CAPRISA
CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

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

February 2016, Volume 15, Issue 2

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Our feature story this month is research by the Musocal Immunology team that describes the genital tract and blood HIV-specific antibody responses in women with breakthrough HIV-infections from the CAPRISA 1% tenofovir microbicide gel trial.

The launch of CAPRISA's "Cure" study that aims to characterize the latent reservoir in African women on treatment is announced on page 2. We also congratulate the ASPIRE team on the results from the dapivirine vaginal ring study that showed a modest reduction in HIV infection in women.

On page 3 we introduce the South African Youth Academy of Sciences (SAYAS) blog aimed at popularising science and provide highlights of the recent visit from CAPRISA collaborators from BroadReach Healthcare, the Institute for Healthcare Improvement and University College London.

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@ukzn.ac.za

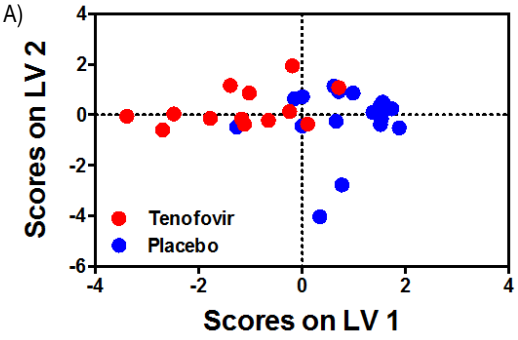
www.caprisa.org.za
caprisaofficial
@CAPRISAofficial

Mucosal antibody responses in women using TFV gel – implications for HIV vaccines

Research by the Mucosal Immunology research team was recently published in the journal Mucosal Immunology, which is is part of the Nature group of journals. The study showcases the genital tract and blood HIV-specific antibody responses in women with breakthrough HIV-infections from the CAPRISA 1% tenofovir microbicide gel trial.

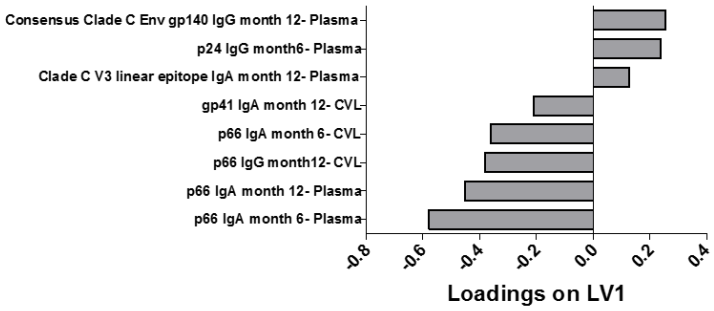
This is the first study to show in detail and in parallel, the kinetics and evolution of antibody responses the blood and genital tract from the primary into the chronic infection state. In this study, Dr Archary et al., showed that women that were exposed to the tenofovir gel had higher antibody responses rates to Env gp120, p66 and p24 in both the blood and genital tract. Additionally, women in the tenofovir gel arm had increased magnitudes of p66 IgG and IgA antibodies in both compartments compared to the women from the placebo arm (Figures A and B). Taken together, these data suggest that humoral immune responses are increased in blood and genital tract of individuals who acquire HIV infection in the presence of tenofovir gel and that prior tenofovir gel usage did not ablate or dampen subsequent humoral immunity in either compartments.

A)



This study informs on strategies where vaccines and PrEP will be used in combination to prevent HIV. This study was a collaboration between CAPRISA, and the Duke Human Vaccine Institute. Dr Archary was given an opportunity to train at Duke University under the mentorship of Dr Tomaras and Dr Yates on the customized binding antibody multiplex assay (BAMA), a technique that is widely used in vaccine research at the HVTN to screen for multiple vaccine immune responses. Dr Archary has subsequently transferred the technology to CAPRISA's Mucosal Immunology Laboratory, and is currently using this technique a wide range of other studies.

B)



For further reading see:
Archary D, et al. Distinct genital tract HIV-specific antibody profiles associated with tenofovir gel. Mucosal Immunol. 2016 Jan 27. doi: 10.1038/mi.2015.145. [Epub ahead of print]

Figure A and B: *Six and 12 month antibody signatures associated with participants in the TFV and placebo arms. LASSO identified a signature of 8 antibody specificities that separated TFV (red- n=13) and placebo (blue-n=18) arms in a PLSDA model with 83% calibration accuracy and 77% cross-validation accuracy (scores plot; A). The loadings plot depicts weighted loadings of individual antibody specificities within the distinguishing signature (B). Five of these specificities were positively associated with TFV (negatively loaded on LV1; plasma p66 IgA at months 6 and 12, plasma p66 IgG at month 12, CVL p66 IgA at month 6, and CVL gp41 IgA at month 12) and three were negatively associated with TFV (positively loaded on LV1; plasma Clade C V3 linear epitope IgA at month 12, p24 IgG at month 6 and Consensus Clade C Env gp140 IgG at month 12.*

Aspire trial results on Dapivirine Ring

CAPRISA congratulates the ASPIRE and the Ring study teams for two well conducted studies. "Both these studies have generated valuable new findings and insights," said Professor Salim S. Abdool Karim, Director of CAPRISA in response to the trial results released at CROI on 22nd February, that showed, overall, the dapivirine vaginal ring reduced HIV incidence by 27% (95% CI: 1% to 46%) in ASPIRE and by 31% (95% CI: 1% to 51%) in the Ring trial. "It is reassuring that the results were consistent across the two studies, including the observation of higher protection in the sub-group of women > 21 years." Dr Lulu Nair, a senior research clinician at CAPRISA, led the MTN study as the Site Principal Investigator at the CAPRISA eThekwini Clinical Research site. CAPRISA was one of 15 sites of this multinational trial.

"There was high hope that the monthly dapivirine ring would remedy the adherence problem seen in past trials of oral & topical pre-exposure prophylaxis (PrEP) and thereby achieve consistently high levels of protection against HIV. While the effectiveness of the dapivirine vaginal ring in preventing HIV is considerably lower than anticipated and hoped for, the success of the two trials in achieving high levels of adherence (82% in ASPIRE and 73% in the Ring Study) and regular monthly vaginal ring insertions, is encouraging, said Prof Abdool Karim.

He explained that, "More research is needed to fully understand and overcome the remaining challenges for sustained adherence in this high-risk population as we look forward to the next set of approaches to HIV prevention in women that are currently being studied, including multi-purpose vaginal rings (for contraception and HIV prevention), injectable long-acting antiretrovirals, as well as injectable broadly neutralising antibodies for protection through passive immunity."

Dr Lulu Nair led the ASPIRE team at the CAPRISA eThekwini site

"The high HIV incidence rates reported in both trials highlight the urgent need for appropriate HIV prevention technologies for women in Africa. Indeed, the ongoing high number of new HIV infections particularly in young women in Africa is one of the major obstacles to current efforts to end the global AIDS epidemic," commented Professor Quarraisha Abdool Karim, Associate Scientific Director of CAPRISA. "These two important studies highlight the challenges in developing technologies to prevent HIV in young women and provide further impetus for research to address this problem."

CAPRISA "Cure" study underway

Professor Carolyn Williamson and Dr Nigel Garrett

CAPRISA's NIH/MRC-funded "cure" study got rolling last week with the recruitment of the first three participants said Dr Nigel Garrett head of Vaccine and Pathogenesis at CAPRISA. The UCT-CAPRISA Pathogenesis team led by Professor Carolyn Williamson (UCT) are working with Professor Ron Swanstrom from the University of North Carolina to characterize the latent reservoir in African women on treatment, to determine when the latent reservoir is established, and to assess host factors that impact the reservoir in this setting.

Life-long treatment is needed to maintain control of HIV infection, and the global sustainability of providing antiretroviral therapy (ART) to the tens of millions of people in need of treatment is a major concern. The only alternative to this scenario is to develop a strategy that can eradicate HIV from the body. An HIV cure has recently been shown to be possible, and requires the elimination of the latent reservoir.

Extending latent reservoir observations to cohorts in less-developed countries where host factors, subtype and gender may differ compared to those in developed countries, will inform the development of a more generalizable approach to any potential cure intervention.

This study will investigate 20 subtype C-infected South African women who were recruited in acute infection, initiated therapy after three years of infection, and who thereafter successfully suppressed HIV replication for at least four years.

Making "Retro"-viruses cool again

Simone Richardson

Simone Richardson, a PhD student from the National Institute for Communicable Diseases (NICD) who is being supervised by Professor Lynn Morris and Dr Nono Mkhize, was recently chosen as one of the 4 PhD bloggers for the South African Youth Academy of Sciences (SAYAS). This competition is to encourage young scientists to share their science and PhD experience widely and not just within their field. Articles are published once a month with topics ranging from the tiny dictatorship of viruses to why standing in a line at home affairs can be hazardous to a virologist's health (coming up in March!). Simone aims to use this platform to impart her experiences to new PhD candidates and share her love for discovery, with a bit of humour. She is passionate about making science something everyone feels they can interact with, not just something people discuss in lab. To see the relevance of one's work fitting into the big picture and being able to translate this for your granny is perhaps the most valuable thing a PhD can give to the world. Look out for Simone's articles (and self-drawn cartoons) published online in the second week of every month here.

Scaling up TB HIV Integration (SUTHI)

CAPRISA hosted key collaborators from Broad-Reach Healthcare (BRHC), Institute for Healthcare Improvement (IHI) and University College London (UCL) to discuss the direction and implementation of the CAPRISA 013, Scaling up TB-HIV Integration (SUTHI) study. The CAPRISA 013 study is testing the effectiveness of a quality improvement model to integrate TB HIV services in Primary Health Care Clinics in two rural districts of uThungulu and Ugu in KwaZulu-Natal. Expertise from the collaborators include quality improvement methodology, implementation science research as well as established relationships with district health facilities. The programme included visits to Mvutshini Primary Health Care Clinic which provides HIV and TB-related treatment. Collaborators had the opportunity to observe quality improvement interventions implemented at the clinic by the CAPRISA team.

L-R : Girlie Shange (DOH), Kogie Naidoo (CAPRISA), Lynne Footit (BRHC), Fikile Dube (DOH), Maryanne Richardson (BRHC), Francois Pretorius (BRHC)

Scientific papers published in 2016

1. Bradley T, Fera D, Bhiman J, Eslamizar L, Lu X, Anasti K, Zhang R, Sutherland LL, Scearce RM, Bowman CM, Stolarchuk C, Lloyd KE, Parks R, Eaton A, Foulger A, Nie X, **Abdool Karim SS**, Barnett S, Kelsoe G, Kepler TB, Alam SM, Montefiori DC, Moody MA, Liao HX, Morris L, Santra S, Harrison SC, Haynes BF. Structural Constraints of Vaccine-Induced Tier-2 Autologous HIV Neutralizing Antibodies Targeting the Receptor Binding Site. *Cell Rep* 2016; 14(1):43-54.
2. Doria-Rose NA, Bhiman JN, Roark RS, Schramm CS, Gorman J, Chuang GY, Pancera M, Cale EM, Ernandes MJ, Louder MK, Asokan M, Bailer RT, Druz A, Frascilla IR, **Garrett NJ**, Jarosinski M, Lynch RM, McKee K, O'Dell S, Pegu A, Schmidt SD, Staupe RP, Sutton MS, Wang K, Wibmer CK, Haynes BF, **Abdool-Karim S**, Shapiro L, Kwong PD, **Moore PL, Morris L,** Mascola JR. New Member of the V1V2-Directed CAP256-VRC26 Lineage That Shows Increased Breadth and Exceptional Potency. *Journal of Virology* 2016; 90(1): 76-91.
3. **Passmore J**, Jaspan HB, **Masson L**. Genital inflammation, immune activation and risk of sexual HIV acquisition. *Current opinion in HIV and* AIDS 2016; 11(2):156-162.
4. **Singh JA**. How Bioethics Is Complementing Human Rights in Realizing Health Access for Clinical Trial Participants: The Case of Formative PrEP Access in South Africa. *Health and Human Rights Journal 2016; 17(1): 58-62.*
5. **Masson L,** Arnold KB, Little F, **Mlisana K,** Lewis DA, Mkhize N, Gamieldien H, **Ngcapu S,** Johnson L, Lauffenburger DA, **Abdool Karim Q, Abdool Karim SS, Passmore JS.** Inflammatory cytokine biomarkers to identify women with asymptomatic sexually transmitted infections and bacterial vaginosis who are at high risk of HIV infection. *Sex Transm Infect* 2015 Oct 28. pii: sextrans-2015-052072. doi: 10.1136/sextrans-2015-052072. [Epub ahead of print]
6. Balkus JE, Brown ER, Hillier SL, Coletti A, Ramjee G, Mgodi N, Makanani B, Reid C, Martinson F, Soto-Torres L, **Abdool Karim SS,** Chirenje ZM. Oral and injectable contraceptive use and HIV acquisition risk among women in four African countries: a secondary analysis of data from a microbicide trial. *Contraception* 2016; 93(1):25-31.
7. **O'Donnell MR, Daftary A,** Frick M, Hirsch-Moverman Y, Amico KR, Senthilingam M, Wolf A, Metcalfe JZ, Isaakidis P, Davis JL, Zelnick RJ, Brust JCM, **Naidu N,** Garretson M, Bangsberg DR, **Padayatchi N,** Friedland G. Re-inventing adherence: toward a patient-centered model of care for drug-resistant tuberculosis and HIV. *Int J Tuberc Lung Dis* 2016; 20(4): http://dx.doi.org/10.5588/ijtld.15.0360
8. Jeena L, **Naidoo K.** Tuberculosis outcomes among peri-urban children receiving doorstep tuberculosis care. The International Journal of Tuberculosis and Lung Disease, 2016; 20(2): 235-239
9. **Archary D,** Seaton KE, **Passmore JS, Werner L,** Deal A, Dunphy LJ, Arnold KB, Yates NL, Lauffenburger DA, Bergin P, **Liebenberg LJ, Samsunder N,** Mureithi MW, Altfeld M, **Garrett N, Abdool Karim Q, Abdool Karim S, Morris L,** Tomaras GD. Distinct genital tract HIV-specific antibody profiles associated with tenofovir gel. Mucosal Immunol. 2016 Jan 27. doi: 10.1038/mi.2015.145. [Epub ahead of print]
10. Baeten JM, Palanee-Phillips T, Brown ER, Schwartz K, Soto-Torres LE, Govender V, Mgodi NM, Matovu Kiweewa F, **Nair G,** Mhlanga F, Siva S, Bekker L-G, Jeenarain N, Gaffoor Z, Martinson F, Makanani B, Pather A, Naidoo L, Husnik M, Richardson BA, Parikh UM, Mellors JW, Marzinke MA, Hendrix et al. Use of a Vaginal Ring Containing Dapivirine for HIV-1 Prevention in Women. New England Journal of Medicine 2016; February 22, 2016: DOI: 10.1056/NEJMoa1506110

Scientific Reviews

Abstracts submitted for review		Manuscripts submitted for review		Ancillary studies submitted for review	
Total#	Cumulative^	Total#	Cumulative^	Total#	Cumulative^
8	348	0	221	1	66

 # for month, ^ since committee initiation

Conference & Workshop Reminders

Conference	Dates	Deadlines: Abstracts	Deadlines: Registration	Website
Conference on Retroviruses and Opportunistic Infections - Boston, Massachusetts, USA	22-25 Feb 2016	30 Sept 2015	26 Jan 2016	http://www.croiconference.org/
21st International AIDS Conference (AIDS 2016) - Durban, South Africa	18-22 July 2016	4 Feb 2016	18 Feb 2016	http://www.aids2016.org/
HIV Research for Prevention - Chicago, Illinois	17-20 Oct 2016	11 Apr 2016	1 Jul 2016	http://hivr4p.org/

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

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

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