



CAPRISA

CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

Newsletter

April/May 2021 Volume 20 Issue 5

Mitigation of chronic immune activation could reduce the rates of TB recurrence

In this Issue

Our feature story this month focuses on the study published in the journal *Frontiers in Immunology* showing that TB reactivation in HIV co-infected individuals is associated with chronic immune activation.

Professors Salim and Quarraisha Abdool Karim's appointments to the WHO and UN committees as well as the Friends of the Global Fight Against AIDS, Tuberculosis and Malaria is highlighted on page 2.

On page 3, we report on the NIH-funded study that will provide crucial information on the role of IFN signalling in HIV infection. We also congratulate Dr Simone Richardson, Dr. Cathrine Scheepers and Dr. Rebecca van Dorsten on their recent early career awards and honours.

A summary of the provincial research symposium is provided on page 4. We also congratulate all our new graduates and award winners.

CONTACT DETAILS

CAPRISA
Doris Duke Medical
Research Institute (DDMRI)
2nd Floor
University of KwaZulu-Natal
Private Bag X7, Congella 4013
South Africa

T: +27-31-260 4555
F: +27-31-260 4566

E-mail: caprisa@caprisa.org

www.caprisa.org.za



Caprisaofficial



@CAPRISAofficial

CAPRISA researchers Ms. Kimesha Pillay (Masters student) and Dr. Aida Sivro (Senior Scientist) led a study, published in the journal, *Frontiers in Immunology*, that demonstrated that the increased risk of TB recurrence in HIV infected individuals on ART is likely driven by the HIV mediated translocation of microbial products and the resulting chronic immune activation.

The study was performed using stored plasma samples drawn from the CAPRISA TB Recurrence upon Treatment with HAART (TRuTH) study, in which individuals with previously treated pulmonary TB were screened for recurrence quarterly for up to 4 years.

Recurrent TB cases (n = 37) were matched to controls (n = 102) by original trial study arm assignment and ART start date. Plasma concentrations of soluble adhesion molecules (sMAdCAM, sICAM and sVCAM), lipopolysaccharide binding protein (LBP) and transforming growth factor-beta (TGF-β1, TGF-β2, TGF-β3) were measured by multiplex immunoassays and ELISA.

The following analytes were associated with increased risk of TB recurrence in the multivariable model: sICAM (aOR 1.06, 95% CI: 1.02-1.12, p = 0.009), LBP (aOR 8.78, 95% CI: 1.23-62.66, p = 0.030) and TGF-β3 (aOR 1.44, 95% CI 1.01-2.05, p = 0.044).

Additionally, the researchers observed a positive correlation between LBP and sICAM (r= 0.347, p<0.0001), and LBP and IL-6, identified to be one of the strongest predictors of TB risk in a previous study (r=0.623, p=0.03, Sivro et al CID 2017).

The results support the notion of HIV associated chronic immune activation as the driving force in TB reactivation/reinfection in HIV co-infected individuals.

Mitigating chronic immune activation through utilization of immune based interventions could significantly reduce the rates of TB recurrence and have a profound impact on reducing TB disease burden in HIV endemic settings.

- Aida Sivro, PhD

TABLE 1 | Univariable and multivariable analysis of TRuTH plasma analytes (sMAdCAM, sICAM, sVCAM, LBP, TGF-β1, TGF-β2 and TGF-β3) as biomarkers of TB recurrence.

Cytokine	Univariable		Multivariable ¹	
	OR (95% CI)	p-value	aOR (95% CI)	p-value
sMAdCAM	0.99 (0.39 – 2.52)	0.984	0.94 (0.26 – 3.33)	0.922
sICAM	1.05(1.01 – 1.08)	0.005*	1.06 (1.02 – 1.12)	0.009
sVCAM	1.02 (0.99 – 1.04)	0.142	1.02 (0.99 – 1.05)	0.222
LBP	3.28 (1.02 – 10.59)	0.047	8.78 (1.23 – 62.66)	0.030
TGF- β1	1.05 (0.97 – 1.12)	0.222	1.05 (0.98 – 1.14)	0.179
TGF- β2	1.09 (0.93 – 1.29)	0.274	1.15 (0.93 – 1.43)	0.194
TGF- β3	1.21 (0.95 – 1.55)	0.120	1.44 (1.01 – 2.05)	0.044

¹Multivariable analysis adjusted for WHO stage of the disease, BMI, lung cavities, age, CD4 count, VL, gender and previous history of TB. *Statistically significant association after FDR adjustment using 0.05 threshold.

Bold values: p-value < 0.05.

For further reading see:

Pillay K, et al. Plasma biomarkers of risk of tuberculosis recurrence in HIV co-infected patients from South Africa. *Front Immunol.* 2021; 12:631094. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8026888/>



Salim and Quarraisha Abdool Karim invited to serve on leading global organisations

Professors Salim and Quarraisha Abdool Karim, internationally recognised for their pioneering research in HIV, have been invited to serve on three leading global organisations.

CAPRISA’s Director, Professor Salim Abdool Karim has been invited to serve on the **WHO Science Council** alongside 9 of the world’s eminent scientists including Nobel Laureate Dr Harold Varmus. The announcement was made at the inaugural meeting of the Council on 27th April by WHO Director General Dr Tedros Ghebreyesus.

Chaired by Dr Harold Varmus, the Council will provide guidance including the identification of current and new science and technology issue that will impact global health and strategic advice to WHO on science, research and innovation in relation to the future impact of scientific developments.

Ghebreyesus explained that this step is part of the organisation’s deep-rooted transformation embarked upon four years ago. “A key part of that transformation has been to strengthen WHO’s scientific work, so that we are not just keeping up with the latest scientific developments but staying ahead of the curve and harnessing the best science for global health”.

“Individually you each represent scientific excellence in your domain”, said Dr Soumya Swaminathan, Chief Scientist at the WHO. “And collectively you are an outstanding group of researchers and scientists, and Dr Tedros Ghebreyesus, and I are grateful of your commitment to WHO and health for all.”

“Pandemics such as AIDS and Covid-19 have highlighted the important role of science in global health, “ said Abdool Karim who served as the chair of the South African ministerial advisory committee on COVID-19. “I am looking forward to participating in this Council providing scientific advice to WHO on future developments in health that the world needs to be better prepared for.”

Professor Quarraisha Abdool Karim, Associate Scientific Director of CAPRISA was appointed by the United Nations Secretary-General, António Guterres, on 4th May as **Co-chair to the new 10-Member Technology Facilitation Mechanism (TFM) Group** to support the Sustainable Development Goals (SDGs).

“It is an honour and a privilege to be appointed by the UN Secretary General to co-chair the high level 10-Member Technology Facilitation Mechanism Group, said Abdool Karim. “The Sustainable Development Goals provide an important framework to address inequities and vulnerabilities globally.”

The 10-Member-Group will work with the UN Inter-agency Task Team on Science, Technology, and Innovation for the Sustainable Development Goals (IATT) to

provide ideas, guidance, and recommendations accelerate progress on the SDGs. It represents and mobilises inputs from civil society, private sector, and scientific communities around the world with diverse experience and expertise across a wide range of fields including science, technology, and innovation.



On 11th May, **Friends of the Global Fight Against AIDS, Tuberculosis and Malaria (Friends)**, announced the appointment of Dr Quarraisha Abdool Karim and former U.S. congresswoman Martha Roby to its Board of Directors.

“It’s an honour to welcome Dr. Abdool Karim and former Representative Roby to our Board,” said Chris Collins, president and CEO of Friends. “They bring a wealth of experience and expertise in their respective fields of scientific research and public policy. We greatly look forward to working with them.”

Responding to her appointment Abdool Karim said “Friends does invaluable work harnessing U.S resources to support the Global Fund and end the HIV/AIDS epidemic. I see my role on the Board as a natural extension of my scientific work on the disease.”



NIH study to assess mechanisms of type I IFN signalling & HIV risk in female genital tract

A CAPRISA led study aimed to define the mechanisms of IFN α 2 induction and its impact on interferon signalling and target cell phenotypes at the site of HIV transmission using longitudinal mucosal sampling from an ongoing clinical trial has been funded by National Institute of Allergy and Infectious Diseases.

CAPRISA senior scientist and PI of the study, Dr Aida Sivro, said the study will provide “crucial information on the role of IFN signalling in HIV infection”. “The results of this study will provide key information on the role of pre-existing mucosal inflammation and the role of timing and duration of exogenous IFN stimulation on generation of potent antiviral immune responses in prevention and treatment of viral infections,” said Sivro.

The study, which will be conducted over 5 years, is in collaboration with scientists, Drs Steven Bosinger (Emory, Atlanta, USA), Lyle McKinnon (University of Manitoba, Winnipeg, Canada), and Prof Tulio de



Photos: (L-R): Drs Aida Sivro, Tanuja Gengiah and Nonhlanhla Yende Zuma

Oliveira (KRISP, SA).

CAPRISA co-investigators include Drs Tanuja Gengiah, senior scientist, and Nonhlanhla Yende Zuma, head of Statistics and Data Management at CAPRISA.

Early Career Investigator Awards and accolades for young investigators

We congratulate Dr Simone Richardson (top) who was awarded the Norman Letvin Early Career Investigator Award from the Collaboration for AIDS Vaccine Discovery (CAVD). Richardson delivered a talk entitled: “IgG3 HIV broadly neutralizing antibodies show improved neutralization potency and phagocytosis compared to IgG1 variants” during the 9th Norman L Letvin Early Career Investigator Virtual Meeting on 23 March 2021.

This award recognizes the young or early career investigators who have made significant contributions to research conducted within the CAVD.

Dr. Cathrine Scheepers (middle), Senior Medical Scientist at the National Institute for Communicable Diseases (NICD) was awarded the University of the Witwatersrand Faculty of Health Sciences Prize for Research for 2020 for her paper published in Cell Reports (IF:8.109), entitled: “Antibody isotype switching as a mechanism to counter HIV neutralization escape”. This prestigious award held in May recognises excellence in research and goes to the first author of publication of exceptional quality.

Congratulations to Dr. Rebecca van Dorsten (bottom), who was awarded her PhD degree from the University of the Witwatersrand. Rebecca’s PhD focused on exploring the potential of engineered antibodies to prevent HIV cell-free and cell-cell transmission. She was supervised by Prof. Lynn Morris and Prof. Penny Moore at the NICD.





KZN CTU engages Civil Society

The KwaZulu-Natal (KZN) Provincial Council on AIDS (PCA), led by the office of the KZN Premier, in collaboration with the Provincial Civil Society, organised a Scientific Research Symposium with KZN Research Institutions, on 8 and 9 April 2021. The KZN PCA provides leadership, coordination and monitoring and evaluation on the provinces' integrated response to HIV, STI and TB.

Members of the KwaZulu Natal Clinical Trials Unit: Prof Kogie Naidoo, Dr Nigel Garrett, Dr Cheryl Baxter, Dr Reshmi Dassaye, Ms Neeta Morar, Ms Zanele Gwamanda and Mrs Ivy Kaunda shared their research activities, and engaged in robust discussion on strategies to meaningfully engage communities in therapeutic and prevention research in HIV, TB and COVID-19.

“The need to educate communities on the scientific research process and commonly used research lexicon will help strengthen collaboration between researchers and communities, and help improve translation of new scientific advances to affected communities”, said Prof Kogie Naidoo, eThekweni CRS leader.



Civil society called for more regular updates on progress on research activities, and resolved to lobby for greater recognition of the research sector in the response to AIDS, TB and COVID at a local, provincial and national level.

Congratulations to our graduates...

CAPRISA celebrates the graduation of eight colleagues - four staff members (one former) and four fellows who successfully completed their degrees and graduated at the University of KwaZulu-Natal's virtual graduation ceremonies held in May.

Fellows, Ms Nabeela Paruk (MMedSc), Dr Andile Mtshali (PhD) and Ms Mandisa Zuma

(MMedSc) received funding from the DSI-NRF Centre of Excellence grant.

Training co-ordinator, Ms Sma Mzobe, congratulated the graduates and said it was personally rewarding to have “colleagues graduate despite the challenges posed by COVID-19 pandemic on the 2020 academic year”.



Photo: (L-R top): Nonzwakazi Ntombela, Study Co-ordinator, *PhD*; Ross Cromarty, former staff, *PhD*; Andile Mtshali, Fellow, *PhD (Medical Sciences)*; Callin Chetty, Study Co-ordinator, *Master of Social Science (Research Psychology)*; (L-R bottom) Franco Musiello, Study Co-ordinator, *Master of Social Science (Research Psychology)*; Nabeela Paruk, Fellow, *Master of Medical Science*; Mandisa Zuma, Fellow, *Master of Medical Science*, and Qondeni Ndlangamandla, *Master of Science (Statistics)*.

MSc Awarded to Tai Ncube at NICD

Tai Ncube, supervised by Dr Cathrine Scheepers, Dr Bronwen Lambson, Dr Claire Cutland and Professor Penny Moore, was awarded his MSc (Med) in Vaccinology degree through WITS. His MSc project was entitled: "Characterisation of IgA1 and IgG1 constant region diversity in South Africa". In this pilot study using only 6 CAPRISA donors he uncovered 2 IgG1, 8 IgA1 and 5 IgA2 genes that have previously not been described. Five of these genes showed amino acid changes, some of which were within Fc receptor binding sites and may alter the function of these antibodies. Future studies will continue to study isotype genetic diversity within the CAPRISA cohort on a larger scale.





Scientific papers published in 2021

- *22 Amusa L, Zewotir T, North D, **Kharsany AB, Lewis L**. Medical male circumcision and HIV prevention among men in Kwazulu-Natal, South Africa: A propensity score analysis. *Scientific African* 2021; 11:e00683. <https://doi.org/10.1016/j.sciaf.2020.e00683>
- 23 **Tanser FC**, Kim HY, Mathenjwa T, Shahmanesh M, Seeley J, Matthews P, Wyke S, McGrath N, Adeagbo O, Sartorius B, Yapa HM, Zuma T, Zeitlin A, Blandford A, Dobra A, Bärnighausen T. Home-Based Intervention to Test and Start (HITS): a community-randomized controlled trial to increase HIV testing uptake among men in rural South Africa. *Journal of the International AIDS Society* 2021 ; 24(2):e25665.
- 24 **Naidoo K, Mansoor LE**, Katz AW, Garcia M, Kemigisha D, Morar NS, Zimba CC, Chitukuta M, Reddy K, Soto-Torres L, Naidoo S, Montgomery ET. Qualitative perceptions of dapivirine vaginal ring adherence and drug level feedback following an open-label extension trial. *Journal of Acquired Immune Deficiency Syndromes* 2021; 86(4):e90-e96.
- 25 Baeten JM, Palanee-Phillips T, Mgodini NM, Mayo AJ, Szydlo DW, Ramjee G, Gati Mirembe B, Mhlanga F, Hunidzarira P, **Mansoor LE**, Siva S, Govender V, Makanani B, Naidoo L, Singh N, Nair G, Chinula L, Parikh UM, Mellors JW, Balán IC, Ngure K, van der Straten A, Scheckter R, Garcia M, Peda M, Patterson K, Livant E, Bunge K, Singh D, Jacobson C, Jiao Y, Hendrix CW, Chirenje ZM, Nakabiito C, Taha TE, Jones J, Torjesen K, Nel A, Rosenberg Z, Soto-Torres LE, Hillier SL, Brown ER; MTN-025/HOPE Study Team. Safety, uptake, and use of a dapivirine vaginal ring for HIV-1 prevention in African women (HOPE): an open-label, extension study. *Lancet HIV* 2021; 8(2):e87-e95.
- 26 **Dorward J**, Sookrajh Y, Ngobese H, **Lessells R, Sayed F**, Bulu E, Moodley P, **Samsunder N, Lewis L**, Tonkin-Crine S, Drain PK, Hayward G, Butler CC, **Garrett N**. Protocol for a randomised feasibility study of Point-Of-care HIV viral load testing to Enhance Re-suppression in South Africa: the PwER study. *BMJ Open* 2021; 11(2):e045373. doi: 10.1136/bmjopen-2020-045373
- 27 **Maharaj B, Abdool Karim Q**. Engaging young women in Africa for PrEP use and adherence. *Lancet HIV* 2021, 8(3):e122-e123.
- 28 **Baxter C, Abdool Karim Q, Abdool Karim SS**. Identifying SARS-CoV-2 infections in South Africa: Balancing public health imperatives with saving lives. *Biochemical and Biophysical Research Communications* 2021; 538:221-225.
- 29 Fontanet A, Autran B, Lina B, Kieny MP, **Abdool Karim SS**, Sridhar D. SARS-CoV-2 variants and ending the COVID-19 pandemic. *Lancet* 2021; 397(10278):952-954.
- 30 Reid M, **Abdool Karim Q**, Geng E, Goosby E. How will COVID-19 transform global health post-pandemic? Defining research and investment opportunities and priorities. *PLoS Medicine* 2021; <https://pubmed.ncbi.nlm.nih.gov/33705396/>
- 31 Lazarus G, Tjoa K, Iskandar AWB, Louisa M, Sagwa EL, **Padayatchi N**, Soetikno V. The effect of human immunodeficiency virus infection on adverse events during treatment of drug-resistant tuberculosis: A systematic review and meta-analysis. *PLoS One* 2021 March; 16(3):e0248017. doi: 10.1371/journal.pone.0248017.
- 32 **Pillay K, Lewis L, Rambaran S, Yende-Zuma N, Archary D, Gengiah S, Govender D, Hassan-Moosa R, Samsunder N, Abdool Karim SS, McKinnon LR, Padayatchi N, Naidoo K, Sivro A**. Plasma Biomarkers of Risk of Tuberculosis Recurrence in HIV Co-Infected Patients from South Africa. *Frontiers in Immunology* 2021; 12:631094. doi: 10.3389/fimmu.2021.631094

HIV TRANSMISSION
2021
PRINCIPLES OF INTERVENTION
BETHESDA, MD, USA | 9 - 10 NOVEMBER 2021

The 16th edition of the International Workshop on HIV Transmission will take place on 9-10 December 2021 at the National Institutes of Health (NIH), Bethesda, Maryland, United States, as a hybrid meeting. Access information on the website here: <https://academicmedicaleducation.com/hiv-transmission-2021>



CAPRISA hosts a DST-NRF Centre of Excellence in HIV Prevention



UNAIDS
CAPRISA is the UNAIDS Collaborating Centre for HIV Research and Policy



CAPRISA hosts a MRC HIV-TB Pathogenesis and Treatment Research Unit
CAPRISA hosts a DoH-MRC Special Initiative for HIV Prevention Technology



Partner Institutions:



Board of Control: B Ntuli (Chair) • M Rajab (Deputy Chair) • Q Abdool Karim • SS Abdool Karim • AC Bawa • JM Frantz • LP Fried (US) • S Harrison • K Naidoo • LV Theron

Scientific Advisory Board: F Barré-Sinoussi (Chair) • T Quinn (Vice Chair) • P Godfrey-Faussett • R Hayes • J Mascola • Y Pillay • S Swaminathan

Registration number: 2002/024027/08 • PBO number: 930 018 155