



# CAPRISA

CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

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## Immune correlates of TB recurrence

### In this Issue

Our feature article this month focuses on the recent publication in *Clinical Infectious Diseases* on predictors of tuberculosis recurrence in antiretroviral-treated HIV-infected individuals.

On page 2 we congratulate the NICD team on their new NIH grant that is part of the H3Africa initiative. We also provide highlights of Professors Salim and Quarraisha Abdool Karim's recent trip to Japan and feature the Young Adults Work Experience Programme.

An update on the results of the APPROACH vaccine study that the CAPRISA HIV Vaccine research Team participated in is provided on page 3. We also congratulate Dr Aida Sivo on being awarded the European and Developing Countries Clinical Trials Partnership (EDCTP) Career Development Fellowship.

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Research from the TB-HIV Treatment group was recently published in *Clinical Infectious Disease*. Sivo et al. describe immune correlates of TB recurrence in a cohort of HIV-infected individuals on antiretroviral therapy with a history of prior TB cure.

The study included a subset of participants from the CAPRISA 005 TB Recurrence upon Treatment with HAART (TRuTH) cohort based at the CAPRISA eThekweni clinic in Durban, South Africa. Selection of 23 different soluble immune markers were measured in plasma samples from 63 cases (patients with recurring TB) and 123 controls (patients with no evidence of recurring TB).

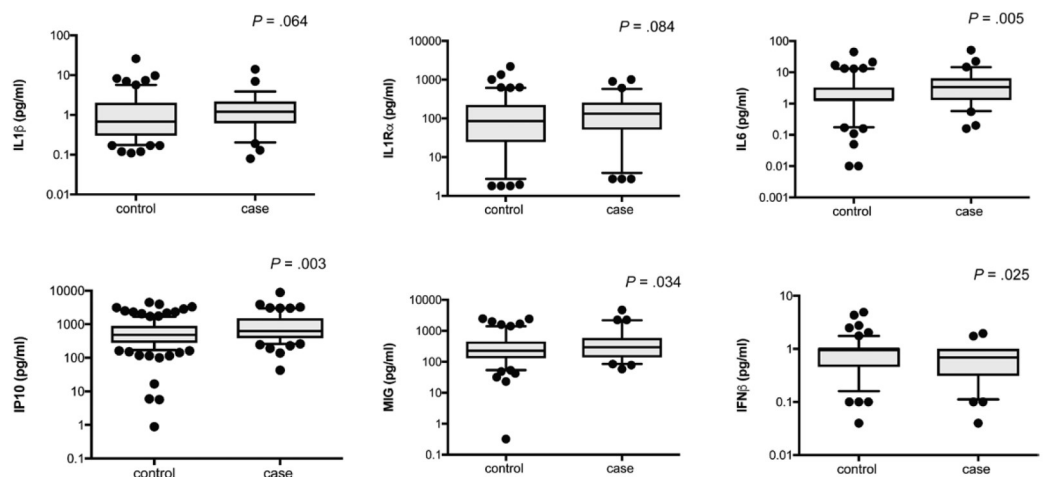
Pro-inflammatory cytokines, Interleukin 6 (IL6), interleukin 1b (IL1b)

and interleukin 1Ra (IL1Ra) were associated with increased risk of TB recurrence while Type I interferon, IFN $\beta$  was associated with decreased TB risk (Figure). Longitudinal analysis of samples during active TB and following successful TB treatment identified several markers of active disease and TB treatment response (IL6, IP10, sCD14 and IFN $\gamma$ ).

Sivo et al. wrote: "Because all HIV-infected individuals now qualify for ART, but ART does not completely ameliorate HIV-associated TB risk, the population for this study is important for defining TB risk factors."

### For further reading see:

Sivo A et al. Plasma Cytokine Predictors of Tuberculosis Recurrence in Antiretroviral-Treated HIV-infected Individuals from Durban, South Africa. *Clinical Infectious Diseases* 2017; 65(5): 819-826.



**Figure:** Cytokines/chemokines differentially expressed between controls ( $n = 123$ ) and cases ( $n = 63$ ) by univariate conditional logistic regression. Five cytokines were associated with increased rates of TB recurrence, including IL6 (OR 2.66, 95% CI 1.34–5.27,  $P = .005$ ), IP10 (OR 4.62, 95% CI 1.69–12.65,  $P = .003$ ), MIG (OR 3.11, 95% CI 1.10–8.82,  $P = .034$ ) and IL1 $\beta$  (OR 1.89, 95% CI 0.97–3.68,  $P = .064$ ) and IL1Ra (OR 1.52, 95% CI 0.95–2.45,  $P = .084$ ), whereas IFN $\beta$  was associated with decreased risk (OR 0.34, 95% CI 0.13–0.87,  $P = .025$ ). Abbreviations: CI, confidence interval; IL, interleukin; IFN, interferon; IP, interferon gamma induced protein; MIG, monokine induced by IFN- $\gamma$ ; OR, odds ratio; TB, tuberculosis.



## NIH grant awarded as part of the H3Africa initiative



*From L-R: Professor Lynn Morris CAPRISA Research Associate, and Dr. Bronwen Lambson, Simone Richardson and Dr. Cathrine Scheepers from the HIV Virology Section at the National Institute for Communicable Diseases.*

**A** National Institutes of Health U01 grant was recently awarded to CAPRISA Research Associate Professor Lynn Morris as part of the H3Africa initiative. This grant aims to examine antibody gene diversity and its impact on neutralizing and non-neutralizing functions. It builds on previous studies by

Catherine Scheepers showing a high frequency of novel alleles in the CAPRISA cohort as well as work by Bronwen Lambson and Simone Richardson, at the National Institutes of Communicable Diseases (NICD), on how changes in the Fc region impact effector functions. It is hoped, "that this work will help to better understand the

human antibody response to HIV infection and ultimately inform vaccine development," explained Morris, who is a Research Professor in the Faculty of Health Sciences at the University of Witwatersrand and is the Head of the HIV Virology Laboratory in the Centre for HIV & STIs at the NICD.

## Scientific exchange with health officials in Japan



*Professors Salim Abdool Karim and Quarraisha Abdool Karim with Dr Aikichi Iwamoto (left) and Dr Makoto Suematsu (right) from the Japan Agency from Medical Research and Development*

Prof Salim Abdool Karim Director of CAPRISA and Prof Quarraisha Abdool Karim Associate Scientific Director of CAPRISA recently visited Japan to attend the International Epidemiological Association's conference. While in Japan, Professors Abdool Karim had an opportunity to meet with several leading Japanese scientists including Dr Aikichi Iwamoto from the Japan Agency from Medical Research and Development (AMED); Dr Kuniaki Miyake from the Japanese Department of Health; Dr Hiroyuki Yamamoto from the AIDS Research Center, National Institute of Infectious Diseases; Dr Makoto Suematsu, President of AMED and Professor Edo, Dean of the St Lukes School of Public Health. Professor Salim Abdool Karim delivered a presentation at the St Lukes School of Public Health on the Global HIV epidemic: Successes, Challenges & Prospects.

## CAPRISA hosts the Young Adults work experience programme

**E**leven enthusiastic learners from secondary schools in Durban spent three informative days at the CAPRISA headquarters and the CAPRISA eThekweni Research Clinic which formed part of their experiential learning and invaluable career knowledge and guidance. The Young Adults Work Experience programme, which was facilitated by the Human Resources Department aimed to create an awareness on the wide range of careers in a clinical research organisation and provide participants with insights to make informed career

choices. The programme included a career assessment with a clinical psychologist and interactions with both administrative and clinical departments. The programme is an annual initiative held over the July vacation and forms part of CAPRISA's outreach to empower youth said Marietjie Geldenhuys, head of CAPRISA's Human Resources department. "The young adults were fascinated by the various facets of careers in clinical research and demonstrated keen inter-



*Learners proudly hold up their certificates after successfully completing the CAPRISA Young Adults Work Experience programme.*

est to acquire new knowledge from CAPRISA staff."



## Toward the next HIV vaccine efficacy trial

**T**he CAPRISA Vaccine team under Dr Nigel Garrett and Dr Kathy Mngadi completed follow up of 29 participants in the APPROACH study, a randomized safety and immunogenicity trial, that enrolled 400 participants across sites in South Africa, Rwanda, Uganda, the United States, and Thailand.

The study was sponsored by Janssen Vaccines and Prevention B.V., and participants received four vaccinations over 48 weeks, two priming immunizations at months 0 and 3 with Ad26.Mos.HIV followed by two booster immunizations at months 6 and 12 with either Ad26 or MVA vectors and high or low dose trimeric clade C gp140 protein in alum adjuvant.

Results of APPROACH were presented at the International AIDS Society conference in Paris in July 2017. After the final boost, 80% or more of participants displayed the requisite immune responses at levels above the desired magnitude, greatly exceeding the targets set for making the go/no go decision about proceeding to efficacy testing. The efficacy trial, HVTN 705, is planned to start later in the year, and aims to enrol 2600 sexually active women aged 18 – 35, randomized 1:1 to receive either the active vaccine regimen or placebo. The CAPRISA team is proud to contribute to the trial, and Dr Mngadi will Co-Chair the study.



*The team that worked on the APPROACH study included (Front L-R): Nigel Garrett, Kathy Mngadi, Kaminee Ramseroop, Fathima Sayed, Zanele Msimango (Back row L-R): Siphesihle Gumede, Yajna Duki, Ivy Kaunda, Jason Naidoo, and Nivashnee Naicker*

### CAPRISA Postdoc Fellow receives EDCTP fellowship

**C**APRISA postdoctoral Fellow Dr Aida Sivro was awarded the European and Developing Countries Clinical Trials Partnership (EDCTP) Career Development Fellowship. The objectives of the fellowship are to promote career development and retention of post-doctoral researchers and postgraduate medical researchers in the research field and in sub-Saharan Africa and to equip the fellows with the ability to establish themselves as independent researchers. Dr Sivro was awarded funding for a three-year period to look at the role of the interferons and interferon signalling in HIV acquisition.



*Dr Aida Sivro*

### Sichuan CDC and Provincial Health and Family Planning Commission visit CAPRISA

**D**r Fan Wei, Chief of Family Department, Sichuan Provincial Health and Family Planning Commission led a delegation of six health officials from the Sichuan CDC and provincial health and family planning commission to CAPRISA on 7 August. The purpose of the visit was to develop cooperation and exchange between South Africa and Sichuan Province in the areas of public health, specifically in the management and treatment of HIV/AIDS and tuberculosis co-infection, data analysis and paper writing of HIV/AIDS control. The delegation met with Dr Kogie Naidoo Head of CAPRISA's HIV and TB Treatment and sen-

ior scientists at the CAPRISA eThekweni Research Clinic. The officials also held discussions with Professor Dhayendre Moodley, Principal Investigator, IMPAACT studies, at the CAPRISA Umlazi Research Clinic and with the Director of CAPRISA, Professor Salim Abdool Karim at the CAPRISA headquarters.



*Front Row: Dr Nigel Garrett (L) and Dr Kogie Naidoo (right) with officials from Sichuan at the CAPRISA eThekweni Research Clinic*



# Scientific papers published in 2017

- 52\* Livant E, Heaps A, Kelly C, Maharaj R, **Samsunder N**, Nhlangulela L, Karugaba P, Panchia R, Marrazzo J, Chirenje ZM, Parikh UM; VOICE Study Team. The fourth generation AlereTM HIV Combo rapid test improves detection of acute infection in MTN-003 (VOICE) samples. *Journal of Clinical Virology* 2017; 94:15-21. doi: 10.1016/j.jcv.2017.06.006.
- 53 Mclvor A, Koornhof H, **Kana BD**. Relapse, re-infection and mixed infections in tuberculosis disease. *Pathogens and Disease* 2017; 75(3):1-16. doi: 10.1093/femspd/ftx020
- 54 Tomita A, Vandormael AM, Cuadros D, Slotow R, **Tanser F**, Burns JK. Proximity to healthcare clinic and depression risk in South Africa: geospatial evidence from a nationally representative longitudinal study. *Social Psychiatry and Psychiatric Epidemiology* 2017; 52(8):1023-30.
- 55 Schomaker M, Leroy V, Wolfs T, Technau KG, Renner L, Judd A, Sawry S, Amorissani-Folquet M, Noguera-Julian A, **Tanser F**, Eboua F. Optimal timing of antiretroviral treatment initiation in HIV-positive children and adolescents: a multiregional analysis from Southern Africa, West Africa and Europe. *International Journal of Epidemiology* 2017; 46(2):453-465.
- 56 Akullian A, Bershteyn A, Klein D, Vandormael A, Bärnighausen T, **Tanser F**. Sexual partnership age pairings and risk of HIV acquisition in rural South Africa. *AIDS* 2017; 31(12):1755-64.
- 57 **Sivro A, McKinnon LR, Yende-Zuma N, Gengiah S, Samsunder N, Abdool Karim SS, Naidoo K**. Plasma Cytokine Predictors of Tuberculosis Recurrence in Antiretroviral-Treated HIV-infected Individuals from Durban, South Africa. *Clinical Infectious Diseases* 2017; 65(5): 819-826.
- 58 Ngandu NK, Carlson JM, Chopera DR, Ndabambi N, **Abdool Karim Q, Abdool Karim S, Williamson C**. Selection of HIV-1 Variants with Higher Transmission Potential by 1% Tenofovir Gel Microbicide. *JAIDS* 2017; 76(1):43-47.

\*continuation from previous newsletter

## Scientific Reviews

Abstracts submitted for review		Manuscripts submitted for review		Ancillary studies submitted for review	
Total#	Cumulative <sup>^</sup>	Total#	Cumulative <sup>^</sup>	Total#	Cumulative <sup>^</sup>
1	389	2	222	2	82

# for month, <sup>^</sup> since committee initiation



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CAPRISA is the UNAIDS Collaborating Centre for HIV Research and Policy



CAPRISA hosts a MRC HIV-TB Pathogenesis and Treatment Research Unit

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