obtained from the databases revealed high proportion of common pharmacogene variants in population of malaria endemic areas (MAF>0.5) versus non-malaria endemic areas (MAF<0.5) and higher proportion of rare variants (MAF<1%) where obtained in populations of non-malaria areas. Allele frequency spectrum of pharmacogenes variants within each pharmacogenes showed a disproportionally higher number of variants in the cytochrome P450 enzymes such as CYP2A13 and CYP2F1 in populations of malaria endemic areas. The ATP-binding cassette (ABC) drug transporters such as ABCC4, ABCC1 and ABCC2 showed higher proportion of pathogenic SNPs in populations of malaria endemic areas compared with non-endemic areas (>50% vs 0%). Principal component analysis (PCA) based on pharmacogene variants also showed clear differentiation into different groups of population.

DISCUSSION:

In our study, we have found high proportion of cytochrome p450 pharmacogene variants in the malaria endemic areas. This may be caused by the selective pressure caused by the antimalarial drugs on the genes. Moreover, we have found high proportion of pathogenic SNPs in the efflux drug transporter genes. This may be caused by the resistance of the plasmodium parasites to antimalarial drugs in patients having the mutated ABC transporter genes.

POS25	Assessing morphological mandibular traits for sex estimation in Holocene San and Khoekhoe populations
Full names of Authors *Presenting Author	**Sadiyah Malek*,** Victoria E. Gibbon, Judith C. Sealy
Department	Human Biology

ABSTRACT:

Sex estimation is a key element in bioarchaeology and forensic anthropology. The mandible, the largest and most sexually dimorphic facial bone, is commonly used for sex estimation with high accuracy. However, accurate population-specific sex estimation standards do not exist for the southern African Holocene San and Khoekhoe (S-K) population. Due to their markedly small stature, skeletal gracility, and physically active lifestyle, this population exhibits reduced sexual dimorphism. The following study assessed the accuracy of morphological mandibular traits for estimating sex in a southern African Holocene S-K sample.

MATERIALS AND METHODS:

Three commonly assessed mandibular traits (mandibular shape, gonial eversion/flaring, mental eminence) were analysed in a sample of 155 adult Holocene S-K mandibles. Mandibular sex estimates were compared to the individual's pelvic sex (Phenice method) to determine the classification accuracy of each trait. Results were statistically analysed using chi-squared tests.

RESULTS:

Mandibular shape produced the highest classification accuracy (72%), followed by gonial flaring (63%), and mental eminence that produced the lowest (55%). When assessed by sex, traits producing the highest classification accuracies were gonial eversion (81%) in males, and mental eminence (95%) in females. Traits producing the lowest accuracies were mental eminence (16%) in males, and gonial eversion (39%) in females.

DISCUSSION:

Whilst the mandible is highly sexually dimorphic, existing morphological assessments of mandibular traits are not sufficient for accurate sex estimation. The range of sexual dimorphism exhibited by this population does not conform to current sex estimation methods, suggesting a need for population-specific optimisation of existing methods, for accurate application in the Holocene S-K population.

POS26	Magnetic resonance imaging characterisation of heap hydrolysis
Full names of Authors *Presenting Author	**Jia Fan*,** Tomas Hessler, Stephen Jermy, Rob Huddy, Sue Harrison, Marijke Fagan-Endres, Ernesta Meintjes
Department	Human Biology

ABSTRACT:

Magnetic resonance imaging (MRI) has been considered a novel technology to non-invasively examine the effect of liquid flowrate on heap hydrology. Diffusion-weighted imaging (DWI) allows us to detect the random microscopic motion of free water molecules known as Brownian movement. The aim of the study was to examine liquid flowrate distribution in heap leaching.

MATERIALS AND METHODS:

DWI was performed on a 3T Skyra MRI (Siemens, Erlangen, Germany) located at CUBIC. The flowrates of an MR compatible bioreactor were varied from 18.5 through 22.17 to 27.67 mm3/s. Once the water stream reached steady state, apparent diffusion coefficient (ADC) maps were acquired at 3 different diffusion weightings (b = 300, 500 and 1000 s/mm2) to evaluate the average speeds at different flowrates.

RESULTS:

The average speeds increased from 2.18 through 2.98 to 4.95 mm/s as the flowrates increased. The directions of the flow were determined from colour-coded diffusion images.

DISCUSSION:

Discussion: The average speeds of the water stream in the bioreactor were evaluated and were proportional to the flowrates. Moreover, MRI provided unique insight into the direction and pattern of the flow.

POS27	Generation of anti-FAPα(scFv)-SNAP-based antibody fusion protein for in vivo radioimaging/-immunotherapy application
Full names of Authors *Presenting Author	**Grace Mayuni***, Dharanidharan Ramamurthy, Stefan Barth
Department	Integrative Biomedical Sciences

ABSTRACT:

Glioblastoma Multiforme accounts for 45 % of all brain tumours. Standard treatment is challenged by high recurrence and drug resistance. FAPα presents a potential antigen target because of its high expression in a glioblastoma microenvironment and low expression in healthy adult brain tissue. The SNAP-tag is a modified version of the human O6-alkylguanine-DNA-alkyltransferase (AGT), which undergoes covalent self-labelling reactions with benzyl guanine (BG) modified substrates. Recombinant constructs containing antibody fragments linked to the SNAP-tag have been developed to create a highly specific antigen targeting tool. This study aims to improve targeted in vivo diagnosis of Glioblastoma as well as investigate a tool that can be used to deliver a specific payload to glioblastoma tumours that express FAPα.

MATERIALS AND METHODS:

A pCB vector for the expression of anti-FAP (scFv)-SNAP is designed in silico, cloned, verified and transformed into HEK293T cells. Purified anti-FAP (scFv) SNAP-fusion protein is characterized by immunoblotting analysis followed by functional conjugation studies using BG-Alexa 488 and BG-Alexa647. Binding of fusion protein to FAP+ cells is analysed by flow cytometry & confocal microscopy. Radiolabeled SNAP-tag based fusion protein will be used to investigate the in vivo imaging and immunotherapeutic activity in human tumour xenograft mouse models

RESULTS:

Experimental results so far agree with the predicted functional properties of the intact and full-length anti-FAP (scFv) SNAP-fusion protein. The optimal binding ratio of Ab:BG-substrate conjugate for downstream experiments was determined to be 1:1.

DISCUSSION:

The application of the antibody explored might pave the way for a novel method of treatment that may impact treating resistant metastasis among glioblastoma patients.

POS28	Creating and analysing an African pan-genome
Full names of Authors *Presenting Author	**Jess Bourn*,** Nicola Mulder, Gerrit Botha
Department	Integrative Biomedical Sciences

ABSTRACT:
The human reference genome is the foundation for understanding the role of genetics in human health, disease and variation. However, there is a significant amount of genetic variation still missing from the reference genome. With African populations harbouring the most genetic diversity, the lack of variation represented within the reference sequence hinders our ability to identify important genetic variants in health and disease in African populations, which prevents the development of potential clinical interventions. One approach to address this shortcoming of the reference genome is a pan-genome, which is a collection of all the DNA sequences present within a population.

MATERIALS AND METHODS:
In this study, an African pan-genome was created and analysed using high coverage whole genome sequences from diverse African populations. The HUman Pan-genome ANalysis (HUPAN) system - a previously developed pipeline - was used to assemble the genomes and identify over 85 Mb sequences that failed to align to the current reference genome.

RESULTS:
These sequences have been classified as individual-, population- or African-specific, with a majority being specific to populations or regions, and fewer than 2000 out of the 64 000 sequences being common to all populations. 59 novel protein-coding genes have also been predicted from the non-reference sequences and are currently being annotated.

DISCUSSION:
These results confirm that the human reference genome lacks significant amounts of genetic sequence and validates the need for multiple reference genomes for distinct human populations. In future, novel African non-reference sequences such as these could be an important resource for improving genomic studies in Africa.

POS29	Intersection of traditional African medicine and Western biomedicine in patient-held explanatory models of Mseleni Joint Disease.
Full names of Authors *Presenting Author	Robea Ballo, Victoria Gibbon, **Elizabeth Sarah Dinkele***
Department	Human Biology

ABSTRACT:

Limited insight into patient-held explanatory models of osteoarthritic diseases in rural regions in South Africa poses a challenge to effective disease management. Until beliefs, perceptions and experiences of the endemic Mseleni Joint Disease (MJD) are understood, this disease will remain a leading cause physical disability in Northern KwaZulu-Natal.

MATERIALS AND METHODS:

The aim of this qualitative pilot study was to examine the relationship between explanatory models and treatment-seeking behaviours associated with MJD. In-depth interviews conducted with MJD patients (n=6), nurses (n=7) and doctors (n=9) at the Mseleni Hospital were analysed thematically.

RESULTS:

MJD patients generally invoked supernatural (witchcraft), natural (nutritional deficiencies, soil or water); and/or social (gender-based practices and lifestyle) explanatory models. In contrast, doctors invoked environmental and social explanatory models, while nurses expressed beliefs common to both doctors and patients. Patients most commonly cited soil as the cause of MJD, and conceptualised disability as an inevitable reality. Consequently, patients reported few interventions to prevent functional impairment, focussing instead on pain management. Patients reported seeking traditional African medical care prior to western biomedical care.

DISCUSSION:

MJD patients generally invoked supernatural (witchcraft), natural (nutritional deficiencies, soil or water); and/or social (gender-based practices and lifestyle) explanatory models. In contrast, doctors invoked environmental and social explanatory models, while nurses expressed beliefs common to both doctors and patients. Patients most commonly cited soil as the cause of MJD, and conceptualised disability as an inevitable reality. Consequently, patients reported few interventions to prevent functional impairment, focussing instead on pain management. Patients reported seeking traditional African medical care prior to western biomedical care.

POS30	Implementation, evaluation and refinement of a targeted gene panel for inherited retinal diseases in Africa
Full names of Authors *Presenting Author	**Nicole Midgley*,** George Rebello; Raj Ramesar; Lisa Roberts
Department	Pathology

ABSTRACT:

Inherited retinal diseases (IRDs) encompass a highly variable group of disorders characterised by vision loss. The clinical and genetic heterogeneity impedes obtaining a molecular diagnosis, which is vital as it may inform the clinical diagnosis and is a prerequisite for participation in gene-based clinical trials. Next-generation sequencing (NGS) has revolutionised the speed and cost of genetic testing, improving diagnostic rates. Targeted gene panels, an NGS technology, are the basis of much of the genetic testing taking place globally with a detection rate of 50-70%, however, no such panel for IRDs exists that has been locally implemented and optimised for the diverse South African populations.

MATERIALS AND METHODS:

We aim to screen >130 IRD patients using an NGS panel we have designed to sequence over 100 known IRD genes in parallel.

RESULTS:

To date, 72 patients have been screened using the panel to genetically resolve 54% of the cohort.

DISCUSSION:

The panel will be supplemented by interrogating the NGS data for the presence of copy number variants, and furthermore by screening for seven functional deep intronic variants via restriction enzyme digest or Sanger sequencing. Finally, to further address missing heritability, we will investigate the controversial mutational load hypothesis, where the disease phenotype is due to the total genetic burden from accumulated deleterious variants across the genome.

POS31	Design and Development of an Open-Source ADL-Compliant Prosthetic Arm for Trans-radial Amputees.
Full names of Authors *Presenting Author	Sudesh Sivarasu, Lara Timm, **Maureen Etuket***
Department	Human Biology

ABSTRACT:

Open-source prostheses have the potential to increase the accessibility of functional prosthetic arms. At present, they are not optimised to assist the dominant hand in performing bimanual ADL. This research study was thus geared towards the design and experimental validation of an open-source below-elbow prosthetic arm, called the ADL arm, that is functionally optimised for the performance of ADL in the unilateral trans-radial amputee population.

MATERIALS AND METHODS:

The ADL arm is 3D printed; the design validation involved functional assessment - using the Anthropomorphic Hand Assessment Protocol (AHAP) and simulated use assessment - a practical ADL verification, and a usability assessment with healthy volunteer participants after obtaining Ethics approval.

RESULTS:

In accordance with AHAP, the ADL arm presented with an overall grasping ability score (GAS) of 68% and a partial GAS of greater than 75 % for four of five ADL grasps. Usability Assessment involved the performance of ADAL tasks coupled with the completion of the system usability scale (SUS). The perceived usability of the device was found to increase with increased device familiarity, yielding an overall score of 84:29.

DISCUSSION:

Through the tests conducted, the ADL arm was found to be functionally competent with proven ability to assist in the performance of ADLs in a simulated-use environment. The participants found the experience with the device to be `good' overall. A number of design modifications are however recommended to overcome the limitations of the current design, which should be tested in the trans-radial amputee population to corroborate the results obtained in this study.

POS32	FlexiGyn – A Flexible Mobile Office Hysteroscopy System
Full names of Authors *Presenting Author	Sudesh Sivarasu, **Edmund Wessels***
Department	Human Biology

ABSTRACT:

In the field of gynaecology, hysteroscopy is currently regarded as the gold standard for abnormal uterine conditions and allows clinicians to directly observe and treat conditions in a single procedure. However, the usage of existing hysteroscopy systems is limited due cost, facility requirements, and equipment mobility. Patient access to hysteroscopy procedures is greatly reduced as a result. This project prosed to develop an innovative hysteroscopy system to overcome the current limitations of existing systems.

MATERIALS AND METHODS:

A prototype of a mobile, handheld hysteroscopy system was developed that included a camera, lighting, and screen for visualisation. A 4.9mm small diameter, flexible scope was connected to a novel bending system that allows for user controlled bending in of up to 130° in two directions. A usability trial was conducted with gynaecologists performing mock procedures with the prototype on cadavers, afterwards participants completed a system usability scale to evaluate the device.

RESULTS:

Bench testing on the anatomical model was successful, with the prototype able to navigate into, and fully observe the uterine cavity. A disposable sheath was also developed to isolate the device from the environment during testing. The usability trial concluded with participants giving the device an average rating of 76 on the usability scale placing it in the 'good to excellent' range.

DISCUSSION:

The prototype developed successfully performed the mock procedures on cadavers and models which confirmed its potential as a solution the current shortcomings of hysteroscopy systems. Feedback from the usability trial is currently being incorporated into a second prototype.

POS33	Design and development of novel anatomical scapular fracture fixation plates: population-based and fracture-focused design
Full names of Authors *Presenting Author	**Habtamu Yimam*,** Roopam Dey, Steven Roche, Sudesh Sivarasu
Department	Human Biology

ABSTRACT:

Precise anatomical reduction and stable internal fixation are required an open reduction internal fixation of displaced and unstable scapular fractures to restore functional anatomy and a full range of shoulder movement. Anatomically contoured scapular plates are designed for specific anatomical regions of the scapula to guide the reduction, serve as a template, and stabilize the fixation. However, due to morphometric variations between the individual scapula and the complexity of the fracture patterns limit the usability of these plates. The aim of this study was to design and develop population-specific novel anatomical scapular plates by identifying the common scapular fracture patterns.

MATERIALS AND METHODS:

A reference average 3D template scapula, representing the target population (South African), was created from a 3D CT reconstruction of 22 intact cadaver scapulae using the Statistical Shape Modelling (SSM) technique. The frequent fracture regions of the scapula were identified by creating fracture and heat maps of 70 virtually reduced and superimposed patterns of fractured scapulae. Using the average 3D template scapula and the fracture information, the CAD model of novel anatomical plates was developed at the selected anatomical regions of interest using reverse engineering and surface modeling techniques.

RESULTS:

A total of five anatomical plates with two size options (large and small) were designed for the lateral border, medial border, glenoid fossa extending to the neck, glenoid fossa with body extension, and acromion fracture patterns. The plates have 2.5 mm thickness, 8.5 mm width, and different lengths and shapes (including the number of screw holes) based on the anatomical regions.

DISCUSSION:

Integrating 3D medical images, 3D statistical analysis, and CAD method in the design of orthopaedic implants could be used to standardize the design process, reduce time, and design anatomically enhanced implants. In this study, a methodology is proposed for the quick design of population-based anatomical scapular plates for common scapular fracture patterns. The method could also be used to design patient-specific anatomical implants. Future works will be evaluating the biomechanical performance of the novel plates using Finite Element (FE) simulation and the quantitative evaluation of bone-plate fitting.

POS34	A retrospective analysis of fatal ground level falls and falls from a height: A 5-year review
Full names of Authors *Presenting Author	**Lorraine R. Chonyera*,** Calvin G. Mole
Department	Pathology

ABSTRACT:

Falls are the second leading cause of unintentional fatalities globally. Such deaths are considered unnatural, and therefore undergo medico-legal investigation. Trauma may be utilized to assess circumstances surrounding death, however further research is necessary to assess fall height based on trauma. Research is necessary to assess the risk of fatal falls in a South African context. The aim of this study was to assess the prevalence and injury patterns associated with ground level falls and falls from a height.

MATERIALS AND METHODS:

A five year (1 January 2014 - 31 December 2018) retrospective review of fatal fall cases investigated at Salt River mortuary was conducted. The prevalence and patterns of injuries were assessed with regard to fall height, impacting surface and victim demographics.

RESULTS:

During the period, 360 (2%) cases were due to falls. The number of fall cases per year ranged from 63 to 79. Most cases were accidental and involved the elderly. Alcohol was detected in 122 (37%) cases. Head and lower extremity injuries were seen in ground level falls while injuries to the head and at least one other region were observed in high falls. Trauma and its complications were predominant causes of death.

DISCUSSION:

Accidental falls constitute the majority of fatal falls cases and alcohol appears to play a significant role in such cases. As expected, trauma associated with falls varies based on the height of the fall. Unfortunately fall height is not consistently recorded on death scenes which may limit investigations. Further studies will improve injury interpretation.

POS35	Caught in the act: impact of Crematogaster spp. (Hymenoptera: Formicidae) necrophagous behaviour on neonate pigs (Sus scrofa domesticus L.) in the Western Cape Province of South Africa
Full names of Authors *Presenting Author	**Adeyemi Daniel Adetimehin***, Calvin Gerald Mole, Devin Finaughty, and Marise Heyns
Department	Pathology

ABSTRACT:

Different ant species have been documented as part of the entomo-sarcosaprophagous community. They have been known to alter the process of carcass decomposition due to their ability to feed on fly eggs/larvae and create post-mortem skin injuries. However, studies on the impact of ants on decomposing carcasses are scarce, especially within the Western Cape Province of South Africa.

MATERIALS AND METHODS:

This study was part of a research project that utilized two (2) neonate pig carcasses in each month of the year to establish baseline data on the insect species associated with decomposing carcasses in the Western Cape Province of South Africa.

RESULTS:

In the early spring (September 2020), mid-autumn (April 2021) and mid-winter (July 2021) trials respectively, several individuals of Crematogaster spp. colonized the pig carcasses shortly after deployment. There, they fed on the flesh of the carcasses and further inflicted bite marks and conspicuous post-mortem skin injuries. Following the reduction in the presence of Crematogaster spp., specifically in the mid-winter trial, bleeding was observed as a consequence of the skin lesions. In the early spring, mid- & late autumn (May 2021) and early (June 2021) & mid-winter trials respectively, Crematogaster spp. prevented the formation of large maggot masses, principally through the predation of live maggots and flies.

DISCUSSION:

The observations recorded in this study are of enormous importance in forensic investigations as the effect of the necrophagous behaviour of Crematogaster spp. on decomposing remains can be misinterpreted by inexperienced investigators during crime scene investigations and post-mortem interval estimations.

POS36	Motion of the glenoid edge under load in 3 degrees of freedom: Development of an augmented ASTM F2028 Test Rig and Preliminary Results
Full names of Authors *Presenting Author	**Leanne Haworth*,** Bhushan Borotikar, Stephen Roche, Sudesh Sivarasu
Department	Human Biology

ABSTRACT:

The most common cause of failure of a shoulder joint prosthesis is loosening of the glenoid component. The American Society for Testing and Materials (ASTM) standardised a test to evaluate glenoid loosening, in which the glenoid is cyclically loaded and the vertical displacement of the edges is measured. However, laboratory experiments of the glenoid under load report the edges also deflect horizontally and with a tilting motion. Therefore, the standardized test does not fully quantify the glenoid motion. This study developed an augmented ASTM test rig to investigate the glenoid component's loosening process.

MATERIALS AND METHODS:

The test rig developed measures vertical, horizontal and tilt motions of the glenoid using sets of LVDT sensors, which track the motion of blocks connected to the glenoid edges by lever arms. An analytical algorithm in MATLAB converts the sensor readings to glenoid edge motion. Rig validation testing was performed using excised glenoid components. Once validation testing was complete, measurement of the motion of an established glenoid design could begin.

RESULTS:

The results of the rig validation show the sensor assembly system successfully acquiring the three types of motion at the glenoid edge. Edge motions in the order of 1mm vertical deflection, 1mm horizontal deflection and 5° tilt were observed in the rig validation testing. Analysis of the preliminary results of the established glenoid is in progress.

DISCUSSION:

The test rig and the results of the established glenoid will later be compared to the loosening behaviour of a novel glenoid design, developed at the UCT Orthopaedic Biomechanics Laboratory.

POS37	Development and validation of a quantitative method to measure retinol and retinyl palmitate using high performance liquid chromatography
Full names of Authors *Presenting Author	Diederick Johannes van der Westhuizen, Joanne Pillay, **Sarah Grace Lampert***
Department	Pathology

ABSTRACT:

Vitamin A is a group of essential lipid-soluble vitamins (retinol, retinyl esters, carotenoids) involved in a number of important physiological processes including sight and immune function. Retinol is a precursor to bioactive vitamin A and retinyl esters act as the storage form of retinol, the most abundant of which is retinyl palmitate. Retinol is measured to confirm vitamin A deficiency or toxicity, and retinyl palmitate is measured to investigate fat or nutrient malabsorption disorders or to evaluate vitamin A liver reserves.

MATERIALS AND METHODS:

Chromatographic separation was performed on an Agilent 6230 HPLC system using a Poroshell 120 SB-C18 (4.6 x 100 mm, 2.7 µm) column and a gradient elution with water as mobile phase A and methanol: acetonitrile (80:20, v:v) at a pH of 5-6 as mobile phase B. Analytes were detected using a DAD at 325 nm.

RESULTS:

The method was optimized to have a final run time of 11.6 minutes, with good inter- and intra-run reproducibility and high specificity. The developed method selectively separates retinol, retinyl palmitate and retinyl acetate (internal standard) from plasma. The calibration curves for retinol and retinyl palmitate were linear in the range of 0.2 – 10 mg/L with a limit of detection (LOD) of 0.2 mg/L for both compounds.

DISCUSSION:

The developed HPLC-DAD method is highly specific for the quantification of retinol and retinyl palmitate in plasma. The final method has been applied to a large number of clinical samples to monitor the clearance of intestinally derived lipoproteins.

POS38	Design, development and validation of a system for the prediction of adrenaline concentration in solution containing degradation by-products
Full names of Authors *Presenting Author	**Ashraf Vahed*,** Roopam Dey, Sudesh Sivarasu
Department	Human Biology

ABSTRACT:

Adrenaline Auto-Injectors (AAIs) are the most common mode of treatment for anaphylaxis. Literature finds the expiry date and visible discoloration to be inaccurate predictors of AAI potency. This project aimed to develop a spectrophotometric system for the prediction of adrenaline concentration (in solutions containing degradation by-products) for the eventual application as an AAI accessory.

MATERIALS AND METHODS:

The spectrophotometric analysis of adrenaline standards and 1mg/ml ampoules through High Pressure Liquid Chromatography (HPLC) was used to converge on analytical wavelengths for predicting adrenaline concentration. This informed the development of a device which used wavelength specific LEDs for spectrophotometry. The system was validated using standardized protocols.

RESULTS:

HPLC revealed optimum analytical wavelengths of 246+-1nm or 276+-1nm for ampoules and standards respectively, while the device used 255+-10nm and 275+-10nm LEDs. Fitting absorbance and known concentration to a linear regression model, the system showed an error of 0.12mg/ml (r=0.96, R^2=92%) for standards containing adrenaline with negligible degradation, and 0.10mg/ml (r=0.79, R^2=63%) for ampoules containing significant levels of oxidative by-product. Precision was measured as RSD=0.47-1.75%.

DISCUSSION:

The optimum wavelength for the prediction of adrenaline concentration in solution depended on the degradation by-product contained, where accuracy varied significantly with wider bandwidths. When accounting for sample temperature, a multiple regression model decreased the prediction error in standards from 0.12mg/ml to 0.003mg/ml, however this method resulted in negligible improvements for ampoules, where the presence of by-product and the wide LED bandwidth were concluded to be the primary sources of error.

POS39	Security for networked smart healthcare systems: A systematic review
Full names of Authors *Presenting Author	**Nyamwezi Parfaite Ndarhwa*,** Bessie Malila
Department	Human Biology

ABSTRACT:

Smart healthcare systems use technologies such as wearable devices, Internet of Medical Things and mobile internet technologies, to dynamically access health information, connect patients to health professionals and health institutions, and actively manage and respond intelligently to the medical ecosystem's needs. However, smart healthcare systems are affected by many challenges in their implementation and maintenance. Key among these is ensuring the security and privacy of patient health information. To address this challenge, several mitigation measures have been proposed and some have been implemented. Techniques that have been used include data encryption and biometric access. In addition, blockchain is an emerging security technology that is expected to address the security issues due to its distributed and decentralized architecture which is similar to that of smart healthcare systems. This study reviewed articles that identified security requirements and risks, proposed potential solutions, and explained the effectiveness of these solutions in addressing security problems in smart healthcare systems.

MATERIALS AND METHODS:

This review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines and was framed using the Problem, Intervention, Comparator, and Outcome (PICO) approach to investigate and analyse the concepts of interest. However, the comparator is not applicable because this review focuses on the security measures available and in this case no comparable solutions were considered since the concept of smart healthcare systems is an emerging one and there are therefore, no existing security solutions that have been used before. The search strategy involved the identification of studies from several databases including the Cumulative Index of Nursing and Allied Health Literature (CINAL), Scopus, PubMed, Web of Science, Medline, Excerpta Medical database (EMBASE), Ebscohost and the Cochrane Library for articles that focused on the security of smart healthcare systems. The selection process involved removing duplicate studies, and excluding studies after reading the titles, abstracts, and full texts. Studies whose records could not be retrieved using a predefined selection criterion for inclusion and exclusion were excluded. The remaining articles were then screened for eligibility. A data extraction form was used to capture details of the screened studies after reading the full text.

RESULTS:

Of the searched databases, only three yielded results when the search strategy was applied, i.e., Scopus, Web of science and Medline, giving a total of 1742 articles of which 14 studies were considered for a detailed review. 436 duplicate studies were removed, 801 were excluded after reading the title, 342 after reading the abstract, 163 after the full text and a further 4 could not be retrieved. 159 articles were screened for eligibility and as a result, 14 studies were included for the detailed review. Each of the 14 final articles was then analysed using the PICO and formulated research questions. Each of the 14 included articles presented a description of a smart healthcare system and identified the security requirements, risks and solutions to mitigate the risks. Each article also summarised the effectiveness of the proposed security solution. The key security requirements reported included data confidentiality, integrity and availability of data within the system, with authorisation and authentication used to support these key security requirements. The security requirements were then used by the authors to guide them in the design and implementation of the proposed security measures. The identified security risks include loss of data confidentiality due to eavesdropping in wireless communication mediums, authentication vulnerabilities in user devices and storage servers, data fabrication and message modification attacks during transmission as well as while the data is at rest in databases and other storage devices. The proposed mitigation measures included use of biometric accessing devices; data encryption for protecting the confidentiality and integrity of data; blockchain technology to address confidentiality, integrity, and availability of data; network slicing techniques to provide isolation of patient health data in 5G mobile systems; and multi-factor authentication when accessing IoT devices, servers, and other components of the smart healthcare systems. The effectiveness of the proposed solutions was demonstrated through its ability to provide a high level of data security in smart healthcare systems. For example, proposed encryption algorithms demonstrated better energy efficiency, and improved operational speed; reduced computational overhead, better scalability, efficiency in data processing, and better ease of deployment.

DISCUSSION:

This systematic review has shown that the use of blockchain technology, biometrics (fingerprints), data encryption techniques, multifactor authentication and network slicing in the case of 5G smart healthcare systems has the potential to alleviate possible security risks in smart healthcare systems. The benefits of these solutions include a high level of security and privacy for Electronic Health Records (EHRs); improved speed of data transaction without the need for a decentralized third party, enabled by the use of Blockchain. However, the proposed solutions do not address data protection in cases where an intruder has already accessed the system. This may be potential avenues for further research and inquiry.

POS40	Predicting Cognitive Performance Using Multimodal MR Neuroimaging—comparing classification performance of decision trees, SVM, and generalized linear models in children with perinatally-acquired HIV
Full names of Authors *Presenting Author	**Isaac L Khobo*,** Marcin Jankiewicz, Martha J Holmes, Francesca Little, Mark F Cotton, Barbara Laughton, Kaylee van Wyhe, Andre JW van der Kouwe, Allison Moreau, Emmanuel Nwosu, Ernesta M Meintjes, Frances C Robertson
Department	Human Biology

ABSTRACT:

It is not yet known how well a multimodal neuroimaging combination of structural magnetic resonance (MR) imaging (sMRI), diffusion tensor imaging (DTI), and proton MR spectroscopy (1H-MRS) predicts current or future cognitive outcomes of children with perinatally-acquired HIV (CPHIV). We compared the predictive ability of support vector machines (SVM), decision tree ensemble (DTE), and generalised linear models (GLM) on multimodal MRI in distinguishing classes of cognitive performance of CPHIV.

MATERIALS AND METHODS:

We studied 72 virally suppressed, 7-year-old CPHIV from the Children with HIV Early Antiretroviral trial and 55 controls from a related vaccine trial. All underwent sMRI, DTI, and 1H-MRS neuroimaging. Neuropsychological testing was conducted to assess psychomotor, receptive language, learning and attention domains. We grouped the children into 2 cognitive performance classes: low-to-normal and normal-to-high composite scores using hierarchical clustering, then used 10-fold cross validated SVM, DTE, and GLM on the MRI measures to predict class membership. Models were compared via cross-validation accuracy and the area under receiver operating characteristic curve (AUC).

RESULTS:

Performances were: SVM - 77% accuracy, 0.63 AUC, DTE - 76% accuracy, 0.64 AUC, and GLM - 57% accuracy, 0.51 AUC. Brain measures important in the prediction model included right posterior cingulate cortex thickness and gyrification, total choline in midfrontal grey matter, and axial diffusivity in the left hippocampal cingulum.

DISCUSSION::

Although predictive accuracy is only moderate, we provide a framework for using neuroimaging measures to predict cognitive performance in CPHIV and identify brain measures contributing to developmental issues over time.

POS41	A systematic review of research on coaches in rugby union and rugby league
Full names of Authors *Presenting Author	Sharief Hendricks, **Lara Paul***
Department	Human Biology

ABSTRACT:
Coaches play an instrumental role in the development of skills, knowledge, and cognitive processes of players. Coaches are key stakeholders in the implementation of any new training programme or intervention in rugby, whether it be for performance or injury prevention. As such, we need to learn and understand more about rugby coaches. The aim of this review is to synthesize the current literature on rugby union and rugby league coaches.

MATERIALS AND METHODS:
A systematic search using key words was done on five different databases (EBSCOhost, PubMed, Scopus, SPORTDiscus, Web of Science). The combined key words were 'coach*' AND 'rugby union' OR 'rugby league' OR 'rugby sevens'.

RESULTS:
Ninety studies were included in the final review, with the majority of studies focusing on rugby union while only twelve explored rugby league and only one explored rugby sevens. Furthermore, the studies were divided into categories. These categories include coach profession knowledge (67%), coach pedagogies (29%) and coach development (4%). Most of the studies used interviews or questionnaires to investigate coaches.

DISCUSSION:
This review showed that concussion knowledge of coaches has improved over the years. Education of coaches has simultaneously increased over the years to ensure that coaches have the knowledge to manage and act on serious injuries, such as concussions, appropriately. Another main finding from this review is that coaching is starting to shift from coach-centred learning to player-centred learning. Coaches are moving away from being the sole leader in the rugby team to encouraging players to have more responsibility, make decisions and solve problems on their own.

POS42	A pathway-based analysis of polymorphisms within angiogenesis-related genes and shoulder pain and disability in breast cancer survivors
Full names of Authors *Presenting Author	**Trevor S. Mafu*,** Alison V. September, Delva Shamley.
Department	Human Biology

ABSTRACT:

Shoulder pain and disability are well-documented sequelae of breast cancer treatment. Angiogenesis signalling may have a role in the development of shoulder pain or disability in breast cancer survivors. Moreover, angiogenesis signalling interacts with the regulation of structural components of the extracellular matrix and other signalling factors such as integrin beta 2. The aim of this study was to follow a pathway-based investigation of the interactive associations between polymorphisms within key angiogenesis-related genes, VEGFA, ITGB2 and COL5A1, and shoulder pain/disability following breast cancer treatment in women.

MATERIALS AND METHODS:

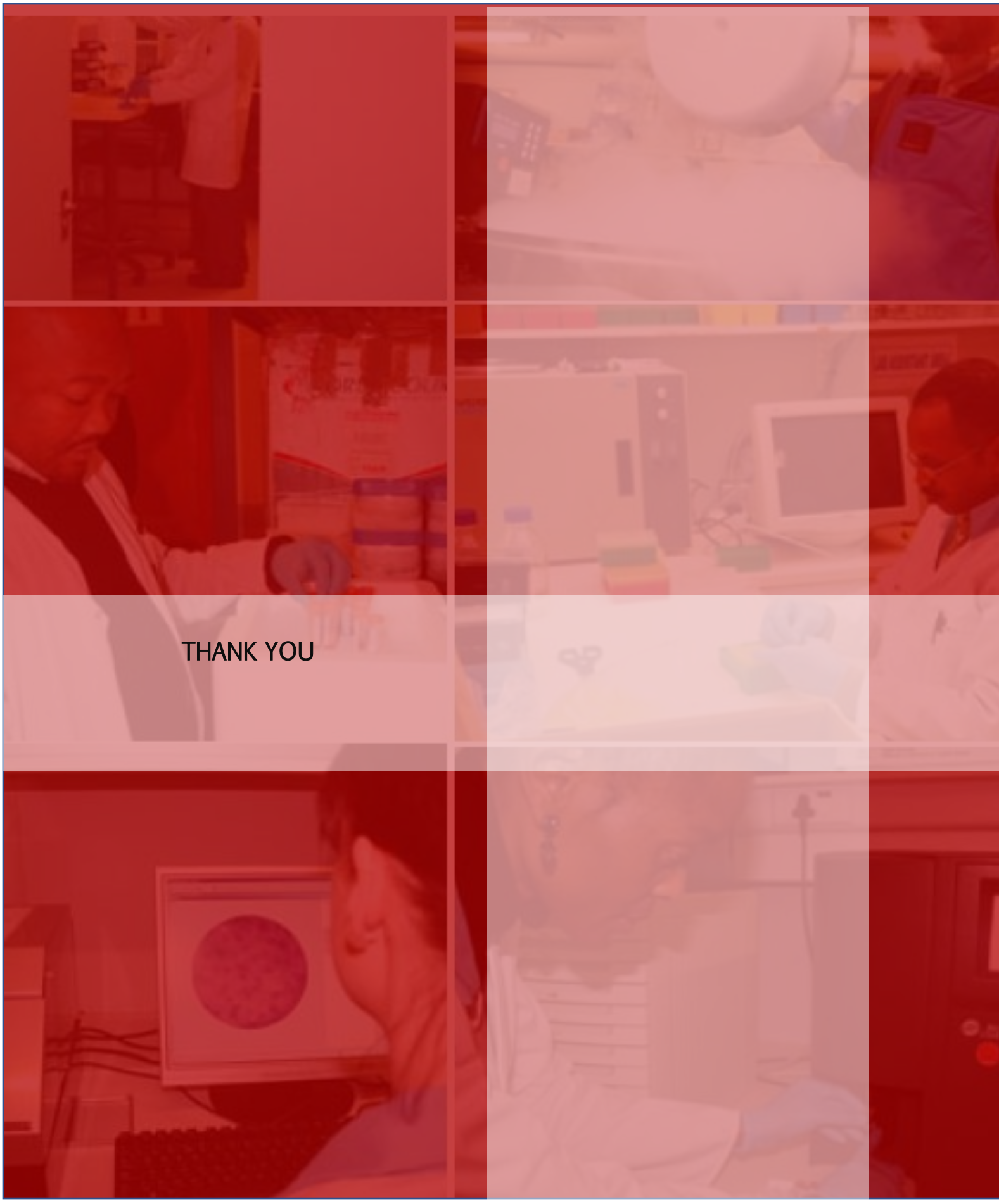
A cross-sectional study was conducted on 226 South African breast cancer survivors. We aimed to evaluate associations between shoulder pain/disability and six single nucleotide polymorphisms (SNPs) within three candidate genes: VEGFA (rs699947 A>C; rs1570360 G>A; rs2010963 G>C), ITGB2 (rs2230528 C>T) and COL5A1 (rs12722 C>T; rs13946 T>C). Participants were grouped into no–low and moderate–high shoulder pain/disability based on total pain/disability scores: ≤30 and >30, respectively, using the shoulder pain and disability index (SPADI).

RESULTS:

Despite that no independent genotype associations were noted for all SNPs, the T allele of ITGB2 rs2230528 C>T was associated with an increased risk of being in the moderate–high shoulder pain category (P=0.033; OR=1.770, 95% CI=1.050–2.970) after adjusting for significant covariates. In addition, several allele combinations among VEGFA, ITGB2 and COL5A1 SNPs were associated with risk (P<0.050) of being in the moderate–high shoulder pain or disability category.

DISCUSSIONS:

Our findings highlight that complex interactions in key genes may modulate risk of shoulder pain and disability in breast cancer survivors; Adding to the growing body of evidence implicating genetic factors in the development of such side effects. Future studies in independent populations with larger sample sizes are warranted to replicate our findings, further characterize the reported associations, and explore more complex interactions that modulate risk of shoulder pain and disability in breast cancer survivors.


THANK YOU