



### Pharmacogenomics of drug transporters for antiretroviral long-acting pre-exposure prophylaxis for HIV

#### In this Issue

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We highlight the enrolment milestones achieved in the SHERPA and Ubuntu Covid-19 vaccine trials, and report on the awarding of honorary degrees by McMaster University to the Abdool Karims on page 3.

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In this CAPRISA-led review, drug transporters and biological factors modulating drug transporter disposition are used to explain discrepancies in PrEP drug efficacies observed in PrEP clinical trials.

The review titled, 'Pharmacogenomics of drug transporters for antiretroviral long-acting pre-exposure prophylaxis for HIV' published in the journal *Frontiers in Genetics*, also provides insight at a pharmacological level of how these factors further increase the susceptibility of the female genital tract to HIV infections, subsequently contributing to ineffective PrEP interventions in African women.

Clinical trials testing the effectiveness of Truvada® [a combination of tenofovir disoproxil fumarate/tenofovir and emtricitabine] as oral or topical PrEP in African women yielded mixed results in preventing the sexual transmission of HIV infections.

Since oral and topical PrEP effectiveness is dependent on adequate drug delivery and availability to cells and tissues tar-

geted by HIV, different host biological factors have been proposed to play an integral role in these women. These include transmembrane drug transporter proteins expressed in various cells. Their expression levels and function has been implicated as key regulators of PrEP pharmacokinetics [which is absorption, distribution, metabolism and excretion] which determines effectiveness. Compartment differences of these drug transporters between the blood and genital tract remain largely undescribed.

Other biological factors such as genetic polymorphisms, specifically the presence of single nucleotide polymorphisms (SNPs) in drug transporter genes and genital inflammation have been shown to directly affect drug transporter disposition.

This review shows that the FGT, renal system and blood are subject to a variety of host biological factors that may undermine PrEP efficacy by affecting drug transporter expression levels and function.

Nomusa M. Zondo and Derseree Archary (PhD)

For more reading see here: Zondo NM, et al. *Frontiers in Genetics* 2022. doi: 10.3389/fgene.2022.940661 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9557974/>

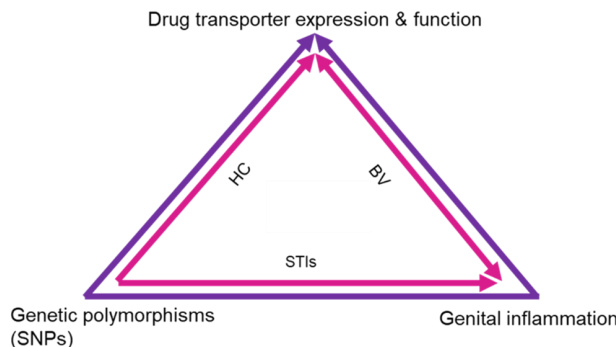


Figure: Proposed mechanisms that impact drug transporter expression and function. This diagram depicts the inextricable links between biological factors and varied drug transporter expression levels and function that subsequently affect PrEP pharmacokinetics and effectiveness.



## Professor Quarraisha Abdool Karim is elected President of The World Academy of Sciences (TWAS)

Professor Quarraisha Abdool Karim is the President-Elect of The World Academy of Sciences (TWAS) for the advancement of science in developing countries in Trieste, Italy. She is the first woman to hold this position and will serve as its seventh President for the next 4 years.

TWAS, which is hosted by the United Nations Educational, Scientific and Cultural Organization (UNESCO), has 1,296 elected fellows, including several of the world's most accomplished scientists and engineers. Eleven TWAS Fellows are Nobel laureates. TWAS has Fellows in over a hundred countries, about 84% from developing nations, and the rest are scientists from the developed world whose work has had a significant impact in the South. This Academy supports sustainable prosperity through research, education, policy and diplomacy.

"It is a real honour and privilege to be elected as President of TWAS," said Abdool Karim "and to have the opportunity to build on the strong foundations established over four decades by my predecessors in realizing the aspirational vision of the founder, Nobel Laureate Abdus Salam, on the use of science to improve the lives of the most vulnerable in the developing world."

Dr Mohamed Hassan, the current President and a Sudanese mathematician said Abdool Karim "is an accomplished scholar, scientist and health policy leader, with deep knowledge of what it takes to training developing world scientists and to make a powerful

real-world impact with her research. I am confident the Academy will not only continue to build scientific capacity through research, education, policy and diplomacy, but also expand its activities and programmes, taking TWAS to new heights."




Abdool Karim said she is taking up the position at an "important juncture with unprecedented social, political and economic upheavals; where science is even more important but also politicised," adding the role of "TWAS globally and specifically in LMICs is even more critical. The focus on sustainable development through scientific solutions remains a key part of the vision as set out by the founders of TWAS and remains current."

Abdool Karim co-chairs the United Nations Sustainable Development Goal 10 Member Technology Facilitation Mechanism (TFM). She is an elected member of the National Academy of Medicine (USA), and Fellow of the Royal Society of South Africa, Academy of Science of South Africa and the African Academy of Science.

## Dr Nonhlanhla Yende-Zuma is a Gates's 'Hero in the Field'

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**STATISTICALLY SIGNIFICANT**

### Dr. Nonhlanhla Yende-Zuma is saving lives with math

She's a statistician who faced impossibly long odds.

By Bill Gates | December 01, 2022

Dr Nonhlanhla Yende-Zuma, Head of Statistics at CAPRISA features on Gates Blog, 'Heroes in Field. "Growing up in a rural community with high rates of HIV and TB, Nonhlanhla Yende could have been just another statistic. Instead, she became a world-class statistician, one who's using her expertise to save lives around the globe," writes Bill Gates. 'Watch the video here: <https://www.gatesnotes.com/>



## Abdool Karims awarded Honorary Degrees from the University of McMaster

Professors Salim and Quarraisha Abdool Karim, Director and Associate Scientific Director CAPRISA, were awarded honorary degrees by the University of McMaster in Ontario, Canada in recognition of their ‘professional achievements and tireless advocacy and lifelong efforts that have helped shape health policy, including measures that slowed the spread of HIV/AIDS in Africa.’

The Doctor of Science (DSc) degrees were conferred at the Faculties of Engineering and Science graduation ceremony held on 18 November. The Abdool Karims addressed the graduating class of 2022 and participated in the 624<sup>th</sup> Convocation ceremony at the First Ontario Concert Hall presided by Vice-Chancellor and President Professor David Farrar.



Photo: (L-R) Chancellor of MacMaster University Ms Santee Smith, Prof Quarraisha Abdool Karim, Prof Salim Abdool Karim, Vice-Chancellor of McMaster University, Professor David Farrar

McMaster confers honorary degrees to distinguished scholars; educators; and individuals who have made outstanding contributions to the creative or performing arts; those with a record of public service or with long, distinguished and impactful careers in their field, and those who have made important and noteworthy contributions to McMaster University or the community.

## COVID-19 vaccine trials reach enrolment milestones at Research Sites

The eThekweni and Vulindlela Research teams, led by Site-Principal Investigators Dr Nivashnee Naicker and Dr Disebo Potloane, completed enrolment of more than 1200 participants into the SHERPA (*Sisonke Heterologous mRNA-1273 boost after prime with Ad26.COv2.S*) trial and the COVPN 3008 Ubuntu trial.

The SHERPA trial evaluates the effectiveness of a Moderna mRNA vaccine boost among 12 000 healthcare workers who previously received either one or two doses of the Ad26.CoV2.S Johnson and Johnson vaccine in the Sisonke trial.

The Ubuntu trial is investigating different mRNA vaccine strategies among people living with HIV within the context of new circulating SARS-CoV-2 variants in Southern and East Africa.

Recently, the new bivalent (BA.4/BA.5/ ancestral) Moderna vaccine was added to the trial to assess its utility in this setting. Both trials will provide important safety and efficacy data in this setting, with a view to obtain licensure of the vaccine in South Africa.

Dr Naicker highlights that it was no easy feat meeting ambitious enrolment targets at record pace. “The teams have worked tirelessly over the past



Photo: (L-R) Drs Disebo Potloane, Nivashnee Naicker and Professor Nigel Garrett

2 years to support the COVID-19 response locally and globally,” she said.

Professor Nigel Garrett, National Co-PI of SHERPA, and International Co-Chair of Ubuntu added that the “COVID-19 response will go down in history as one of the most collaborative periods in research, and the CAPRISA clinical and scientific teams have made a remarkable contribution to the national and international effort.”



## H.E. Ambassador of Japan to South Africa presents fourth Noguchi Africa Prize to Salim and Quarraisha Abdool Karim



On 9<sup>th</sup> November His Excellency the Ambassador of Japan to South Africa, Mr Maruyama Norio hosted a special ceremony and lunch at his official residence to present the certificate and mementos of the 4<sup>th</sup> Hideyo Noguchi Africa Prize, in the category Medical Research to Professors Salim and Quarraisha Abdool Karim. The prize was officially announced at TICAD 8, held in Tunis on 28<sup>th</sup> August.

On 22<sup>nd</sup> November H.E, Excellency, Mr Maruyama Norio visited CAPRISA's headquarters and held discussions with senior scientists to gain insights into CAPRISA's core research studies following a tour of the facilities led by Professor Salim Abdool Karim.



Senior Scientists held discussions with H.E. Ambassador Mr Maruyama Norio *Photo front row (L-R): Dr Sharana Mahomed, Research Clinician; Dr Tanuja Gengiah, Head of Pharmacy; Associate Scientific Director, Prof Quarraisha Abdool Karim and Dr Leila Mansoor, Senior Scientist.*

*Back row (L-R) Prof Salim Abdool Karim, CAPRISA Director; Prof Lenine Liebenberg, Senior Scientist; His Excellency Mr Norio Maruyama, Ambassador of Japan to South Africa; Dr Nonhlanhla Yende-Zuma, Head of Statistics; Prof Derseree Archary, Senior Scientist; Dr Nivashnee Naicker, Research Clinician and Prof Nigel Garrett, Head of Vaccines & Pathogenesis Research.*

## Call for new solutions to prevent and reduce new HIV infections at World AIDS Day event

CAPRISA Head of Community Programmes Mr Patrick Mdletshe was a panellist at the World AIDS Day event hosted by the University of KwaZulu-Natal (UKZN) and Research partners on Tuesday 29<sup>th</sup> November, themed "EQUALISE".



*(L-R) Head of UKZN's Department of Internal Medicine Prof Nombulelo Magula; Mr Patrick Mdletshe and AHRI Director for Basic and Translational Science Prof Thumbi Ndung'u*

Mdletshe joined Deputy Vice Chancellor of the College of Health Sciences Prof Busisiwe Ncama and officials from AHRI, UKZN, HEARD, SANTHE and the SRC for a round table discussion.

"While significant gains in HIV treatment have been made the rate of new HIV infections in South Africa is not coming down fast enough," said Mdletshe. "In 2021, there were around 198 000 new HIV infections in South Africa, with particularly high rates of HIV infection in young women and girls. We urgently need new solutions in preventing and reducing new HIV infections and improve adherence to ARVs," he added.

## Prof Carolyn Williamson receives UCT Excellence Award



Congratulations to Professor Carolyn Williamson, who was given an Excellence Award by the University of Cape Town in recognition of her exceptional contribution to research in the field of HIV vaccines and

prevention, as well as SARS-CoV-2 genomic surveillance.

She is further recognised for her role in leadership of the University, in particular taking on the role of Interim Dean of the Faculty of Health Sciences and guiding the Faculty through a particularly difficult time following the passing of the previous Dean.



## Scientists hosted at the Gates Foundation Rising Stars session



Photo: (L-R) Second Row, Dr Sharana Mahomed third from the left; and fourth row, third from the left, Dr Rubeshan Perumal

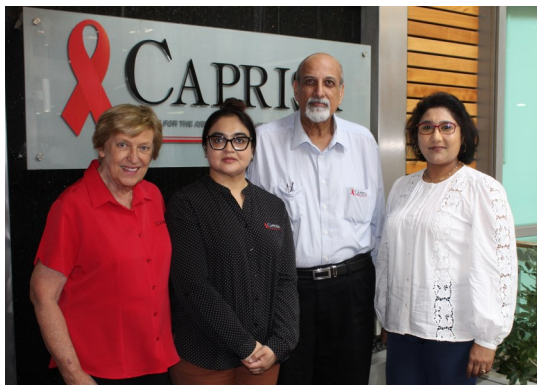
Dr Sharana Mahomed, CAPRISA Research Clinician and Dr Rubeshan Perumal, Senior Scientist were hosted at the Bill and Melinda Gates Foundations' Global Health Africa Teams "Rising Stars" session in Durban, on 16th November. The format of the session was an engaging dinner at the Oyster Box hotel with a set of dynamic researchers who have shown excellence and high potential. The aim of the dinner was to help improve the Foundation's intentionality around diversity and capacity building in the region. This was also an opportunity for CAPRISA scientists to share their interesting research and journey with the representatives.



Dr. Thandeka Moyo-Gwete, Senior Medical Scientist in the Moore lab at NICD, was nominated to meet with members of the Bill and Melinda Gates Foundations' Global Health and Africa Teams for a "Rising Stars" event which took place over dinner on 17 November at Ten Bompas Hotel in Johannesburg.

The sessions were part of a 5-day countrywide event where the foundation met with individuals across the South African R&D ecosystem. It was an engaging dinner and opportunity to share Thandeka's research and journey with the Gates Foundation.

## CAPRISA Achievement Awards recognises excellence



CAPRISA Achievement Awards were awarded to Deputy Director and Head of Treatment Research Prof Kogie Naidoo, Research Clinician Dr Sharana Mahomed, and Personal Assistant to the Directors Mrs Norma Hatcher. The awards presented on 1st December recognises outstanding work accomplishments, said Prof Salim Abdool Karim.

Photo: (L-R) Mrs Norma Hatcher, Dr Sharana Mahomed, Professor Salim Abdool Karim CAPRISA Director and Professor Kogie Naidoo

## eThekwini Research Site Engaging with the communities

CAPRISA eThekwini Research Site Vaccine team led by Ms Ivy Kaunda CAPRISA Community Liaison Officer (second row, second from the left) celebrated South Africa's cultural diversity together with 180 study participants attending the event dressed in their cultural attire representing the isiZulu, Indian, isiXhosa, seSotho and amaNdebele cultures.



This engagement strengthened partnerships and understanding of CAPRISA's scientific studies with the research participants in the ENSEMBLE, HVTN 139, HVTN 140, and CoVPN 3008 research studies. The participation of the research participants provided relevant insights and allows for addressing any challenges and concerns around the studies and finding solutions.

"Empowering communities to understand the process of scientific research and the impact of findings in saving lives is critical in building partnerships." said Kaunda.



# Congratulations to our students for their outstanding achievements

## Dr Kapil Narain is awarded a 2023 Rhodes Scholarship



On 7<sup>th</sup> November, Dr Kapil Narain was inducted as a Rhodes Scholar to pursue his postgraduate studies at the University of Oxford following a rigorous selection process. Narain is an alum of the University of KwaZulu-Natal and of the CAPRISA Research Placement programme.

Prof Salim Abdool Karim, Director CAPRISA said he had personally mentored Narain as part of the CAPRISA Research Placement Programme to 'develop the next generation of clinical research leaders in South Africa.' "All my previous mentees have been recipients of the Rhodes Scholarship – one is still at Oxford at present," he said. "Dr Narain possesses several qualities that will one day make him an excellent researcher; he has a quick grasp of highly complex questions, the ability to think laterally, and to analyse a topic holistically and thoroughly."

## Fellows receive awards at UKZN Research Symposium



**C**APRISA fellows Ms Nomusa Zondo (*top left in the photo*) and Ms Nonsikelelo Ndlela won prizes for their oral presentations at the annual UKZN Research Symposium of the College of Health Sciences, School of Laboratory Medicine, and Medical Sciences, held on 27<sup>th</sup> November at the ICC in Durban.



Ndlela (*left*), a master's fellow won the best oral poster presentation prize for her study titled, 'Investigating the impact of point-of-care STI/BV testing and treatment on the genital epithelial barrier integrity of the CAPRISA 083 participants'. She is supervised by Prof

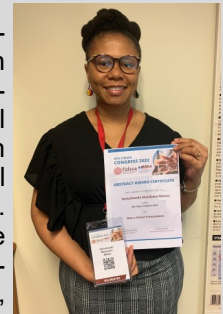
Lenine Liebenberg, Senior Scientist at CAPRISA. Zondo a PhD fellow won the second prize for the best oral presentation and is supervised by Prof Desh Archary, Senior Scientist at CAPRISA and Dr Parveen Sobia. Her study is titled: *continued...*

## CAPRISA Fellows scoop FIDSSA Congress prizes

The 9th Federation of Infectious Diseases Societies of South Africa (FIDSSA) Congress was held in Durban from 3<sup>rd</sup> – 5<sup>th</sup> November and focused on infectious diseases, infection prevention and control, clinical microbiology, and paediatric infectious diseases.

CAPRISA Fellows Ms Noluthando Mazibuko-Motau, Mr Kwabena Asare, and Ms Makhosazane Zondi were awarded prizes for their presentations at the Congress.

Mazibuko-Motau, a PhD fellow received the Best Poster Presentation prize for her presentation on the impact of daily oral tenofovir disoproxil fumarate in combination with emtricitabine for PrEP on vaginal microbiota in South African women. She is supervised by Drs Sinaye Ngcapu, (Senior Scientist, CAPRISA) and Douglas S Kwon, (Ragon Institute).



Asare, who is a PhD fellow in Public Health, under the supervision of Prof Nigel Garrett, (Head of Vaccine and Pathogenesis Research, CAPRISA) and Dr Andrew Tomita (UKZN) received the prize for the Best Short Presentation on Bacterial Vaginosis incidence and recurrence among women living with HIV in South Africa.



Zondi, a master's fellow in Research Psychology won the top prize for Best Oral Presentation. Her presentation examined the efficacy of Women's Experiences of an Expedited Partner Treatment Intervention in KwaZulu-Natal, in reducing sexually transmitted diseases reinfection and prevalence. Zondi is supervised by Prof Garrett, Professor Mary van der Riet and Ms Kershia Sunjeevan



...continued...**Fellows receive awards**

..., 'Impact of single nucleotide polymorphisms in ABC drug transporter genes on circulating Tenofovir in healthy South African women exposed to pre-exposure prophylaxis (PrEP)'.



## A selection of scientific papers published in 2022

- 118 **Zondo NM, Sobia P, Sivro A, Ngcapu S, Ramsuran V, Archary D.** Pharmacogenomics of drug transporters for antiretroviral long-acting pre-exposure prophylaxis for HIV. *Frontiers in Genetics* 2022; 13:940661 doi: 10.3389/fgene.2022.940661
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- 126 Dookie N\*, Ngema SL\*, **Perumal R, Naicker N, Padayatchi N, Naidoo K.** The Changing Paradigm of Drug-Resistant Tuberculosis Treatment: Successes, Pitfalls, and Future Perspectives. *Clinical Microbiology Reviews* 2022. doi: 10.1128/cmr.00180-19.
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- 130 Bateman M, Wolf A, **Chimukangara B**, Brust JCM, **Lessells R**, Amico R, **Boodhram R**, Singh N, Orrell C, Friedland G, **Naidoo K, Padayatchi N, O'Donnell MR**. Adherence measured using electronic dose monitoring is associated with emergent antiretroviral resistance and poor outcomes in patients co-infected with HIV/AIDS and multidrug-resistant tuberculosis. *Clinical Infectious Diseases* 2022; 75 (9):1489-1496.
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For the complete list of publications see here: <http://bit.ly/3FwekeC>



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