CAPRISA
CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA
Newsletter
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Understanding the latent *HIV-1 reservoir* is critical for developing strategies for cure

Immune activation, measured on CD8+ T cells, just prior to antiretroviral therapy (ART) initiation, was an independent predictor of the size of the replication-competent HIV-1 reservoir, according to a study by the collaborative team of researchers from CAPRISA and the Universities of Cape Town and North Carolina.

The study, *Immunological correlates of the HIV-1 replication-competent reservoir size,* was recently published in the journal *Clinical Infectious Diseases.*

Researchers carried out a longitudinal study of 20 women enrolled in the CAPRISA 002 acute infection cohort and quantified the frequency of resting CD4+ T-cells harbouring replication-competent HIV-1 after 5 years of suppressive ART that was initiated during chronic infection and investigated immune correlates of reservoir size. Viral loads and $CD4^+$ T-cell counts also predicted the size of the reservoir, but models that included immune activation improved their predictive value (Figure). This is important because the longer HIV infection proceeds, the more acti-vation accumulates, and therefore early therapy in a less tem may improve the chances of achieving an HIV cure. "The results are consistent with the hypothesis that the host immune milieu near the time of ART initiation plays an important role in shaping the durable reservoir of HIV infection that persists on ART," says *Dr Lyle McKinnon*, Honorary Senior Scientist at CAPRISA.

The latent HIV reservoir is a major barrier to curing HIV infection, and recent efforts have accelerated with respect to solving fundamental problems, such as where the reservoir is located, how best to measure it, when it is established, and ways that it can be targeted therapeutically.

The new knowledge regarding the contribution of immune to activation to HIV reservoir formation may assist with the design of novel cure and/or therapeutic vaccine approaches.

For further reading see:

Ismail SD, et al. Immunological correlates of the HIV-1 replication-competent reservoir size. Clinical Infectious Diseases 2021. doi: 10.1093/cid/ciab587. https://pubmed.ncbi.nlm.nih.gov/34181706/

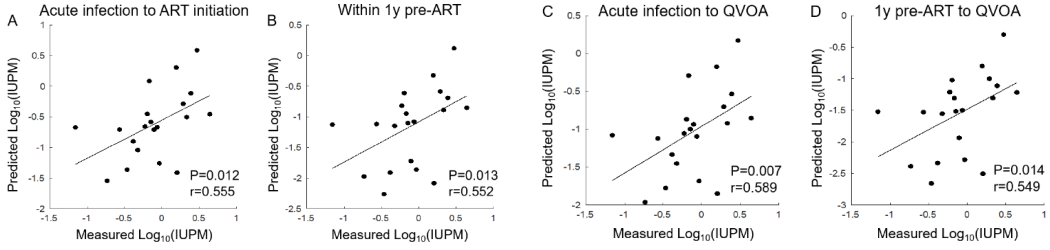

Figure: Correlations between model predictions and measured frequency of latently infected cells. *Correlation between replication-competent HIV-1 in resting memory CD4+ T-cells [log10 (infectious units per million, IUPM)] and the predicted IUPM resting CD4+ T-cells over the time period from* ***(A)*** *acute infection to ART initiation (n=20),* ***(B)*** *over the final year prior to ART initiation (n=20),* ***(C)*** *acute infection to QVOA (n=20), and* ***(D)*** *from a year prior to ART initiation to QVOA (n=20). Non-parametric Spearman rank correlation coefficients and the P-value of the correlation are given at the bottom of each panel.*

In this Issue

Our feature story this month focusses on the study by a collaborative group of scientists on the immunological correlates of the HIV-1 replication-competent reservoir size, published in the journal, *Clinical Infectious Diseases.*

We feature the Kader Asmal lecture delivered by Prof Salim Abdool Karim on page 2, and report on a cross-sectional survey to assess the impact of the COVID-19 crisis on women and girls living with HIV in South Africa.

On page 3, we highlight the GIISER grant awarded to Prof Penny Moore and feature CAPRISA & the NICD's celebrations by colleagues on Heritage Day.

The study on metronidazole for the treatment of bacterial vaginosis is featured on page 4

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'A crime against humanity – the tragedy of vaccine apartheid'- Salim Abdool Karim delivers the 2021 Kader Asmal lecture

The Council for the Advancement of the South African Constitution (CASAC) hosted the Kader Asmal lecture on Wednesday, 14th September to mark the 10th anniversary year of the passing of the eminent human rights activist and academic, Professor Kader Asmal described as 'a relentless advocate for human rights.

Professor Salim Abdool Karim, CAPRISA's Director delivered the lecture, titled: *COVID-19 and Human Rights: A tiny virus magnifies society's inequalities*, to an audience which included Ireland's Ambassador to South Africa, H.E. Gilsenan Fionnuala.

In his address he referred to one of the biggest tragedies of the Covid-19 pandemic. "And that's the tragedy of vaccine Apartheid," he said, "which for me is nothing short of a crime against humanity." He questioned the gross inequities that underpin vaccine access to poorer nations. "In the midst of billions of doses of vaccines being made available across the world, how is it that Africa has been pushed to the back of the queue?" Abdool Karim said that Africa does not have access to the doses of vaccines it needs, "even in the midst of five and a half billion people across the world receiving at least one dose."

What would Kader Asmal have said when he looked at all of this? he asked. "I think he would have said and I'm quoting Kader Asmal, 'human dignity, individually and collectively, cannot be determined by the pricing mechanisms of the market'."

"We have to find a different way, we have to find a new world order for the distribution of pandemic vaccines in the future," said Abdool Karim.

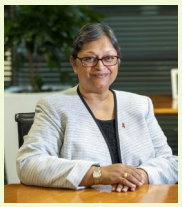
Watch the lecture here: https://youtu.be/ThYS-Gi2T5s

Survey to assess the impact of COVID-19 among women and girls living with HIV in South Africa

The COVID-19 pandemic has had a profound impact worldwide. Efforts to curb the spread of the virus are challenging societies socially and economically. Already vulnerable communities, such as adolescent girls and women, especially those in key and vulnerable populations are bearing the highest burden of these impacts.

CAPRISA, the UNAIDS Collaborating Centre for Research and Policy, in partnership with UNAIDS Geneva is implementing a cross-sectional survey to assess the impact of the COVID-19 crisis on women and girls living with HIV in South Africa, including high risk populations. The project includes leading civil society organisations in the country – AIDS Foundation of South Africa, African Alliance, and Youth Health Africa.

The national level survey is being rolled out in Eastern Cape, KwaZulu Natal, Gauteng, and Western Cape. The project is co-led by principal investigators, Professor Quarraisha Abdool Karim *(top right)* , and Dr Hilton Humphries *(bottom right)* .



This survey will provide "greater insight into the impact of COVID-19 on vulnerable populations in South Africa and will help us develop gender-responsive economic and social policies that place women's economic lives at the heart of the pandemic response and recovery plans" says Dr Hilton Humphries.

For more information, contact Dr Hilton Humphries (Hilton.Humphries@caprisa.org) or Dr Shakira Choonara, Project Manager (shakira@shakirachoonara.com)

Bill & Melinda Gates Foundation GIISER Grant awarded to Prof Penny Moore

Prof. Penny Moore was recently awarded a Global Immunology and Immune Sequencing for Epidemic Response (GIISER) Grant by the Bill & Melinda Gates Foundation. This two-year project will leverage existing expertise at the National Institute for Communicable Diseases (NICD) and an international network of GIISER sites and contribute to a global effort to pre-emptively respond to emerging SARS-CoV-2 variants of concern in the sub-Saharan region.

It will support and build immunological capacity at key sub-Saharan sites designated as African GIISER sites and in the longer term, develop capacity and readiness to respond to other emerging pathogens of public health importance, as part of a globally coordinated network. The Gates Foundation envisions the GIISER Program to be an integral part of country-led efforts to discover, develop and manufacture locally relevant vaccines, diagnostics and therapeutics.

Congratulations to our NICD colleagues!

Dr. Simone Richardson has been appointed to the South African Immunology Society's (SAIS) 2022 Committee. The goal of the SAIS is to grow basic, applied and translational immunology research nationally, regionally and with international partners. SAIS connects researchers and clinicians working in infectious and other diseases and its membership includes internationally acclaimed researchers in HIV and Tuberculosis immunology.

Ms Nelia Manamela, a Medical Scientist based at the NICD, received the runner-up prize for the best oral presentation during the South African Immunology Society (SAIS) Conference, held virtually on 30 August – 2 September 2021, for her talk entitled: "Distinct humoral trajectories associated with both HIV co-infection and COVID-19 survival in a hospitalized South African SARS-CoV-2 cohort"

CAPRISA & NICD celebrate the richness and diversity of our culture on Heritage Day

On Friday 24th September, Heritage Day, South Africans celebrated the rich cultural diversity and heritage of the country's rainbow nation. Heritage Day provides an opportunity to promote mutual understanding, respect, and social cohesion in our society as we continue to learn about the significance of diverse cultural traditions and practices in our society, explained Professor Kogie Naidoo, Deputy Director CAPRISA. "Our unique cultural heritage defines our individual identities that we should treasure with pride. It provides an opportunity to recognise, understand and acquire knowledge on the diverse cultural traditions and practices of our nation," she said. Staff at the NICD and CAPRISA joined the call to celebrate the richness of our diversity by wearing traditional attire.

Study highlights the interplay between vaginal microbiota and genital inflammation in response to treatment

In a recent collaborative CAPRISA-led study, researchers concluded that metronidazole for the treatment of BV induced short-term shifts in the vaginal microbiota and mucosal cytokines, while treatment failures promoted persistent elevation of pro-inflammatory cytokine concentrations in the genital tract.

The study, *Temporal changes in vaginal microbiota and genital tract cytokines among South African women treated for bacterial vaginosis,* published recently in the journal *Frontiers in Immunology,* researchers investigated the effects of metronidazole treatment on the vaginal microbiota and genital cytokines among 56 symptomatic South African women with BV [defined as Nugent score (NS) ≥4] using 16S rRNA gene sequencing and multiplex bead arrays.

Among 56 BV-positive women, researchers observed short-term BV clearance (NS <4) in a proportion of women six weeks after metronidazole treatment, with more than half of these experiencing recurrence by 12 weeks post-treatment.

BV treatment temporarily reduced the relative abundance of BV-associated anaerobes and increased lactobacilli species (mainly *L. iners*), resulting in significantly altered mucosal immune milieu over time (Figure).

In a linear mixed model, the median concentrations of pro-inflammatory cytokines and chemokines were significantly reduced in women who cleared BV compared to pre-treatment.

BV persistence and recurrence were strongly associated with mucosal cytokine profiles that may increase the risk of HIV acquisition. Concentrations of these cytokines were differentially regulated by changes in the relative abundance of BVAB1 and *G. vaginalis*.

"The data suggest the need to improve clinical management of BV to minimize BV related reproductive risk factors," says lead author, Dr Andile Mtshali, at the CAPRISA Mucosal Immunology Laboratory.

For further reading see:

Mtshali A, et al. Temporal changes in vaginal microbiota and genital tract cytokines among South African women treated for bacterial vaginosis. Frontiers in Immunology 2021; 12:730986. https://doi.org/10.3389/fimmu.2021.730986

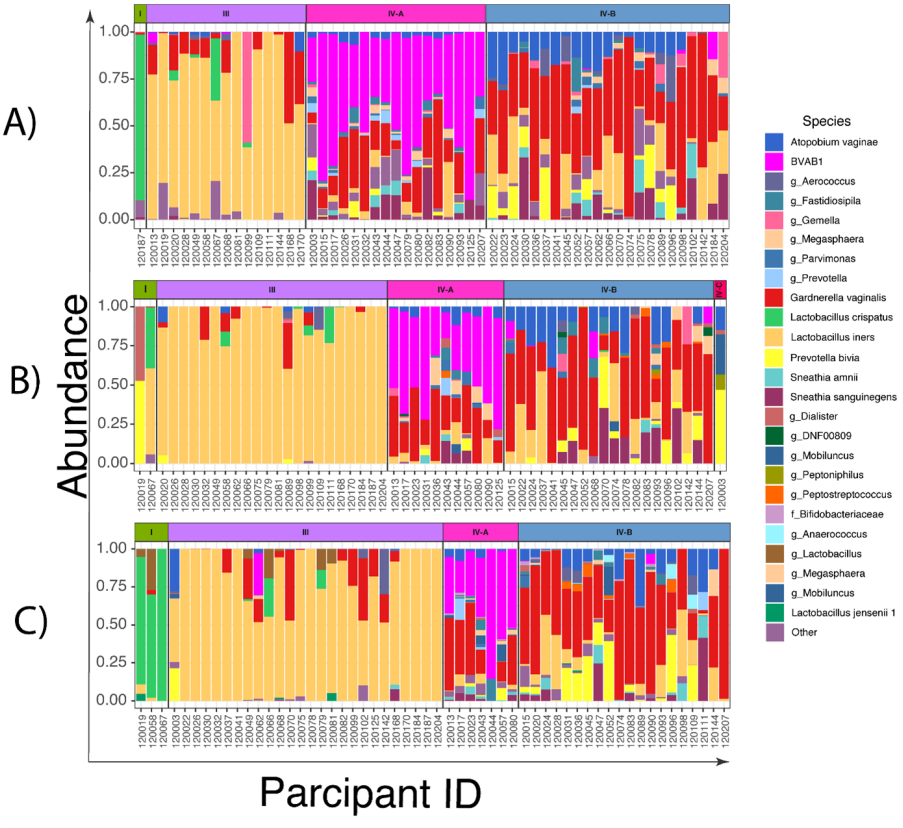


Figure: *Relative abundance of the twenty most common taxa in cervicovaginal bacterial communities in women (n=56) before and aftertreatment with metronidazole with and without sexually transmitted infection (STI) treatment (A) at baseline; (B) at 6 weeks post-treatment, and (C) at 12 weeks post-treatment*

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CIDRZ seeks a senior Director for The Enteric Disease and Vaccine Research Unit (EDVRU)

CIDRZ has an exciting opportunity for the senior leadership position of Director of The Enteric Disease and Vaccine Research Unit (EDVRU) based at CIDRZ in Zambia. The Director will provide scientific leadership to the EDVRU team and will lead strategy development and supervise teams to drive growth and productivity. The Director will oversee current clinical and basic science research studies on rotavirus, shigella, cholera, enterotoxigenic E-coli, corona virus and will oversee multiple teams of clinical and biomedical research fellows as well as the administrative support teams and will assume the function of principal investigator on a range of ongoing and new studies.

For further information contact Dr Izukanji Sikazwe at Izukanji.Sikazwe@cidrz.org

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