



# CAPRISA

CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

Newsletter

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## The broadly neutralizing antibody from patient CAPRISA 256 (CAP256-VRC26.25) protects monkeys from SHIV

### In this Issue

Our featured story this month focuses on the recent publication in *Science Translational Medicine* that shows the protective efficacy of the CAP256-VRC26.25LS broadly neutralizing antibody in an experimental monkey model.

On page 2 we report on the recent DST-NRF Centres of Excellence Directors' Forum and congratulate Drs Anushka Naidoo and Gugulethu Mzobe on being awarded their PhDs at the UKZN Spring graduation ceremony.

On page 3 we feature the "Berlin patient" Timothy Brown who was a speaker at the South African Immunology Society held in Cape Town. We also report on the site visit by officials from DAIDS VRP and OCSO and congratulate Dr Sherika Hanley on being awarded a 4-year competitive DRILL grant.

A study published in *Science Translational Medicine* on 6<sup>th</sup> September 2017 shows the protective efficacy of the CAP256-VRC26.25LS broadly neutralizing antibody in an experimental monkey model.

The CAP256-VRC26.25LS antibody, isolated from a woman in the CAPRISA 002 cohort, targets the V2 apex of the HIV envelope glycoprotein and is highly potent against clade C viruses in laboratory assays. Importantly, this potency translated to *in vivo* efficacy, as all animals treated with the lowest dose were fully protected against a clade C SHIV challenge (see Figure below).

In this study, Rhesus macaques received a single infusion of CAP256-VRC26.25LS at 3 different concentrations (2, 0.4, and 0.08 mg/kg) before challenge with SHIV-325c. CAP256-VRC26.25LS was fully protective even at the 0.08 mg/kg dose, which correlated with its greater *in*

*vitro* neutralization potency against the challenge virus. Serum antibody concentrations required for protection were <0.75 mg/ml for CAP256-VRC26.25LS.

These data demonstrate exceptional potency and protective efficacy of V2-specific neutralizing antibodies in non-human primates and validate V2 as a potential target for the prevention of HIV infection in passive immunization strategies in humans.

These results lay the foundation for the human studies using CAP256-VRC26.25 that are due to start in 2018 as part of the **S**ubcutaneous **A**dministration of **M**onoclonal **B**roadly-neutralizing **A**ntibodies (SAMBA Trial - CAPRISA 012).

### For further reading see:

Julg B, et al. Broadly neutralizing antibodies targeting the HIV-1 envelope V2 apex confer protection against a clade C SHIV challenge. *Science Translational Medicine* 2017; 9(406): eaal1321. <http://stm.sciencemag.org/content/9/406/eaal1321>

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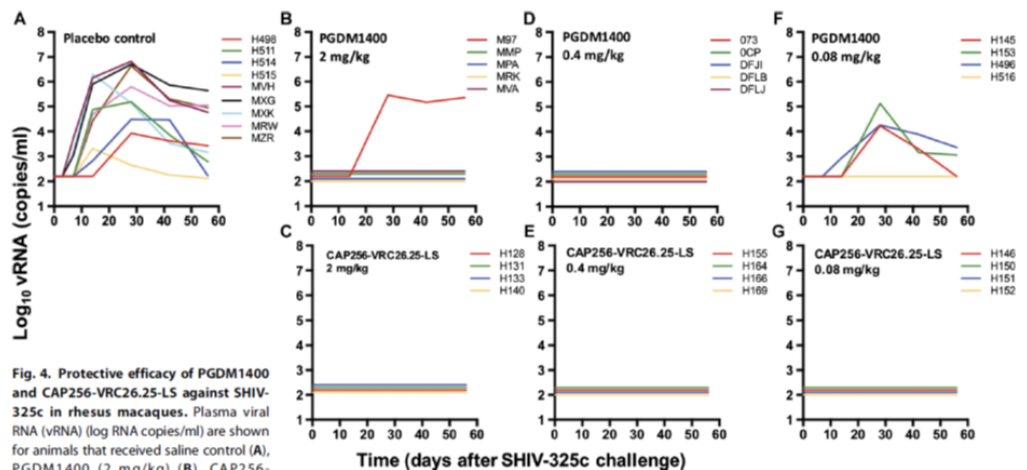


Fig. 4. Protective efficacy of PGDM1400 and CAP256-VRC26.25-LS against SHIV-325c in rhesus macaques. Plasma viral RNA (vRNA) (log RNA copies/ml) are shown for animals that received saline control (A), PGDM1400 (2 mg/kg) (B), CAP256-VRC26.25-LS (2 mg/kg) (C), PGDM1400 (0.4 mg/kg) (D), CAP256-VRC26.25-LS (0.4 mg/kg) (E), PGDM1400 (0.08 mg/kg) (F), or CAP256-VRC26.25-LS (0.08 mg/kg) (G). The assay sensitivity limit was >50 RNA copies/ml.



## CAPRISA participates at the DST-NRF Centres of Excellence Directors' Forum

As a designated DST-NRF Centre of Excellence in HIV Prevention, CAPRISA participated in the annual Department of Science and Technology (DST) and the National Research Foundation (NRF) Centres of Excellence (CoEs) Directors' Forum on 31 August—1 September held in Port Elizabeth. The theme “*Triumvirate Transformation in the CoEs*” with special reference to the three pillars of People, Knowledge Enterprise and Engagement with Society resonated in the keynote address delivered by the Honourable Minister of Science and Technology, Dr Naledi Pandor. She highlighted the need for social transformation and taking the lead in knowledge generation on the African continent. CAPRISA's associate scientific Director Professor Quarraisha Abdool Karim was an invited speaker and delivered an address entitled: “How HIV prevention research can achieve an AIDS free generation of young women in Africa”. She said that reducing HIV in young women could change the course of the epidemic in Africa and reverse current poor global progress in HIV prevention. Whilst several promising technologies were in development the root cause of vulnerability among women was gender-power disparities, she said. The impressive list of speakers at the Forum included the former Vice-Chancellor of UCT Dr Mamphele Ramphela and Prof Barney Pitso, former Vice-Chancellor of UNISA. Learners from disadvantaged and urban schools attended the open sessions and participated in the interactive exhibits showcased by the Centres of Excellence.



L—R: The Honourable Minister of Science and Technology, Dr Naledi Pandor visits the CAPRISA stand and discusses the progress of the CAP 256-VRC26.25 bNAb studies with Professor Salim Abdool Karim, Director CAPRISA. Also present are, Nigel Makoah from the National Institute of Communicable Diseases and Dr Sinaye Ngcapu, CAPRISA Research Associate.

The DST-NRF CoE in HIV Prevention offers scholarships to postgraduate students at Honours, Masters, doctoral and post-doctoral levels which has supported the training of 120 postgraduate and 95 medical students since 2015.

## CAPRISA duo graduate with PhDs



Dr Anushka Naidoo



Dr Gugulethu Mzobe

We congratulate CAPRISA's Dr Anushka Naidoo and Dr Gugulethu Mzobe who graduated with PhDs at the University of KwaZulu-Natal's Spring Graduation ceremony.

**Dr Anushka Naidoo**, Senior Research Pharmacist at CAPRISA, was awarded a PhD in Pharmacology at UKZN's Spring graduation. Her study, entitled: “Moxifloxacin, Pharmacokinetics (PK-PD) in the treatment of drug susceptible Tuberculosis”, investigated if a clinically significant drug interaction that may affect drug exposure, exists between moxifloxacin and tuberculosis drug rifampicin or antiretroviral drugs in TB-HIV coinfecting patients enrolled in a clinical trial at CAPRISA. She also studied the effects of pharmacogenetic variation in genes coding of drug metabolising and drug

transporter enzymes on moxifloxacin concentrations in African patients.

**Dr Gugulethu Mzobe**, a postdoctoral Research Fellow at CAPRISA, was awarded a PhD in Medical Microbiology. Her thesis examined temporal gene expression of *Chlamydia trachomatis* in keratinocytes at 37°C. Her study confirms that mid-and-late cycle chlamydial gene expression levels are different to the published research conducted in HeLa cells at 37°C and that temperature has an effect on the level of Chlamydial gene expression when grown in keratinocytes. Her study also showed that two hours post infection, chlamydia retains its elementary body (EB) structural conformation in keratinocytes at 37°C, and that L2 reference strain 434 is different from the clinical L2 US151 as indicated by the difference in the gene expression pattern.



## Living proof that HIV can be cured



Left: Timothy Ray Brown with CAPRISA Research Associate Professor Lynn Morris at the SAIS meeting held in Gordon's Bay recently.

**T**imothy Ray Brown, better known as the "Berlin patient" was a speaker at the recent South African Immunology Society (SAIS) meeting held in Gordon's Bay. He gave a fascinating talk about his life-changing decision to undergo a bone-marrow transplant to treat his leukemia using stem cells that lacked the CCR5 receptor. Since these cells do not support HIV replication, this was an experimental attempt to simultaneously treat his HIV infection. After the transplant he decided to stop taking antiretroviral therapy and remarkably HIV could no longer be detected. Timothy has been HIV-free for over 10 years and is living proof that HIV is curable.

## Visit from DAIDS VRP and OCSO



Front Row: Tina Tong (Health Specialist - VRP), Joanne Csedrik (Programme Officer - OCSO), Tanuja Gengiah (Head: Pharmacy), Lutchemee Eswarlal (Laboratory Manager), Jacqueline Kasavan (QA -Lab) . Back Row: Kevin Ryan (Deputy Director - VRP), Kathy Mngadi (PI HVTN), Mary Marovich (Director - VRP), Nesri Padayatchi Deputy Director CAPRISA), Yajna Duki (HVTN Study Coordinator)

**T**he CAPRISA Vaccine team hosted officials from the DAIDS Vaccine Research Programme (VRP) and OCSO (Office of Clinical Site Oversight) on 19 September at the eThekweni CAPRISA Research clinic where the HVTN studies are currently underway. The purpose of the visit was to gain insight into the challenges experienced in conducting multiple vaccine protocols simultaneously. The officials had an opportunity to observe the infusion of a participant in the AMP study.

Dr Kathy Mngadi who led the tour of the Prevention facility, the onsite laboratory and pharmacy units, highlighted the challenges experienced in undertaking the vaccine studies which included space constraints.

A visit to the CAPRISA headquarters followed and officials had a tour of the main laboratory.

The vaccine team is currently conducting five HVTN studies; three phase I studies and two efficacy studies. The current combined cohort size is approximately 220 participants, with an expected accrual of about 25 participants per month until the end of September 2018.

The delegation met with Dr Nesri Padayatchi Deputy Director CAPRISA, Dr Kathy Mngadi HVTN Principal Investigator and senior CAPRISA staff.

## DRILL fellowship awarded to CAPRISA research clinician



**D**r Sherika Hanley (left), CAPRISA research clinician at the Umhlabi Research Clinic, has been awarded a DRILL Fellowship, a four-year research

training scholarship, by UKZN. The Developing Research Innovation, Localisation and Leadership in South Africa (DRILL) grant is funded by the National Institutes of Health in the US, aims at developing world-class scientists who are able to lead high-impact

research to find solutions to problems afflicting communities in resource-constrained settings in South Africa.

Dr Hanley, a specialist family physician who recently registered for her PhD entitled "Integration of Cardiovascular Disease Screening and Prevention in the HIV Management Plan for Women of Reproductive Age", will undertake training and research in the field of HIV under the supervision of Prof Daya Moodley, Head of the Women's Health and HIV Research Unit at UKZN and Dr Mergan Naidoo Head of Clinical Unit School of Nursing and Public Health, UKZN. The study proposes an algorithm which includes

point of care predictors of, and interventions for, cardiovascular disease risk, integrated into the HIV management guidelines for women receiving HIV care in resource-constrained settings.

Dr Hanley said that if the study is proven to be feasible and effective, "study findings could potentially offer a platform for further research which may allow for possible policy amendment in the direction of a simple to administer, but comprehensive integrated HIV chronic care model to be implemented at all levels of Primary Health Care in South Africa."



# Scientific papers published in 2017

\*59 **Naranbhai V**, Carrington M. Host genetic variation and HIV disease: from mapping to mechanism. *Immunogenetics* 2017; 69(8-9):489-498.

60 **Liebenberg L, Archary D, Sivro A**, Kwon DS. Bugs, drugs, and HIV: the role of the vaginal microbiome in HIV risk and antiretroviral efficacy for HIV prevention. *Genome Medicine* 2017; 9(1):74. DOI 10.1186/s13073-017-0469-2

61 **Naicker N, Naidoo A, Werner L, Garrett N, Majola N, Asari V, Baxter C, Grobler A, Abdool Karim Q, Abdool Karim SS**. Efficacy and safety of tenofovir-containing antiretroviral therapy in women who acquired HIV while enrolled in tenofovir gel prophylaxis trials. *Antiviral Therapy* 2017; 22(4):287-293.

62 Schopper D, Ravinetto R, Schwartz L, Kamaara E, Sheel S, Segelid MJ, Ahmad A, Dawson A, **Singh J**, Jesani A, Upshur R. Research Ethics Governance in Times of Ebola. *Public Health Ethics* 2017; 10(1):49-61.

63 Vandormael A, Rego F, Danaviah S, Carlos Junior Alcantara L, Boulware DR, **de Oliveira T**. CD4+ T-cell Count may not be a Useful Strategy to Monitor Antiretroviral Therapy Response in HTLV-1/HIV Co-infected Patients. *Current HIV Research* 2017; 15(3):225-231

64 Kufa T, **Kharsany A**, Cawood C, Khanyile D, **Lewis L, Grobler A**, Chipeta Z, Bere A, Glenshaw M, Puren A. Misdiagnosis of HIV infection during a South African community-based survey: implications for rapid HIV testing. *Journal of the International AIDS Society* 2017; 20(Suppl 6):35-43.

65 Julg B, Tartaglia LJ, Keele BF, Wagh K, Pegu A, Sok D, Abbink P, Schmidt SD, Wang K, Chen X, Joyce MG, Georgiev IS, Choe M, Kwong PD, Doria-Rose NA, Le K, Louder MK, Bailer RT, **Moore PL**, Korber B, Seaman MS, **Abdul Karim SS, Morris L**, Koup RA, Mascola JR, Burton DR, Barouch DH. Broadly neutralizing antibodies targeting the HIV-1 envelope V2 apex confer protection against a clade C SHIV challenge. *Science Translational Medicine* 2017; 9(406): eaa11321. DOI: 10.1126/scitranslmed.aa11321

\*continuation from previous newsletter

## Scientific Reviews

Abstracts submitted for review		Manuscripts submitted for review		Ancillary studies submitted for review	
Total#	Cumulative^	Total#	Cumulative^	Total#	Cumulative^
1	390	2	224	0	82

# for month, ^ since committee initiation



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