Biological mechanisms underpinning the development of Long COVID

There is a need to elucidate the pathobiological mechanisms underlying the clinical manifestations of Long Covid.

In the review “Biological mechanisms underpinning the development of Long Covid” published in the journal *iScience*, a complete and well-characterized understanding of the biological mechanisms responsible for generating the diverse clinical phenotypes of Long Covid aims to underpin the development of diagnostic tests, biomarkers for risk-stratification, and therapeutic interventions.

The precise biological basis for the diverse range of problems that Long Covid patients develop is complex and likely multifactorial. In this review, Dr Rubeshan Perumal, Senior Scientist et al., provide an in-depth analysis of the evidence on potential mechanisms of Long Covid.

The analysis shows a significant proportion of survivors experience a diversity of long-lasting clinical sequelae and have an increased risk for new morbidity and possibly mortality.

This review identified several potential mechanisms supported by published evidence, including viral persistence, SARS-CoV-2 antigen persistence, micro clot formation, autoimmunity, reactivation of latent viruses, persistent systemic inflammation, dysbiosis, persistent central nervous system inflammation and metabolic dysfunction/bioenergetic failure.

The analysis highlighted people living with HIV/AIDS (PLWHA) are at a higher risk of developing severe Covid-19 complications because of dysregulated inflammation and a functionally impaired immune system, especially in the setting of high-level HIV viremia.

There is an urgent need to further delineate the pathobiology underpinning the development of this major public health threat through well-characterized and deeply phenotyped clinical cohorts, and through clinical trials to also assess the effectiveness of candidate therapeutic options directed at key biological mechanisms in different populations, concluded the review.


**Figure:** “Putative biological mechanisms underpinning Long COVID*"
CAPRISA celebrates 20 years of scientific excellence

Leading scientists, policy makers and collaborators join the celebrations

W e “are celebrating 20 years of extraordinary achievement in responding to HIV, HIV-TB co-infection, and more recently, Covid-19. CAPRISA’s work is setting a new path in global health and is playing a pivotal role in promoting a network of research organizations in Africa.”

These were the words of Nobel Laureate and Chair of the CAPRISA Scientific Advisory Board Professor Françoise Barré-Sinoussi in her congratulatory message at CAPRISA’s 20th anniversary celebrations.

Dr Tedros Ghebreyesus, DG of the WHO congratulated CAPRISA on an impressive legacy, that positively affected the trajectory of our global public health responses, while working to address the challenges of its community.

The 20-year celebratory symposium and gala dinner held on Monday 26 June at the Inkosi Albert Luthuli International Convention Centre Complex in Durban was an extraordinary event bringing together leading scientists from the US, UK and the WHO, policy makers, government, ambassadors and consulates and South African scientists to mark two decades of scientific excellence since its establishment in 2002.

CAPRISA, has reached a 20-year milestone in research addressing the two biggest AIDS challenges in Africa: reducing HIV-TB co-infection deaths and preventing new HIV infections in young women, said Prof Quarraisha Abdool Karim (Associate Scientific Director and co-founder of CAPRISA) acknowledging CAPRISA’s five founding partner institutions. “It is wonderful to have this opportunity to meet and interact with each of you. It really is so heart-warming, to me... this is what humanity is about. It’s our interactions. It’s our connections and it’s our friendships. And it is that, that has brought us to this milestone event in CAPRISA.”

Established during the height of the HIV epidemic and AIDS denialism in South Africa as a multi-institutional independent non-profit AIDS Research Organisation working with many partners across the world, CAPRISA has grown into an international research organization recognized for excellence in science, policy, and scientific leadership. Prof Salim Abdool Karim (Director & co-founder of CAPRISA) outlined CAPRISA’s achievements in his presentation titled: CAPRISA: A 20-year journey which focused on scientific leadership, science advice and impact on policy in 3 key areas: improving TB-HIV treatment, preventing HIV in young women, and understanding SARS-CoV-2 variants. Over the last 20 years CAPRISA scientists have produced 1430 journal articles, said Abdool Karim. Of these, 40% had a CAPRISA scientist as the first author and 42% of the articles are published in high-impact journals with impact factors higher than 5. “A CAPRISA article appears in Nature and Science about 3 and 2 times a year, respectively. They appear 2 times every 12 months—in the New England Journal of Medicine. A Lancet journal article is produced every 2 months,” he said.

The award-winning South African research organization provided the first scientific evidence and proof-of-concept showing that antiretrovirals prevents the sexual transmission of HIV and that integrated TB-HIV treatment halves co-infection deaths which is included in the WHO guidelines on HIV-TB co-infection treatment. The results won widespread acclaim and were published in the prestigious journal Science in 2010 and made headlines in the New York Times, the Wall Street Journal, the Washington Post and the Guardian. CAPRISA’s seminal research paved the way for pre-exposure prophylaxis (PrEP) which is widely used in HIV prevention today. CAPRISA is now studying broadly neutralizing antibodies (bnAbs) as a potential long-acting injectable HIV prevention strategy.

Continued on page 4
...Celebrating 20 years of scientific excellence...

Photo: Top row (L–R): Prof Salim Abdool Karim, Director CAPRISA delivers his presentation on CAPRISA’s 20-year journey. Prof Thomas Quinn Director: John Hopkins Center for Global Health & Vice-Chair of CAPRISA’s Scientific Advisory Board delivers his address. Seated: L—R Dr Disebo Potloane CAPRISA Valindela Site Director; Prof Linda Fried, Dean Mailman School of Public Health, Columbia University; Justice Leona Theron, Judge of the Constitutional Court, SA; Prof Wafaa El Sadr, Director Columbia World Projects & ICAP; Prof Sten Vermund Anna Lauder Professor, School of Public Health, Yale University; & Prof Quarraisha Abdool Karim, Associate Scientific Director, CAPRISA

Second row (L–R) Delivering keynote addresses: Prof Peter Piot, Special Advisor on Covid-19 to the President of the European Commission; Minister of Health Dr Joseph Phaahla; Ambassador John Nkengasong, U.S. Global AIDS Coordinator & Special Representative for Global Health Diplomacy

Bottom row (L) Prof Jeremy Farrar, Chief Scientist, WHO delivers a keynote address.

Group photo (L–R): Dr Sibongiseni Dhlomo, Deputy Minister of Health; Profs Quarraisha and Salim Abdool Karim; Dr Barry Kistnasamy, Department of Health; and Prof Busiwe Ncama, Deputy Vice-Chancellor University of KwaZulu-Natal
The discovery of the CAPRISA 256 bnAb provides the opportunity to evaluate passive immunization as a potential long-acting injectable HIV prevention strategy.

A high-level panel discussion on CAPRISA’s research and future challenges followed Abdool Karim’s presentation and included eminent scientists: Prof Thomas Quinn (Director: John Hopkins Center for Global Health & Vice-Chair of CAPRISA’s Scientific Advisory Board); Prof Linda Fried (Dean, Mailman School of Public Health, Columbia University); Prof Sten Vermund Anna Lauder Professor, School of Public Health, Yale University; Prof Wafaa El Sadr, Director Columbia World Projects & ICAP; & Justice Leona Theron, Judge of the Constitutional Court, SA). Quinn praised “both the depth and breadth of the science that CAPRISA practices every day… and he underscored “the mentorship that CAPRISA does by example to all the young scientists, because they're our future," he said.

Ambassador John Nkengasong, U.S. Global AIDS Coordinator & Special Representative for Global Health Diplomacy; Prof Peter Piot Special Advisor on Covid-19 to the President of the European Commission; and Prof Jeremy Farrar Chief Scientist, World Health Organisation (who attended the symposium in his personal capacity) delivered keynote addresses. CAPRISA has received recognition with over 30 prestigious awards from South Africa, Canada, the United Kingdom, the United States, India and Japan. Earlier this year the government of Japan hosted Salim and Quarraisha Abdool Karim laureates of the prestigious Fourth Hideyo Noguchi Africa Prize, medical research category for “outstanding achievements to combat infectious and other diseases in Africa, thus contributing to the health and welfare of the African people and of all humankind.” The Abdool Karims serve on several high-level bodies - Quarraisha Abdool Karim is the president of The World Academy of Sciences TWAS, the first woman to hold this position and Salim Abdool Karim is the Science Advisor to the Director General of the WHO.

Minister of Health in South Africa, Dr Joseph Phaahla paid tribute to CAPRISA in his keynote address, saying “we as South Africans and on behalf of the Health Ministry and also on behalf of government are proud to be associated with your work and look forward to more cutting-edge research which will continue to shape the way we develop policy and continue to change the lives of people.”

At the celebratory gala dinner Deputy Minister of Health, Dr Sibongiseni Dhlomo presented 20-year awards for long service to CAPRISA staff. The awards were presented to Prof Kogie Naidoo (Deputy Director & Head: HIV&TB Treatment research), Dr Tanuja Gengiah (Head Pharmacy & Senior Scientist) and Ms Joyce Mchunu, (Counsellor) at the Vulindlela Research Clinical site. He presented CAPRISA Awards to Profs Quarraisha Abdool Karim (Associate Scientific Director) and Ayesha Kharsany (Senior Scientist). The awards were presented “in recognition of two decades of exceptional commitment/ contributions and dedication to research excellence”.

Photos: Top: Prof Kogie Naidoo, Deputy Director CAPRISA delivers the closing address

Middle (L-R): Dr Yogan Pillay, Country Director of the Clinton Health Access Initiative in South Africa; Prof Thomas Quinn; Prof Salim Abdool Karim; Prof Sten Vermund; Profs Quarraisha Abdool Karim, Kogie Naidoo and Peter Godfrey Faussett, UNAIDS Senior Adviser on Science

Bottom (L-R) Prof Salim Abdool Karim with Inkosi Zondi, Head of the Inadi ward in Vulindlela on the right and Mr Patrick Mdletshe, Head: Community Programmes
Salim Abdool Karim’s book: “Standing up for Science” is launched

“His work is a reminder of the enduring value of science in the service of global health” - DG WHO

In his foreword of Standing up for Science: A Voice of Reason, Dr Tedros Adhanom Ghebreyesus, Director-General, World Health Organization wrote: “His work is a reminder of the enduring value of science in the service of global health. His strong sense of social justice is tempered by a commitment to remain true to the science. As this book illustrates, Slim does not shy away from highlighting the injustices that often attend those inequalities, including those inequities that emerged so starkly, particularly in the early phases of the global distribution of the Covid-19 vaccine.”

Standing up for Science: A Voice of Reason authored by Prof Salim Abdool Karim, South Africa’s Chief Covid-19 Science Adviser was launched by publishing house Pan Macmillan South Africa on 26 June at the Durban ICC. Leading international scientists, government officials and collaborators listened intently to Abdool Karim’s brief account of his personal, behind-the-scenes experience of the first three years of the pandemic, the ground-breaking and globally recognized achievements made through science in a battle against an unprecedented time in our history.

Ambassador John Nkengasong, Prof Jeremy Farrar and Peter Piot participated in a panel discussion, moderated by Prof Cate Hankins, (McGill University & member of the Canadian Covid-19 committee) and shared valuable insights and lessons learned during the Covid-19 pandemic. Prof Peter Piot, EU Chief Scientific Adviser on Epidemics said Standing up for Science was ‘A must-read to understand the complex and vital interaction between science and politics by one of the world’s thought leaders in science and health, sharing precious, first-hand experience during the Covid pandemic.’

“This is more than just a personal and captivating narrative about the events that transpired during and after the pandemic – the intricacies of translating science into policy, the international linkages and coordination of effective Covid response plans, and the important lessons learnt that will better prepare leaders and nations for future epidemics,” explained Andrea Nattrass, Publisher at Pan Macmillan. “Standing Up for Science is a stimulating read and ode to science from one of the world’s leading epidemiologists.”


Watch the launch here: https://bit.ly/3rbbPJS
Recognised for two decades of commitment and contributions

Deputy Minister of Health, Dr Sibongiseni Dhlomo presented 20-year awards for long service to CAPRISA staff at the 20-year celebratory gala dinner on 26 June held at the Durban ICC. The awards were presented “in recognition of two decades of exceptional commitment/contributions and dedication to research excellence”. Twenty year Long Service Awards were presented to: Professor Kogie Naidoo Deputy Director CAPRISA; Dr Tanuja Gengiah (Head Pharmacy & Senior Scientist) and Ms Joyce Mchunu, (Counsellor) at the Vulindlela Research Clinical site.

Dhlomo presented CAPRISA Awards for two decades of contributions to research excellence to Professor Quarraisha Abdool Karim (Associate Scientific Director) and Ayesha Kharsany (Senior Scientist).

Robust discussions at Scientific Advisory Board meeting

CAPRISA’s two-day Scientific Advisory Board (SAB) meeting held from 27 – 28 June at the Coastlands Musgrave hotel brought together distinguished global and local scientists, collaborators and policymakers to learn about recent and forthcoming research in CAPRISA’s four priority areas: Vaccines, Pathogenesis & Broadly Neutralising Antibodies; Epidemiology, Prevention and Mucosal Immunology; HIV and TB Treatment and Pandemics and Epideimics. The presentations elicited robust discussions and insights on the challenges in public health particularly in low-income countries and in medical research. Professor Thomas Quinn Vice-Chair of SAB said: “I personally believe this has been the most outstanding SAB that we have had, the most insightful, the most outstanding presentations. CAPRISA... but also to the leaders of CAPRISA, of each of the sections and to the overall leaders for their vision, their leadership, the organizational skills, their mentorship.”
TWAS president launches celebrations for the Academy’s 40th Anniversary

TWAS President Professor Quarraisha Abdool Karim marked the Academy’s 40th anniversary with discussions on public health issues such as HIV, tuberculosis, and COVID-19 during her visit to Trieste.

Abdool Karim met with TWAS secretariat staff as well as the Academy’s sister organizations, InterAcademy Partnership and the Organization for Women in Science in the Developing World, and its host institution, the Abdus Salam International Centre for Theoretical Physics. The visit culminated in the TWAS 40th Anniversary Launch event at the Savoia Excelsior Palace Hotel in Trieste, and a public lecture from Abdool Karim on public health, academic excellence, and Africa’s past and future. Abdool Karim is a 2015 TWAS Fellow, and the winner of the Academy’s prestigious TWAS-Lenovo Science Award in 2014. She is currently serving her first of four years as the president of TWAS. Abdool Karim is the first woman to serve in the role of TWAS President and leads a 16-member council comprised of eight men and eight women.

Source: https://bit.ly/3XSWnhM

DUT confers an honorary degree on Prof Salim Abdool Karim

The Durban University of Technology (DUT) awarded an honorary Doctor of Philosophy Degree in Health Sciences to Prof Salim Abdool Karim for “his exceptional contributions in the global health environment and his outstanding service to humanity. His expertise has extensively contributed to the HIV/AIDS prevention and treatment, as well as the COVID-19 response, thereby saving many lives.”

The honorary doctorate was conferred by the DUT Vice Chancellor and Principal, Professor Thandwa Mthembu at the Olive Convention Centre in Durban at the Autumn ceremony. Abdool Karim shared three key concepts to succeed as an academic, as a professional and in leadership positions.

“The first is find your passion, find the thing that makes you wake up in the morning, the thing that lights the fire in you. It will find you and don’t despair if you have not found it already. It is going to be the basis in which you will find your calling in life, you will find what excites you and makes a difference to each day in your life. Secondly, persevere, nothing comes to those who don’t have patience and perseverance. If something comes easily it means that other people also have it. You have to take on the difficulties in life and never give up as obstacles are put in your way. You have been given an education to overcome those obstacles. Lastly, be the best that you can be and never settle for second best,” advised Abdool Karim. Source: https://bit.ly/3roNKPU

Kwabena Asare receives HVTN Young Investigator Award

Kwabena Asare, a PhD candidate and statistician at CAPRISA, supervised by Prof Nigel Garrett, Head of Vaccine and Pathogenesis Research, received the HVTN Bonnie Mathieson Young Investigator award for his publication titled "Impact of Point-of-Care Testing on the Management of Sexually Transmitted Infections in South Africa: Evidence from the HVTN702 Human Immunodeficiency Vaccine Trial."

Collaborating with the HIV Vaccine Trials Network (HVTN), Asare’s research focused on the impact of point-of-care testing on the management of sexually transmitted infections (STIs) in South Africa. The study found that this rapid diagnostic approach significantly improved STI management by enabling timely diagnoses, treatment and detection of adverse events highlighting the utility of point-of-care testing for STI care in resource-limited settings. Asare’s achievement highlights the importance of collaboration and showcases his contributions to the field of HIV and STI research. “The award serves as an encouragement for young researchers”, said Garrett “and underscores the potential of their work in advancing global health and addressing critical challenges.”
Presentations at the SA AIDS conference: deliberating strategies to eliminate HIV as a public health threat

CAPRISA scientists participated in the 11th SA AIDS conference held in Durban, which brought together policymakers, scientists, social activists and people living with HIV to review and reflect on progress made towards HIV/AIDS and TB epidemic control. Senior Scientist Prof Lenine Liebenberg served on the conference organising committee and led the Basic and Clinical Sciences track. The track included several abstract-driven sessions discussing research advances and opportunities for innovations in HIV prevention, refining the treatment landscape, and cure research. Additionally, track symposia explored humoral immunity in HIV prevention and cure, opportunities for innovation in managing HIV and other STIs, and controlling the consequences of HIV and ageing. Liebenberg chaired the session: HIV and other STIs – Challenges and Opportunities, and co-chaired the plenary: “Re-connecting - are we on track towards Epidemic control?”

Prof Quarraisha Abdool Karim chaired the plenary: Unpacking the next steps, with co-chair Patrick Mdletshe, Head: Community Programmes. Dr Sinaye Ngcapu, Senior Scientist, discussed his current research on understanding and manipulating the genital microbiome to limit susceptibility to HIV and other STIs; Prof Desh Archary, Senior Scientist, chaired the session: Humoral Immunity in HIV Prevention and Cure; and Dr Melissa-Rose Abrahams (UCT) chaired the abstract session: HIV Cure and presented in a session: Humoral Immunity in HIV prevention and Cure.

CAPRISA staff and fellows were also featured in other tracks. Oral presentations were made by Dr Upasna Singh, Research Clinician, titled: Patients Perceptions on Starting Antiretroviral Therapy During Implementation of Universal Test and Treat, in track: Innovation for Service Delivery; and by Mr Mxolisi Mathenjwa, Study Coordinator– Prevention Studies, eThekwini CRS, titled: Safer Conception for Women: Delivering Adherence Counselling to Women taking Oral PrEP wishing to Conceive with Partners Living with HIV or with Unknown sero-status in South Africa, in the session: Community Intervention; and Ms Makhosazane Zondi, Research Psychology MSS Student, titled: Can STI testing in pregnancy improve partner management?, in the satellite session: Sexually transmitted infections in pregnancy: towards best practice.

Dr Nicola Bodley, Research Clinician, presented a poster titled: “Point-of-care urine tenofovir testing to improve antiretroviral treatment adherence and HIV outcomes in South Africa”.

Prof Dooley shares insights into clinical research

During her recent visit to CAPRISA research clinics, Professor Kelly Dooley, Professor of Medicine and Director of the Division of Infectious Diseases, Department of Medicine at Vanderbilt University Medical Center (VUMC) engaged in discussions with the INSIGHT and ORCHID study research teams and explored potential avenues for future collaborations. Accompanied by Dr Anushka Naidoo, CAPRISA Research Fellow and CAPRISA INSIGHT and ORCHID Studies’ Principal Investigator, she visited the CAPRISA Springfield and eThekwini Research Clinics. Dooley’s research focuses on tuberculosis therapeutics, clinical trials of TB drugs and HIV/TB co-treatment, and clinical pharmacology of TB and HIV drugs.
A selection of scientific papers published in 2023


* continuation from previous newsletter

For the complete list of publications see here: http://bit.ly/3IRvjZd