



CAPRISA

CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

Newsletter

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Superinfection does not promote broadly neutralizing antibodies to HIV

In this Issue

The feature story this month focuses on a recent CAPRISA study which revealed that superinfection does not boost memory neutralizing antibody (nAb) responses primed by the first infection or promote nAb responses to epitopes conserved in both infecting viruses.

On Page 2 we report on the visit by the UNAIDS PCB members as part of their visit to South Africa to gain insights and an understanding of the AIDS response in South Africa and we highlight the SAMRC visit to assess the extramural MRC HIV-TB research Unit.

We summarise the CAPRISA-affiliated researchers contributions to the 2018 HIVR4P Conference that was recently held in Madrid on page 3.

Eliciting bNAbs that neutralize a broad range of circulating HIV strains, represents a key priority for vaccine development. In some cohorts, superinfection has been implicated in driving such responses. However, a recent CAPRISA study revealed that superinfection does not boost memory neutralizing antibody (nAb) responses primed by the first infection or promote nAb responses to epitopes conserved in both infecting viruses.

In the study published in *Cell Host and Microbe*, PhD student Daniel Sheward at the University of Cape Town supervised by CAPRISA honorary senior scientists, Profs Carolyn Williamson and Penny Moore, characterized the nAb responses in four superinfected CAPRISA female participants.

To assess whether the onset of nAb responses to superinfection was accelerated, Sheward compared the time from primary infection and superinfection until the first detection of neutralizing antibodies. The nAb responses to superinfecting viruses reached detectable levels by a median of 9–17.5 weeks following superinfection comparable with the time to first detection of nAbs to the primary infecting viruses in each of the four superinfected individuals. This was also comparable with the timing of nAb responses following primary HIV infection in 22 other participants, which were detectable by a median of 9–16 weeks post-infection. As the onset of nAbs to the superinfecting viruses were not accelerated, this suggested that they likely represented *de novo* responses, rather than secondary, memory responses.

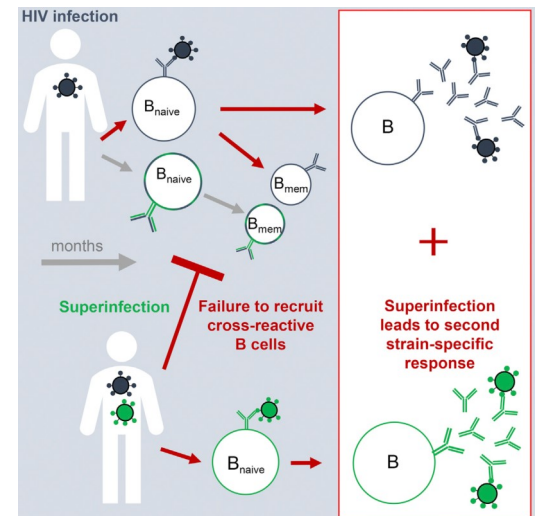
While one superinfected individual, CAP256, developed potent broadly neutralizing antibodies (bnAbs), superinfection was likely not the driver as the nAb re-

sponse did not target an epitope conserved in both viruses.

Rather, sequential exposure led to nAbs specific to each HIV envelope glycoproteins (Env) but did not promote bnAb development. This study has major implications for vaccine design, and suggests that sequential immunization with differing Envs may not be sufficient to focus the immune response onto conserved epitopes.

Penny L. Moore and Carolyn Williamson

For further reading see: Sheward D et al. *Cell Host and Microbe* 2018; <https://doi.org/10.1016/j.chom.2018.09.001>



HIV-infected individuals can be reinfected with a second strain (superinfection), providing a model that informs the use of sequential immunizations in future vaccines. Superinfection fails to boost memory B cells primed by the first infection and does not promote bnAbs to HIV

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The UNAIDS Programme Coordinating Board's visit to CAPRISA focuses on research for policy



Members of the UNAIDS Programme Coordinating Board (PCB), including the outgoing and incoming-Chair together with Gunilla Carlsson (the newly appointed Deputy Director of UNAIDS and UN Assistant Secretary-General), visited CAPRISA, which is a UNAIDS Collaborating Centre for Research and Policy, on 16th October as part of their visit to South Africa to gain insights and an understanding of the AIDS response in South Africa.

The 24 person delegation was led by UNAIDS Regional and Country Directors, Drs Catherine Sozi and Mbulawa Mugabe.

Quarraisha Abdool Karim, CAPRISA's Associate Scientific Director and UNAIDS Special Ambassador for Adolescents and HIV, provided the delegation with an

overview of CAPRISA highlighting the impact CAPRISA's research has on global and national policy and saving lives.

Her science update included an update of the evolving HIV epidemic in a hyper-endemic epidemic setting underscoring the magnitude of the epidemic in the region; the importance of reducing new infections in adolescent girls and young women; new data on understanding vulnerability of young women, planned studies to prevent HIV and the need for HIV to be integrated into health care delivery including the importance of integration of HI and TB services to reduce mortality rates. She cautioned that whilst significant gains have been achieved globally, there is a perception that AIDS is no longer a global priority, posing a threat to reverse the gains made to date.

Visit to assess the progress of the SAMRC extramural TB Unit at CAPRISA



The South African Medical Research Council's (SAMRC) Vice President of Research Prof Jeffrey Mphahlele and Dr Eunice Zwane Senior Programme Manager visited CAPRISA, the host to an extramural MRC HIV-TB Pathogenesis and Treatment Research Unit, recently for an update on the progress and research output made in TB treatment and research studies.

The SAMRC officials met with Drs Nesri Padayatchi PI of the INDEX and PRAXIS studies, Kogie Naidoo, Head of HIV-TB Treatment research and held discussions with staff at the CAPRISA Springfield Research clinic where the MDR and XDR TB research team is located. The visit included a tour of the laboratory and the new TB and HIV BSL 3 laboratories at the DDMRI.

From Left to right: Dr Kogie Naidoo; Prof Quarraisha Abdool Karim, Prof Jeffrey Mphahlele, Vice-President Research (SAMRC); Dr Eunice Zwane, Senior Programme Manager (SAMRC); Prof Salim Abdool Karim and Dr Nesri Padayatchi.



Representing CAPRISA at the 2018 HIVR4P in Madrid



Some of the CAPRISA-affiliated researchers who gathered in Madrid, Spain to share research findings on bnAbs and HIV prevention studies

CAPRISA collaborators and researchers participated in several sessions at the 2018 HIVR4P conference held in Madrid, Spain from 21 – 25 October where the latest biomedical prevention research was presented. The presentations by CAPRISA focused largely on broadly neutralizing antibodies and vaccine research. One of the highlights at the conference was understanding how to tweak the broadly neutralizing antibody structural characteristics itself to better preserve function and half-life for translational passive immunization studies in humans to prevent HIV.

Invited speakers included Profs Lynn Morris and Penny Moore, CAPRISA honorary senior scientists, and NICD Postdoctoral Fellow, Dr

Simone Richardson. Morris delivered a talk entitled, “Antibody Mediated Protection (AMP): Where Are We? Which Antibodies to Use and How Will We Know If It’s Working?” and Moore presented two talks at satellite sessions entitled: “The impact of antibody isotype on neutralization” and “Broadly neutralizing antibodies in HIV-infected children”. Richardson’s talk in a satellite session was entitled: “The Link Between Fc Effector Function and Neutralization”.

CAPRISA-affiliated researchers were represented in 8 oral and 13 poster presentations (Box 1). CAPRISA scientist Dr Sinaye Ngcapu chaired the oral poster session entitled: “Microbiome: When Microorganisms

Presenting their posters at HIVR4P (L) Thevani Pillay, (M) Ross Cromarty and (R) Kalendri Naidoo

BOX 1: CAPRISA-affiliated research contributions to the 2018 HIVR4P conference (CAPRISA-affiliated researcher (bold), presenting author)

Invited talks

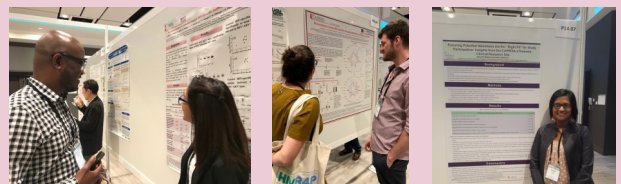
- **Morris L.** Antibody Mediated Protection (AMP): Where Are We? Which Antibodies to Use and How Will We Know If It’s Working?
- **Moore P.** The impact of antibody isotype on neutralization
- **Moore P.** Broadly neutralizing antibodies in HIV-infected children

Orals

- **Richardson SJ,** Lambson BL, Crowley A, Mkhize NN, **Garrett N, Abdool Karim S, Moore PL, Ackerman ME, Morris L.** IgG3 Hinge Length Enhances Neutralization Potency and Fc Effector Function of an HIV V2-Specific Broadly Neutralizing Antibody.
- **Sacks D,** Bhiman JD, Gorman J, Kwong PD, **Morris L, Moore PL.** Somatic hypermutation to counter a rare viral immunotype drove off-track antibodies in the CAP256-VRC26 V2-directed bNAbs lineage.
- **Mabvakure BM,** Scheepers C, **Garrett N, Abdool Karim SS, Williamson C, Morris L, Moore PL.** Targeted viral selection is associated with the development of HIV broadly neutralizing antibodies.
- **Umotov J,** Bagaya B, Ver L, Kilembe W, Poignard P, Sok D, **Moore P,** et al. Fast and Focused Maturation of VH1-2-restricted HIV-Env CD4-binding Site Targeting bNAbs.
- **Sacks D,** Bhiman JN, Gorman J, Kwong PD, **Morris L, Moore PL.** Somatic hypermutation to counter a rare viral immunotype drove off-track antibodies in the CAP256-VRC26 V2-directed bNAbs lineage
- **Ellen Tolley EE,** Zangeneh S, Chau G, Eron J, Grinsztejn B, **Dawood H,** et al. Acceptability of Long-acting Injectable Cabotegravir (CAB LA) in HIV-uninfected Individuals: HPTN 077.
- **Mielke D,** Ziki R, Anthony C, Ochsenauber C, **Garrett N, Abdool Karim SS, Montefiori D, Moore P, Morris L, Ferrari G, Williamson C.** Neutralizing and ADCC Activity of Anti-HIV-1 Antibodies Against Acute Subtype C Envs: Implications for Prevention and Treatment of HIV-1 Infection.
- **Landovitz RJ,** Li S, Eron JJ, Grinsztejn B, **Dawood H,** et al. Tail-phase Safety, Tolerability and Pharmacokinetics of Long-acting Injectable Cabotegravir in HIV-uninfected Individuals: HPTN 077 Final Results.

Posters

- **Cromarty R, Liebenberg L, Mckinnon L, Abdool Karim Q, Abdool Karim SS, Sigal A, Passmore J-A, Archary D.** Betamethasone Reduces HIV Infection Through Modulation of Cytokine Expression
- **Naidoo K, Mansoor LE.** Ensuring Potential Volunteers Are the “Right Fit” for Study Participation: Insights From the CAPRISA eThekweni Clinical Research Site.
- **Garrett N, Mtshali A, Osman F, Singh R, Masson L, Mitchev N, McKinnon L, Ngobese H, Abdool Karim SS, Mlisana K, Passmore J-A, Rompalo A, Mindel A, Liebenberg L.** Reducing Genital Inflammation and HIV Risk: Assessing the Role of Point-of-care STI/BV Testing With Expedited Partner Therapy.
- **Pillay T, Olivier AJ, Parveen S, Narain K, Liebenberg L, Ngcapu S, Mhlongo M, Burgers WA, Passmore J-A, Archary D.** Pro-inflammatory Cytokine Profiles and HIV-specific Antibody Responses in the Male Genital Tract.
- **Mtshali A, Garrett N, Mhlongo M, Ngcapu S, Liebenberg L.** Clearance of Sexually Transmitted Infections and the Impact of Genital Inflammation in HIV-infected Women.
- **Tanko RF, Coussens A, Dabee S, Mbulawa ZZA, Barnabas S, Hu NC, Jaumdally SZ, Gamielidien H, Jaspan HB, Bekker L-G, Williamson A-L, Passmore J-A.** Relationship Between Vitamin D Deficiency and Genital Mucosal Immunity in Young South African Women Related to Risk for HIV and HPV Infections.
- **Kitchin D, Bhiman JN, Scheepers C, Mvududu D, Oosthuysen B, Lambson BE, Madzorera VS, Anthony C, Abdool Karim SS, Garrett NJ, Williamson C, Doria-Rose NA, Mascola JR, Morris L, Moore PL.** Divergent Members of a HIV-1 Broadly Neutralizing Antibody Lineage that Share a Common Mode of Recognition within the N332-Glycan Supersite.
- **Makoah NG,** van den Berg FT, Ali S, Scott TA, Ziki RE, Mutsunguma, Mkhize NN, Lambson B, Crowther C, **Abdool Karim SS, Balazs AB, Weinberg MS, Moore PL, Ely A, Arbutnot P, Morris L.** Vector-mediated delivery of broadly neutralizing antibodies targeting the V2 apex
- **Manhanzva MT,** Abrahams A, Gamielidien H, Jaspan H, Jaumdally S, Barnabas SL, Dabee S, **Masson L.** Immunoregulatory Properties of Clinical Lactobacillus Isolates From South African Women at High Risk of HIV Acquisition
- **Roberts ST,** van der Straten A, Rael CT, Gorbach PM, Chinula L, Palanee-Phillips T, **Naidoo K,** et al. Intimate Partner Violence and Engagement in the HIV Care Continuum Among Women in sub-Saharan Africa: A Prospective Cohort Study.
- **Ximba P,** Chapman R, Meyers A, van Diepen M, Margolin E, **Morris L,** et al. Exploring the Use of Nano-particulate Zera®-induced HIV-1 Env “Protein Bodies” as Vaccines.
- **Abrahams AG,** Manhanzva M, Chetwin E, Froissart R, Gamielidien H, Jaspan H, Jaumdally S, Barnabas SL, Dabee S, **Masson L.** Pathogen Inhibitory Properties of Vaginal Lactobacillus Isolates From South African Women at High Risk of HIV Infection.
- **Alisoltani A,** Potgieter M, Bell L, Waldron E, Iranzadeh A, McDonald Z, Allali I, Mulder N, Dabee S, Barnabas S, Jaspan H, Tabb D, Bekker L-G, **Passmore J-A, Masson L.** Analysis of the Genital Tract Metaproteome in South African Women: From Bacterial Vaginosis Biomarkers to HIV Prevention.





Scientific papers published in 2018

72 Drain PK, Bajema KL, Dowdy D, Dheda K, **Naidoo K**, Schumacher SG, Ma S, Meermeier E, Lewinsohn DM, Sherman DR. Incipient and Subclinical Tuberculosis: a Clinical Review of Early Stages and Progression of Infection. *Clinical Microbiology Reviews* 2018; 31(4): e00021-18.

73 Barre-Sinoussi F, **Abdool Karim SS**, Albert J, Bekker LG, Beyrer C, Cahn P, Calmy A, Grinsztejn B, Grulich A, Kamarulzaman A, Kumarasamy N, Loutfy MR, El Filali KM, Mboup S, Montaner JS, Munderi P, Pokrovsky V, Vandamme AM, Young B, Godfrey-Faussett P. Expert consensus statement on the science of HIV in the context of criminal law. *Journal of the International AIDS Society* 2018; 21(7):e25161.

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75 Ginsburg C, Bocquier P, Beguy D, Afolabi S, Kahn K, Obor D, **Tanser F**, Tomita A, Wamukoya M, Collinson MA. Association between internal migration and epidemic dynamics: an analysis of cause-specific mortality in Kenya and South Africa using health and demographic surveillance data. *BMC Public Health* 2018; 18(1):918.

76 Govender E, **Abdool Karim Q**. Understanding women and men's acceptability of current and new HIV prevention technologies in KwaZulu-Natal, South Africa. *AIDS Care* 2018; 30(10):1311-1314.

77 Ealand C, Rimal B, Chang J, Mashigo L, Chengalroyen M, Mapela L, Beukes G, Machowski E, Kim SJ, **Kana B**. Resuscitation-Promoting Factors Are Required for Mycobacterium smegmatis Biofilm Formation. *Applied and Environmental Microbiology* 2018; 84(17): e00687-18.

78 Ditse Z, Muenchhoff M, Adland E, Jooste P, Goulder P, **Moore PL**, **Morris L**. HIV-1 Subtype C Infected Children with Exceptional Neutralization Breadth Exhibit Polyclonal Responses Targeting Known Epitopes. *Journal of Virology* 2018; 92(17): e00878-18.

79 Jaumdally SZ, **Masson L**, Jones HE, Dabee S, Hoover DR, Gamielien H, Langwenya N, Myer L, Todd CS, **Passmore JS**. Lower genital tract cytokine profiles in South African women living with HIV: influence of mucosal sampling. *Scientific reports*. 2018; 8(1):12203.

80 Sheward DJ, Marais J, Bekker V, Murrell B, Eren K, Bhiman JN, Nonyane M, **Garrett N**, Woodman ZL, **Abdool Karim Q**, **Abdool Karim SS**, **Morris L**, **Moore PL**, **Williamson C**. HIV Superinfection Drives De Novo Antibody Responses and Not Neutralization Breadth. *Cell Host & Microbe* 2018; <https://doi.org/10.1016/j.chom.2018.09.001>

CAPRISA iSpot U Award for Innovation

We congratulate Patience Nomthandazo Mbatha, at the CAPRISA Springfield Research clinic, a tracker and counsellor on the INDEX study, who was presented with the CAPRISA iSpot U Award in recognition of showing innovation in her work.

Dr Nesri Padayatchi (left) Deputy Director of CAPRISA presents the award to Nomthandazo (centre) with Ms Natasha Gounden (right), study coordinator INDEX.



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



UNAIDS
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



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