CAPRISA
CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

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## In this Issue...

*In our cover story we summarise findings from the CAPRISA 004 trial that indicate that consistently high tenofovir concentrations during sexual exposure may be necessary to achieve high levels of protection against HIV.*

*On page 2 we provide highlights from the MRC SHIP TB Biomarker meeting and report on a new initiative, "Tea talks" with the Director.*

*The Harvard Transmed course, the visit of scientists and medical students from Harvard's Ragon Institute and the visit of French Ambassador, Elisabeth Barbier, is featured on page 3.*

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# Genital tenofovir concentrations correlate with protection against HIV infection

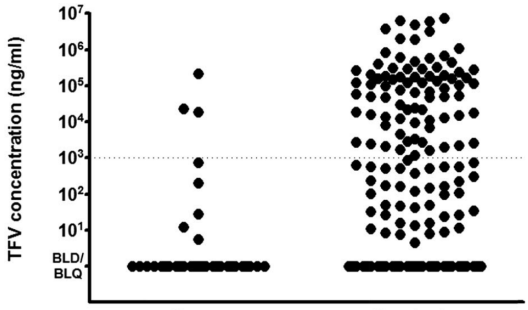
**Data from the CAPRISA 004 trial provides further insights into a potential correlate of protection against HIV infection.**

This case control study, which was published this week in the Journal of AIDS, showed that a tenofovir concentration of ≥100 ng/mL in cervicovaginal fluid (CVF) was associated with 65% (95% CI: 6% to 87%) protection against HIV, whereas a ≥1000 ng/mL concentration correlated with 76% (95% CI: 8% to 92%) protection against HIV infection.

The CAPRISA 004 trial showed that coitally dosed tenofovir 1% gel reduced HIV acquisition by 39% overall and 54% when used consistently. The objective of this analysis was to ascertain its pharmacokinetic–pharmacodynamic relationship to protect against HIV acquisition.

Genital and systemic tenofovir concentrations in 34 women who acquired HIV (cases) were compared with 302 randomly selected women who remained HIV uninfected (controls) during the CAPRISA 004 trial. In total, 336 CVF, 55 plasma, and 23 paired cervical and vaginal tissue samples were assayed by validated methods for tenofovir and tenofovir diphosphate (tenofovir-DP) detection.

Tenofovir was detected in the genital tract in 8 (23.5%) cases and 119 (39.4%) controls (P = 0.076). Among those with detectable genital tract tenofovir, the median CVF concentrations were 97% lower in cases compared with controls, 476 versus 13,821 ng/mL (P = 0.107). A total of 14.7% (5/34) of cases and 32.8% (99/302) of controls were found to have tenofovir CVF concentrations above 100 ng/mL [odds ratio (OR): 0.35, P = 0.037] (Figure). At a higher threshold, 8.8% (3/34) of cases and 26.2% (79/302) of controls were found to have tenofovir CVF concentrations above 1000 ng/mL (OR: 0.27, P = 0.036). Plasma tenofovir concentrations were ,1 ng/mL in all women and were detected only in controls (16.7%) and not in cases (0%), (P = 0.031). Returned used tenofovir gel applicators and CVF concentrations were correlated (Spearman r = 0.22, P = 0.001).




| | Cases | Controls |
|---|---|---|
| N | 34 | 302 |
| % detected (n) | 23.5% (8) | 39.4% (119) |
| | p=0.076 | |
| Median (IQR) TFV (ng/ml) among detectable | 476 (20-20674) | 13821 (300-171920) |
| | p=0.107 | |

*Figure: Cervicovaginal tenofovir concentrations for HIV cases and controls*

Based on this analysis, the attainment of this concentration during sexual exposure consistently may be necessary to achieve high levels of protection against HIV.

**For further reading see:**
Kashuba et al. http://journals.lww.com/jaids/Abstract/2015/07010/Genial_Tenofovir_ Concentrations_Correlate _With.2.aspx

# Hosting the MRC SHIP TB biomarker meeting

*Participants at the TB biomarker meeting included: Front (L-R) : Dr Andre Loxton (SUN-IRG), Rizwana Mia (MRC), Dr Christina Thobakgale (HPP/CAPRISA), Dr Kogie Naidoo (CAPRISA), Dr Novel Chegou (SUN-IRG), Dr Aishe Sivno (CAPRISA), Dr Nesri Padayatchi (CAPRISA) . Back (L-R): Dr Roxana Rustomjee (MRC), Dr Mark Hatherill, SATVI, Dr Gerhard Walzl (SUN-IRG), Ms Leya Hassanally (SATVI), Dr Tom Scriba (SATVI), Dr Lyle Mckinnon (CAPRISA), Dr Daniel Zak (CIDR formerly Seattle Biomed), Dr Adam Penn-Nicholson (SATVI), and Dr Navisha Dookie (CAPRISA).*

Drs Kogie Naidoo, Head of HIV and TB Treatment, and Nesri Padayatchi, Deputy Director of CAPRISA, hosted the 2nd Annual Investigators Meeting of the MRC Strategic Health Innovation Partnerships (SHIP) TB Biomarker consortium with researchers from the University of Cape Town's South African Tuberculosis Vaccine Initiative (SATVI), Stellenbosch University's Immunology Research Group (SUN-IRG), Seattle's Centre for Infectious Disease Research (CIDR) and CAPRISA.

This multi-institutional team has been awarded three years of funding for a systems immunology project that aims to identify and validate correlates of risk of TB disease, treatment success or recurrent TB disease, and to improve understanding on the biology of TB pathogenesis from latent to active TB disease. The project is leveraging new opportunities for biomarker discovery and validation from a number of completed and currently active clinical studies in South Africa. Valuable specimens from HIV-uninfected or HIV-infected persons at risk of TB disease, those who have been diagnosed with TB and are on TB treatment or who are at risk of recurrent TB have been or are being analysed in various sub-studies to address the project objectives.

The group reviewed early project results, deliberated about the proposed next steps and approaches and much discussion revolved around how best to account for degree of immunocompromise in case/control matching in HIV-infected populations. A number of very exciting scientific questions are being addressed that enhance our knowledge of TB immunopathogenesis and inform development of new tests for TB diagnosis, predicting incident TB, monitoring TB treatment and predicting recurrent TB.

# In conversation with the Director

Launched in May this year the CAPRISA Tea Talks initiative has created an opportunity for employees to engage on a personal level or in groups with the Director ,Professor Salim Abdool Karim. Conversations range from seeking advice regarding careers, future scientific studies or advice for their children's career. Employees have welcomed the initiative which is held at all the CAPRISA research sites. "It is not a forum for confidential discussions as staff can meet with the Director at his offices for these discussions," explained Ms Marietjie Geldenhuys Manager of Human Resources at CAPRISA. She said that the initiative is extremely successful and it is "unique to have the Director create opportunities to interact in an informal setting and encourage meaningful conversations".

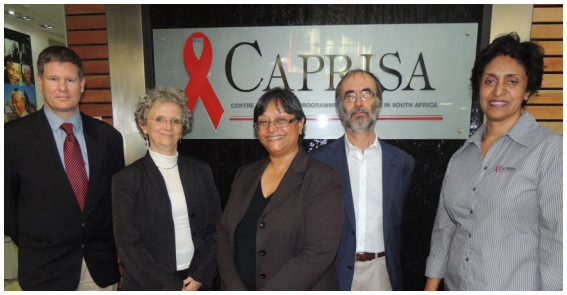
*Staff at the Vulindlela Clinical Research site who participated in the Tea Talks with Prof Salim Abdool Karim*

# Scientists from Ragon Institute visit CAPRISA

*Back (L-R): Travis Hughes, Marc Wadsworth, Alex Shalek, Lyle McKinnon, Jo-Ann Passmore, Aleth Gaillard. Middle (L-R): Andile Mtshali, Carly Ziegler, Jay Prakadan, Derseree Archary, Alex Genshaft. Front (L-R): Kellie Kolb, Refilwe Molatlhegi and Sam Kazer*

Dr Alex Shalek, from the Ragon Institute of MGH, MIT and Harvard and his laboratory team of first year graduate students, was recently hosted by Dr Desh Archary Research Associate and senior scientists at CAPRISA. Dr Shalek's research uses an interdisciplinary approach that incorporates chemical biology, nanoscale technologies and microfluidics and transcriptomics to extensively profile and precisely control cells and their interactions within the context of complex systems. This integrative research is directed towards the development and application of new technologies that will facilitate the understanding of how cells collectively perform systems-level functions in healthy and diseased states.

# French Ambassador visit




During her visit to CAPRISA, Ambassador of France to South Africa, Elisabeth Barbier, expressed a keen interest to forge closer links with the Instit Pasteur and CAPRISA. Participating in the visit were (L-R): Dr Carl Montague Chief Operations Officer CAPRISA, Ambassador Elisabeth Barbier, Professor Quarraisha Abdool Karim Associate Scientific Director CAPRISA, Dr Philippe Tabard, Regional Consellor for Health Cooperation French Embassy and Dr Nesri Padayatchi Deputy Director CAPRISA.

# CAPRISA participates in Harvard's Transmed course

Dr Kogie Naidoo hosted medical students from the Ragon Institute at Harvard and participated in the Transmed course organised by Harvard's Ragon Institute. As part of scientific capacity building in Africa, three students from South Africa, one from CAPRISA and two from the HPP, and one from Zimbabwe received support from the Ragon Institute to attend the course.

Dr Fillipos Porichis Director of International Programs, Ragon Institute of MGH, MIT and Harvard who led the delegation explained that the main goal of the course 'was to educate students on how to identify unmet medical needs and how to employ translational solutions'. He said that the visit to the CAPRISA research clinic provided students 'with a unique opportunity to identify the unmet medical needs of HIV and/or TB infections and through the different talks, the students were able to see firsthand the design, execution and analysis of clinical trials addressing some of the medical needs that were identified'.

The visit and participation at the CAPRISA ECRS was significant as it contributed to the development of the curriculum said Dr Kogie Naidoo. "This course is a great example of collaborative efforts in finding innovative solutions to unmet medical needs that contribute daily to unnecessary suffering and death. I was struck by the interest and motivation in the group in accessing first world technologies to find novel interventions for the scourge of HIV and TB."

*Dr Kogie Naidoo lectures to medical students from the Ragon Institute at Harvard at the CAPRISA eThekwini Research clinic*

# Scientific papers published in 2015

| | |
|---|---|
| 33* | **Naidoo K, Grobler AC,** Deghaye N, Reddy T, **Gengiah S,** Gray A, **Abdool Karim SS.** Cost-effectiveness of initiating antiretroviral therapy at different points in TB treatment in HIV-TB co-infected ambulatory patients in South Africa. *JAIDS 2015; DOI: 10.1097/QAI.0000000000000673* |
| 34 | Kashuba ADM, **Gengiah T, Werner L,** Yang K-H, White N, **Karim Q, Abdool Karim SS.** Genital tenofovir concentrations correlate with protection against HIV infection in the CAPRISA 004 trial: Importance of adherence for microbicide effectiveness. *JAIDS 2015, 69(3): 264–269.* |
| 35 | Izulla P, **McKinnon LR,** Munyao J, Ireri N, Nagelkerke N, Gakii G, Gelmon L, Nangami M, Kaul R, Kimani J. Repeat Use of Post-exposure Prophylaxis for HIV Among Nairobi-Based Female Sex Workers Following Sexual Exposure. *AIDS Behav 2015: DOI 10.1007/s10461-015-1091-1.* |
| 36 | Cohen KA, Abeel T, McGuire AM, Desjardins CA, Munsamy V, Shea TP, Walker BJ, Bantubani N, Almeida DV, Alvarado L, Chapman S, Mvelas NR, Duffy EY, Fitzgerald MG, Govender P, Gujja S, Hamilton S, Howarth C, Larimer JD, Maharaj K, Pearson MD, Priest ME, Zeng Q, **Padayatchi N,** Grosset J, Young SK, Wortman J, **Mlisana KP, O'Donnell MR,** Birren BW, Bishai WR, Pym AS, Earl, A.M. Evolution of extensively drug-resistant tuberculosis over four decades revealed by whole genome sequencing of Mycobacterium tuberculosis from KwaZulu-Natal, South Africa. *International Journal of Mycobacteriology 2015; 4(Supplement 1): 24–25.* |
| 37 | Mendelsohn JB, Calzavara L, **Daftary A**, Mitra S, Pidutti J, Allman D, Bourne A, Loutfy M, Myers T. A scoping review and thematic analysis of social and behavioural research among HIV-serodiscordant couples in high-income settings. *BMC Public Health 2015; DOI: 10.1186/s12889-015-1488-9.* |
| 38 | Parida SK, Madansein R, Singh N, **Padayatchi N**, Master I, Naidu K, Zumla A, Maeurer M. Cellular therapy in Tuberculosis. *International Journal of Infectious Diseases* 2015; 32: 32-38. |
| 39 | Knight LC, Van Rooyen H, **Humphries H**, Barnabas RV, Celum C. Empowering patients to link to care and treatment: qualitative findings about the role of a home-based HIV counselling, testing and linkage intervention in South Africa. *AIDS Care 2015; DOI: 10.1080/09540121.2015.1035633.* |
| 40 | Wibmer CK, **Moore PL, Morris L**. HIV broadly neutralizing antibody targets. *Current Opinion in HIV & AIDS* 2015; 10(3): 135-142. |
| 41 | **Williamson C,** Swanstrom R. HIV-1 replication capacity: Setting the pace of disease. *Proceedings of the National Academy of Sciences of the United States of America* 2015: 112(12): 3591-3592. |
| 42 | Schopper D, Dawson A, Upshur R, Ahmad A, Jesani A, Ravinetto R, Segelid MJ, Sheel S, **Singh J**. Innovations in research ethics governance in humanitarian settings. *BMC Medical Ethics* 2015; DOI: 10.1186/s12910-015-0002-3. |

**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 | 327 | 2 | 211 | 0 | 61 |

*# for month, ^ since committee initiation*

# Conference & Workshop Reminders

| Conference | Dates | Deadlines: Abstracts | Deadlines: Registration | Website |
|---|---|---|---|---|
| **8th IAS Conference on HIV Pathogenesis, Treatment and Prevention (IAS 2015)** - Vancouver, British Columbia, Canada | 19-22 July 2015 | 27 Jan 2015 | 25 Feb 015 | http://www.ias2015.org/ |
| **46th Union World Conference on Lung Health** - Cape Town, South Africa | 2-6 Dec 2015 | 24 Apr 2015 | 20 Aug 2015 | http://capetown.worldlunghealth.org/ |
| **World STI & HIV Congress** - Brisbane, Australia | 13-16 Sept 2015 | 13 April 2015 | 31 August 2015 | http://www.worldsti2015.com/ehome/index.php?eventid=91027& |
| **International Conference on AIDS & STI in Africa (ICASA)** - Hammamet, Tunisia | 8-13 Nov 2015 | May 2015 | 29 Oct 2015 | http://icasa2015tunisia.org/ |



Registration number: 2002/024027/08