IMMUNOLOGY
AT THE CENTRE OF ONE HEALTH

10th ANNUAL CONFERENCE

30 October-01 November 2025
Garden Court Marine Parade, Kwazulu-Natal

South African Immunology Society

ABSTRACT BOOK

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2025 Local Organising Committee

Dr Luyanda Kwofie (Department of Immunology, National Health Laboratory Service) – Chairperson

Dr Sven Parsons (University of Pretoria) – Programme Chairperson

Prof. Theresa Rossouw,(Department of Immunology, University of Pretoria) – President of SAIS

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Prof. André van Niekerk (University of Pretoria)

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Contents

Words of welcome from the Conference Chairperson

Dear Fellow Immunologists,

It is my great pleasure to welcome you to the 10th South African Immunology Society Conference.

As Chairperson of this inspiring conference, I am honoured to host a gathering of over 90 scientists, researchers, and industry partners who share a commitment to advancing the field of immunology

This year's theme, "Immunology at the Centre of One Health", places our field exactly where it belongs – at the heart of global health, discovery, and innovation.

Get ready for one of the **biggest highlights on the immunology calendar**, where leading minds come together to exchange ideas, build collaborations, and push the boundaries of research across infectious diseases, primary immunodeficiency, allergy, rheumatology, transplantation, reproductive immunology, and veterinary medicine.

What to expect:

- 6 world-class plenary speakers sharing cutting-edge insights
- 80+ oral and poster presentations from rising and established experts
- 17 accredited CPD hours
- 6 dynamic scientific sessions
- 2 interactive workshops designed to sharpen your skills
- A programme built on diversity, inclusion, and collaboration

Beyond the science, this conference is about **connection and inspiration** – meeting old friends, forging new partnerships, and igniting fresh motivation for our vital work.

On behalf of the organising committee, I extend our warmest welcome and encourage you to actively engage in all aspects of SAIS2025. We wish you a memorable event and look forward to an inspiring and productive conference, and to creating lasting connections within our community, both scientifically and socially – enjoy your stay in Kwazulu-Natal!

Warm regards,

Dr Luyanda Kwofie
10th Annual SAIS Conference Chairperson

Welcoming address by the President of the South African Immunology Society

Dear distinguished colleagues, invited guests, partners, and friends of the South African Immunology Society.

It is both an honour and a profound pleasure to welcome you to the 10th Conference of the South African Immunology Society. This gathering marks not only a milestone in our Society's history but also a celebration of the growing impact of immunology - across disciplines, across borders, and across species.

Our theme this year, *"Immunology at the Center of One Health,"* reminds us that the immune system is more than a biological defence mechanism - it is a universal language connecting human, animal, and environmental health. As we navigate an era of pandemics, antimicrobial resistance, climate-driven disease, and ecological disruption, it becomes ever clearer that health is a shared responsibility.

Immunology lies at the very heart of that responsibility. It teaches us about balance, adaptation, and resilience: lessons that apply not only to our cells and systems but also to our scientific community. We, too, are part of an interconnected ecosystem: clinicians, veterinarians, environmental scientists, molecular biologists, and public health experts working together toward a healthier and more sustainable future.

This conference offers us the opportunity to reflect on what we have achieved, to showcase the extraordinary breadth of African immunology, and to strengthen collaborations that transcend institutional and national boundaries. Over the next few days, I encourage you to engage with openness, to challenge ideas constructively, and to share generously - for it is through these exchanges that innovation and progress emerge.

As President of SAIS, I am immensely proud of how far we have come. From our modest beginnings, we have built a vibrant, multidisciplinary community that continues to grow in scientific excellence and global relevance. Yet our greatest strength remains our sense of purpose: our shared commitment to harnessing immunological insight for the benefit of all life.

I would like to extend my deepest thanks to the organizing committee, our sponsors, and all of you - the participants - for making this conference possible. Your presence here affirms that immunology is not only a field of study, but a cornerstone of the *One Health* vision.

Let us use this 10th SAIS Conference as a platform for discovery, dialogue, and connection - and as an inspiration to keep immunology at the centre of solutions for a healthier world.

Welcome to the conference and thank you for being part of this journey.
Together, we are One Health - and immunology is at the centre.

Sincerely

Prof. Theresa Rossouw
President of the South African Immunology Society

With appreciation to the following people for their assistance during the conference

Session Chairpersons

Dr Luyanda Kwofie
Dr Sven Parsons
Dr Bongiwe Ndlovu
Dr Sabelo Hadebe
Prof. André van Niekerk
Dr Khanyisile Kgoadi
Dr Heena Ranchod
Dr Nancy Meulenberg
Dr Roanne Keeton

The oral and Poster adjudication committee

With appreciation to the KwaZulu-Natal Convention Bureau for sponsoring our Gala Dinner

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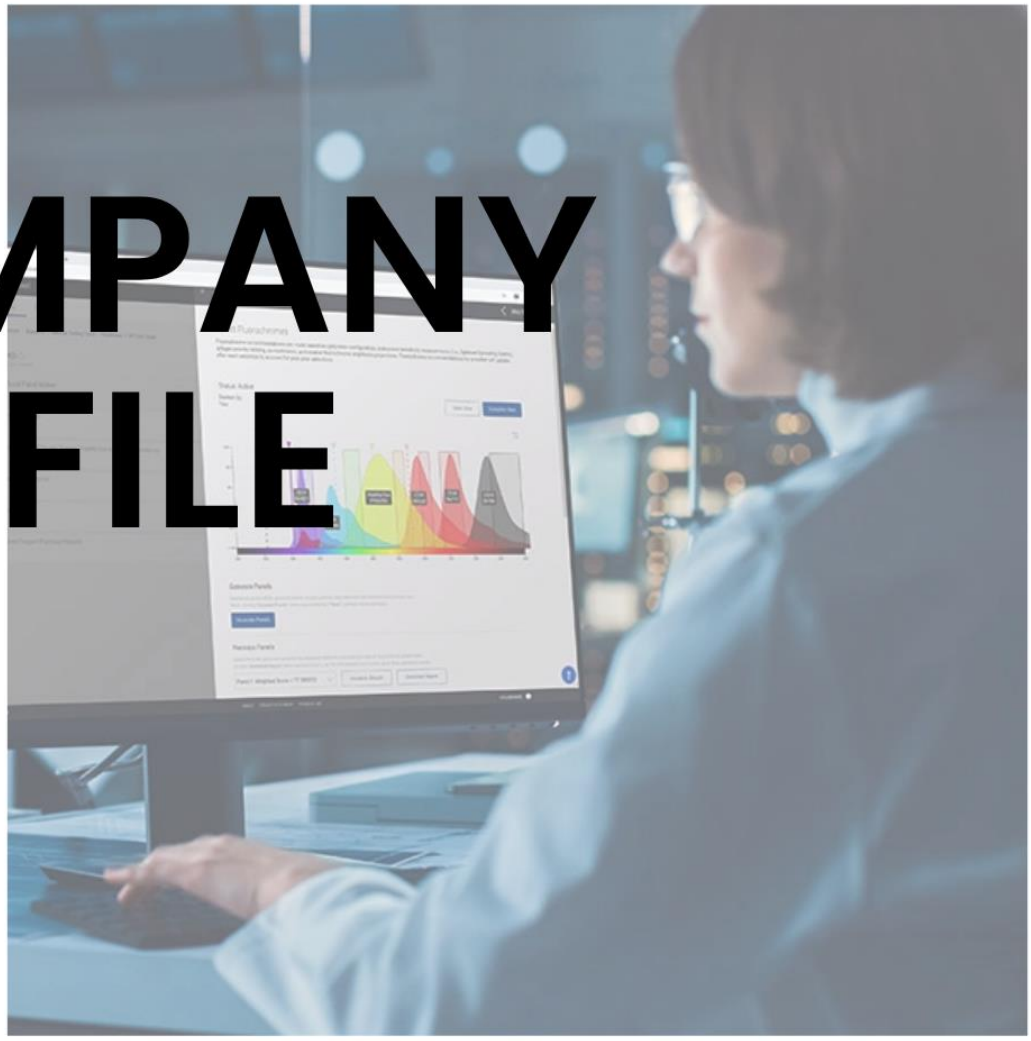

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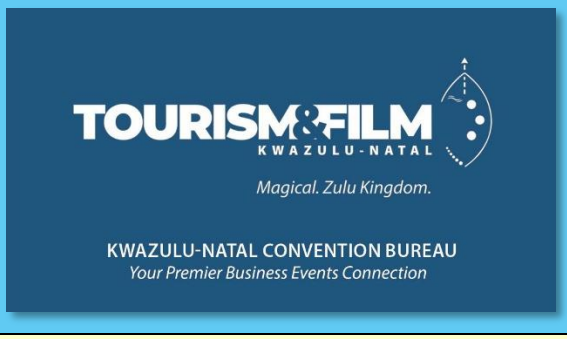
Programme Overview

DAY 1 – THURSDAY 30 OCTOBER		
07:30	Registration and arrival refreshments in the DHS 1 & 2 Foyer	
08:00	Pre-Conference Workshop - Immunological memory: A One Health approach	
10:00	Mid-morning Refreshments & Industry Networking in the Kearsney Room	
10:30	Workshop Continues	
12:30	Workshop wrap-up/outcomes	
13:00	Lunch in the Peppa Restaurant	
13:00	SAIS 2025 Conference Registration Opens	
Session 1 - Tolerance, Auto-Immunity & Allergy *Session Chair: Dr Luyanda Kwofie*		
Time	**Theme & Topic**	**Speaker**
15:00	Welcome and Introduction	Dr Luyanda Kwofie, Conference Chairperson
15:15	Opening Plenary Presentation **Systemic immune activation: lessons from viral infections in humans and animals**	Prof. Theresa Rossouw, University of Pretoria
16:00	[017] Investigating new immune mechanisms for severe asthma	Nontobeko Mthembu
16:10	[046] Bradykinin pathway dynamics in ACE inhibitor-induced angioedema: evidence of distinct endotypes in a South African cohort	Sarah Pedretti
16:20	Discussion / Questions and Answers	
16:30	**POSTER SESSION 1 & Mid-afternoon Refreshments (Glenwood & Hilton)**	
17:00	Close of Day 1	
17:00	Welcome Reception in the Exhibition Venue (Kearsney)	

DAY 2 – FRIDAY 31 OCTOBER		
07:30	Registration and arrival refreshments in the Kearsney Room	
Session 2 - Non-communicable diseases – inborn errors, lifestyle, diabetes, nutrition, cancer, reproduction *Session Chair: Dr Sabelo Hadebe & Dr Heena Ranchod*		
Time	**Theme & Topic**	**Speaker**
08:30	Plenary Session 1 **From fat to fate: Adipose-derived stromal/stem cells at the crossroads of obesity and cancer**	Prof. Melvin Ambele, University of Pretoria
09:15	[003] Establishing an in-house real-time polymerase chain reaction assay to quantify T-cell receptor excision circles and kappa-deleting recombination excision circles for use in screening newborn babies for inborn errors of immunity	Shudufhadzo S Singo

Time	Theme & Topic	Speaker
09:25	[038] *Datura stramonium* and *Catha edulis* extracts display cytoprotective activity in an SH-SY5Y Parkinson's disease cell model	Tidimalo Mogale
09:35	[052] Platelet activation and T-helper cytokine profiles in patients living with diabetes in sub-Saharan Africa	Bongani B. Nkambule
09:45	[041] The immunopathogenic mechanisms of severe cutaneous adverse drug reactions to first line anti-tuberculosis drugs	Phuti Choshi
09:55	Discussion / Questions and Answers	
10:05	Mid-morning Refreshments & Industry Networking in the Kearsney Room	
Session 3 - One Health Focus on Influenza *Session Chair: Dr Sven Parsons*		
10:45	Plenary Session 2 **How immunology can support bacterial vaccine development to help combat AMR**	Prof. Adam Cunningham, University of Birmingham
11:30	Seasonal drift and avian threats: Update on influenza in humans	Dr Nicole Wolter, NICD
11:50	Avian Influenza in South Africa: Patterns, pathways, and Public Health implications	Dr Lia Rotherham, ARC
12:10	Building vaccine sovereignty for the next pandemic	Prof. Wendy Burgers, University of Cape Town
12:30	Panel Discussion	
13:00	Lunch in the Peppa Restaurant	
Session 4 - Clinical and Diagnostic Immunology Workshop *Session Chair: Prof. André van Niekerk*		
14:00	Background: Vaccine response testing in clinical practice: why, what and when?	Prof. Theresa Rossouw
14:20	[067] Clinical immunology: awareness, structured laboratory evaluation, and immunogenetic sequencing are key in diagnosing & treating Inborn Errors of Immunity (IEI)	Prof. André van Niekerk
14:30	Case presentation: An HIV-non-infected child presents with bronchiectasis	Prof. André van Niekerk
14:35	Questions	
14:40	Vaccine response testing: why do we need alternative options?	Prof. André van Niekerk
14:50	Serotype specific vaccine testing: challenges & solutions	Dr Lizelle Nagel
15:10	Conclusion: Questions, discussion & formulation of a congress position statement	Congress Chair & Panel
15:30	**POSTER SESSION 2 & Mid-afternoon Refreshments (Glenwood & Hilton)**	
16:15	SAIS AGM	
17:30	SAIS AGM Ends	
17:30	Close of Day 2	
18:30	**Depart for Gala Dinner @ uShaka Marine World**	

19:00	**GALA DINNER @ Ushaka Marine World** • 19:00 – Arrival of Guests • 19:00 – Welcome mocktails & entertainment by Uzuko Marimba Band • 19:20 – Welcome by newly elected SAIS President • 19:30 – Starters served • 20:00 – Introduction of the Guest Speaker by the Conference Chair, ***Dr Luyanda Kwofie*** • 20:30 – Mains and dessert on buffet • 22:30 – End of event ***Sponsored by:*** 
22:30	**Busses return to the Garden Court**

DAY 3 – SATURDAY 01 NOVEMBER		
07:30	Registration and arrival refreshments in the Kearsney Room	
Session 5 - Infectious diseases (1) *Chair: Dr Nancy Meulenberg & Dr Bongiwe Ndlovu*		
Time	Theme & Topic	Speaker
08:30	Plenary Session 3 **The role of immunotherapy in achieving functional cures in people living with HIV**	Prof. Thumbi Ndung'u, University of KwaZulu-Natal
09:15	[012] Chimpanzee adenovirus vector-based vaccination: A promising approach for inducing T cell responses against HIV	Anele Mbatha
09:25	[077] Development of a novel serological assay capable of differentiating between animals vaccinated or naturally infected with lumpy skin disease virus	Antoinette van Schalkwyk
09:35	[022] HIV-1 reprograms t cell metabolism and inflammatory responses based on virus replicative capacity	Murunwa Maimela
09:45	[079] Brain antigen presenting cells and T cells promote regulated Th1 immune responses during central nervous system tuberculosis	Khanyisile Kgoadi
09:55	[064] How asymptomatic sexually transmitted infections alter the epithelial-immuno barrier of the penile genital tract	Cosnet Lerato Rametse
10:05	Discussion / Questions and Answers	
10:20	Mid-morning Refreshments & Industry Networking in the Kearsney Room **Guests to check out of Hotel**	

Session 6 - Infectious diseases (2) *Chair: Dr Khanyisile Kgoadi & Dr Roanne Keeton*		
11:00	Plenary Session 4 **Platelet activation and thromboinflammation in canine babesiosis**	Prof. Amelia Goddard, University of Pretoria
11:45	[023] Interleukin 4-induced gene 1 is a major tryptophan catabolising enzyme that regulates Type 2 immunity in a tissue-specific manner	Sabelo Hadebe
11:55	[049] CD68+ follicular macrophages harbour HIV reservoirs in human lymph node tissues during suppressive ART	Merantha Moodley
12:05	[034] Diabetes mellitus affects alveolar- and monocyte-derived macrophage effector function during latent tuberculosis	Tariq Webber
12:15	[050] Resistance to SARS-CoV-2 infection is not associated with pre-existing antibody responses to common cold coronavirus fusion peptides	Strauss van Graan
12:25	[055] Altered immune activation and function in antigen-presenting cells of South African HIV-1 elite controllers	Asisipo Mohamed Lekoloane
12:35	Discussion / Questions and Answers	
12:45	Awards & Prize Giving	Prof. Theresa Rossouw & Dr Luyanda Kwofie
13:00	Close of the Conference	
13:00	Lunch in the Peppa Restaurant & Depart at leisure	

Poster Session 1

30 October | 16:40-17:10

Abstract Nr.	Topic	Speaker
002	A comparative study of the effects of lopinavir and dolutegravir on the pro-inflammatory activities of human neutrophils *in vitro*	Atlehang K. Letsiri
005	The potential role of red blood cells in the innate immune response to Mycobacterium tuberculosis	Kondwani Alyce Kapisa
006	Immunological features associated with the development of broadly neutralizing antibodies and Fc-effector functions in people living with HIV-1 subtype C	Hlelolwenkosi Z. Mlimi
009	Migration of intestinal CD4+ T cells promote vaginal eosinophil accumulation following hookworm infection	Alisha Chetty
010	Characterization of activin expression and its role in host immune responses in a murine model of cutaneous leishmaniasis	Gina de Klerk
013	Identification of somatic hypermutations responsible for the development of neutralization breadth in an HIV-1 N332-directed antibody lineage	Nomcebo Shusha
014	Exploring gartanin and long non-coding RNA-286 as a host-directed drug therapy for tuberculosis	Whoghuwah Muntonia Heidi Makena
015	Optimization of BD flow cytometer high throughput sampler (HTS) system loader settings for high-throughput laboratories and rare cell analysis	Saleha Omarjee
016	Interleukin 4-induced gene 1 regulates Type 2 immunity during Schistosoma mansoni infection	Nomthandazo Msipha
019	Regulators of neuroimmune function in the manifestation of Central Nervous System Tuberculosis in the absence of microglia	Limpho Thipane
020	Enhancing the reliability of immune cell-type identification in scRNA-seq through improved damaged cell quality control	Alicen Joy Henning
021	Novel insights into the biology and functional relevance of innate lymphoid type 2 cells in cutaneous leishmaniasis using a mouse model of infection	Laura Emery
029	Comparative immunogenicity of reduced vs. standard dose *Brucella abortus* S19 vaccine in cattle administered via different routes	Itumeleng Moeketsi and Lehlohonolo Tabane
031	Antemortem diagnosis of *Mycobacterium bovis* infection in African lions (*Panthera leo*)	Rachiel Gumbo
032	Rural cattle as reservoirs of zoonotic mycobacteria: genomic insights from KwaZulu-Natal, South Arica	Tristen Lourens
035	TB and the male sex bias: Investigating the effect of sex hormones on mycobacterial killing *in vitro*	Raadhiyah Mathee
036	The impact of inflammatory and metabolic breast milk profiles associated with maternal HIV on infant growth and development	Tafadzwa Nerwande
037	Host responses to chikungunya infection and their association with long-term arthritis	Mario Rankin

Abstract Nr.	Topic	Speaker
039	Characterization of T cell immune responses to SARS-CoV-2 and cross-reactivity to variants of concern in South African children	Ntombi S.B. Benede
040	Investigating the process of neutrophil extracellular trap formation using imaging and cytometric techniques	Claudia C. du Plessis
042	The effect of cationic DNA-binding proteins on HIV-1 latency	Senzo Cebekhulu
043	Characterization of antigens to assess T cell responses in the HVTN 605 TB vaccine trial	Boitumelo Mosito

Poster Session 2

31 October | 15:30-16:00

Abstract Nr.	Topic	Speaker
044	Phenotyping positive sequential additive challenge reactions following severe cutaneous adverse reactions to anti-TB medications	Rose Selim
045	Insulin-like growth factor 1 (IGF-1) signalling in tuberculosis and tuberculosis/diabetes co-morbidity	Thobekile S. Leyane
047	*In vitro* immunomodulatory effects of African traditional medicines in H1299-ACE2 cells co-cultured with peripheral blood mononuclear cells in response to SARS-CoV-2 infection	Ata Thabo Mokoena
048	Characterization of the naïve B-cell repertoire and antigen-specific precursors in South African populations	Zama Dlamini
053	Investigating the function of host gene factors in *listeria monocytogenes* infection	Robert Ruhangariyo
054	Targeting the monocyte: lymphocyte ratio and osteopontin as potential diagnostic markers for TB disease and treatment response	Bongani Motaung
056	Evolution of the extensively mutated SARS-CoV-2 BA.3.2 Omicron subvariant	Zesuliwe Jule
057	Assessing the burden of dengue virus infection in northern KwaZulu-Natal, South Africa	Siphokazi Silangwe
058	Variations in HIV-1 subtype C env sequences and neutralization sensitivity between lymph nodes, peripheral blood mononuclear cells and plasma-derived sequences	Keyura Velan
060	Evaluating the immunomodulatory potential of atorvastatin in reducing inflammation and tissue damage post-tuberculosis treatment	Jesse R. Conradie
061	Cytomegalovirus infection in preterm and HIV-exposed infants: a prospective South African cohort study	Tariq Webber
063	Phenotypic profiling of TST-induced local T cell immune responses in Mtb-exposed individuals	Mahlatse K. Maseeme
065	Seroprevalence of pre-existing neutralising antibody responses to clinically relevant adenoviruses in a Southern African population	Mamodiane Anna Patjane
066	Oral pre-exposure prophylaxis does not modulate lymphoid/myeloid HIV target cell density in the foreskin: results from the CHAPS clinical trial	Cosnet Lerato Rametse

Abstract Nr.	Topic	Speaker
068	Association between total IgE levels and multiple allergen sensitizations in patients undergoing allergy testing at a tertiary immunology laboratory	Lucas Tabata
069	Association of aldosterone, protein levels, and inflammatory markers in Angora Goats affected by Swelling Disease	Refilwe Bokaba
073	Animal-friendly diagnostic reagents: a renewable, universal source based on avian genes	Jeanni Fehrsen
074	Host proteins associated with strong neutralizing antibody responses to SARS-CoV-2 infection	Afrah Khairallah
075	Mechanisms driving colorectal cancer (CRC) formation and differentiation in people with HIV (PWH)	Bronwyn L. Ramsamy
078	Immune activation and thrombotic risk in African adult patients with B-cell acute lymphoblastic leukaemia on maintenance therapy	Zekhethelo A. Mkhwanazi
080	Antibody responses elicited by different SARS-CoV-2 vaccines: Durability and impact of HIV infection	Shannon Ramkistan
081	BactiVac, the Bacterial Vaccines Network	Jamie Pillaye

Participant Information

Your Event Squad

Ms Corné Engelbrecht
+27 82 925 9241

Ms Melanie Pretorius
+27 82 410 1202

Venue

The conference will take place at the Garden Court Marine Parade in KwaZulu-Natal.

- Registration – DHS 1 & 2 Foyer
- Workshop Venue – DHS 1 & 2
- Plenary Venue – DHS 1 & 2
- Poster Venue – Glenwood & Hilton
- Exhibition & Refreshment Venue – Kearsney
- Lunch – Peppa Restaurant
- Gala Dinner – uShaka Marine World

Registration Information

Each participant must register in person at the Registration Desk to collect a Conference kit and badge before attending any of the sessions or events.

Registration Times

- Thursday 30 October, 07:30-08:00 – Registration for the Pre-Conference Workshop
- Thursday 30 October, 13:00-14:30 – Registration for the SAIS 2025 Conference Registration opens
- Friday 31 October, 07:30-08:30 – Registration
- Saturday 01 November, 07:30-08:30 – Registration

Badges

Identification badges are required for admission to all sessions, official functions, and social events of the conference. Participants who lose their badges must report to the Registration Desk, presenting proof of identity.

CPD

The conference has been accredited for 17 CPD points. A kind reminder to scan the CPD QR **on each morning** of your attendance to be able to claim CPD points.

Attendance Certificates

Attendance certificates will be distributed electronically after the conference.

Presenters, Chairs & Facilitators

All speakers are required to report to the Registration Area at least 60-minutes before their presentation to ensure that we have uploaded the correct presentation onto the presentation laptop in the respective venues. If you are not attending the full day of your presentation or the full conference, please arrive at least 2 hours before your presentation to ensure the correct version has been uploaded onto the presentation laptop in the venue.

Poster Presentations

POSTERS WILL BE ON DISPLAY DURING THE FULL CONFERENCE IN THE GLENWOOD AND HILTON ROOMS.

1. Poster Session 1 – Thursday 30 October, 16:30-17:00
2. Poster Session 2 – Friday 31 October, 15:30-16:00

- Setup Posters – Wednesday 29 October, 15:00-17:00 & Thursday 30 October, 07:00-08:00
- Take Down – Saturday 01 November, from 11:00-13:00

Presenters are requested to be at their posters during their assigned times to present their work.

All posters not removed by the designated times will be subject to disposal.

Exhibitors

EXHIBITORS WILL BE ON DISPLAY DURING THE FULL CONFERENCE IN THE KEARSNEY ROOM.

All exhibitors will be provided with one trestle table, one table cloth and two chairs.

- Setup: Wednesday 29 October, between 13:00-17:00
- Breakdown: Saturday 01 November, from 11:00-13:00

Welcome Reception

Thursday 30 October from 17:15-19:00

Kearsney Room

Attendance to the Welcome Reception is included in your registration fees. Join us on Thursday 30 October in the Exhibition venue for some light refreshments and drinks.

Official Gala Dinner – pre-registration required

Friday 31 October from 18:30-22:30

uShaka Marine World

If you pre-registered for the Gala Dinner at uShaka Marine World, you will have an ORANGE dot on your name badge, indicating the number of tickets purchased. Tickets to the Gala Dinner can unfortunately not be purchased on site.

IMPORTANT:

- Registration for the Gala Dinner is closed.
- This is a ticketed event and pre-registration is required. If you have registered to attend, you will have ORANGE dot on your name badge.
- Busses will depart from the Garden Court Marine Parade at 18:30 and will return to the hotel at 22:00.
- Dress Code: **Cocktail / Traditional**

Conference Onsite Service

Meals and Snacks

Arrival, mid-morning, mid-afternoon, lunch and beverages will be provided to attendees as indicated in the programme, during Conference times. All additional meals will be for the attendees' own account. The Welcome Reception on Thursday 30 October is included in your registration fee.

Emergency Medical Assistance

For assistance with any medical emergencies, please visit the Registration area. Medical procedures and medicine will be for the attendee's own account. For any medical emergencies, please contact +27 (0) 82 925 9241 during conference hours.

Safety and Security

In the interest of personal safety and security, attendees should only display their identity tags in the conference area premises and within the restricted conference areas.

Lost property can be handed in at the Registration Desk. Any losses should be reported to the Conference Organisers.

Although every effort will be made to retrieve lost personal belongings, the responsibility for securing his/her personal belongings remains that of each person attending the conference.

Accommodation and Transport

IMPORTANT: Excluding sponsored participants, all accommodation and transport arrangements will be for your own account.

Dress Code

The suggested dress code for the conference is business casual, but please do bring something warm along as the rooms will be air-conditioned.

Disclaimer

The programme is correct at the time of publishing. The organisers reserve the right to delete, modify or alter items from the programme or to delete, modify or alter any aspect of the Conference timetabling and delivery at their sole discretion and without notice. Neither the host organisation(s) nor the Conference Organisers will accept any liability for any loss or inconvenience caused to any party consequent to such changes.

Code of Conduct

The Organiser and Host/s of SAIS 2025 (the "Event") reserve the right to remove from the venue/Event at any time any attendee deemed to be causing, or potentially causing, a disturbance or exhibiting disruptive or inappropriate behaviour. Such removal does not constitute a right to refund of any fees paid.

Liability

Neither the Conference Organisers nor any of its contracted service providers will be responsible for the safety of articles of any kind brought into the Conference facilities by attendees, whether registered or not, their agents, contractors, visitors and/or any other person/s whatsoever. The Conference attendee shall indemnify and not hold the organisers and associates of the organisers and their subcontractors liable in respect of any cost, claims, demands and expenses as a result of any damage, loss or injury to any person howsoever caused as a result of any act or default of the Conference Organisers or a person representing the Conference Organisers, its contractors, or guests. In addition, the Conference attendee shall take all necessary precautions to prevent any loss or damage to his/her property with special regard to mobile phones, carry or handbags and computing equipment.

Contents

Plenary Presentations

Opening Plenary Presentation - Systemic immune activation: lessons from viral infections in humans and animals

Prof. Theresa Rossouw *MBChB, MPH, DPhil, PhD*

Acting Head of Department, Department of Immunology, Faculty of Health Sciences University of Pretoria; Chairperson: Faculty of Health Sciences Research Ethics Committee; President: South African Immunology Society - theresa.rossouw@up.ac.za

Systemic immune activation is a critical factor in viral pathogenesis across both human and animal hosts; however, the resultant effects can vary due to differences in viral adaptation, host immune history, and specific inflammatory responses. In humans, particularly during zoonotic infections, there is often a more detrimental "neopathogenesis" as the immune system encounters a novel virus. In contrast, animals may experience an adapted "orthopathogenesis" within their natural reservoirs or exhibit a more generalized response in laboratory models. A significant distinction lies in the potential for severe, and at times chronic, immune activation in humans, as observed in influenza A infection and HIV respectively, which is less prevalent or presents differently in animal models. This presentation will examine several underlying immune pathways that contribute to systemic immune activation and could inform potential therapeutic strategies.

***

Biography: Professor Theresa Rossouw describes herself as a clinician first and foremost, though she has been involved in research at the University of Pretoria (UP) since 2008. She says she conducts research so that the treatment and outcomes of patients can be improved. Prof Rossouw leads the research of the HIV Immunopathology Laboratory, working on understanding the pathophysiology of HIV infection, especially with regard to ongoing systemic immune activation and inflammation. This has been associated with the development of long-term complications such as heart disease, neurocognitive dysfunction, renal disease, drug resistance; and the effect of in utero HIV exposure on the immunological, neurological and growth development of infants. Prof Rossouw says her academic role model is Prof Ronald Anderson (retired HOD of UP's Immunology Department, who still works in a post-retirement UP position), who is "the epitome of a true academic": fiercely intelligent and greatly accomplished, yet humble, generous with his time and always willing to assist and mentor. She adds that her research matters as it aims to improve the outcomes of patients with dreaded conditions. "I have special empathy for potentially vulnerable people, such as pregnant women and children living with HIV, and I strive to improve their well-being." She hopes to empower a new generation of researchers, especially female researchers, to embrace the incredible opportunities offered by science. Her advice to school learners and undergraduates is to never give up on their dreams. Her interests are philosophy, literature, travel, wine, jogging and gardening.

Thursday 30 October – 15:15

Plenary 1 - From fat to fate: Adipose-derived stromal/stem cells at the crossroads of obesity and cancer

Prof. Melvin Ambele

Associate Professor in the Department of Oral and Maxillofacial Pathology at the School of Dentistry, University of Pretoria - melvin.ambele@up.ac.za

Adipose-derived stromal/stem cells (ASCs) play a central role in lipid metabolism and immune modulation, with implications for both obesity and cancer metastasis. This study integrates transcriptomic profiling of human ASCs during adipogenesis with in vivo models to identify key molecular regulators. The solute carrier SLC7A8 emerged as a novel adipogenic factor, with knockout mice showing resistance to diet-induced obesity, improved glucose tolerance, and depot-specific metabolic adaptations. Parallel investigations in a spontaneous breast cancer model revealed that murine ASCs influence the metastatic microenvironment, reducing lung metastases and altering cytokine profiles. These findings highlight the dual role of ASC-mediated lipid-handling processes in modulating metabolic and metastatic pathways—particularly involving SLC7A8 and CD36—as promising therapeutic targets to address metabolic dysfunction and metastatic progression.

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Biography: Prof. Melvin Ambele is an Associate Professor in the Department of Oral and Maxillofacial Pathology at the School of Dentistry, University of Pretoria. He is a distinguished researcher with specialized expertise in translational research, focusing on the molecular and genetic aspects of cancer and obesity, with active national and international collaborations. Prof. Ambele serves as an Academic Editor for *PLOS ONE*, a Guest Editor for *Frontiers in Genetics*, and has authored over 40 peer-reviewed publications, including book chapters. In addition, he is deeply committed to teaching and lectures in undergraduate and postgraduate Health Sciences modules at the University of Pretoria. He is a key member of the School of Dentistry's PhD Committee and the Faculty of Health Sciences Research Ethics Committee. He supervises and mentors young research fellows, postdoctoral fellows, PhD, and MSc students across diverse disciplines, including Dentistry, Genetics, Pharmacology, and Medical Immunology. Prof. Ambele is a member of several professional scientific organizations, including the African Society of Human Genetics (AfSHG), the African Society of Dental and Craniofacial Genetics (ASDCG), the American Society of Human Genetics (ASHG), and the New York Academy of Sciences (NYAS).

Friday 31 October – 08:30

Plenary 2 - How immunology can support bacterial vaccine development to help combat AMR

Prof. Adam Cunningham

Professor of Functional Immunity & Director of BactiVac, University of Birmingham, UK - a.f.cunningham@bham.ac.uk

Biography: Adam Cunningham gained his PhD from University of Southampton for studies on antibody responses to Chlamydia pneumoniae. He then moved to the University of Birmingham to study how antibody responses develop and are regulated. This work developed to include how helpful and harmful immune responses develop to Salmonella and its antigens. Adam is also the Director of BactiVac, the Bacterial Vaccines Network which was established in August 2017.

Friday 31 October – 10:45

Plenary 3 - The role of immunotherapy in achieving functional cures in people living with HIV

Prof. Thumbi Ndung'u

Africa Health Research Institute and University of KwaZulu-Natal - thumbi.ndungu@ahri.or

Antiretroviral therapy (ART) can reduce morbidity and mortality but does not eradicate HIV. Combination approaches using ART and immunotherapies are showing some promise in inducing HIV remission. We characterised immune profiles and reservoir characteristics in women who initiated ART in acute versus chronic HIV infection and conducted a phase 2a HIV cure study to evaluate the safety of a regimen of 2 broadly neutralizing antibodies (bnAbs), VRC07-523LS and CAP256V2LS, and a TLR7 agonist, vesatolimod (VES), who started on ART in acute infection in South Africa (NCT05281510). We identified and longitudinally followed women identified with acute HIV-1 infection. Twenty women who started ART in acute HIV infection, who were suppressed on ART for ≥12 months and sensitive to at least 1 bnAb, were enrolled into the clinical trial. Participants received up to 10 oral doses of VES (6 mg, dose escalation to 8 mg) every 2 weeks starting on day 0 and IV infusions of VRC07-523LS (20 mg/kg) and CAP256V2LS (20 mg/kg) on day 7. Participants began an analytical treatment interruption (ATI) on day 35 and remained off ART until day 336 or until they met ART restart criteria (HIV-1 RNA ≥1000 copies/mL for 8 consecutive weeks and without a drop of 0.3$\log_{10}$; or confirmed HIV-1 RNA >100,000 copies/mL; or confirmed CD4 count <350 cells/µL). The primary endpoint was safety. Secondary endpoints included time to viral rebound (HIV-1 RNA >200 copies/mL), time to ART restart, and pharmacokinetics. Early ART was associated with lower levels of CD4 T cell activation, lower reservoir size and lower inducible reservoir after one year of ART compared to chronic treatment. Among 20 women enrolled into the ATI-inclusive clinical trial, there were no treatment-related serious adverse events. Three distinct virological outcomes were noted namely early restart (ER; <16 weeks, n=7), delayed restart (DR; 16-44 weeks, n=7), and long-term delayed restart or virologic control (LTDR; >44 weeks, n=6). Eight participants had evidence of partial virologic control with oscillating rebound, characterized by fluctuating levels of viremia with periods of undetectable viral load. This first-in-Africa HIV cure trial demonstrates that complex cure studies can be successfully conducted in resource-limited settings with great unmet need. VES, VRC07-523LS, and CAP256V2LS were safe and well tolerated in acutely treated South African women. Potential mechanisms for the variable patterns of virologic control observed in this novel study are under investigation.

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Biography: Thumbi Ndung'u is a faculty member at the Africa Health Research Institute (AHRI) in Durban, South Africa; Professor and Victor Daitz Chair in HIV/TB Research at the HIV Pathogenesis Programme, University of KwaZulu-Natal; Programme Director for the Sub-Saharan African Network for TB/HIV Research Excellence (SANTHE); Professor of Infectious Diseases at University College London, UK; Associate Member of the Ragon Institute; Adjunct Professor of Immunology and Infectious Diseases at Harvard T.H. Chan School of Public Health; and Provost's Visiting Professor of HIV Virology and Immunology at Imperial College London, UK. He graduated with a Bachelor of Veterinary Medicine degree from the University of Nairobi, Kenya, completed a PhD in Biological Sciences in Public Health from Harvard University, USA and performed post-doctoral research in Virology at Harvard Medical School. He is the recipient of several awards for scientific excellence and leadership contributions, including the South African Medical Research Council Gold Scientific Achievement Award, the Leadership Award in Public Health Practice from the Harvard T. H. Chan School of Public Health, and the KT Jeang Retrovirology Prize in recognition of outstanding work on HIV. He is a member of the Academy of Science of South Africa, a fellow of the African Academy of Sciences and a member of the United States National Academy of Medicine. Ndung'u has received grant funding from the Bill and Melinda Gates Foundation, the Wellcome Trust, the Science for Africa Foundation, the Howard Hughes Medical Institute, the South African National Research Foundation, the National Institutes of Health, and others. He has mentored more than 50 postgraduate students and has a special interest in capacity building for biomedical research in Africa. He has co-authored more than 320 original research publications. His research focuses on understanding interactions between HIV and the immune system and how these may be harnessed and translated for HIV prevention or cure.

Saturday 01 November – 08:30

Plenary 4 - Platelet activation and thromboinflammation in canine babesiosis

Prof. Amelia Goddard *BVSc BVSc(Hons) MMedVet PhD*

Department of Companion Animal Clinical Studies, Faculty of Veterinary Science, University of Pretoria - amelia.goddard@up.ac.za

Immunothrombosis is a physiological defence mechanism whereby the innate immune and haemostatic systems collaborate to restrict pathogen dissemination. When dysregulated, this process evolves into thromboinflammation, a maladaptive state characterised by excessive activation of coagulation and inflammation, resulting in microthrombus formation and organ dysfunction. *Babesia rossi* infection, a severe tick-borne haemolytic disease, elicits a pronounced proinflammatory response accompanied by marked coagulation abnormalities. Complications frequently include disseminated intravascular coagulation (DIC), multiorgan failure, and death. Poor clinical outcomes have been associated with the presence of DIC and widespread capillary microthrombosis. Despite severe thrombocytopenia, dogs infected with *B. rossi* typically do not exhibit spontaneous bleeding at presentation. Instead, platelet activation and the formation of platelet-leukocyte aggregates contribute to tissue factor expression, endothelial cell injury, and neutrophil extracellular trap (NET) formation, establishing a self-perpetuating prothrombotic cycle. Transmission electron microscopy (TEM) of thrombi from affected dogs reveals extensive platelet activation, with large platelet aggregates, numerous pseudopodia, and early microvesicle release. Extensive platelet membrane fragmentation observed already during early clot formation may further enhance thrombogenic potential and influence thrombus resolution and platelet clearance. Thromboelastography (TEG) demonstrates delayed clot initiation and propagation, reflecting the significant depletion of coagulation factors present in these dogs; some that are more severe in dogs that did not survive. Antithrombin activity is markedly reduced, reinforcing a hypercoagulable and proinflammatory state. Despite severe thrombocytopenia and factor consumption, overall clot strength remains preserved due to the combined effects of platelet activation and hyperfibrinogenemia.

Evidence of fibrinolytic shutdown includes low TEG fibrinolysis variables and increased α2-antiplasmin activity. TEM analysis further reveals a predominance of thin, densely packed, highly branched fibrin fibres that progress to thick, matted bundles, consistent with increased clot rigidity, reduced deformability, and resistance to fibrinolysis, resulting in more occlusive thrombi. In summary, dogs with *B. rossi* infection exhibit profound dysregulation of immunothrombosis leading to thromboinflammation. This state is characterised by thrombocytopenia, platelet hyperactivation, coagulation factor consumption, antithrombin depletion, and impaired fibrinolysis, culminating in persistent microvascular thrombosis. These findings underscore the central role of thromboinflammation in the pathogenesis, severity, and fatal outcomes of canine babesiosis and parallel mechanisms recognised in severe human infectious diseases.

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Biography: Amelia Goddard is a Professor in Veterinary Clinical Pathology in the Department of Companion Animal Clinical Studies, Faculty of Veterinary Science, University of Pretoria. After 6 years in small animal practice, she returned to academia as a lecturer and completed a specialist residency in Veterinary Clinical Pathology. For her PhD degree she investigated "Biomarkers of haemostatic and inflammatory changes in canine babesiosis". She has presented over 65 international scientific congress presentations and has delivered more than 50 regional and national CPD lectures. She currently has 78 publications in peer-reviewed journals and has written three book chapters. She has a C1 NRF rating. Her main research interest is investigating thromboinflammation in systemic inflammation, using various animal models such as canine babesiosis, canine parvovirus enteritis, canine spirocercosis, snake envenomation, African horse sickness and cancer in dogs.

Saturday 01 November – 11:00

Oral Presentations as they appear in the Programme

Thursday 30 October 2025

Pre-Conference Workshop

Immunological memory: A One Health approach

Dr Sven Parsons[1], Dr Roanne Keeton[2] & Prof. Melvin Ambele[3]

[1]*Extraordinary Lecturer, Department of Anatomy and Physiology, Faculty of Veterinary Science, University of Pretoria – sven.parsons@up.ac.za*
[2]*Senior Research Scientist and viral immunologist based in the Division of Virology at the University of Cape Town - roanne.keeton@uct.ac.za*
[3]*Associate Professor in the Department of Oral and Maxillofacial Pathology at the School of Dentistry, University of Pretoria - melvin.ambele@up.ac.za*

The Workshop will explore the mechanisms and significance of immunological memory across humans, animals, and the environment. This interdisciplinary workshop highlights how memory responses to infections and vaccinations impact health outcomes in diverse species, emphasizing shared challenges and collaborative strategies in the context of zoonotic diseases, emerging pathogens, and global health. By integrating veterinary, medical, and ecological perspectives, the session promotes a holistic understanding of immune memory to inform more effective and sustainable health interventions.

Key Topics:

1. Immune Regulation, Tolerance, and Exhaustion
2. Long vs Short-Term Memory in Response to Infection and/or Vaccination
3. Variation/Outcome in T vs B Cell Memory Response to COVID Vaccination (Obesity, ageing, etc.)
4. Original Antigenic Sin (OAS)

Thursday 30 October – 08:00-12:30

Session 1 - Tolerance, Auto-Immunity & Allergy

[017] Investigating new immune mechanisms for severe asthma

Nontobeko Mthembu[1], Nomthandazo Msipha[1]; Ephie Geza[1,2]; Frank Brombacher[1] & Sabelo Hadebe[1]

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[2]*Division of Computational Biology, Department of Integrative Biomedical Sciences, University of Cape Town, South Africa*

Asthma is a complex and multifaceted disease with multiple distinct endotypes, some of which respond poorly to corticosteroids (CSs), the primary treatment approach. Therefore, efforts to enhance existing asthma therapeutics have explored various avenues including monoclonal antibody therapeutics. However, the heterogeneous nature of asthma, where patients may exhibit Th2/eosinophilic, neutrophilic, mixed granulocytic, or paucigranulocytic inflammation, renders standard and interventional treatments ineffective for many individuals. To investigate the mechanisms underlying steroid-insensitive severe asthma, we sensitised and intranasally challenged mice with house dust mites

(HDM) combined with 2',3'-cyclic dimeric adenosine monophosphate (c-di-AMP). This model mimics the airway inflammation observed in asthmatic patients. Immune responses, pathology, and airway hyperresponsiveness were evaluated using flow cytometry, ELISA, and histology, alongside RNA sequencing to examine disease-associated gene expression patterns. Additionally, we investigated the role of IL-4i1 deficiency (IL-4i1$^{-/-}$) in severe asthma using IL-4i1$^{-/-}$ mice. Our findings revealed a mixed eosinophilic/neutrophilic inflammation in adult mice. Notably, neutrophilic inflammation in mice demonstrated poor responsiveness to dexamethasone, indicating a degree of steroid insensitivity. Furthermore, RNA sequencing identified key genes involved in severe asthma, including *Cyp1a1*, a downstream target of IL-4i1, which plays a pivotal role in modulating airway inflammation in mice. The absence of IL-4i1 exacerbated airway inflammation, underscoring its role as a critical immunoregulator. These findings highlight the importance of understanding the diverse forms of severe asthma and their various molecular mechanisms that contribute to steroid insensitivity. Further research is essential to advance the development of precise and effective treatment strategies tailored to disease's varying forms.

Thursday 30 October – 16:00

[046] Bradykinin pathway dynamics in ACE inhibitor-induced angioedema: evidence of distinct endotypes in a South African cohort

Sarah L Pedretti[1] & Diamante Ngoie[2] & Sumayah Salie[3] & Nokukhanya Tenza[4] & Min-ghah Kariem[5] & Jonathan G Peter[6]

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Angiotensin-converting enzyme inhibitor-induced angioedema (ACEi-AE) is a rare but potentially life-threatening adverse drug reaction. It is thought to result from the accumulation of vasoactive peptides, primarily bradykinin (BK) and substance P (SP), due to impaired enzymatic degradation. To investigate the pathophysiology of ACEi-AE by measuring plasma levels of BK and SP, threshold-stimulated plasma kallikrein (TSK) activity, and serum tryptase during acute and recovery phases. We analysed samples from 32 ACEi-AE patients during acute angioedema episodes and again at follow-up (3–6 months post-attack). BK and SP levels were quantified using ELISA. TSK activity, reflecting contact system sensitivity, was assessed via fluorometric assay. Serum tryptase was measured using UniCAP-Tryptase fluoroimmunoassay. Overall, plasma BK levels did not differ significantly between acute and follow-up phases. However, patients segregated into two subgroups: 50% had elevated BK during the acute episode ("BK-high"), while 50% had lower BK levels ("BK-low"). Plasma TSK activity was significantly higher in the BK-high group (2.00 ± 2.26 vs 0.88 ± 0.90 nmol/min/mL). In contrast, serum tryptase levels were elevated in the BK-low group (6.8 ± 3.1 vs 4.3 ± 2.5 µg/L), suggesting a distinct, possibly mast cell–mediated mechanism. Plasma SP levels remained unchanged across groups. These findings support the hypothesis of heterogeneous pathophysiological mechanisms in ACEi-AE, with distinct BK-driven and non-BK-driven phenotypes. Further biomarker-driven research is essential to improve diagnosis, risk stratification, and management in diverse patient populations, particularly in African settings.

Thursday 30 October – 16:10

[003] Establishing an in-house real-time polymerase chain reaction assay to quantify T-cell receptor excision circles and kappa-deleting recombination excision circles for use in screening newborn babies for inborn errors of immunity

Shudufhadzo Singo[1], Pieter W.A. Meyer[1,2], Catherine M. Worsley[1,2] & Luyanda L.I. Kwofie[1,2]

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Inborn errors of immunity (IEI) are genetic disorders that hinder immune responses and are underdiagnosed, particularly in large populations. These disorders occur in one in every 500 live births. Early detection is crucial to prevent health complications. The need for early detection of IEI has led to the development of newborn screening (NBS) programs, but many countries lack routine NBS due to financial and technological challenges. This study developed an in-house screening technique for T-cell receptor excision circles (TREC) and kappa-deleting recombination excision circles (KREC) quantification using real-time polymerase chain reaction (PCR) to screen IEI in newborn babies. The study developed an in-house real-time PCR technique to detect and quantify TREC and KREC in HIV-exposed uninfected (HEU) and HIV-unexposed uninfected (HUU) neonates using preserved DBS samples from the Siyakhula study cohort. DNA was extracted from DBS samples, and TREC and KREC genes were simultaneously detected using a newly developed real-time PCR technique. Results showed HUU infants had more TREC quantity, but no significant difference (p-value > 0.05) in KREC quantity. This indicates reduced TREC levels in immunologically vulnerable babies (HEU). Babies born to mothers living with HIV are at a higher risk of immune dysfunction due to exposure to HIV and antiretroviral therapy. The TREC and KREC assays show significant potential for IEI screening, and the simultaneous TREC/KREC detection provides a cost-effective method.

Friday 31 October – 09:15

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[038] *Datura stramonium* and *Catha edulis* extracts display cytoprotective activity in an SH-SY5Y Parkinson's disease cell model

Tidimalo Mogale[1], Andries D. de Beer[1] & Vanessa Steenkamp[2]

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[2]*Department of Pharmacology, Health Sciences, University of Pretoria, Pretoria, South Africa - vanessa.steenkamp@up.ac.za*

Parkinson's disease (PD) is characterised by the loss of dopaminergic neurons and is attributed to oxidative stress and mitochondrial dysfunction. Medicinal plants are widely used to treat neurological disorders. The aim of this study was to evaluate the effects of crude and fractionated extracts of *Datura stramonium* and *Catha edulis* in SH-SY5Y human neuroblastoma cells in which cytotoxicity was induced using 6-hydroxydopamine (6-OHDA), as a model for PD. Plant extracts were prepared using

dichloromethane/methanol (50:50) and methanol, fractionated via solid-phase extraction, and analysed by liquid chromatography–mass spectrometry (LC-MS). Inherent cytotoxicity and following 6-OHDA exposure were assessed using the sulforhodamine B assay, and cell morphology using light microscopy. Mechanistic assays included reactive oxygen species (ROS) measurement via flow cytometry and dichlorofluorescein assay, assessment of mitochondrial membrane integrity, and evaluation of anti-apoptotic activity using the Ac-DEVD-AMC assay. Lastly, *in silico* analysis assessed binding of plant-derived chemotaxonomic markers to D1 and D2 dopamine receptors. The *D. stramonium* extract contained biomarker compounds hyoscyamine, noradrenaline, and atropine, whereas *C. edulis* contained cathine and norephedrine. Both plant extracts induced negligible cytotoxicity. Three fractions of *D. stramonium* and four fractions of *C. edulis* provided cytoprotection between 8.00 and 12.52%, and 3.39 and 10.5%, respectively. Microscopic analysis confirmed these results. Fraction 1 of *C. edulis and* Fraction 2 of *D. stramonium* presented the highest reductions in ROS generation by 1.72-fold and 1.33-fold, respectively. The fractions significantly ($p < 0.05$) reduced caspase 3/7 activation and mitochondrial membrane potential compared to the 6-OHDA control. *In silico* analysis, norephedrine and noradrenaline exhibit high binding affinities to D1 and D2 receptors, with noradrenaline showing greater affinity as reflected by lower binding free energies. Both plant extracts preserved cell viability, demonstrated cytoprotective effects, and reduced ROS levels, indicating their potential for further research to assess *in vivo* activity and therapeutic applications.

Friday 31 October – 09:25

[052] Platelet activation and T-helper cytokine profiles in patients living with diabetes in sub-Saharan Africa

Bongani B. Nkambule[1], Zekhethelo Mkhwanazi[1] & Maurice T. Nyambuya[2]

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Platelets are hyperactivated in patients living with type 2 diabetes and platelet glycoprotein Ib (GPIb) which is abundantly expressed on membrane of peripheral blood platelets in patients with type 2 diabetes (T2D) has been associated with vascular thrombosis. A pivotal role of activated platelets in the initiation of acute inflammation and atherosclerosis has been established. However, the association between well characterized mediators of inflammation such as the T helper 1 (Th1) and T helper 2 cytokines with platelet activation levels in overt T2D remains unclear. The primary aim of this study was to assess platelet activation and Th1/Th2 cytokines in an African cohort of patients living with diabetes. We recruited participants from the Rundu state Hospital, Namibia from September 2023 to November 2024. This study comprised of 156 patients living with type 2 diabetes and 20 healthy controls. Platelet activation was measured using quantitative platelet flow cytometry and T-helper 1 (interferon gamma, interleukin 2, tumour necrosis factor beta) and T-helper 2 (interleukin 4, interleukin 10) cytokines were measured using cytometric bead arrays. This study included 156 patients who were diagnosed with type 2 diabetes and 20 healthy controls. There were age differences between patients with T2D compared to controls, $p<0.0001$. Patients with T2D had a higher BMI (28.02±5.98) compared to controls (24.69±4.49), $p=0.0237$. In patients with T2D, the BMI inversely associated with plasma TNF-α levels ($r=-0.412$, $p=0.0066$). Notably, platelet counts were higher in patients with T2D (300.10±82.98), $p= 0.0318$. There was a 2.5-fold increase in the platelet membrane CD61 antigen density in patients with T2D when compared to controls ($p=0.0050$). Moreover, the levels of activated peripheral blood platelets were elevated in patients with T2D (6.40±3.29) when compared to controls (3.38±1.88), $p=0.0024$. However, the levels of platelet activation and CD61 antigen density were not associated with glycated hemoglobin (HbA1c levels). In our cohort GPIb levels were two-fold higher in patients with T2D. The levels of platelet activation are not associated with Th1/Th2 cytokines in patients with T2D.

Friday 31 October – 09:35

[041] The immunopathogenic mechanisms of severe cutaneous adverse drug reactions to first line anti-tuberculosis drugs

Phuti Choshi[1], Sarah Pedretti[2], Amy Palubinsky[6], Rama Gangula[6], Ramesh Ram[7], Andrew Gibson[7], Rannakoe Lehloenya[8], Graeme Meintjes[3,4,5], Elizabeth Phillips[6,7] & Jonny Peter[1,2]

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[7]Institute for Immunology and Infectious Diseases, Murdoch University, Murdoch, WA, Australia;
[8]Division of Dermatology, Department of Medicine, University of Cape Town, South Africa

First-line anti-tuberculosis drugs(FLTD) are the commonest cause of severe immune mediated adverse drug reactions, including SJS/TEN and DRESS in PLHV. The mechanisms of these life-threatening reactions are poorly understood, making diagnosis and treatment challenging in patients who can ill-afford suboptimal anti-TB treatment. We aimed to identify genetic markers for FLTD-induced SJS/TEN and DRESS through HLA, ERAP and KIR typing, and used an integrated single-cell approach involving: i) CyTOF2 (n=8), and ii) ScRNA-seq (n=3) to characterise peripheral blood immune cells activated *in vivo* and *in vitro* by offending drug. Rifampicin (RIF)-associated DRESS was commonest. IFN-gamma ELISPOT, optimised for FLTDs, was most sensitive(75%) for RIF-DRESS. RIF-DRESS/SJS/TEN cases were associated with HLA-B*44:03, and single-cell work was restricted to these cases and matched controls. HIV-related chronic immune activation drove expansion of exhausted CD8+ T cells in cases and controls. However, a subpopulation of these CD8+ T cells in cases expressed co-stimulation (CD28+CD27+) markers. We confirmed these with ScRNA-seq, as KLRG1^{low}CX3CR1^{high} CD8+ T-cells with RIF-specific proliferative and cytotoxic capabilities. The CDR3αβ analysis showed a unique TCR repertoire for each case, with predominantly CD8+ oligoclonality. GLIPH2 analysis of TCRβ sequences found eight common T-cell groups across the three cases. Differential gene expression identified the SQVP TCR-motif as having RIF-induced proliferative and cytotoxic profiles. We propose that, despite expanded, exhausted CD8+ T-cell populations characteristic of HIV-related advanced immunosuppression, RIF-DRESS patients have drug-specific cytotoxic CD8+ T cells, potentially sharing low-frequency TCR-motifs like SQVP. Future site-of-disease and in-vitro work is required to better define proposed pathogenic T-cell populations.

Friday 31 October – 09:45

Session 3 - One Health Focus on Influenza

Seasonal drift and avian threats: Update on influenza in humans

Nicole Walter

National Institute for Communicable Diseases (NICD), Johannesburg, South Africa - nicolew@nicd.ac.za

Seasonal influenza continues to impose a substantial global burden, resulting in significant morbidity, mortality, and pressure on healthcare systems. At the same time, avian influenza remains a persistent public health concern due to sporadic human infections and the risk of viral adaptation enabling sustained transmission. This presentation will summarise current epidemiological and virological trends in human influenza, with a focus on recent seasonal influenza activity in South Africa and updates on

avian influenza cases in humans. Data from national surveillance systems will be reviewed, including viral antigenic and genetic characterisation, with discussion of implications for vaccine strain selection and pandemic preparedness.

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Biography: Dr Nicole Wolter is a Principal Medical Scientist in the Centre for Respiratory Diseases and Meningitis (CRDM) at the National Institute for Communicable Diseases in Johannesburg, South Africa. She also holds a joint appointment as a Lecturer within the School of Pathology at the University of Witwatersrand. She received her PhD in Molecular Microbiology in 2007 from the University of Witwatersrand, and an MSc in Epidemiology from the London School of Hygiene and Tropical Medicine (LSHTM) in 2019. Dr Wolter is an NRF-rated scientist and has published more than 70 publications in peer-reviewed journals. In her position at the NICD, she leads a team of scientists in surveillance and research focused on the epidemiology, advanced diagnostics and molecular characterisation of pathogens causing respiratory disease in South Africa. Her research interests include understanding the burden, epidemiology and transmission of respiratory diseases in order to guide public health policy and action.

Friday 31 October – 11:30

Avian influenza in South Africa: Patterns, pathways, and Public Health implications

M Romito, M Molefe, BA Lubisi & LS Rotherham

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Avian Influenza (AI), commonly known as bird flu, is a contagious viral disease caused by influenza A viruses that are adapted to birds. Of particular concern are highly pathogenic avian influenza (HPAI) viruses of the H5 subtype, which have resulted in the deaths of millions of birds globally and pose a significant threat to both animal and human health. In South Africa, AI outbreaks have been recorded since 2004, with initial cases primarily involving ostriches. However, since 2017, the emergence and continued circulation of HPAI H5 viruses belonging to clade 2.3.4.4b have been documented in wild birds, ostriches, and commercial poultry, marking a notable shift in the virus's epidemiology. The impact of these outbreaks extends far beyond avian mortality. AI poses serious economic and social risks, affecting the livelihoods of farmers, disrupting food security, and raising concerns about zoonotic potential. While South Africa has not yet observed transmission to mammalian hosts—unlike trends seen globally—the dynamic evolution of AI viruses and the increasing incidence of mass mortality events in wild birds underscore the need for vigilant surveillance and response mechanisms. This presentation will explore the patterns, pathways, and Public Health Implications of AI in the South African context, including viral pathogenesis, touching on some host immune responses, and the necessity of robust biosecurity, vaccination strategies, and early detection systems to mitigate current and future outbreaks. Understanding the interplay between virus evolution, host susceptibility, and environmental factors remains essential in guiding effective public health and veterinary responses.

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Biography: Dr Lia Rotherham completed her PhD in Microbiology in 2012 at the University of Pretoria. After completion of her PhD, she joined the ARC-OVR in 2013 as a postdoctoral fellow that had a focus on research for vaccine development of Foot-and-Mouth Disease. This work included using reverse genetic systems to try and broaden the neutralisation properties of the viruses. In 2015, she joined the Vaccine and Diagnostic Development group of the ARC-OVR with a research focus on avian influenza and Newcastle disease. A large part of her research focuses on pathogen characterisation of circulating strains and the potential of these pathogens to become zoonotic outbreaks.

Friday 31 October – 11:50

Building vaccine sovereignty for the next pandemic

Wendy Burgers

Professor and Deputy Director of the Institute of Infectious Disease (IDM) at the University of Cape Town (UCT) - wendy.burgers@uct.ac.za

The COVID-19 pandemic revealed how vulnerable Africa remains to global vaccine inequities. Since then, South Africa has made major strides toward vaccine self-reliance, establishing local manufacturing, strengthening translational research capacity, and nurturing expertise in vaccine development. This talk explores these advances and how they can build both technological and immune readiness for future pandemic threats. With growing attention to zoonotic spillover and One Health principles, the discussion will highlight the adaptability of the mRNA vaccine platform for emerging pathogens such as avian influenza. Ultimately, achieving vaccine sovereignty in Africa is both a scientific and strategic health-security imperative, essential to ensuring readiness for the next pandemic.

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Biography: Wendy Burgers is a Professor and Deputy Director of the Institute of Infectious Disease (IDM) at the University of Cape Town (UCT). She is a viral immunologist, studying the human immune response to infections. She established and directs the Cellular Immunology Platform at UCT, a hub for clinical immunology research, vaccine evaluation (preclinical and clinical) and capacity building, for new and existing pathogens and future epidemics and pandemics. In the past her research group focused on understanding the cellular immune response to HIV and TB. During the COVID-19 pandemic, her research group studied T cell responses to SARS-CoV-2 infection and vaccination, addressing globally relevant and timely questions on T cell cross-reactivity to viral variants. She led the Cellular Immunity subgroup of the South African National COVID Variants Consortium and was a member of the Ministerial Advisory Committee on COVID vaccines. Her group is funded by the South African MRC, Wellcome Trust, European Commission and Gates Foundation. Wendy was awarded the **South African MRC Silver Medal for outstanding contributions to science in 2024, and in 2023 was elected a Fellow of UCT in recognition of exemplary scholarly work.** Wendy leads a group of 25 postgraduate students, postdoctoral fellows, early and mid-career investigators and laboratory scientists. Her training and mentoring efforts are focused primarily on Black women, who remain severely underrepresented in biomedical science in South Africa. She also teaches infectious disease immunology to undergraduates at UCT.

Friday 31 October – 12:10

Session 4 - Clinical and Diagnostic Immunology Workshop

Background: Vaccine response testing in clinical practice: why, what and when?

Prof. Theresa Rossouw *MBChB, MPH, DPhil, PhD*

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Friday 31 October – 14:00

[067] Clinical immunology: awareness, structured laboratory evaluation, and immunogenetic sequencing are key in diagnosing & treating Inborn Errors of Immunity (IEI)]

André van Niekerk[1], Sylvia van den Berg[2], Sarah Walters[2] & Celeste Kock[3]

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We present a case of XMEN syndrome (X-linked immunodeficiency with magnesium defect, Epstein–Barr virus [EBV] infection, and neoplasia), illustrating the importance of clinical awareness of inborn errors of immunity (IEI), structured immunologic evaluation, and integration of clinical and laboratory data. A 6-year-old HIV-negative Caucasian male presented with recurrent upper respiratory tract infections (requiring tympanostomy tube insertion on four occasions) and problematic herpes labialis. Chronic abdominal pain led to referral to a gastroenterologist, who recognised a SPUR (Severe, Persistent, Unusual, or Recurrent) infection pattern suggestive of an underlying IEI. This prompted immunological investigation. The full blood count was normal. Serum IgG and IgA were markedly reduced (below –3 Z-scores), with elevated IgM (above +3 Z-score). Lymphocyte subset analysis showed increased B cells, decreased NK cell percentage, poor response to tetanus toxoid, but preserved response to pneumococcal polysaccharide antigens. Further findings included decreased CD40L expression, reduced memory B cells, and impaired T-cell proliferation to varicella antigen, consistent with a combined immunodeficiency. Genetic sequencing confirmed a pathogenic *MAGT1* mutation, diagnostic of XMEN syndrome. *MAGT1* mutations impair intracellular magnesium transport and N-linked glycosylation, resulting in multisystem abnormalities and disrupted immune receptor expression (particularly NKG2D) leading to dysfunction of $CD4^+$, $CD8^+$, and NK cells. Affected individuals are predisposed to various recurrent infections, EBV infection, EBV-driven lymphoproliferation, and autoimmune manifestations. This case highlights the critical role of IEI awareness, stepwise immunologic work-up, and genetic testing in diagnosing immunodeficiencies and informing appropriate long-term management.

Friday 31 October – 14:20

Case presentation: An HIV-non-infected child presents with bronchiectasis

Prof. André van Niekerk

University of Pretoria -Ampath Chair for Inborn Errors of Immunity & Allergology, School of Medicine, University of Pretoria, andre.vanniekerk@up.ac.za

Friday 31 October – 14:30

Vaccine response testing: why do we need alternative options?

Prof. André van Niekerk

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Friday 31 October – 14:40

Serotype specific vaccine testing: challenges & solutions

Dr Lizelle Nagel

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Friday 31 October – 14:50

Saturday 01 November 2025

Session 5 - Infectious diseases (1)

[012] Chimpanzee adenovirus vector-based vaccination: A promising approach for inducing T cell responses against HIV

Anele Mbatha[1], Zelda Euler[1], Sharon Khuzwayo[1], Valentin Voillet[1], Faatima Laher-Omar[1], Saleha Omarjee[1], Anneta Naidoo[1], Zinhle Mgaga[1], Hildegund Ertl[3], Edith Swann[5], Youyi Fong[2], Pei-Chun Yu[2], Manuel V. Villaran[2], Vimla Naicker[2], Ameena Goga[4], Brodie Daniels[4], M. Juliana McElrath[2], Stephen C. De Rosa[2] & Erica Andersen-Nissen[1,2]

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Effective HIV vaccines must generate strong cell-mediated immune responses, especially CD8+ T cells, to prevent infection, control disease progression, and potentially enable a functional cure. Adenovirus vectors are promising tools due to their ability to express diverse immunogens and elicit potent adaptive immune responses. The HVTN 139 trial (NCT05182125) evaluated chimpanzee-derived, replication-defective adenovirus vectors (AdC6-HIVgp140 and AdC7-HIVgp140) encoding codon-optimized HIV

clade C Env, with a CH505TF gp120 protein boost. Healthy adults received either a single low dose ($1x10^{10}$ viral particles; N=10) of AdC6-HIVgp140 (AdC6) or AdC7-HIVgp140 (AdC7) or a high-dose ($5x10^{10}$ viral particles; N=20) combination regimen administered at 0 and 3 months, followed by a protein boost at month 6. HIV-specific CD4+ and CD8+ T-cell responses were assessed using a 17-color intracellular cytokine staining assay. Key endpoints were IFNγ and/or IL-2 production. An unbiased clustering analysis identified unique HIV-specific T cell subsets altered by vaccination. High-dose AdC7 elicited stronger CD4+ responses than AdC6 one-month post-vaccination (p=0.038). Protein-boosted participants primed with AdC7 showed greater CD4+ and CD8+ T cell responses than those primed with AdC6 at both month 6.5 and 12. CD4+ T cells were more responsive to the protein boost. Clustering revealed 13 distinct CD8+ T cell subsets, with higher frequencies of $IFN\gamma^+/TNF^+$ effector-memory cells in AdC7-primed groups. AdC7-HIVgp140 priming induced durable HIV-specific T cell responses, highlighting its potential in vaccine strategies. These findings support further research in larger human trials to confirm efficacy.

Saturday 01 November – 09:15

[077] Development of a novel serological assay capable of differentiating between animals vaccinated or naturally infected with lumpy skin disease virus

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The sustainability of global livestock is under threat due to the increase in the spread of transboundary animal diseases. Lumpy skin disease (LSD), caused by the poxvirus lumpy skin disease virus (LSDV), is a World Organisation for Animal Health notifiable disease. Due to the severe economic impact, there are restrictions on the trade and movement of cattle. Vaccination is one of the most cost-effective methods to control the spread of the disease. There is no serological assay capable of distinguishing between vaccinated and naturally infected animals (DIVA) which would enable regions conducting vaccination campaigns to demonstrate disease freedom, resulting in improved food security, particularly for developing farmers. To identify DIVA diagnostic reagents, two fragmented-genome phage display libraries were constructed, derived from the OBP vaccine and a virulent field isolate (Warmbaths). Phages were selected based on the ability of the individually expressed peptides to bind to LSDV antibodies from vaccinated or naturally infected cattle. Following high-throughput sequencing of bound phages, sequence analysis identified twenty-eight putative diagnostic antigens. Several of the predicted protein encoding genes were cloned, the proteins expressed in bacteria and empirically tested for binding specificity. P4 and P17 were able to detect natural infections by virulent isolates in an indirect ELISA. Even though the test needs further optimisation, the two potential diagnostic reagents are a key step toward developing a serological LSD DIVA assay. This would lead to more efficient approaches to vaccination and disease control, enhanced surveillance, all while ensuring the protection of animal health and food security.

Saturday 01 November – 09:25

[022] HIV-1 reprograms T cell metabolism and inflammatory responses based on virus replicative capacity

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HIV-1/AIDS remains a major global health challenge, necessitating innovative interventions. HIV-1 disrupts immune responses by targeting CD4+ T cells and their function. However, the role of viral replicative capacity (RC) in modulating CD4+ T cell function remains unclear. We hypothesized that higher viral RC correlates with increased inflammation and metabolic dysregulation in CD4+ T cells. We previously analysed the immunomodulatory effects of chimeric HIV-1 viruses encoding gag-proteases from subtypes B and C in the NL4-3 backbone using T cell lines. Here, we extended this approach to primary CD4+ T cells isolated from peripheral blood mononuclear cells. Cells were infected, and infection was measured via flow cytometry, while mitochondrial function was evaluated using the Seahorse XFe Analyzer. Infection supernatants were used for cytokine profiling and metabolic assessment. Liquid chromatography-tandem mass spectrometry was used to assess the metabolome from archived plasma samples. Subtype B viruses exhibited higher RC and infection rates than subtype C. Several cytokines, including FGF-basic, IFN-γ, MCP-1, and PDGF-bb, correlated positively with viral RC ($p < 0.05$). Glutamine consumption increased significantly from 24 to 72 hours ($p = 0.0078$), particularly in subtype B infections. Metabolomics analysis detected 209 plasma metabolites, with 28 significantly altered based on RC, affecting pathways such as glutamine and nucleotide metabolism. Subtype B viruses induce greater CD4+ T cell infection, cytokine production, and metabolic dysregulation than subtype C. HIV-1 alters the plasma metabolome based on RC, potentially influencing clinical outcomes. Targeting metabolic pathways may provide novel therapeutic strategies for HIV-1 control.

Saturday 01 November – 09:35

[079] Brain antigen presenting cells and T cells promote regulated Th1 immune responses during central nervous system tuberculosis

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Central nervous system tuberculosis (CNS-TB), which commonly manifests as TB meningitis, is a severe form of TB associated with high morbidity and approximately 50% mortality rates due to challenges in both diagnosis and treatment. Despite its significant impact on public health, our understanding of the immune mechanisms and specific cell types involved in CNS-TB is currently limited. Our study characterized the roles of brain antigen presenting cells (APCs), namely, dendritic cells (DCs), infiltrating macrophages, microglia, and T cells in a CNS-TB mouse model. Wild-type female C57BL/6J mice were intracerebrally infected with *Mtb* H37Rv or *Mycobacterium bovis* BCG, while control animals were inoculated with saline. Mice were euthanized at weeks 2, 4 and 6 for histopathological and flow cytometric analysis. Infected mice presented with acid-fast bacilli in the brain and inflamed meninges. Despite the effective control of bacterial burdens in the brain of both *Mtb*- and BCG-infected mice, dissemination was observed in the spleen and lungs. Mycobacterial infection of the CNS induced the recruitment and expansion of microglia, brain-infiltrating macrophages, and DCs, exhibiting an activated mature phenotype (MHCII+, CD80/D86+, CCR7+) in both the brain and cervical lymph nodes (CLNs). These APCs were mainly pro-inflammatory, secreting IFN-□, TNF-□, IL-1□, IL-6 and/or IL-12; and some IL-10-producing APCs (anti-inflammatory) were also detected. At week 4 post intracerebral infection, increased numbers of activated T cells expressing transcription factors T-bet (Th1) and FoxP3 (Treg) were observed. *Mtb*-infected DCs from CLNs of CNS-TB mice cocultured with sorted naive CD3+ T cells demonstrated increased expression of IFN-□+, IL-4, IL-10 and TGF-□ responses by CD4+ and CD8+ T cells compared to co-culture with uninfected DCs. Our findings suggest that protection against mycobacterial infection of the CNS involves the expansion and recruitment of functional mature brain APCs capable of promoting a Th1- and Treg-polarized T cell response at the site of infection.

Saturday 01 November – 09:45

[064] How asymptomatic sexually transmitted infections alter the epithelial-immuno barrier of the penile genital tract

Cosnet Lerato Rametse[1], Riyaadh Roberts[1], Micheal Mndini[1], Asiphe Besethi[1], Berenice Alinde[2], Yacoeb Ganief[1], Aubrey Shoko[3], Thomas J. Hope[4] & Clive Gray[2]

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The presence of an asymptomatic sexually transmitted infections (aSTI) is ubiquitous and may induce changes in the penile genital tract such as in foreskin tissue which renders an uncircumcised male to be more vulnerable to HIV infection. To assess changes in foreskin inflammation, epithelial tight junction (TJ) genes: claudin, filaggrin, e-cadherin and involucrin and *in vivo* penile epithelial barrier function changes in the presence of an aSTI. Foreskin (FS) tissue was collected from 96 males following voluntary medical male circumcision (vMMC). FS tissue was examined histologically and for TJ gene expression using RT-qPCR and stratified by any of the measured STI: *Chlamydia trachomatis, Neisseria gonorrhoea, Trichomonas vaginalis & Mycoplasma genitalium*, Vapometers and moisture meters SC and D were used to measure trans-epithelial water loss (TEWL), dermal and surface hydration in the absence/presence of an aSTI. Inflammatory cell density was higher in aSTI+ (n=38) vs aSTI- males (n=58), in the epidermis (24.6 vs 10.4 cells /m^2 p=0.002), papillary dermis (119.9 vs 61.4 cells/m^2,p=0.014) and reticular dermis (13.6 vs 6.5 cells/m^2 ,p=0.03). These were predominantly lymphocytic infiltrates that were largely in the papillary dermis. Claudin-1 expression was significantly decreased in the inner foreskin compared to the outer foreskin in the presence of an aSTI. This was matched by increased penile glans surface hydration in the presence of an aSTI (58.3 vs 105.6 au, p=0.003). The presence of an aSTI significantly increases inflammatory cells in the foreskin epidermis and dermis, with most of the infiltrates localised within the papillary dermis. This is associated with decreased expression of Claudin- in the inner foreskin (hence reduced barrier integrity) & increased moisture in the glans. Our findings show that aSTI's alter epithelial characteristics

Saturday 01 November – 09:55

Session 6 - Infectious diseases (2)

[023] Interleukin 4-induced gene 1 is a major tryptophan catabolising enzyme that regulates Type 2 immunity in a tissue-specific manner

Sabelo Hadebe[1]*, Nontobeko Mthembu[1]*, Amkele Ngomti[1]*, Paballo Mosala[1]*, Nada Abdel Aziz[1], Inam Makhabane[1], Fungai Musaigwa[1] & Frank Brombacher[1,2]

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Type 2 immunity is involved in homeostatic functions including tissue repair, haemostasis,

thermogenesis and metabolism. Distress signals such as interleukin 33 (IL-33), thymic stromal lymphopoietin (TSLP) and IL-25 released by barrier cells activate Type 2 immunity and are thought to be a unifying feature that guides tissue-specific cues. How metabolic processes especially amino acid availability influence Type 2 immunity is less understood. Here we focussed on the role of interleukin 4 induced gene 1 (IL-4I1), a tryptophan catabolising enzyme in the induction of Type 2 immunity. To investigate the role of IL-4I1 in the induction of Type 2 immunity across barrier sites in mouse and human. We measured IL-4I1 and its metabolites using LC-MS in patients with moderate to severe atopic dermatitis (AD) and in mice. We also deleted or inhibited IL-4I1 in human keratinocytes to validate our findings. In vivo we induced acute AD in IL-4I1-deficient mice and restored IL-4I1 function with downstream metabolites. We also infected IL-4I1-deficient mice with *Nippostrongylus brasiliensis* (*N. brasiliensis*) and restored IL-4I1 function with downstream metabolites. Tryptophan pathway and IL-4I1 metabolites were elevated in moderate to severe AD patients. Deletion of IL-4I1 by CRISPR-cas9 or inhibition by a putative inhibitor led to reduced Type 2 markers in vitro. Lack of IL-4I1 in mice led to reduced AD Type 2 inflammation which could be restored by IL-4I1-derived metabolites indole-3-aldehyde and kynurenine. IL-4I1-deficient mice displayed increased worm burden and reduced Type 2 immunity when infected with *N. brasiliensis*. Exogenous restoration of IL-4I1 function through IL-4I1-derived metabolites restored Type 2 immunity leading to worm expulsion. Conclusion. Here we demonstrate that IL-4I1 is a major tryptophan catabolising enzyme that has critical functions in Type 2 immunity especially at barrier sites.

Saturday 01 November – 11:45

[049] CD68+ follicular macrophages harbour HIV reservoirs in human lymph node tissues during suppressive ART

Merantha Moodley[1], Caroline Chasara[1], Trevor Khaba[1,2], Bongiwe Mahlobo[1], Nicole Reddy[1], Sifundo Nxele[1,2], Sibongiseni Msipa[1], Kavidha Reddy[1], Thandekile Ngubane[2], Ismail Jajbhay[3], Johan Pansegrouw[3], Thumbi Ndung'u[1,2,4,5] & Zaza M. Ndhlovu[1,2,4,5*]

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Uncertainty persists regarding the contribution of macrophages to HIV reservoirs, largely due to insufficient characterization of these reservoirs within their native tissue microenvironments. This study aimed to characterize and quantify macrophage reservoirs in human lymph node (LN) tissues in terms of their phenotype, location, and their potential for sustained productive infection during suppressive antiretroviral therapy (ART). We examined the topology, nature, and size of macrophage reservoirs in LNs from 45 PLWH subtype C on suppressive ART and 14 matched controls using *in situ* imaging and multiplexed immunofluorescence microscopy. Germinal center $CD68^+$ macrophages harboured HIV *gag-pol* DNA, *gag-pol* RNA and Gagp24 protein. Digital droplet PCR confirmed the presence of proviral reservoirs in myeloid cells within LNs. High-resolution imaging techniques revealed that infected macrophages within GCs displayed distinct morphological characteristics, featuring larger and irregular shapes. In contrast, phagocytic macrophages exhibited intracellular staining for $CD4^+$ T cells, had regular

shapes, and were predominantly found outside the GCs. Our findings provide detailed quantitative, spatial, and phenotypic characterization of macrophage reservoirs in LNs, offering a clear estimation of the extent to which macrophages contribute to HIV reservoir persistence. These findings establish a basis for developing targeted strategies aimed at reservoir eradication in LN tissues.

Saturday 01 November – 11:55

[034] Diabetes mellitus affects alveolar- and monocyte-derived macrophage effector function during latent tuberculosis

Léanie Kleynhans[1,2], Carine Kunsevi-Kilola[1], Happy Tshivhula[1], Tariq Webber[1], Stephanus T Malherbe[1], Blanca I Restrepo[3,4,5], Larry S Schlesinger[3] & Katharina Ronacher[1,2,6]

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Patients with type 2 diabetes (T2D) are more susceptible to *Mycobacterium tuberculosis* (*M.tb*) infection and severe tuberculosis (TB). The underlying mechanisms contributing to this remain largely unknown. To fill this critical knowledge gap, we simultaneously obtained human alveolar macrophages (HAMs) and monocyte-derived macrophages (MDMs) from TB-exposed individuals with (n=12) and without (n=11) T2D in South Africa. We infected HAMs and MDMs *ex vivo* with live *M.tb* to investigate their phenotype and function. HAMs from T2D patients expressed less CD32, had reduced capacity to control *M.tb* growth (24h post infection) and produced more TNF and CCL3 in response to *M.tb* infection ($p<0.05$). Frequencies of CD32, CD36 and CD180 expressing MDMs were lower in T2D, but the ability of MDMs to control *M.tb* growth was not affected by T2D. MDMs from T2D patients also produce less CCL2. Functional changes in T2D HAMs were associated with delays in *M.tb*-induced gene expression and overall hypermethylation of DNA, except for genes linked to TNF signaling that were hypomethylated. Taken together, we provide the first in-depth analysis of diabetic HAMs and MDMs in the context of recent TB exposure, providing potential mechanistic explanations for increased TB susceptibility in diabetes patients.

Saturday 01 November – 12:05

[050] Resistance to SARS-CoV-2 infection is not associated with pre-existing antibody responses to common cold coronavirus fusion peptides

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Individuals who resist SARS-CoV-2 infection are rare but may be used to identify novel immune correlates of protection. Coronavirus fusion peptides (FPs) are highly conserved across multiple genera. Therefore, we investigated whether pre-existing coronavirus anti-FP responses were associated with resistance to SARS-CoV-2 infection. We used a longitudinal household transmission cohort (PHIRST-C) with intensive SARS-CoV-2 testing (bi-weekly PCR) and serology (2-monthly ELISA) between July 2020-August 2021. After August 2021, individuals were classified as resistors (n=21) or controls (n=21) if they remained uninfected or were infected with SARS-CoV-2 respectively. Binding antibodies (IgG) were measured using a bead-based multiplex assay across four successive blood draws: enrolment, pre-Delta, pre-BA.1 and post-BA.1 waves. We evaluated coronavirus spike (NL63, 229E, OC43, HKU-1, and SARS-CoV-2 D614G) and fusion peptide (NL63, 229E and OC43) binding. Associations between IgG binding responses in longitudinal and cross-sectional samples were assessed using hierarchical clustering and ANOVA. In both groups, binding titres were highest against OC43 spike (176744 MFI) and lowest against 229E FP (6358 MFI). Barring undetectable SARS-CoV-2 binding antibodies in resistors, no significant differences in binding to other spikes and FPs were observed between resistors and controls at each blood draw. Longitudinal area under the curve analysis demonstrated similar binding profiles in the resistors and controls across all antigens. Prior antibody immunity in the periphery, to common cold coronaviruses, targeting the whole spike or fusion peptides, did not correlate with SARS-CoV-2 resistance. Future studies should investigate whether pre-existing mucosal antibody or T cell immunity is associated with the resistor phenotype.

Saturday 01 November – 12:15

[055] Altered immune activation and function in antigen-presenting cells of South African HIV-1 elite controllers

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HIV controllers can spontaneously control viral replication without antiretroviral therapy but remain at risk of developing non-AIDS-related conditions due to persistent immune activation. The mechanisms underlying chronic activation of innate immune cells in elite controllers remain poorly understood. We investigated markers of immune activation and functional profiles of antigen-presenting cells (APCs) in South African elite controllers compared to other people with HIV (PWH). We recruited different phenotypes of PWH, including elite controllers (PWH_{EC}, n=16), HIV progressors (PWH_{PROG}, n=20), ART-suppressed individuals (PWH_{ART}, n=19), and individuals without HIV ($PWOH_{HIV-}$, n=18). T cell activation (CD38+/HLA-DR+), monocyte (CD86 and CD69) activation and cytokine production (TNF-α, IFN-α, and IL-1β) by monocytes, myeloid (mDCs) and plasmacytoid (pDCs) dendritic cells were assessed using multi-colour flow cytometry. Cells were stimulated with Toll-like receptor (TLR) ligands: TLR4 (LPS), TLR7/8 (CL097), and TLR9 (CpG). Plasma levels of soluble CD14 (sCD14) and D-dimer were measured by ELISA. PWH_{EC} displayed elevated T cell activation compared to PWH_{ART} and $PWOH_{HIV-}$ ($p<0.05$). PWH_{EC} demonstrated reduced TNF-α and IL-1β production in monocytes and mDCs following TLR4 and TLR7/8 stimulation compared to $PWOH_{HIV-}$ ($p<0.05$). Plasma sCD14 levels were higher in PWH_{EC} compared to $PWOH_{HIV-}$ ($p=0.01$), while D-dimer levels were elevated in PWH_{PROG} compared to PWH_{ART} ($p=0.01$) and PWH_{EC} ($p=0.04$). In conclusion, PWH_{EC} exhibits heightened T cell activation, reduced monocyte activation, decreased pro-inflammatory cytokine production, and elevated biomarkers associated with adverse outcomes. These results suggest that, despite viral control, altered immune responses may contribute to persistent inflammation, underscoring the importance of targeted anti-inflammatory interventions in PWH_{EC}.

Saturday 01 November – 12:25

END ORAL PRESENTATIONS

Poster Presentations as they appear in the Programme

Poster Session 1

[002] A comparative study of the effects of lopinavir and dolutegravir on the pro-inflammatory activities of human neutrophils *in vitro*

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Both lopinavir (LPV) and dolutegravir (DTG) are part of the South African HIV anti-retroviral (ARV) treatment regimen. Both drugs have been associated with side effects, mainly hyperlipidaemia and unexplained weight gain, respectively. Systemic inflammation as a result of drug-mediated pro-inflammatory activities, may underpin the pathophysiology of these side effects. Isolated human neutrophils were exposed to the drugs at a concentration range of 2.5-20 µg/mL and reactive oxygen species (ROS) production, neutrophil degranulation and intracellular calcium fluxes were quantified using luminol-enhanced chemiluminescence, spectrophotometry and spectrofluorometry respectively. Exposure of neutrophils to lopinavir resulted in the abrupt, dose-related, and significant (P=0.0205-P<0.0001) generation of ROS that was attenuated by inclusion of inhibitors of NADPH oxidase (diphenyleneiodonium chloride, DPI), myeloperoxidase (sodium azide), phospholipase C (U73122), inositol triphosphate receptors (2-aminoethoxydiphenylborane, 2-APB) and phosphoinositol-3-kinase (wortmannin), while the calcium (Ca^{2+}) chelating agent, EGTA, was ineffective, whereas a more potent effect was observed in DTG exposed neutrophils at a significance of P<0.0001 at all concentrations tested (2.5-20 mg/mL). Exposure of neutrophils to LPV also resulted in a significant (P=0.0286) increase in granular lysozyme release at all concentrations tested (2.5-20 mg/mL). Similarly, exposure of neutrophils to DTG resulted in significant (P=0.0194-P<0.0001), dose related increases in granular elastase release at all concentrations tested (2.5-20 mg/mL). The addition of DTG to neutrophils resulted in an abrupt, marked, and sustained increases in cytosolic Ca^{2+} that was dose-dependent at concentrations of 5-20 mg/mL. While it seems clear that mobilisation of intracellular Ca2+ is the probable mechanism of lopinavir-mediated neutrophil activation and extracellular Ca2+ mobilisation is the probable mechanism of dolutegravir-mediated neutrophil activation, it is uncertain whether the pro-inflammatory interactions of lopinavir described in the current study may contribute to the pathophysiology of the side-effects such as hyperlipidaemia and weight gain in the setting of HIV infection. This uncertainty merits further investigation.

[005] The role of red blood cells in the innate immune response to *Mycobacterium tuberculosis*

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The exact role of red blood cells (RBCs) in the body's initial immune response to infection is relatively unknown. When it comes to Mycobacterium tuberculosis (M.tb), there is even less research on how RBCs may potentially function in the presence of this pathogen. Recent studies have focused on the role of RBCs and other non-M.tb mycobacteria and these have shown that RBC surfaces may allow for the attachment or internalisation of mycobacteria. These studies have also revealed other interactions that may occur between these two entities. Further research on these finding is required, specifically to establish the role of RBCs during M.tb infection. Therefore, this thesis aims to investigate the immunological relationship between M.tb and RBCs, including the location of the bacterium on these cells during the early stages of infection. Using peripheral whole blood from healthy donors, different blood cells (red blood cells, PBMCs and whole blood) will be isolated using various isolation techniques and then infected with a laboratory strain of M.tb H37Rv. Following infection, multiple experimental readouts including: enumeration of bacilli post-infection to determine the contribution of RBCs in the internalisation and killing of M.tb, the production of various soluble mediators released by samples will be measured via Luminex, the functions, viability and phenotypes of cells will be determined using flow cytometry and microscopy will be used to assess the attachment and location of M.tb on the different blood cells. Overall, this thesis aims to provide more information and broaden the knowledge and understanding of the functions of RBCs and how they aid in the pathogenesis of M.tb.

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[006] Immunological features associated with the development of broadly neutralizing antibodies and Fc-effector functions in people living with HIV-1 subtype C

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The induction of broadly neutralizing antibodies (bnAbs) is highly desired for an effective vaccine against HIV-1. Few host genes and immune profiles were associated with the development of bnAbs. However, impact of host genes in immune cell subsets and their association with the development of bnAbs are not fully understood. This study aims to assess the role of host gene transcripts and immune profiles associated with development of bNAbs and fc mediated function during acute HIV-1 clade C infection. This study performed bulk RNA-sequencing (RNA-seq) on peripheral blood mononuclear cells (PBMCs) from 25 chronically HIV-1-subtype C infected individuals, seven who developed bnAbs and 18 who did not. Transcriptomic analysis identified genes, HLA-DPA1, CCR6, SP100 and TLR4 upregulated in participants who developed bNAbs at 1- and 3 years post-infection. Following Pathway enrichment analysis these genes were associated with positive regulation of molecular mediator of immune response, immunoglobulin-mediated immune response, and leukocyte proliferation pathways. Expression level of these gene in NK, CD8 T cells and monocytes will be measured with qPCR. Additionally, determine the functional impact of NK cells in antibody response, performed invitro co-

culture. And there was reduction in the frequency of plasmablasts and IgM antibody in the presence of NK cells, with increased frequency of class-switched memory B cells. Furthermore, Elisa showed a trend towards the increase of IgG antibodies in the absence of NK cells. This study may generate crucial information on host immune factors that should be considered in the design of future neutralizing antibody-based therapeutic and preventive vaccines.

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[009] Migration of intestinal CD4$^+$ T cells promote vaginal eosinophil accumulation following hookworm infection

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Highly pathogenic sexually transmitted infections (STIs) disproportionately affect women in Sub-Saharan Africa (1, 2). A critical contributor to this may be the systemic effects of other distal infections on vaginal immunity (3-5). Using a murine hookworm model *Nippostrongylus brasiliensis*, we demonstrate that T cells elicited by intestinal helminth colonization, traffic to the vagina and promote eosinophil accumulation, leading to eosinophil-mediated exacerbation of HSV-2-associated pathology: We show that GI colonisation by *N. brasiliensis* is sufficient to drive vaginal eosinophil accumulation. This process requires the ability of intestinal CD4+ T cells to traffic from GI-associated immune system. Trafficking of intestinal CD4$^+$ T cell drives the accumulation of eosinophils in the vagina which enhances HSV-2-driven epithelial ulceration in co-infected mice. This introduces a significant paradigm shifts in our understanding of vaginal immunity and the regulation of pathology related to STIs. These findings hold substantial importance for women's health in Sub-Saharan Africa, indicating that prevalent GI infections can substantially impact vaginal immunity, thereby influencing the severity of pathology from STIs.

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a T-Helper Type 2 Cytokine Signature in Cervical Fluids. The Journal of infectious diseases. 2016;213(5):723-30.
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[010] Characterization of activin expression and its role in host immune responses in a murine model of cutaneous leishmaniasis

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Cutaneous leishmaniasis is a neglected tropical disease caused by transmission of *Leishmania major* parasites, transmitted via *Phlebotomus* sandflies, and is characterised by localized necrotic lesions. With no effective preventative vaccines available and current treatments posing toxic threats to the host, research has increasingly focused on understanding the host-parasite interaction in order to identify host targets as potential immunotherapeutic agents. Cytokines are key molecules that regulate host immunity and susceptibility during infection. Activins, prominent members of the transforming growth factor-β (TGF-β) superfamily, are such cytokines known to mediate inflammation, stress and immunity. Activin A, B and AB are the main functional isoforms of activins, distinguished by the dimerization of inhibin (Inh) βA and/or InhβB subunits. Although implicated in susceptibility to various diseases, the role of activins in immune regulation during cutaneous leishmaniasis remains unknown. This study aims to determine whether activins are potential targets for host-directed therapies by investigating their expression and roles in immunity during *Leishmania major* infection. BALB/c and C57BL/6 murine strains, model organisms of susceptibility and resistance respectively to *L. major* infection, will be used to examine parasitological and immune responses. Using RT-qPCR, flow cytometry and advanced imaging techniques, the expression profiles of activin isomers and their potential association with resistant or susceptible immune responses can be elucidated. These findings are expected to provide novel insights into the immunomodulatory role of activins in immunity during *L. major* infection.

[013] Identification of somatic hypermutations responsible for the development of neutralization breadth in an HIV-1 N332-directed antibody lineage

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Broadly neutralizing antibodies (bNAbs) neutralize diverse HIV-1 strains, and an effective HIV-1 vaccine will need to induce these antibodies. Understanding their ontogeny, particularly which somatic hypermutations (SHMs) drive the development of neutralization breadth, is important for informing vaccine design. We previously isolated CAP255.G3, a N332-directed bNAb (55% breadth) from participant CAP255. Heavy chain variable region sequencing revealed extensive SHMs in CAP255.G3 compared to its closest clonal relative, IntF. This study assessed which SHMs contributed to breadth in CAP255.G3 bNAb lineage. Three SHMs (P40S, T57A, Q77H) were selected based on the significance of the biochemical changes of their amino acid side chains and were introduced individually and in combination into IntF, using site-directed mutagenesis. Mutant antibodies were expressed, purified, and tested for neutralization breadth and potency against autologous and heterologous viruses using an HIV-1 Env pseudotyped neutralization assay. Against autologous viruses, mutants showed slight, non-significant potency improvements compare to IntF against 23 and 39 wpi, however, none neutralized the 51 wpi virus, unlike CAP255.G3. Heterologous breadth improved with all mutants gaining activity against RHPA4259.7, and the triple mutant showing modest, non-significant IC_{50} values reductions against DU156 and TRO11. The introduced SHMs led to subtle gains in breadth and potency but did not recapitulate the full activity of CAP255.G3. This suggests that additional SHMs, not included here, likely played a critical role in the development of breadth in the CAP255.G3 lineage.

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[014] Exploring Gartanin and long non-coding RNA-286 as a host-directed drug therapy for tuberculosis

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Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb), remains a significant global health issue, worsened by rising drug resistance and comorbidities like HIV and diabetes. Host-directed therapies (HDTs) offer promising alternatives to traditional antibiotics. Gartanin, a xanthone compound derived from *Garcinia mangostana* (Mangosteen), is known for its anti-inflammatory, antioxidant, and autophagy-inducing properties. In parallel, CAGE (Cap Analysis Gene Expression) analysis has identified the long non-coding RNA (lncRNA)-286 as being upregulated following stimulation with IFN-γ, IL-4, and IL-13 Mtb-infected macrophages, suggesting a potential immunomodulatory role. This study investigates the roles of Gartanin and lncRNA-286 as candidate HDTs in the context of TB. Specifically, we examined the effects of Gartanin therapy and lncRNA-286 knockdown in Mtb-infected macrophages. Our preliminary findings indicate that a combination therapy of lncRNA-286 knockdown and Gartanin pre-treatment significantly improves macrophage viability and reduces intracellular Mtb burden. Conversely, knockdown of lncRNA-286 using a GapmeR antisense oligonucleotide led to increased bacterial burden and a marked decrease in the production of pro-inflammatory cytokines TNF-α and IL-12p70. These results suggest that Gartanin enhances host cell resilience and bacterial clearance, while lncRNA-286 is crucial for effective immune activation and bacterial control. Together, these findings underscore the therapeutic potential of modulating host factors, specifically via Gartanin administration, whose implications may help address drug resistance and improve patient outcomes.

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[015] Optimization of BD flow cytometer high throughput sampler (HTS) system loader settings for high-throughput laboratories and rare cell analysis

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Rare immune cell populations, including antigen-specific B and T cells, are important indicators of durable immune protection. Our laboratory uses intracellular cytokine staining (ICS) and flow cytometry to detect these responses at the single-cell level. Our ICS assay is performed in 96-well plates, and we employ a high throughput sampler (HTS) system for acquisition of stained cells on the cytometers. Determining optimal cytometer settings to maximise per sample cell recovery but decrease acquisition time is critical to our high-throughput analysis of vaccine trial samples. We evaluated four acquisition conditions using the BD FACS Symphony A5 with HTS. The current standard loader settings of 200µL per well at 2.0µL/second, were compared to 200µL at 2.5µL/second, 170µL at 2.5µL/second and 200µL at 3.0µL/sec. One million PBMC from Cape Town Area Control cohort samples were stained using a 5-color ICS panel. FlowJo software was used for data analysis. Percent decrease in cell recovery and acquisition

time per well were evaluated relative to the standard setting. The 200µL at 2.5µL/sec condition provided the highest T cell recovery with under 1% loss, in contrast to up to 14% loss with 170µL at 2.5µL/sec. This setting also reduced acquisition time by 20 seconds per well (80 seconds vs. 100 seconds), improving throughput while preserving assay sensitivity by reducing loss of cell counts of rare populations. Using 200µL at 2.5µL/second is recommended for ICS assays to enhance efficiency and maintain cell yield. These results support optimized protocols for rare-cell studies in high-throughput laboratories.

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[016] Interleukin 4-induced gene 1 regulates Type 2 immunity during Schistosoma mansoni infection

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Tryptophan, an essential amino acid, is metabolized primarily through the kynurenine pathway, serotonin pathways and indole pathways. Dysregulation of tryptophan metabolism leads to various psychiatric disorders (such as Alzheimer, depression), inflammatory and autoimmune diseases (multiple sclerosis, inflammatory bowel disease) and metabolic diseases (type 2 diabetes, obesity). For a long time, it's been known that tryptophan is metabolized in the liver by indoleamine 2,3-dioxygenase 1 (IDO) and TDO2. Our lab has recently shown that there is another pathway that catabolizes tryptophan in extrahepatic sites such as the gut, skin and lung. We identified interleukin 4 induced gene 1 (IL-4I1) as a major tryptophan catabolising enzyme that regulates Type 2 immunity in a tissue specific manner. Objective. To investigate the role of IL-4I1 in regulating Type 2 immunity during Schistosoma mansoni infection. Method. We infected IL-4I1-deficient mice and littermate controls with 100 Schistosoma mansoni (S. mansoni) cercaria for acute infection and 35 cercaria for chronic infection. We measure survival, egg counts (gut and liver), hydroxyproline (liver and gut) and cytokines (mesenteric lymph nodes, serum, gut, liver and spleen) and granulomatous inflammation in the gut and liver. Results. We found that deletion of IL-4I1 led to increased egg counts in the gut but not liver. Interestingly lack of IL-4I1 led to reduced Type 2 inflammation including eosinophils, CD4 derived IL-4, IL-5, IL-10 and IL-13 and ILC2s in the liver, but not the gut of mesenteric lymph nodes. No changes were observed in hydroxyproline or granuloma inflammation. In chronic infection models, we observed no changes in survival. Conclusion. Here we demonstrate that IL-4I1 is important in regulating innate and adaptive Type 2 cytokines. More studies are required to understand the significance of IL-4I1 during acute and chronic Schistosoma mansoni infection.

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[019] Regulators of neuroimmune function in the manifestation of central nervous system tuberculosis in the absence of microglia

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Tuberculosis (TB) is an ancient, chronic disease triggered by the bacillus *Mycobacterium tuberculosis (M. tuberculosis).* Among the most devastating forms of extrapulmonary TB, central nervous system tuberculosis (CNS-TB) is strongly associated with elevated mortality and morbidity, even in the setting of suitable anti-tubercular therapy. Several studies have reported that resident central nervous system (CNS) cells, particularly microglial cells form part of the initial line of defence and are regulators of the innate host immune response in CNS-TB. The colony-stimulating factor 1 factor (CSF-1R) receptor is a crucial regulator of microglia. To specifically eliminate microglia with PLX5622 and subsequently investigate the response of the CNS resident cells when exposed to *M. tuberculosis H37Rv* in the absence of microglia. C57BL/6 female adult mice were orally administered with the AIN-76A (normal diet) and PLX5622 rodent diet and through oral gavage. After set time points, cell pallets of harvested brains from both groups were processed and analysed by immunohistochemistry and flow cytometry to determine microglial depletion. To assess the impact of microglia depletion on bacterial dissemination and organ-specific infection severity, colony forming units (CFU) enumeration was performed on the homogenized organs (brains, lungs, spleens) 24 hours and 3 weeks post-infection. The treated group illustrated microglial population decrease by 67,67% with the specific CSF-1R inhibitor (PLX5622), however control group did not experience microglia depletion. Flow cytometry demonstrated no significant differences in percentages of both neurons and astrocytes. Additionally, the differences in microglial depletion demonstrated that PLX5622 also affects other immune cells. These findings establish that microglia cells are dependent on CSF-1R signaling and by significantly eliminating the cells, microglia's important functions are silenced, however both astrocytes and neurons are functional during infection. In the context of CNS-TB, the off-target effects of PLX5622 on other immune cells needs to be elucidated.

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[020] Enhancing the reliability of immune cell-type identification in scRNA-seq through improved damaged cell quality control

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Single-cell RNA sequencing (scRNA-seq) is a powerful tool in immunology, from identifying novel cell types to characterising treatment responses. However, its reliability depends on upstream pre-processing, with cell-level quality control (QC) being a fundamental component. Damaged cells, an artifact resulting from the capture of cells with stress-induced plasma membrane rupture, introduce technical variability that distorts functionally relevant variability in scRNA-seq data. While filtering damaged cells is a standard task of scRNA-seq QC, it lacks standardisation in practice. Many protocols rely on manual thresholding that assumes true cells follow a unimodal distribution, an assumption that fails when faced with the reality of cellular heterogeneity. While automated tools exist to improve reproducibility in filtering, most also depend on this assumed unimodality. Recent tools address this by

defining damage within distinct distributions, but in so doing, assume all distributions correspond to viable cell populations, risking leaving abundant damage undetected. We present *DamageDetective*, an R-based tool that detects damage by comparing cells to artificially damaged profiles of themselves, simulated through cytoplasmic RNA escape, a characteristic of lost plasma membrane integrity. In experimental (n = 3) and simulated (n = 30) ground truth datasets, *DamageDetective* emerged favourably, achieving the highest balanced performance among existing methods (MCC = 0.61, CI: 0.44–0.85). This was demonstrated in a non-ground truth bronchoalveolar lavage (BAL) dataset where output from existing methods showed expected immune cell type clusters to be either absent or distorted—suggesting over- or underestimation of damage prevalence—compared to *DamageDetective*, which preserved and refined these clusters.

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[021] Novel insights into the biology and functional relevance of innate lymphoid Type 2 cells in cutaneous Leishmaniasis using a mouse model of infection

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Innate lymphoid cells (ILCs) are tissue-resident lymphocyte cells that lack adaptive receptors, differentiating them from B and T cells, and act as the innate counterpart of T lymphocytes. ILC2s mirror $CD4^+$ T helper 2 cells, which are involved in Type 2 immunity against large extracellular parasites and allergens. Functionally, ILC2s produce effector molecules such as type 2 cytokines (IL-4, IL-5, IL-13, and IL-9), express amphiregulin and large amounts of the transcription factor GATA3. The functional contribution of ILC2s to disease is still being ascertained, particularly in parasitic diseases, such as leishmaniasis. Leishmaniasis, a neglected tropical disease caused by a protozoan parasite called *Leishmania* spp., is transmitted to humans by the bite of the female sandfly (*Phlebotomus* sp.). There are three main clinical manifestations: visceral, mucosal, and the most common, cutaneous (CL). Cutaneous leishmaniasis results in skin lesions at the site of the bite and often leaves scars. Self-healing can occur, resulting in some immunity, but not a sterile cure. Therefore, long-term immunity is attainable through vaccination. However, there is no effective vaccine. A common species to cause CL is *Leishmania major*. Mouse models have elucidated immunological data and host immune responses related to CL caused by *L. major*, highlighting that host factors may influence disease response. However, the contribution of ILC2s remains unclear. This project will focus on ILC2s in two aspects: (1) signals inducing ILC2 expansion and secretion (specifically parasite-specific and non-parasite-specific stimulants), and (2) ILC2-cell interactions with significant immune cells, such as T cells, B cells and macrophages.

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[029] Comparative immunogenicity of reduced vs. Standard dose *brucella abortus* S19 vaccine in cattle administered via different routes

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Brucellosis is a zoonotic disease of significance caused by *Brucella spp*. primarily affecting livestock resulting in abortions, decline in productivity and immunocompromised offspring that ultimately affect both the national and international livestock trade. Live attenuated *Brucella abortus* S19 vaccine is a widely used vaccine in controlling bovine brucellosis and it has been for many years administered subcutaneously. However, this vaccination route and dose have proven to present several disadvantages, one of them being the persistence of high antibody levels post-vaccination, which prevents the differentiation between infected and vaccinated animals (DIVA), a critical diagnosis for trade. This study evaluates the immunogenic response elicited by a reduced dose of a commercial live attenuated *Brucella abortus*S19 vaccine compared to the standard dose, administered via different vaccination routes (subcutaneous and conjunctival) in cattle. Serological and cellular immune responses were monitored over a 6-month period post-vaccination using indirect-enzyme linked immunosorbent assay (i-ELISA) and RT^2 Profiler PCR arrays to monitor the expression of innate and adaptive immune response gene. using Real Time PCR (RT-PCR), as well as residual shedding of vaccine strain, as a safety measure using quantitative polymerase chain reaction (q-PCR). Preliminary findings suggest that a reduced-dose vaccination, particularly via the conjunctival route, may offer comparable immunogenicity to the standard dose while minimizing adverse effects and diagnostic interference during screening. These results support the potential for dose and route optimization in brucellosis vaccination strategies, contributing to more effective and sustainable disease control program.

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[031] Antemortem diagnosis of *Mycobacterium bovis* infection in African lions (*Panthera leo*)

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Animal tuberculosis, caused by *Mycobacterium bovis* (*M. bovis*) infection, remains a significant zoonotic and ecological concern at the human–livestock–wildlife interface. In South Africa, this chronic infectious disease affects many of the country's most iconic wildlife species including African lions (*Panthera leo*). This study aimed to identify *M. bovis*-infected lions using a combination of available antemortem

diagnostic tools. Samples, including blood, bronchoalveolar lavage (BAL) fluid and aspirates from elbow hygromas, were collected from free-ranging lions in Kruger National Park (KNP) as part of a larger approved project. Direct detection of *M. bovis* infection was performed using mycobacterial culture and the GeneXpert® MTB/RIF Ultra (GXU®) assay. In parallel, immunological assays were performed to screen for sensitization to *M. bovis*. This included a partially validated interferon-gamma release assay (IGRA) using whole blood stimulated with QuantiFERON®-TB Gold Plus tubes, and the Chembio DPP® Vet TB serological test (for detection of mycobacterial antibodies). *Mycobacterium bovis* was successfully isolated from an elbow hygroma aspirate of one lion. Although no *M. bovis* was isolated from BAL fluid, non-tuberculous mycobacteria (NTMs), including *M. littorale*, *M. novocastrense*, *M. peregrinum*, and members of the *M. avium* complex, were detected. However, the GXU® detected *Mycobacterium tuberculosis* (MTB) complex DNA in 6/79 (7.6%) BAL samples, at "trace" (n=5) and "high" (n=1) levels. While IGRA identified 61/79 (77.2%) lions as sensitized to *M. bovis*, only two individuals (2.5%) were seropositive using the DPP® assay. A comparison of direct and indirect *M. bovis* infection detection methods revealed substantial differences, which might be due to variability in stage of infection, host immune response, as well as technical challenges of using paucibacillary samples. Previous studies suggest that the QFT-IGRA is highly sensitive for detecting *M. bovis* infection, whereas serological responses are only present in cases of advanced disease in lions. These findings suggest that multiple tools are required to provide accurate antemortem detection of *M. bovis* infection in African lions, especially since test performance may vary with progression of TB. Inclusion of wildlife health in global disease prevention is critical for managing the risks of zoonotic transmission and understanding disease dynamics at their shared interfaces.

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[032] Rural cattle as reservoirs of zoonotic mycobacteria: genomic insights from KwaZulu-Natal, South Africa

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This study aimed to analyse secreted mycobacterial communities from KwaZulu-Natal (KZN) rural cattle positive on the GeneXpert MTB/RIF Ultra assay (Ultra), using next-generational sequencing (NGS). Oronasal swabs (n = 12) and faeces (n = 93) were collected in 2023 from rural KZN cattle (n = 93). The Ultra was performed on all samples, of which 3/12 and 9/93 had *Mycobacterium tuberculosis* complex (MTBC) DNA present, respectively. Samples were further subjected to the Mycobacteria growth indicator tube (MGIT) system. Subsequently, 77/105 and 5/105 were positive for solid media growth. DNA was extracted from raw specimens, primary MGITs, and solid-media colonies containing MTBC DNA (n = 12). Region-of-difference PCR (RD-PCR) was performed on extracted DNA from all Ultra-positive primary MGITs and solid-media colonies for speciation. Extracted DNA from raw faeces and MGITs was further subjected to mycobacterial-specific PCRs. Targeted amplicon NGS was conducted using the Oxford Nanopore Technologies (ONT) PromethION 2 solo. Finally, whole-genome sequencing (WGS) was performed on DNA from all solid-media-cultured isolates. RD-PCR identified seven culture samples as *M. bovis* (n = 3 MGITs and n = 4 solid-media isolates). Finally, *M. komossense* (n = 1), *M. avium* (n = 1), *M. bovis* (n = 2), and *M. litorale* (n = 1) were confirmed using WGS on solid-media-cultured

isolates. This is the first study to report *M. bovis* isolation from free-ranging rural cattle secretions, providing genomic insights into mycobacterial communities and highlighting how *M. bovis* is masked by other Mycobacteria present in raw specimens.

[035] TB and the male sex bias: Investigating the effect of sex hormones on mycobacterial killing *in vitro*

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Globally, Tuberculosis (TB) incidence rates are nearly twice as high in males compared to females [1]. Despite being widely documented, the underlying biological mechanisms are poorly understood. Epidemiological data shows that the male bias only becomes significant following sexual maturation and reduces again post menopause providing strong evidence for the involvement of sex hormones [2]. Furthermore, even though the male sex bias is less pronounced before sexual maturation, the disparity is still present suggesting a genetic contributing factor. Previous genome wide association studies (GWAS) identified strong sex-specific genetic effects on TB susceptibility [3]. Building on this, the current study aims to functionally investigate the effect of sex hormones on macrophage killing capacity and their gene expression *in vitro*. To date, we have optimized hormone concentrations and infection time points and investigated mycobacterial killing in response to oestrogen and testosterone treatment compared to untreated controls using colony-forming unit enumeration. However, no statistically significant differences were observed between hormone-treated and control groups. In addition, cytokine profiling has been completed on both infected and uninfected macrophages treated with sex hormones, generating a dataset that was used to identify the most relevant time point and concentration for subsequent experiments. Future transcriptomic analyses will explore differential gene expression under hormone stimulation as a potential mechanism underlying the male bias in TB. The analyses generated from this study serve to broaden our understanding of the mechanisms underlying sex-specific effects during *M. tuberculosis* infection and provide preliminary data for further investigation using human samples.

[036] The impact of inflammatory and metabolic breast milk profiles associated with maternal HIV on infant growth and development

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HIV-exposed uninfected (HEU) infants are at increased risk of suboptimal growth and infection despite being HIV-negative. Breast milk composition, shaped by maternal HIV status and antiretroviral therapy (ART) regimen, may influence infant health outcomes. This study investigated the inflammatory, antimicrobial, and metabolic profiles of breastmilk from mothers living with HIV (MLWH) as well as HIV-uninfected mothers, and their association with infant growth trajectories. Breast milk samples were collected from 24 mothers of African descent (15 HIV-uninfected; 9 MLWH on a fixed-dose ART) at birth, 6 ± 4 weeks, and 6 ± 3 months postpartum. Inflammatory cytokines (IL-2, IL-6, IL-8, TNF-α) and antimicrobial peptides (lysozyme, lactoferrin, beta-defensin-2, tenascin C) were quantified using suspension bead array and ELISAs, respectively. Metabolites were profiled using untargeted nuclear magnetic resonance spectroscopy. Although not statistically significant, HEU infants exhibited moderately poorer growth compared to HIV-unexposed uninfected infants. Colostrum from MLWH contained reduced levels of inflammatory cytokines (except for IL-6) and antimicrobial peptides (notably lysozyme and tenascin C). Breast milk from MLWH also showed reduced levels of metabolites, which are essential for immune and developmental support. Maternal HIV status alters the immune and metabolic breast milk profiles, potentially compromising HEU infant development. These findings should be explored in mechanistic studies and warrant closer monitoring of HEU infants and maternal nutritional interventions.

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[037] Host responses to chikungunya infection and their association with long-term arthritis

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Chikungunya virus (CHIKV) is an enveloped alphavirus with an ~11.8 kb genome encoding four non-structural and three structural proteins. The infection is transmitted by the Aedes species of mosquitoes, known to be circulating in the northeastern parts of South Africa. CHIKV causes Chikungunya fever (CHIKF), an acute febrile illness marked by high viremia. A significant clinical concern is persistent polyarthritis, affecting approximately 30% of patients, extending from months to years. While innate immune responses, particularly Type 1 interferons, help control viral replication, the factors underlying chronic disease remain poorly understood. Chondrocytes, the primary cell type in cartilage, are known to be permissive to alphavirus infection and may contribute to joint pathology. In this study, we investigate CHIKV infection in primary human chondrocytes using clinical isolates from the East/Central/South African (ECSA) and West African (WA) lineages. Ethical approval was obtained to harvest hyaline cartilage from participants undergoing clinically indicated surgeries where this tissue would otherwise be discarded for incineration. Preliminary results show that primary chondrocytes are more permissive to CHIKV infection than the highly permissive Vero cell line. We also observed heterogeneity in infection between both the donor and the viral strain, suggesting that host and viral genetic factors influence cellular susceptibility. These findings support the hypothesis that differential host-pathogen interactions may determine the heterogeneity in chronic joint symptoms. This work is ongoing, and future research will focus on understanding the mechanisms driving viral persistence and chronic joint inflammation.

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[039] Characterization of T-cell immune responses to SARS-CoV-2 and cross-reactivity to variants of concern in South African children

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Children infected with SARS-CoV-2 are more likely to exhibit asymptomatic or mild illness compared to the severe clinical outcomes often observed in adults. There are limited studies analysing SARS-CoV-2-specific T cell immunity in children from Africa. The aim of this study was to investigate SARS-CoV-2-specific T cell responses in South African children from the Drakenstein Child Health study to 1) compare responses in children to their mothers; 2) determine durability and 3) measure cross-reactivity to variants of concerns. Children (n=125; median age:7-years) and their mothers (n=81) were recruited from Western Cape, during the COVID-19 pandemic. Samples were taken after the 2nd epidemic wave (Mar-May 2021) and after 1-year (Jun-Dec 2022). SARS-CoV-2-specific T cell responses against spike, nucleocapsid and membrane along with Ancestral, Delta and Omicron spike proteins were quantified using intracellular cytokine staining and flow cytometry. Overall, children mounted a significantly lower SARS-CoV-2-specific T cell responses than their mothers. Polyfunctional analysis revealed distinct CD4 T cell profiles, higher proportions of polyfunctional SARS-CoV-2-specific CD4 T cells (IFN-γ+TNF-α+IL-2+) were detected in mothers, while children had a higher proportion of monofunctional (IFN-γ+) CD4 T cells. After 1-year, 82% of children-maintained SARS-CoV-2-specific T cells and exhibited a predominantly early differentiated (CD27+CD45RA-) memory phenotype. Finally, we showed that SARS-CoV-2-specific T cell responses generated after natural infection in children cross-recognize Delta and Omicron variants. Despite children having a significantly reduced SARS-CoV-2-specific T cell responses compared to their mothers, but this response was maintained up to 1-year and demonstrated cross-reactivity to the Delta and Omicron variants.

[040] Investigating the process of neutrophil extracellular trap formation using imaging and cytometric techniques

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Neutrophil extracellular traps (NETs) are networks of extruded genomic filaments from the genomic DNA of neutrophils. Various quantification techniques are employed to evaluate NETs and the mechanism by which these structures develop, known as NETosis, although there is currently no recognised gold standard for measuring NETosis, complicating research, identification and quantification. In this study, we aim to establish a robust general method to induce NET induction. To do so we stimulated neutrophils to induce NET formation and analysed this through both manual and automated quantification methods using confocal micrographs. The methods were compared to evaluate reliability and reproducibility. Granular proteins, myeloperoxidase (MPO) and citrullinated histone H3 (CitH3), were assessed for their viability as reliable markers of NETosis. Current standard markers of NETosis, MPO and CitH3, were not consistently observed throughout the NETotic process. These markers were also found in unstimulated neutrophils. In addition to granule presence, morphological changes were observed, which include nuclear swelling and rounding. It is unclear whether these changes are always associated with NETosis. Future research should focus on elucidating whether morphological and granule presentation is exclusive to NETosis, or whether these alterations may also indicate neutrophil activation. CitH3 and MPO were found not to be reliable markers for NETosis. Morphological changes such as nuclear swelling, were consistently observed in neutrophils stimulated with pro-NETotic agents. It remains unclear whether these changes represent irreversible commitment to NETosis or if neutrophils retain the capacity to reverse the process.

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[042] The effect of cationic DNA-binding proteins on HIV-1 latency

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Latent HIV-1 reservoirs remain the foremost obstacle to a cure. Cure strategies such as “Shock and Kill”, which uses latency-reversing agents (LRAs) to reactivate and eliminate latent virus, and “Block and Lock” which employs latency-promoting agents (LPAs) to silence the virus, have shown limited long-term success. This study investigates the potential of cationic proteins lysozyme (Lz), lactoferrin (Lf), and HL9 (a lysozyme-derived fragment) to modulate HIV-1 latency. J-Lat cell lines were treated with varying concentrations of cationic proteins, alone or in combination with established LRAs (PMA and SAHA) and LPAs (tanespimycin and spironolactone). HIV-1 latency reactivation was assessed after 24-48 hours by measuring GFP expression by flow cytometry. Our data revealed that cationic proteins had minimal latency-reversing activity on their own but significantly altered LRA and LPA effects, with outcomes depending on cell type. In J-Lat A2 cells (subtype-B), Lf enhanced reactivation by PMA (by 228%) and SAHA (by 3000 %). In contrast, Lf only enhanced reactivation by 112% and 700% in J-Lat T66 cells (subtype-C), respectively. Notably, Lf counteracted the blocking effect of tanespimycin on PMA-induced reactivation by reducing the blocking effect of tanespimycin from 93% to 23% in J-Lat A2 cells, and from 40% to 31% in J-Lat C cells. These findings suggest Lf can enhance latency reversal in permissive contexts and potentially counteracts tanespimycin effect, which was more pronounced in subtype B compared

to subtype C. This highlights Lf as a promising adjunct in HIV-1 cure strategies and underscores the importance of cellular and viral subtype context in therapeutic outcomes.

[043] Characterization of antigens to assess T cell responses in the HVTN 605 TB vaccine trial

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An effective vaccine against TB is urgently needed, especially for people living with HIV. The HVTN 605/ACTG A5421 Phase 2a trial is testing BCG Danish strain 1331 and MTBVAC vaccination of South African adolescents and adults with/without HIV. We will assess T cell responses using a validated 28-color Intracellular Cytokine Staining (ICS) assay. We characterized responses to BCG, MTBVAC, *Mtb* lysate and two new *Mtb* peptide pools. Cryopreserved PBMC isolated from volunteers enrolled in Seattle (low mycobacterial sensitization) and Cape Town (high mycobacterial sensitization) were stimulated with the antigens for 8 hours. BCG and MTBVAC were titrated at a range of multiplicities of infection (MOI); *Mtb* lysate was tested from 1µg/ml to 300µg/ml. Two peptide pools derived from the published MTB300 pool covering immunodominant *Mtb* T cell epitopes were synthesized and characterized to include shorter CD8 epitopes: Mtb213, representing epitopes present in both BCG and *Mtb*, and Mtb253 included additional epitopes unique to Mtb. Data was analyzed in FlowJo. Titration of BCG and MTBVAC concluded that an MOI of 4 was optimal for detecting IFN-γ and/or IL-2 responses in CD4+ T cells in the ICS assay. *Mtb* lysate elicited optimal CD4+ T cell responses at a concentration of 30µg/ml. CD4+ T cell responses to both peptide pools were higher in Cape Town participants and Mtb253 elicited slightly higher response magnitudes than Mtb213. Limited CD8+ T cell responses were detected using these antigens.All antigens were deemed fit for use in the ICS assays for the HVTN 605 trial.

[044] Phenotyping positive sequential additive challenge reactions following severe cutaneous adverse reactions to anti-TB medications

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Sequential additive drug challenge(SADC) allows rapid reinitiation of tolerated medications following severe cutaneous adverse reactions(SCAR). However, rechallenge reactions are clinically heterogeneous meaning differentiating true from transient reactions is challenging. We hypothesised the plasma proteome may discriminate. Validated SCAR(DRESS, SJS/TEN and GBFDE) cases were recruited from Groote Schuur hospital, South Africa as part of the IMARI prospective registry. Samples were collected prechallenge and on development of a positive reaction from 20 patients. Olink analysis(96-inflammation panel), C reactive protein(CRP) and tryptase measurements were performed, and ratios between prechallenge and drug reaction timepoints compared. Incident SCAR included: 84%(21/25) DRESS, 4%(1/25) SJS/TEN and 12%(3/25) GBFDE. Clinical reaction phenotypes were: 56%(14/25) immediate - < 6hours from drug administration, 24%(6/25) delayed, and 20%(5/25) transient. The cohort's mean (SD) age was 38(11) years, 76%(19/25) were female, 84%(21/25) had active TB, and 88%(22/25) were PLWH [median(IQR) CD4 count 144(96-373)]. Amongst clinical features, only skin burning was less common in transient reactions (p=0.03). Classical markers tryptase, CRP and IL-6 did not differentiate reaction phenotypes. Principal component analysis showed a significant overlap across all reactor phenotypes, with positive reactions characterised by increased neurturin, IL-6, MCP-1, IFN-gamma and other markers of monocyte and neutrophil pathways. Although no significant differences in markers were found between immediate and delayed reactors, transient reactions showed lower levels of IFN-gamma and IL-6. Positive drug reactions post SCAR shows consistent inflammatory profile independent of timing of symptom onset. The magnitude of IL-6 and IFN-gamma elevations may help distinguish transient from treatment-limiting reactions, and further work is required.

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[045] Insulin-like growth factor 1 (IGF-1) signalling in tuberculosis and tuberculosis/diabetes do-morbidity

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The convergence of tuberculosis (TB) and diabetes mellitus (DM) presents a growing global health challenge, with DM increasing the risk and severity of TB. While metabolic and immunological dysregulation in TB-DM co-morbidity has been explored, the role of insulin-like growth factor 1 (IGF-1) signalling in this context remains poorly understood. IGF-1, a critical mediator of cellular growth, metabolism, and immune function, may play a pivotal role in host-pathogen interactions during *Mycobacterium tuberculosis* infection, particularly in the setting of hyperglycaemia. This study investigates the involvement of IGF-1 signalling in TB-DM co-morbidity, we hypothesized that elevated IGF-1/IGF-1R expression contributes to impaired immune responses and exacerbated disease outcomes. Using *a* model of macrophage-specific IGF-1 knockout mice ($LysM^{cre}IGF\text{-}1^{flox/flox}$), we examined IGF-1 expression and signalling in TB-infected hosts with DM, by assessing the impact of IGF-1 modulation on bacterial control, inflammatory responses, detailed immune cell profiling, and cytokine production. IGF-1 deficiency does not significantly alter lung bacterial burden at 22 weeks post-infection. The slight reduction in pulmonary CFUs alongside increased splenic dissemination suggests impaired local bacterial containment in the absence of IGF-1. Furthermore, IGF-1-deficient mice demonstrated an expansion of monocyte-derived dendritic cells (moDCs), which may contribute to immune dysfunction during chronic infection. The reduced TNF expression in $CD8^+$ T cells further indicates a compromised T-cell response, hindering effective bacterial clearance. Consequently, IGF-1-deficient mice displayed reduced IGF-1 expression in $CD4^+$ and $CD8^+$ T cells. Our findings suggest the absence of IGF-1 may promote an environment conducive to disease containment.

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[047] *In vitro* immunomodulatory effects of African traditional medicines in H1299-ACE2 cells co-cultured with peripheral blood mononuclear cells in response to SARS-CoV-2 infection

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The hallmark of severe COVID-19 is associated with elevated inflammatory cytokines, contributing to a life threatening systemic inflammatory syndrome known as cytokine storm and resultant poor clinical outcomes. African traditional medicines (ATMs) with immunomodulatory properties may offer prophylactic or therapeutic options. This study assessed the cytotoxicity and immunomodulatory activity of two South African ATMs—Product Nkabinde (ATM-PN) and *Gnidia sericocephala* (ATM-GS) against the SARS-CoV-2 D614G variant *in vitro*. Cell cytotoxicity was evaluated using an ATP-based luminescence assay in H1299-ACE2 epithelial cells and peripheral blood mononuclear cells (PBMCs). Cytokine responses were assessed in PBMCs co-cultured with H1299-ACE2 cells in a pre- or post-treatment strategy in response to SARS-CoV-2 infection. The 50% cytotoxic concentrations (CC_{50}) value which is the concentration of the ATM that kills 50% of the cells for ATM-GS were 1137 µg/mL (H1299-ACE2) and 110.8 µg/mL (PBMCs), whereas ATM-PN showed lesser cytotoxicity with CC_{50} values of 1736 µg/mL and 356.3 µg/mL for H1299-ACE2 cells and PBMCs, respectively. ATM-PN exhibited a robust cytokine response by significantly increasing both pro- and anti-inflammatory cytokines (IL-1β, IL-6, IL-8, TNF-α, IL-10) in both the pre-treatment and post-treatment strategies suggesting a strong antiviral and anti-inflammatory immune response. In contrast, ATM-GS showed a more balanced response particularly in post-treatment strategy by suppressing IL-1β, IL-4, TNF-α, and IL-10 while moderately

elevating IL-6 and IL-8 levels. However, ATM-GS demonstrates a safer therapeutic candidate post-infection without exacerbating inflammation. Further mechanistic and in vivo studies are essential to assess the therapeutic effectiveness of these ATMs in SARS-CoV-2 and other respiratory viral infections.

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[048] Characterization of the naïve B-cell repertoire and antigen-specific precursors in South African populations

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Effective antiretroviral therapy has transformed AIDS from a fatal disease to a manageable chronic disease, HIV-1 remains a major global health burden with 1.3 million new infections annually. South Africa still has the highest median HIV-1 prevalence, especially among young women ages 15-25. Consequently, an effective and safe HIV-1 vaccine is urgently needed. The study aims to determine the presence of bnAb-like features in the naïve B-cell repertoire by identifying the V(D)J recombination patterns and genetic variations that could impact antibody-mediated protection from healthy South Africans. Additionally, we evaluated frequencies and features of antigen-specific naïve B-cell precursors binding to HIV envelope-based antigens eOD-GT8. We performed bulk sequencing using MiSeq on longitudinal samples to characterize Naïve BCR repertoire. We used germline targeting eOD-GT8 immunogen sorting and bulk sequencing using Illumina NextSeq to profile diversity and frequency of circulating broadly neutralizing antibodies (bnAbs) such as VRC01 among HIV-1 positive South African donors, aged 18-25 years. Naïve BCR sequencing revealed dominant gene usage (IGHV3, IGHD3 and IGHJ4), CDRH3 length of 15 amino acids, measurable somatic hypermutation (SHM) and antibody clonotypes. We genetically characterized VRC01-class precursor B cells by VH1-2 gene usage, short CDRL3 length and high rate of SHM.Our findings highlight the genetic diversity and presence of eOD-GT8-reactive naïve B cells, providing evidence for their potential in HIV-1 vaccine design. This supports the feasibility of germline-targeting vaccine strategies in high-prevalence regions like South Africa.

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[053] Investigating the function of Sestrin 1 (SESN1) gene in *listeria monocytogenes* infection

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L. monocytogenes is a facultative intracellular pathogen capable of evading host immune defences and establishing systemic infections. While antibiotics remain the primary treatment option, host-directed therapies (HDT) offer a promising platform to enhance immune responses and improve disease outcomes. We identified Sestrin 1 (Sesn1*)* gene differentially expressed in Mtb-infected macrophages. Sesn1, a stress-inducible protein, plays a significant role in cellular homeostasis and immune regulation, cellular stress responses, autophagy, and immune signaling, however, despite its known involvement in cellular stress responses and immune regulation, the functional role of Sesn1 in the context of infectious diseases, including bacterial pathogens like *L. monocytogenes*, remains largely unexplored and poorly characterized. This study is investigating the role of Sesn1 in listeriosis infection using *in vitro* and *in vivo* approaches. We are utilizing Sesn1 knockout (KO) mouse model to examine bacterial clearance, tissue pathology, innate and adaptive immune cells responses in acute and chronic disease progression. To better understand the relevance of this gene function in humans, we were employing siRNA to knock down approach for Sesn1, and other 2 Sestrin orthologs (Sesn2 and Sesn3) in THP-1-derived human macrophages, and monocyte-derived macrophages (MDMs). This study will provide understanding into the immunomodulatory role of Sesn1 and its potential as a novel therapeutic target in HDTs and may contribute to the development of alternative strategies for managing intracellular listeria infection.

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[054] Targeting the Monocyte: Lymphocyte ratio and Osteopontin as potential diagnostic markers for TB disease and treatment response

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Tuberculosis (TB) remains a global threat with a high mortality rate, resulting from a single infectious agent. Current TB diagnostic and treatment measures suffer challenges, such as high costs, inaccessibility, and lack of adequate infrastructure, particularly in low-income environments. Here, we performed full blood count, analyzed plasma levels of full-length osteopontin (OPN), and measured inflammatory cytokines to determine their potential diagnostic value in pulmonary TB. Study participants were stratified into healthy controls (CTRL) and TB treatment group where peripheral blood and bronchoalveolar lavage (BAL) samples were obtained. Blood samples were collected from the TB treatment group at TB diagnosis (TBDx), week 1 (TBW1), month 2 (TBM2), and month 6 (TBM6) while BAL samples were only collected at TBDx and TBM6. Samples from the CTRL group were collected at a

single time-point. Our data showed significantly increased monocyte: lymphocyte ratio and plasma OPN in TB treatment group at TBDx when compared to the CTRL group. The elevated levels of plasma OPN in TB treatment group was significantly reduced at TBW1 and TBM2 when compared to TBDx time-point. However, plasma OPN was significantly increased in TB treatment group between TBM2 and TBM6 time-points, further showing a significant upregulation when compared to the CTRL group. OPN secretion was significantly upregulated in BAL samples from TB treatment group at TBDx and TBM6, no significant differences were observed with the CTRL group. This study highlights the diagnostic potential of monocyte: lymphocyte ratio and plasma OPN as targets for early TB diagnosis and treatment monitoring.

[056] Evolution of the extensively mutated SARS-CoV-2 BA.3.2 Omicron subvariant

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In November 2021, the Omicron variant of SARS-CoV-2 was first detected in Botswana and South Africa and subsequently divided into three primary lineages: BA.1, BA.2, and BA.3. Nearly three years later, a highly mutated descendant of BA.3, designated BA.3.2, was identified in South Africa. This subvariant contains over 30 additional spike protein mutations relative to BA.3, as well as a large deletion in accessory genes, raising concerns about reduced susceptibility to neutralizing antibodies and differences in viral function. We successfully isolated live Omicron BA.3 and BA.3.2 viruses from diagnostic swab samples collected in South Africa. Using sera from individuals sampled in March 2025, we performed neutralization assays to assess the extent of antibody escape. Preliminary data shows an 8-fold reduction in BA.3.2 neutralization relative to BA.3, indicating increased immune evasion. Our ongoing work is focused on comparative analyses of BA.3 and BA.3.2 replication kinetics cytopathic effects, and innate immune response. These findings highlight the continued evolution of SARS-CoV-2 and the importance of ongoing genomic surveillance and functional characterization of emerging variants.

[057] Assessing the burden of dengue virus infection in northern KwaZulu-Natal, South Africa

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Dengue virus (DENV) is a rapidly spreading mosquito-borne *Flavivirus*, primarily affecting tropical and subtropical regions. Despite favorable conditions for transmission in northern KwaZulu-Natal (KZN), including the presence of *Aedes* mosquito vectors and proximity to dengue-endemic Mozambique, the

burden of DENV in this region remains poorly understood due to limited surveillance. This study aims to assess the seroprevalence and immune responses to DENV in northern KZN using serological, virological, and molecular approaches. Two DENV-positive plasma samples obtained through collaborations were cultured in Vero E6 cells. Viral replication was monitored through cytopathic effects and quantified using RT-qPCR with the Novaplex™ Tropical Fever Virus Assay. Infectious units were confirmed via a live virus focus forming assay. Whole-genome sequencing using Oxford Nanopore Technologies and Genome Detective identified both isolates as DENV serotype 1 (DENV-1). No in vitro mutations were detected, and phylogenetic analysis revealed clustering with global DENV-1 strains. The next phase will analyze sera collected during sentinel surveillance in northern KZN to assess neutralizing antibody responses. Additionally, ELISAs will detect IgM and IgG antibodies, indicating recent or past exposure. These findings will improve understanding of DENV transmission dynamics, inform population-level immunity, and support outbreak preparedness efforts in South Africa.

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[058] Variations in neutralization sensitivity of HIV-1 subtype c between lymph nodes, peripheral blood mononuclear cells and plasma derived viruses

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There are genetic variations in the HIV-1 *env* single genome amplicons (SGA) derived from plasma, polymorphonuclear cells (PBMCs) and lymph node samples. However, the impact of these amino acid variations in the sensitivity of broadly neutralizing antibodies is not known. Therefore, the aim of this study was to evaluate HIV-1 *env* sequence differences within bnAb epitopes and assess their neutralization sensitivity in HIV-1 subtype C between lymph nodes, PBMC and plasma-derived clones. Full-length HIV-1 *env* was amplified from four HIV-1 subtype C infected ART naïve individuals selected from the FRESH cohort based in KwaZulu-Natal, South Africa. Single genome amplicons were produced from plasma, lymph nodes and PBMC samples sequenced by Sanger sequencing and cloned into a TOPO 2.1 vector. Env-pseudotyped viruses were produced and the neutralization sensitivity was assessed against a panel of nine broadly neutralizing antibodies (bnAbs) targeting different epitopes. HIV-1 *env* sequences were analysed within bnAb epitopes and compared between lymph nodes, PBMC and plasma samples. A high frequency of discordant mutations was observed in the V2 and V3 loops, while few discordant amino acid mutations were observed in the conserved regions including the CD4 binding site, MPER and gp120-gp41 interface. Discordant mutations were associated with the differences in neutralization sensitivity between viruses derived from plasma, lymph nodes and PBMCs. The highest number of resistant mutations were observed in the lymph node compartment. Our findings suggest that amino acid variations in viral populations that are circulating in lymph nodes, PBMCs and plasma may lead to differences in neutralization sensitivity to bnAbs. These findings may have implications in immunotherapy or vaccine development.

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[060] Evaluating the immunomodulatory potential of atorvastatin in reducing inflammation and tissue damage post-tuberculosis treatment

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Tuberculosis (TB), caused by *Mycobacterium tuberculosis (Mtb)*, continues to be a leading cause of morbidity and mortality globally, with South Africa being among the 30 countries with the highest TB burden. Despite effective TB treatment, many patients experience chronic lung inflammation and tissue damage following successful treatment, contributing to long-term respiratory complications and increasing the risk of TB relapse. This post-treatment lung pathology is driven by dysregulated macrophage functions, including impairment of phagosome maturation, excessive inflammatory responses, and necrotic cell death. Atorvastatin, a widely used and prescribed cholesterol-lowering agent, has been shown to exhibit immunomodulatory effects in various infectious diseases and may help restore immune homeostasis. This study is embedded in the ongoing StatinTB clinical trial, investigating how atorvastatin modulates immune responses in participants with persistent lung inflammation following TB treatment. Using PBMCs and serum samples isolated from trial participants before and after 12 weeks of atorvastatin or placebo treatment, we assess phagosome maturation, vesicular trafficking and mitochondrial-dependent apoptosis using flow cytometry and confocal microscopy, targeting markers such as LAMP1, Bax, Bcl2 and caspase 3. Luminex multiplex complements these analyses to identify immune signatures associated with atorvastatin treatment. The findings of this study will provide mechanistic insights into how atorvastatin may function as a host-directed therapy to aid in reducing chronic inflammation and preventing pulmonary tissue damage that may persist after TB treatment.

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[061] Cytomegalovirus infection in preterm and HIV-exposed infants: a prospective South African cohort study – Tariq Webber

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Congenital and postnatal cytomegalovirus (cCMV, pCMV) infections can be associated with multi-organ disease in preterm and low birthweight infants, however, there is uncertainty regarding which infants require treatment. We aimed to enhance understanding of CMV acquisition and associated immune responses in this population to inform and guide treatment strategies. Infants <14 days and <1.5kg were enrolled from a South African tertiary hospital neonatal unit. Blood and saliva were collected at enrolment, followed by weekly saliva and clinical data collection. CMV DNA in saliva was quantified by PCR. A CMV ELISPOT assay measured interferon gamma (IFNγ) release from T cells in response to CMV peptides. 154 infants with median gestational age of 28 weeks [IQR 28.0-30.0] and birthweight of 1072.5g [IQR 950-1275.5] were enrolled. 30 (19%) were HIV-exposed uninfected infants (HEU). Eleven (7%) infants had cCMV; two (15%) had neurological abnormalities but no hearing loss. pCMV was acquired in 8 (5%) infants at median age 4.0 weeks [IQR 3.0–5.0]. Peak saliva CMV viral load correlated with longer admissions (r=0.7, p=0.0046). CMV-infected and uninfected infants showed no significant difference in IFNγ T-cell responses, though HEU infants with CMV showed a trend toward low responses. The prevalence of cCMV and pCMV is higher than previously reported in South Africa. High saliva CMV viral load is associated with prolonged hospitalization. HIV-exposure may impair CMV-specific T-cell responses, suggestive of T-cell exhaustion in-utero. Future work will investigate whether CMV-specific immune profiles can identify infants who could benefit from treatment.

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[063] Phenotypic profiling of TST-induced local T cell immune responses in Mtb-exposed individuals

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Understanding protective immune responses to Mycobacterium tuberculosis (Mtb) is critical for advancing TB vaccine development. While systemic immunity has been extensively profiled, less is known about the local immune mechanisms that may contribute to protection. The tuberculin skin test (TST) provides a unique opportunity to study immune responses in vivo. When coupled with skin blistering, it enables direct sampling of immune cells engaged in localized recall responses. We recruited TB household contacts and performed a Mantoux TST. On day 7, we induced a suction blister at the TST site and analyzed the blister cells using high-dimensional flow cytometry. The immune cell infiltrate was dominated by CD8+ T-cells, outnumbering CD4+ T-cells. The CD4+ T-cells were mostly effector memory (TEM), while CD8+ T-cells comprised both TEM and TEMRA subsets. Naive T-cells were nearly absent. Notably, a high frequency of tissue-resident memory (TRM) cells (CD69+CD103+) was detected, with CD8+ TRMs being more prominent than CD4+ TRMs. Both T-cell subsets showed evidence of activation (CD38+, HLA-DR+) and exhaustion (PD-1+, TIM-3+, TIGIT+), suggesting ongoing antigenic stimulation or immune regulation. Interestingly, the CD4+ T-cell compartment exhibited a Th1/Th17-skewed phenotype (CXCR3+CCR6+) rather than a classical Th1-only response. Further, HLA-DR+CD38+ activated T-cells were predominantly CXCR3+, consistent with potential TB antigen-specific cells. The TST blister site reveals a robust, antigen-driven, tissue-localized immune response in asymptomatic, TB-exposed individuals. The predominance of CD8+ TRMs and the presence of activated, Th1/Th17-polarized CXCR3+ T-cells highlight key components of local immune recall.

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[065] Seroprevalence of pre-existing neutralising antibody responses to clinically relevant adenoviruses in a Southern African population

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Adenoviruses (Ads) are widely used as vaccine vectors; however, pre-existing immunity to common Ads like Ad5 can reduce vaccine immunogenicity, as studies have reported anti-vector titers > 200 impact vaccine efficacy. Less common (Ad26) or non-human (gorilla adenovirus, GRAd32) Ad vectors were developed, but their seroprevalence in sub-Saharan Africa is poorly defined. Sera from participants enrolled in the South African Sisonke sub-study (n=100) (pre-Ad26.COV2.S vaccination), the follow-up study "Booster after Sisonke" (Basis) (pre- and post-Ad26.COV2.S), and 40 sera from a pre-COVID cohort in Zimbabwe were tested for Ad5, Ad26, and GRAd32 neutralizing antibodies. Neutralization titers were compared, and the Spearman's test was used to evaluate correlations between antibody (Ab) responses to the different Ads. In the Sisonke cohort, geometric mean titers (GMT) for anti-GRAd32, Ad26, and Ad5 antibodies were 78, 142, and 459, with neutralization titers >200 observed in 14%, 32%, and 68% of responses, respectively. Similarly, in the Zimbabwean cohort, GMTs for GRAd32, Ad26, and Ad5 were 65, 125, and 631, with neutralizing titers >200 seen in 17.5%, 42.5%, and 70% of responses. No correlation was observed between Ab responses to the different Ads across cohorts. At ~9 months post-prime, anti-Ad26 titers in the Basis cohort increased to a GMT of 929, while GRAd32 titers remained comparable at 48. Anti-Ad5 neutralizing responses are common globally, while Ad26 and GRAd32 responses are less frequent. These findings suggest that Ad-vectored priming does not elicit cross-reactive Abs to other Ad-vectors and support the use of the GRAd32-vector in upcoming trials.

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[066] Oral pre-exposure prophylaxis does not modulate lymphoid/myeloid HIV target cell density in the foreskin: results from the CHAPS clinical trial

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Oral on-demand pre-exposure prophylaxis (PrEP) has shown efficacy in preventing HIV acquisition in men-who-have-sex-with-men, but evidence in heterosexual men in Africa is lacking. As a secondary objective of the CHAPS clinical trial in South Africa and Uganda, we investigated the immunologic safety of PrEP in the foreskin. To examine the impact of oral PrEP on lymphoid and myeloid changes in the foreskin. HIV-negative males (n=144) were enrolled in an open-label randomized controlled trial to receive high or low-start doses of Tenofovir/emtricitabine (TDF/FTC) or tenofovir. alafenamide (TAF)/FTC 5h or 21h before voluntary medical male circumcision (VMMC), or to a control arm with no PrEP prior to circumcision. Foreskins were analyzed in a blind manner to determine numbers of CD4 + CCR5 + cells and CD1a + cells using fluorescence microscopy and correlated with tissue-bound metabolites and p24 production after ex vivo foreskin challenge with HIV-1 bal. There was no significant difference in CD4 + CCR5 + or CD1a + cell numbers in foreskins between treatment arms compared with the control arm. Claudin-1 expression was 34% significantly higher (95% confidence interval (CI):11%-62%, p=0.003) in foreskin tissue from participants who received PrEP relative to controls with no difference between FTC/TDF and FTC/TAF observed. These associations were no longer statistically significant after controlling multiple comparisons. There was no correlation between CD4 + CCR5 + , CD1a + cell numbers, and claudin-1 expression with tissue-bound drug metabolites and nor with p24 production after ex vivo viral challenge. Oral dosing of either TDF or TAF over a 21hr window had no effect on in situ drug metabolite levels in tissue, or on numbers or anatomical location of lymphoid or myeloid HIV target cells in foreskin tissue.

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[068] Association between total IgE levels and multiple allergen sensitizations in patients undergoing allergy testing at a tertiary immunology laboratory

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Total immunoglobulin E (tIgE) is widely used as a preliminary marker in allergy diagnostics, yet its clinical utility in predicting multiple allergen sensitizations remains debated. Accurate identification of atopic individuals is critical, especially in resource-limited settings where broad allergy testing is costly. This study aimed to evaluate the association between total serum IgE levels and the number of allergen-specific IgE responses in patients undergoing allergy testing using the ImmunoCAP™ Phadia 250 system. A retrospective, cross-sectional analysis was conducted on 119 patients tested at the NHLS Immunology Laboratory. Data included total IgE and specific IgE results from food and inhalant allergen panels. Linear regression and independent t-tests were used to assess correlations and differences between patients with single vs. multiple sensitizations. Elevated tIgE levels were significantly associated with multiple allergen sensitizations ($p < 0.05$). Patients sensitized to more than one allergen had markedly higher tIgE values compared to those with single allergen sensitization. The most commonly detected allergens included house dust mite (*D. pteronyssinus*), grass pollen, cat dander, cockroach, and peanuts. Total IgE is a valuable preliminary indicator of atopy and may help guide the need for specific IgE testing. This study affirms the role of tIgE in allergy diagnostics and supports its use in integrated testing strategies within public healthcare settings.

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[069] Association of aldosterone, protein levels, and inflammatory markers in Angora Goats affected by Swelling Disease

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Angora goats are a valuable fibre-producing breed in South Africa but are prone to a condition known as swelling disease. The disease is characterized by ventral oedema, hypoproteinaemia, and hyperaldosteronism. In humans, hyperaldosteronism is associated with a pro-inflammatory state, but this has not been investigated in Angora goats. The present study therefore investigated the association between aldosterone and inflammation in swelling disease. Retrospective analysis was conducted using blood samples from goats in the Eastern Cape. Group 1 included weaned kids (n=20) from farm 1; groups 2 and 3 comprised does (n=20) and weaned kids (n=20) from farm 2. Each group had 10 affected and 10 unaffected goats. Group 4 included 14 goats (7 affected, 7 unaffected) from farm 3. Aldosterone, total serum protein (TSP), albumin, and white blood cell counts (WBC) were assessed in groups 1–3, while Serum Amyloid A (SAA) was measured in group 4. Significant differences were found between affected and unaffected goats in aldosterone ($p<0.04$), TSP ($p<0.01$) and albumin ($p<0.01$) levels across groups 1–3. Notably, groups 1 and 3 showed significant differences in WBC (p-value<0.01). Elevated aldosterone levels showed a significant negative correlation with TSP ($r = –0.5$, $p<0.02$) and albumin ($r = –0.5$, $p<0.02$). Group 4 showed no significant difference in SAA ($p>0.05$), though slightly higher values (1.5 – 3.6 mg/l) were observed in affected goats. These findings suggest aldosterone may contribute to fluid retention and a possible inflammatory response in swelling disease. Further investigation into aldosterone's immunomodulatory role may improve understanding of this condition's pathophysiology.

[073] Animal-friendly diagnostic reagents: a renewable, universal source based on avian genes

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Antibodies interact very specifically with their targets. Scientists exploit this interaction not only to find solutions to problems related to animal and human health, but also to develop diagnostic tests. In the past, experimental animals have been used to raise hyper-immune sera. However, in line with the current international trend to minimize the use of experimental animals, we developed sustainable antibody production methods with minimal animal use. Phage display technology uses bacteriophages, which are viruses of bacteria, to produce antibodies of interest. Because these antibodies are made in the laboratory and not by the immune systems of humans or animals, they are called recombinant antibodies (rAbs). Two rAB libraries, the *Nkuku*® and *Inshi*® libraries, were constructed. Each library consists of millions of different antibodies, representing the immune repertoires of both the chicken and ostrich, respectively. The libraries provide a universal, readily accessible pool of rAbs from which binders to a specific target can be retrieved. They can be reproduced an unlimited number of times. While we have applied this technology predominantly to veterinary applications, arenas other than animal health targets can be exploited. Thus far, rAbs to Rift Valley fever virus, African horse sickness virus, bluetongue virus, foot and mouth disease virus, equine encephalosis virus, bovine tuberculosis and equine babesiosis have been identified. Some have been incorporated into diagnostic tests in combination with recombinant proteins as targets, resulting in cost-effective, locally made assays based on completely renewable reagents.

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[074] Host proteins associated with strong neutralizing antibody responses to SARS-CoV-2 infection

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Severe Covid-19 leads to higher neutralizing antibody levels, a key correlate of protection from future infection. However, the host proteins associated with a stronger neutralizing antibody response at moderate disease severity have not been fully characterized. We investigated these associations in a South African cohort during first SARS-CoV-2 infection. Among 71 participants, 17 required supplemental oxygen but none were critically ill. Participants were stratified as high or low neutralizers based on convalescent plasma neutralization capacity; Anti-spike antibody levels were also measured. Using SomaScan proteomics on blood collected soon after diagnosis, we identified proteins linked to neutralization, spike antibody levels, and disease severity. There was strong overlap between proteins associated with neutralization and spike binding (87%), but only moderate overlap with disease severity (36%). High neutralizers, whether they required oxygen or not showed protein signatures and risk factors consistent with greater illness than low neutralizers. Inclusion of oxygen-requiring participants was essential to reveal significant neutralization-associated proteins. Predictive analyses showed that neutralization status could be inferred from individual protein markers. The strongest signal was HSPA8, a molecular chaperone that interacts with viral proteins and supports cross-presentation of extracellular antigens. To our knowledge, this is the first study to define host plasma proteins early in SARS-CoV-2 infection that predict the magnitude of neutralizing antibody responses at convalescence, providing novel insight into pathways shaping protective humoral immunity.

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[075] Mechanisms driving Colorectal Cancer (CRC) formation and differentiation in people with HIV (PWH)

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Colorectal cancer (CRC) is an emerging non-AIDS-defining cancer (NADC). PWH develop CRC nearly two decades earlier than HIV-uninfected individuals often with more advanced disease and worse outcomes. However, the mechanisms driving CRC in PWH are unclear. Chronic HIV infection in the gut causes irreversible CD4+ T-cell depletion, weakening immune surveillance and potentially predisposing individuals to CRC. CRC is also linked to excess mucin production, key marker of gut pathology and tumour progression. We hypothesized mucin to be elevated in the gut of PWH and CRC. In this study, hematoxylin and eosin (H&E)-stained tissue sections from 37 CRC patients (21 male, median age: 64.5), 8 CRC patients PWH (4 male, median age: 65), and 17 normal controls (NC) without HIV and CRC (13 male, age: 48) were analyzed using HALO AI image analysis software. We show that CRC tissues, regardless of HIV status, had more mucin than non-diseased tissues. Notably, CRC tissues from PWH exhibited even higher mucin levels than HIV-negative individuals. Ten normal controls with inflammatory conditions (e.g., colitis, IBS) also showed elevated mucin. Elevated mucin expression in PWH suggests a key role in immune evasion and disease progression, linking HIV-driven immune dysfunction to CRC development and treatment resistance. This insight suggests more studies are required to better understand the complex interplay between HIV gut pathology and CRC development.

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[078] Immune activation and thrombotic risk in African adult patients with B-cell acute lymphoblastic leukemia on maintenance therapy

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Maintenance therapy in B-cell acute lymphoblastic leukaemia (B-ALL) plays a critical role in sustaining remission and preventing relapse. While the efficacy of maintenance regimen is well established, little is known about its impact on immune function and coagulation. Emerging evidence from related malignancies suggests that immune activation and subclinical thrombosis may persist beyond intensive therapy. However, these processes have not been explored in B-ALL during maintenance. This study, therefore, aimed to assess immune activation and thrombotic risk in patients with B-ALL receiving maintenance treatment. This cross-sectional study was conducted at Windhoek Central Hospital and Katutura State Hospital in Namibia. We enrolled patients with B-ALL (n=18) and age- and sex-matched healthy controls (n=18). Plasma levels of D-dimer, thrombin, and platelet factor 4 (PF4) were quantified using an enzyme-linked immunosorbent assay. Flow cytometry was used to characterize activation markers and immune checkpoint expression on $CD4^+$ T cells, $CD19^+$ B cells, and platelets. D-dimer levels were similar between groups ($p=0.75$), whereas thrombin ($p<0.01$) and PF4 levels ($p<0.001$) were elevated in patients with B-ALL. T cells from patients with B-ALL showed increased expression of the early activation marker CD69 ($p<0.001$), along with upregulation of PD-L1 ($p<0.001$) and CTLA-4 ($p<0.001$), while PD-1 expression remained unchanged ($p=0.90$). B cells also showed increased expression of PD-1 ($p=0.02$), PD-L1 ($p<0.001$), and CTLA-4 ($p<0.01$) but no differences in CD69 ($p=0.40$). There was an increase in CD62P expression in platelets from patients with B-ALL ($p<0.001$). Patients with B-ALL on maintenance therapy show ongoing immune dysregulation and subclinical prothrombotic activity. Persistent T cell activation with broad immune checkpoint upregulation suggests chronic immune perturbation and potential exhaustion. Elevated thrombin and PF4 levels, together with platelet activation, indicate a heightened thrombotic risk, even in the absence of clinical events. Together, these findings highlight the need for integrated immuno-thrombotic monitoring during maintenance therapy to identify patients at risk of relapse, immune exhaustion, or thrombotic complications.

[080] Antibody responses elicited by different SARS-CoV-2 vaccines: Durability and impact of HIV infection

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The SARS-CoV-2 pandemic prompted the rapid development of several vaccine platforms. In Africa, where the burden of coinfections such as HIV and tuberculosis is high and vaccine rollout lagged, comparative studies of SARS-CoV-2 vaccine immunogenicity and durability remain limited. This study evaluated neutralizing antibody responses elicited by different SARS-CoV-2 vaccines against representative prototypes of major variants in 255 participants from Botswana who received Pfizer mRNA (BNT162b2), Janssen adenovirus 26 (Ad26.COV2.S), AstraZeneca chimpanzee adenovirus (ChAdOx1-S), or Sinovac whole inactivated virus. Neutralizing antibodies were measured using live virus neutralization assays and focus reduction neutralization tests. Participants were stratified by time since vaccination (≤3 months vs >3 months). At ≤3 months Pfizer (BNT162b2) induced the highest neutralizing antibody titers, significantly exceeding those of AstraZeneca (ChAdOx1-S) and Sinovac. However, only Pfizer showed a significant decline in titers when comparing responses at ≤3 months to those at >3 months. Across all vaccines, neutralizing antibodies were markedly lower against the recently emergent JN.1 variant, often falling below the limit of detection compared with the ancestral D614G strain. No significant differences were observed by HIV status or sex. The findings highlight variability in vaccine-induced immunity, waning antibody levels over time, and reduced efficacy against new variants. In low-resource settings, more durable viral vector vaccines may be advantageous, while mRNA vaccines may require timely boosting. Comparable responses between people living with and without HIV support integrating COVID-19 vaccination into HIV care programs. Continued surveillance of viral variants and investment in next-generation vaccines are essential for pandemic preparedness.

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[081] BactiVac, the Bacterial Vaccines Network

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Bacterial vaccines save lives and constitute a major tool to address the challenge of anti-microbial resistance. Nevertheless, historically there has not been a network that focuses on bacterial vaccines, to promote sharing of approaches and best practices, and provide advocacy. BactiVac, the Bacterial Vaccines Network, was established in 2017 to address this gap. Its mission is to advance vaccine development against global bacterial infections in humans and animals through a One Health approach,

to reduce disease, death, and antimicrobial resistance, and thereby enhance economic development. BactiVac brings together academia, industry, policymakers and funders from high-income countries (HICs) and low- and middle-income countries (LMICs), in a network of over >2300 members from 92 countries, including, 52% from LMICs and 15% from industry. BactiVac supports vaccine development through Catalyst Project Awards, and Catalyst Training Awards. This funding targets bottlenecks and capacity-building in bacterial vaccinology, particularly among LMIC early-career researchers. Annual Network Meetings facilitate exchange of information and ideas, and new collaborations. We provide advocacy for bacterial vaccines nationally and internationally and, by partnering with aligned networks, function as a network within a network of networks. Therefore, through providing financial support and facilitating collaboration, BactiVac supports and enhances the bacterial vaccinology community and helps reduce the devastating burdens caused by bacterial infections.

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