CAPRISA
CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA
Newsletter
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No HBV resistance mutations in women using tenofovir gel as PrEP

A study recently published in the journal *Viruses*, shows that no known tenofovir resistance mutations (M240V/I, L180M, A194T, V214A, N238T) were identified in any hepatitis B virus (HBV)-infected women who used tenofovir gel during the CAPRISA 004 trial.

Intermittent use of a single antiretroviral agent in the presence of a replicating virus could potentially increase the development of antiviral resistance. The before-and-after sex, dosing regimen in the tenofovir gel trial meant that women with HBV infection were exposed intermittently to tenofovir, noting that systemic absorption of tenofovir from gel use is low.

The impact of intermittent tenofovir gel use on HBV resistance was assessed by amplification of the HBV polymerase region from 37 stored plasma samples of women who were HBV surface antigen positive. All samples were HBV genotype A (Figure 1A). Overall, there were no significant differences in the frequency of amino acid substitutions between the tenofovir-exposed and placebo isolates (all $p > 0.05$) (Figure 1B). A similar number of highly conserved sites (≤1% variation) was found between the isolates from women assigned to the tenofovir 181/204 (88.7%) and placebo arms 188/204 (92.2%). Two (0.8%) of the 204 amino acids in the HBVrt domain were highly polymorphic (> 50% variability)—positions P109 and E125—in both arms and at positions S105, H122 and H271 in isolates from women assigned to the placebo arm (Figure 1B).

While it is reassuring that no resistance mutations were found among women using topical tenofovir, the rapidly expanding access to oral tenofovir-containing HIV pre-exposure prophylaxis (PrEP), with higher systemic exposure to the drug, makes monitoring for potential HBV drug resistance important.

For further reading:

Baxter C, et al. Frequency of Hepatitis B Virus Resistance Mutations in Women Using Tenofovir Gel as Pre-Exposure Prophylaxis. Viruses 2019; 11 (6):E569. doi: 10.3390/v11060569. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6630952/

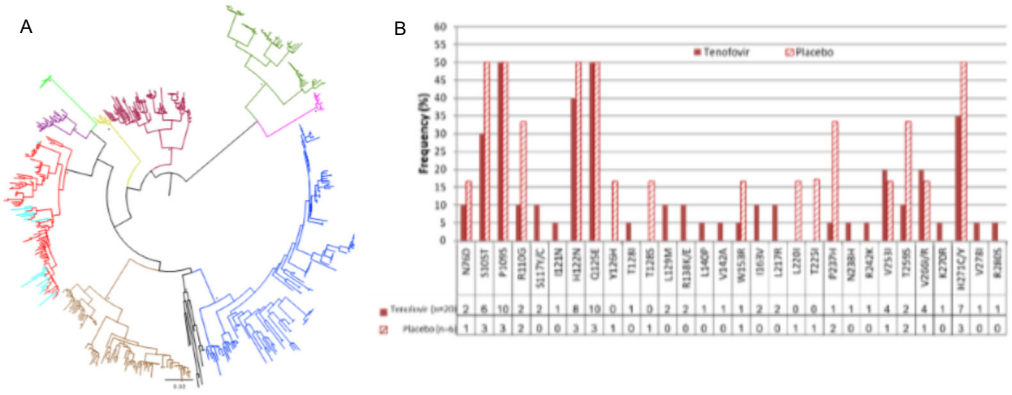

***Figure**: Figure 1. A) Maximum likelihood tree (midpoint rooted) showing the phylogenetic clustering between South African HBV genome sequences and randomly chosen reference sequences (A–J). Bootstrap support values above 70% are shown with an asterisk (*). HBV sequences from this study are highlighted in light blue, while subtype A references are red. Other subtype references are represented by Brown = B, blue = C, maroon = D, yellow = E, dark green = F, luminous green = G, pink = H, purple = I, black = J. B) Frequency of the HBVrt domain associated mutations in the tenofovir and placebo isolates*

In this Issue

Our feature story this month focuses on the study showing no HBV resistance in women using tenofovir gel as PrEP.

On page 2 we report on the UNAIDS Steering committee meeting, 2025 Target Setting, Impact and Resource Needs, held at CAPRISA, and the protocol training led by CAPRISA 018 clinical trial staff. We also congratulate CAPRISA's Statistics Fellow for winning the best poster presentation prize at the SUSAN-SSACAB 2019 Conference.

We announce the launch of the SAMRC Extramural Antibody immunity research Unit, which will be led by CAPRISA Honorary Senior Scientist Prof Lynn Morris, the awarding of the NIH grant for the STREAM 2 study and CAPRISA's participation at the NIH DAIDS Applied Research Training (DART) pilot workshop on page 3

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CAPRISA hosts UNAIDS 2025 Target Setting, Impact & Resource Needs Steering Committee Meeting

Seated: (L-R) Michaela Clayton (Director of the AIDS and Rights Alliance for Southern Africa – ARASA); Quarraisha Abdool Karim (CAPRISA); Peter Ghys (UNAIDS); Adele Benzaken (Global Health Advisor – Brazil); Lucy Wanjiku Njenga (Team Leader, Positive Young Women Voices, Kenya). Middle row: (L-R) Kalipso Chalkidou (Center for Global Development (USA) and Imperial College London (UK)); Paul De Lay (Global Health Advisor -USA); Wafaa El-Sadr (ICAP at Columbia University); Erik Lamontagne (UNAIDS); Aleny Couto (Director of the Mozambique National HIV Programme); Petchsri Sirinirund (Independent Expert, Thailand); Carl Pretorius (Deputy Director for the Center of Modeling, Planning and Policy Analysis Avenir Health); Back row (L-R) Jose-Antonio Izazola UNAIDS); Judy Chang (Executive Director, International Network of People who Use Drugs – INPUD); Smail Mesbah (The Algerian Society of Infectiology, Algeria); Chris Fontaine (UNAIDS); Marvin Manzanero (DG of Health Services, Ministry of Health, (Belize); Sani Aliyu (Director General, NACA, Nigeria); Jorge Saavedra (Global Ambassador, AIDS Healthcare Foundation – AHF); Daniel Low-Beer (WHO)

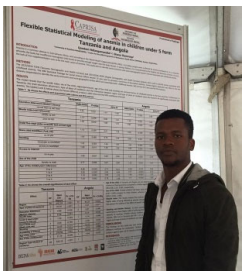
The second face-to-face meeting of the UNAIDS 2025 Target Setting, Impact and Resource Needs Steering Committee was held over three days at the CAPRISA headquarters from 24- 27 September. CAPRISA is a UNAIDS Collaborating Centre for HIV Research and Policy. Twenty-three members of the Steering Committee including key UNAIDS staff participated in the deliberations co-chaired by Paul De Lay (Global Health Advisor - USA) and Adele Benzaken (Global Health Advisor, Brazil).

Clinical Research training for CAPRISA 018

CAPRISA 018 clinical trial staff conducted sponsor-led protocol training at TCD-Global on 4 September in Centurion, Gauteng. TCD-Global is the independent Clinical Research Organisation responsible for external monitoring of both the CAP012A and CAP018 trials.

From L-R: Jaco Koegelenberg (COM,CAP012A), Jaylene Guest (Senior CRA CAP018), Tanuja Gengiah (Co-PI CAP018), Leila Mansoor (CAP018, Project Director), Ishana Harkoo (CAP018, Study clinician), Raphala Seima (COM,CAP018), Leonard Herbst (COO,TCD-Global)

CAPRISA Fellow wins best poster presentation



CAPRISA Biostatisticians, Dr Nonhlanhla Yende Zuma (Head: Biostatistics), Lara Lewis (Statistician), Nobuhle Mchunu (Fellow) and Qondeni Ndlangamandla (Fellow) participated in the Joint Conference of the Sub-Saharan Network (SUSAN) of the International Biometrics Society (IBS) and DELTAS Africa Sub-Saharan Africa Consortium for Advanced Biostatistics (SSACAB). The SUSAN-SSACAB 2019 Conference, was held on 8 - 11 September 2019 at the South African Medical Research Council (SAMRC) in Cape Town. Ndlangamandla (left in the photo) won the first prize for his poster presentation. Nobuhle Mchunu delivered an oral presentation on her MSc work titled: Joint Modelling CD4 Count and Mortality in a Cohort of Patients Initiated on HAART and Yende Zuma chaired a session on Causal Inference.

Launch of SAMRC Extra mural Antibody Immunity Research Unit

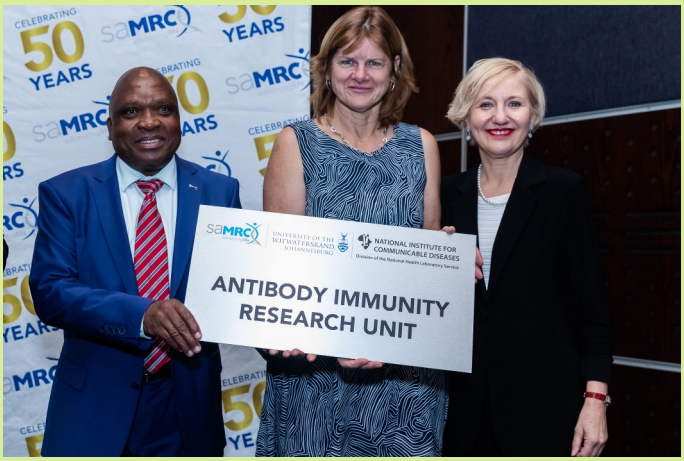


Photo: (L-R) *Dr Joe Phaahla and Prof Glenda Gray present the Extra Mural Unit name plaque to Prof Lynn Morris.*

Prof Lynn Morris from the National Institute for Communicable Diseases (NICD) was recently awarded a SAMRC Extramural Antibody Immunity Research Unit. The official launch took place on 4th September and was attended by Dr Joe Phaahla, the Deputy Minister of Health and Mr Mmboneni Muofhe, the Deputy Director-General from the Department of Science and Innovation (DSI). Also in attendance were Dr Kamy Chetty, acting CEO of the NHLS, Prof Glenda Gray, President and CEO of the SAMRC and Prof Jeffrey Mphahlele, Vice President of the SAMRC.

The mission of the MRC/Wits/NICD AIRU is to apply the team's extensive knowledge and experience of immunology to study the antibody responses to HIV as well as other viral pathogens. There are 3 key focus areas; namely identifying antibody correlates of protection by vaccines, uncovering the genetic diversity in the African antibody repertoire and discovery and engineering of antibodies for passive immunity. In this way, the Unit will help to design better vaccines and antibody treatments for the African region which bears the largest burden of infectious diseases..

The NIH-funded STREAM 2 Study

Nigel Garrett

Paul Drain

Co-Principal Investigators of the Simplifying HIV Treatment and Monitoring (STREAM) study, Paul Drain from the University of Washington and Nigel Garrett at CAPRISA received funding for STREAM 2 from the National Institutes of Health in the US to continue their research on point of care (POC) viral load (VL) testing.

STREAM 1 was a randomized controlled trial assessing the effect of POC VL monitoring and task shifting to enrolled nurses on treatment outcomes for stable patients on antiretroviral therapy (ART). The study found that the intervention increased a combined outcome of VL suppression and retention in care by 14% (95% confidence interval 6 - 21%) over a 12-month period compared to standard laboratory testing.

In STREAM 2, the PIs are now proposing to combine a novel POC urine tenofovir adherence assay with POC VL testing to improve HIV outcomes in South Africa even further. The idea is to use the tenofovir assay as an adherence support tool in the first 6 months after ART initiation, and identify patients struggling with adherence earlier. Later on, POC VL combined with tenofovir testing may help to distinguish patients who either need further adherence support or evaluation for resistance testing. The study will be conducted in collaboration with the eThekwini Municipality at the Prince Cyril Zulu Communicable Diseases Centre and is expected to start in February 2020.

Strengthening GCP and compliance at DART

CAPRISA research team was invited to attend the National Institutes of Health DAIDS Applied Research Training (DART) pilot workshop held in Johannesburg from 16 – 19 September. The training was tailored towards new clinical researchers and all aspects of clinical research were covered. Bongi Zuma, Study Coordinator on the HIV Vaccine Trial Network (HVTN) studies at the CAPRISA eThekwini Clinical Research Site (ECRS) contributed as a subject matter expert and DART facilitator. Nqobile Myeni and Miranda Naidoo, Quality Control Officers at ECRS, Callin Chetty (Study Coordinator) and Sandile Ngubane (Quality Control Officer) from the Vulindlela Clinical Research Site participated in the training. Attendees were given a project that focuses on improving quality and compliance to GCP and ICH at the respective sites, to be completed within 6 months to evaluate the impact of DART 2019.

Scientific papers published in 2019

63*	**Harichund C, Kunene P**, Moshabela M. Feasibility of HIV self-testing: experiences of people seeking HIV testing in rural and urban KwaZulu-Natal, South Africa. *African Journal of AIDS Research* 2019; 18 (2):115-122.
64	Chateau AV, Dlova NC, **Dawood H**, Aldous C. Outcomes of Stevens-Johnson syndrome and toxic epidermal necrolysis in HIV-infected patients when using systemic steroids and/or intravenous immunoglobulins in Pietermaritzburg, South Africa. *Southern African Journal of HIV Medicine* 2019; 20(1):944. doi: 10.4102/sajhivmed.v20i1.944.
65	Palanee-Phillips T, Brown ER, Szydlo D, Matovu Kiweewa F, Pather A, **Harkoo I**, Nair G, Soto-Torres L, Hillier SL, Baeten JM; MTN-020/ASPIRE Study Team. Risk of HIV-1 acquisition among South African women using a variety of contraceptive methods in a prospective study. *AIDS* 2019; 33(10):1619-1622.
66	Umotoy J, Bagaya BS, Joyce C, Schiffner T, Menis S, Saye-Francisco KL, Biddle T, Mohan S, Vollbrecht T, Kalyuzhniy O, Madzorera S, Kitchin D, Lambson B, Nonyane M, Kilembe W; IAVI Protocol C Investigators; IAVI African HIV Research Network, Poignard P, Schief WR, Burton DR, Murrell B, **Moore PL**, Briney B, Sok D, Landais E. Rapid and Focused Maturation of a VRC01-Class HIV Broadly Neutralizing Antibody Lineage Involves Both Binding and Accommodation of the N276-Glycan. *Immunity* 2019; 51 (1):141-154.
67	Mathenjwa T, Kim HY, Zuma T, Shahmanesh M, Seeley J, Matthews P, Wyke S, McGrath N, Sartorius B, Yapa HM, Adeagbo O, Blandford A, Dobra A, Bärnighausen T, **Tanser F**. Home-based intervention to test and start (HITS) protocol: a cluster-randomized controlled trial to reduce HIV-related mortality in men and HIV incidence in women through increased coverage of HIV treatment. *BMC Public Health* 2019; 19 (1):969.
68	**Harichund C, Abdool Karim Q, Kunene P, Simelane S**, Moshabela M. Exploring factors that influence the integration of HIVST with HCT using a qualitative comparative cross-over design in KwaZulu-Natal, South Africa. *Global Public Health* 2019;14(9):1275-1287.
69	**Singh JA**. Informed consent and community engagement in open field research: lessons for gene drive science. *BMC Medical Ethics* 2019; 20(1):54. doi: 10.1186/s12910-019-0389-3.
70	Tomita A, Smith CM, **Lessells RJ**, Pym A, Grant AD, **de Oliveira T, Tanser F**. Space-time clustering of recently-diagnosed tuberculosis and impact of ART scale-up: Evidence from an HIV hyper-endemic rural South African population. *Scientific Reports* 2019; 9(1):10724. doi: 10.1038/s41598-019-46455-7.
71	Roider J, Porterfield JZ, Ogongo P, Muenchhoff M, Adland E, Groll A, **Morris L, Moore PL**, Ndung'u T, Kløverpris H, Goulder PJR, Leslie A. Plasma IL-5 but not CXCL13 correlates with neutralization breadth in HIV-infected children. *Frontiers in Immunology* 2019; 10:1497. doi: 10.3389/fimmu.2019.01497.

**continuation from previous newsletter*

Black Friday against women and child abuse

On 6 September 2019, the NICD HIV Virology Laboratory staff all dressed in black to join the country in taking a stand against women and child abuse.

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

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: University of KwaZulu-Natal; Columbia University Mailman School of Public Health; National Institute for Communicable Diseases; University of Cape Town; University of the Western Cape