



CAPRISA

CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

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Vaginal bacteria modify HIV tenofovir microbicide efficacy in African women

In this Issue

Our feature article this month focuses on the study that shows that vaginal bacteria, especially *Gardnerella* modifies tenofovir microbicide efficacy. These novel findings were first presented at the 2016 Durban International AIDS Conference in 2016.

On page 2 we highlight the roundtable discussions with Dr Francis Collins from the US National Institutes of Health (NIH) and CAPRISA's participation in the World Economic Forum.

We congratulate Quarraisha Abdool Karim on being awarded an honorary doctorate from the University of Johannesburg and Jerome Singh on his appointment to the WHO's International Health Regulations Roster of Experts, as an expert in Health Law, Ethics and Human Rights for a period of four years.

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Research by a Mucosal Immunology research collaboration between CAPRISA's mucosal immunology team in Durban and scientists from the USA and Canada was published in *Science* this week. The study provides new evidence linking vaginal bacteria to microbicide efficacy through tenofovir depletion via bacterial metabolism.

Antiretroviral-based strategies for HIV prevention have shown inconsistent results in women. Although variability in the levels of adherence has been shown to be a major contributing factor for the diverse trial outcomes in women, little is known about what biological factors may also contribute to the variability in these results.

This study, which included biological samples from 688 HIV-negative women from the CAPRISA 004 trial, used a metaproteomic approach to assess whether vaginal bacteria modulate the efficacy of the topical microbicide tenofovir in preventing HIV infection.

Two major vaginal bacterial community types were identified; one dominated by *Lactobacillus* (59.2%), and the other where *Gardnerella vaginalis* predominated with other anaerobic bacteria (40.8%).

Tenofovir reduced HIV incidence by 61% ($P=0.013$) in *Lactobacillus*-dominant women but only 18% ($P=0.644$) in women with non-*Lactobacillus* bacteria - a three-fold difference in efficacy (Figure below).

An *in vitro* culture system was used to assess potential biodegradation of tenofovir by the major bacterial species present in this cohort. The results show that detectible mucosal tenofovir was lower in non-*Lactobacillus* women, negatively correlating with *G. vaginalis* and other anaerobic bacteria, which depleted tenofovir by metabolism more rapidly than target cells convert to pharmacologically active drug.

For more information see: Klatt NR, et al. Vaginal bacteria modify HIV tenofovir microbicide efficacy in African women. *Science* 2017; 356: 938-945

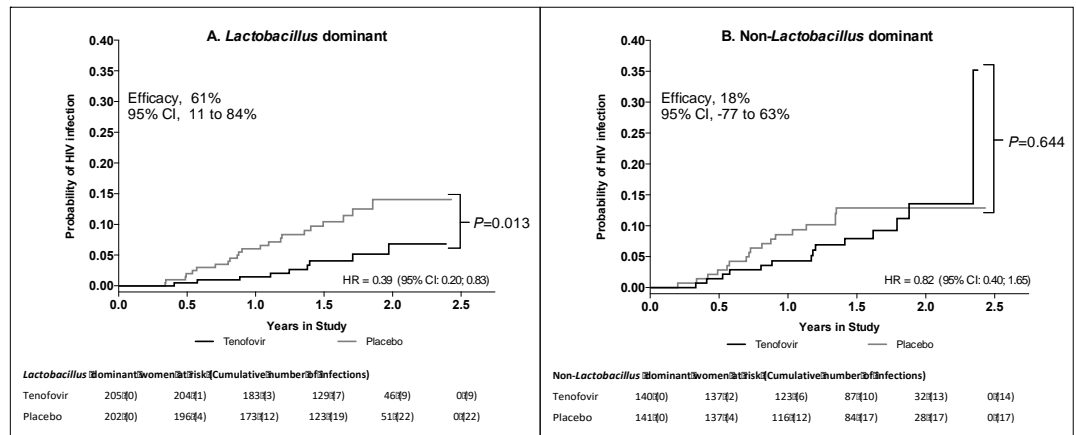


Figure: Cumulative HIV infection probability by treatment assignment in women with (A) vaginal *Lactobacillus* dominance (*Lactobacillus* >50%) (n=407 women) and (B) non-*Lactobacillus* bacterial dominance (*Lactobacillus* ≤50%) (n=281 women). The table below shows the cumulative number of HIV infections in each study arm, corresponding HIV incidence rates, and efficacy of tenofovir gel to prevent HIV acquisition for each additional 6 months of follow-up.



Francis Collins leads roundtable discussion on building international excellence in medical research



Present at the roundtable discussion were: Front Row - seated (L-R): Richard Gordon, Gansen Pillay, Nesri Padayatchi, Robert Eiss, Salim Abdool Karim, Francis Collins, Quarraisha Abdool Karim, Sabiha Essack, Koleka Mlisana, Tanuja Gengiah. Back row – standing (L-R): Frank Tanser, Ayesha Kharsany, Jeffrey Mphahlele, Eliza Govender, Halima Dawood, Kogie Naidoo, Andries Steyn, Cheryl Baxter, Desh Archary, Alex Pym, Arthie Ramkissoon, Gita Ramjee, Nombulelo Magula, Leila Mansoor, Kathy Mngadi, Pamela Gumbi, Sinaye Ngcapu, Bonginkosi Mfuze.

On 5 May CAPRISA hosted a Roundtable discussion with Dr Francis Collins, Director of the US National Institutes of Health (NIH) on building international excellence in medical research. Senior officials and scientists from the South African Medical Research Council, the National Research Foundation, Africa Health Research Initiative, Maternal, Adolescent and Child Health, the University of KwaZulu-Natal and CAPRISA had an opportunity to interact with Dr Collins and Dr Robert Eiss, the senior advisor Fogarty International Centre NIH, and to participate in a robust discussion on

what is needed to build research excellence, with a special emphasis on what the NIH should do. In his position as Director Dr Collins oversees the work of the largest supporter of biomedical research in the world, spanning the spectrum from basic to clinical research. A physician-geneticist, Dr Collins is noted for his landmark discoveries of disease genes and his leadership of the international Human Genome Project, which culminated in April 2003 with the completion of a finished sequence of the human DNA instruction book.

CAPRISA participates at the World Economic Forum for Africa

CAPRISA Director Professor Salim and Associate Scientific Director Quarraisha Abdool Karim participated in sessions at the World Economic Forum (WEF) for Africa held from 3-5 May in Durban. Prof Salim Abdool Karim participated in the Leadership Council of the Coalition for African Research and Innovation (CARI) together with Dr Francis Collins Director of the National Institutes of Health and Dr Michelle Mulder from the Medical Research Council. This session focussed on strategic business models, governance, financial options and African-led networks to develop innovative research platforms and sustain research in Africa.

Professor Quarraisha Abdool Karim was a speaker in the session on Laying the Groundwork for Research and Innovation, which examined how government

and business leaders foster viable pan-African research and innovation ecosystems. The panel, which included representatives from the African Academy of Sciences and the Bill and Melinda Gates Foundation, among others,

explored scenarios on expanding funding mechanisms, building local capacity for R&D and prioritising intra-African science partnerships. To listen to this session click on: <https://www.weforum.org/events/world-economic-forum-on-africa-2017/sessions/laying-the-groundwork-for-research-innovation#>



L-R: Prof Salim Abdool Karim, Dr Francis Collins and Dr Nicola Mulder participate in the forum of the Leadership Council of CARI



An honorary doctorate awarded for AIDS research

Associate Scientific Director of CAPRISA Professor Quarraisha Abdool Karim received plaudits for her remarkable contribution to HIV/AIDS prevention research and her unrelenting fight for the rights of girls and women affected by HIV to live healthy lives and achieve their full potential.

On 24th May, Prof Abdool Karim received the honorary degree Philosophiae Doctor *honoris causa* from the University of Johannesburg (UJ) for her pioneering contributions in understanding the evolving HIV epidemic. Prof André Swart, Executive Dean of the Faculty of Health Sciences at UJ said that the conferral of the honorary doctoral degree is in recognition of her work that has contributed greatly towards improving the quality of life of women in Africa. "Prof Abdool Karim is the embodiment of a true South African ambassador, in the context of both traditional and modern Africa. Her work has had a profound impact on HIV treatment and prevention policies at a national and global level," he said.



Professor Quarraisha Abdool Karim delivers an address at the graduation

Abdool Karim said that she accepted the honorary doctorate in recognition of women in Africa who are unwavering in their commitment to research and the development of effective medical technologies and who are contributing to knowledge generation either by leading research teams, participating in research and advocating for the betterment of women's



lives. "They continue to inspire me to persist with my scientific endeavours. While some progress has been made, much more remains to be done to ensure a non-sexist and just society," she said.

President of Mauritius visits South Africa



Her Excellency Dr Ameenah Gurib-Fakim, President of the Republic of Mauritius (seated left in the front row), visited Prof Salim and Quarraisha Abdool Karim (seated on the right) on 1st May. At the dinner on the occasion of her visit are: Second row (L-R): Nithia Madurai CEO Global Laboratories, Prof Jerry Coovadia (MatCH) and Dr Zubie Hamed, Ms Bongwiwe Ntuli (CEO: Grindrod); Tom Kariuki (Interim Executive Director AAS), Delivette Castor, Katherine Reardon, Back Row (L-R): Prof Salim Abdool Karim, Director CAPRISA and finally, Fine Dining Chef, Markus Banziger

Member of WHO IHR Roster of Experts

CAPRISA's head of Ethics and Law, Professor Jerome Singh, has been invited to serve as a member of the WHO's International Health Regulations Roster of Experts, as an expert in Health Law, Ethics and Human Rights for a period of four years. As a member Prof Singh will participate in special Emergency or Review Committees to which he is appointed and provide technical information and advice on matters within his areas of expertise.



Commenting on his appointment, Prof Singh said, "It is a great honour to have been appointed by the WHO's Director-General to serve on this high-level Roster, and for my appointment to have been supported by the South African government. Experts drawn from the Roster determine whether a disease outbreak should be declared a Public Health Emergency of International Concern (PHEIC). This declaration designates a public health crisis of potentially global reach under the International Health Regulations, which is a legally binding instrument on all countries. This, in turn, triggers strict mandatory reporting and containment strategies on the part of national authorities. To date, a PHEIC has been declared 4 times: H1N1 (Swine Flu) in 2009, Polio in 2014; Ebola in 2014, and Zika in 2016."

Professor Singh is currently the PI of the Bill and Melinda Gates Foundation-funded Ethical, Legal, Social, and Cultural Issues (ELSCI) Program on Synthetic Biology. He is also Adjunct Professor in the Dalla Lana School of Public Health at the University of Toronto in Canada and serves on several oversight bodies, including the International Ethics Review Board of Médecins Sans Frontières (MSF) and as an ad hoc Consultant to several UN entities, including the WHO, UNAIDS, UNICEF, TDR, and UNICRI.



Scientific papers published in 2017

29 Klatt NR, Cheu R, Birse K, Zevin AS, Perner M, Noël-Romas L, **Grobler A**, Westmacott G, Xie IY; Butler J; **Mansoor L, McKinnon L, Passmore JAS, Abdool Karim Q, Abdool Karim SS**, Burgener AD. Vaginal bacteria modify HIV tenofovir microbicide efficacy in African women. *Science* 2017; 356: 938-945

30 Maheu-Giroux M, **Tanser F**, Boily MC, Pillay D, Joseph SA, Bärnighausen T. Determinants of time from HIV infection to linkage-to-care in rural KwaZulu-Natal, South Africa. *AIDS* 2017; 31(7):1017-1024.

31 Chirenje ZM, Gundacker HM, Richardson B, Rabe L, Gaffoor Z, **Nair G**, Mirembe BG, Piper JM, Hillier S, Marrazzo J. Risk Factors for Incidence of Sexually Transmitted Infections among Women in a Human Immunodeficiency Virus Chemoprevention Trial: VOICE (MTN-003). *Sexually Transmitted Diseases* 2017; 44(3):135-140.

32 Hirsch-Moverman Y, **Daftary A**, Yuengling KA, Saito S, Ntoane M, Frederix K, Maama LB, Howard AA. Using mHealth for HIV/TB Treatment Support in Lesotho: Enhancing Patient-Provider Communication in the START Study. *Journal of Acquired Immune Deficiency Syndromes* 2017; 74 (Suppl 1):S37-S43.

33 Cremin I, **McKinnon L**, Kimani J, Cherutich P, Gakii G, Muriuki F, Kripke K, Hecht R, Kiragu M, Smith J, Hinsley W, Gelmon L, Hallett TB. PrEP for key populations in combination HIV prevention in Nairobi: a mathematical modelling study. *Lancet HIV* 2017; 4(5):e214-e222

34 Haber N, **Tanser F**, Bor J, Naidu K, Mutevedzi T, Herbst K, Porter K, Pillay D, Barnighausen T. From HIV infection to therapeutic response: a population-based longitudinal HIV cascade-of-care study in KwaZulu-Natal, South Africa. *Lancet HIV* 2017; 4(5):e223-e230.

35 Alam SM, Aussedat B, Vohra Y, Meyerhoff RR, Cale EM, Walkowicz WE, Radakovich NA, Anasti K, Armand L, Parks R, Sutherland L, Searce R, Joyce MG, Pancera M, Druz A, Georgiev IS, Von Holle T, Eaton A, Fox C, Reed SG, Louder M, Bailer RT, **Morris L, Abdool Karim SS**, Cohen M, Liao H-X, Montefiori DC, Park PK, Fernández-Tejada A, Wiehe K, Santra S, Kepler TB, Saunders KO, Sodroski J, Kwong PD, Mascola JR, Bonsignori M, Moody MA, Danishefsky S, and Haynes BF. Mimicry of an HIV broadly neutralizing antibody epitope with a synthetic glycopeptide. *Science Translational Medicine* 2017; 9(381): eaai7521.

*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^
0	386	1	217	1	77

for month, ^ since committee initiation

**12TH INTERNATIONAL WORKSHOP ON
HIV TRANSMISSION
PRINCIPLES OF INTERVENTION**
PARIS, FRANCE • 21-22 JULY 2017

Don't miss the opportunity to attend the 12th International Workshop of HIV Transmission, which is scheduled to take place on July 21 and 22, 2017 in Paris, France, prior to IAS 2017. Should you wish to attend, please contact Cheryl Baxter cheryl.baxter@caprisa.org

science & technology
NRF National Research Foundation
CAPRISA hosts a DST-NRF Centre of Excellence in HIV Prevention
UNAIDS
CAPRISA is the UNAIDS Collaborating Centre for HIV Research and Policy
MRC
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
STELLENBOSCH UNIVERSITY