

## In this issue...

Our feature article this month focuses on a study aimed at identifying the innate immune correlates of TB recurrence in HIV positive ART-treated individuals with a history of previous successful TB treatment.

On page 2 we feature the first South African 'Advancing HIV Cure Research Workshop' which took place in Stellenbosch on the 6-7<sup>th</sup> October 2016 and congratulate our young colleagues who were invited to participate in the Nickelodeon Genius TV show.

We report on the DataFax training workshop hosted by CAPRISA during October and congratulate the editors (including Professor Quarraisha Abdool Karim) of the "Oxford Textbook of Global Public Health (6th edition)" on being acknowledged by the British Medical Association at the 2016 BMA Medical Book Awards evening on page 3.



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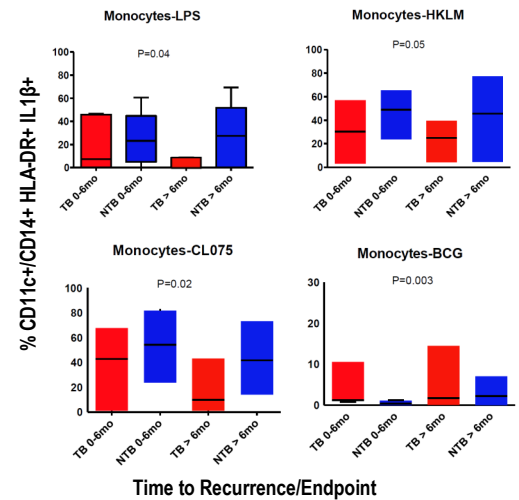
# Correlation between IL-1 $\beta$ production and TB recurrence

Results from the HIV and tuberculosis (TB) treatment Programme were recently published in JAIDS. The study, which was led by CAPRISA's Research Associate, Dr Christina Thobakgale, showed that the production of IL-1 $\beta$  by innate immune cells following Toll like receptors (TLR) and Bacillus Calmette-Guérin (BCG) stimulations correlated with differential TB recurrence outcomes in patients with a history of previous successful TB treatment.

The incidence rate of TB recurrence in the overall cohort was 4.07 % (95%CI. 3.24-5.06). In this pilot study, 12 patients with a recurrent episode of TB (cases) were matched, based on age, sex, time on ART, and pre-ART CD4 count, with 12 participants who did not develop recurrent TB in 60 months of follow-up (controls). All patients were known to be HIV infected on ART with a previously-defined history of successfully treated pulmonary TB. Cryopreserved peripheral blood mononuclear cells from time points prior to TB recurrence were stimulated with ligands for TLR including TLR-2, TLR-4, and TLR-7/8. Multi-colour flow cytometry and intracellular cytokine staining was used to detect IL-1 $\beta$ , TNF- $\alpha$ , IL-12 and IP10 responses from monocytes and myeloid dendritic cells (mDCs).

An elevated production of IL-1 $\beta$  from monocytes following TLR-2, TLR-4 and TLR-7/8 stimulation was associated with reduced odds of TB recurrence. In contrast, production of IL-1 $\beta$  from both monocytes and mDCs following BCG stimulation was associated with increased odds of TB recurrence, where the risk of recurrence increased by 30% in monocytes and 42% in mDCs respectively.

These findings show that expression of IL-1 $\beta$  from monocytes was the best predictor of TB recurrence and may indicate a



Representative predictive (0-6month & 6month time points) cytokine (IL-1 $\beta$ ) response profiles in monocytes of individuals with TB recurrence (cases) during successful treatment of TB prior to TB recurrence (TB) versus controls (NTB) over time

functional defect in monocytes. In addition, the study showed that APC responses to BCG stimulation were associated with increased risk of TB recurrence and may mark an important difference in innate host response to TB in cases compared to controls.

TB remains a major cause of global morbidity and mortality, especially in the context of HIV co-infection, since immunity is not completely restored following ART. The identification of immune correlates of risk for TB disease could help in the design of host-directed therapies and clinical management. These results highlight differences in host response to TB.

## For further reading see:

Thobakgale C, Naidoo K, McKinnon LR, Werner L, Samsunder N, Abdool Karim SS, et al. 1-beta (IL-1 $\beta$ ) production by innate cells following TLR stimulation correlates with TB recurrence in ART-treated HIV infected patients. JAIDS 2016 Sep 19. DOI: 10.1097/QAI.0000000000001181



## Advancing HIV Cure Research Workshop



*Back row (L-R): Walter Nevondo, Simone Richardson, Thumbi Ngund'u, Colin Anthony, Rebecca Van Dorsten, Penny Moore, Lynn Morris, Britt Hanson, Deelan Doolabh, Sherazaan Ismail, Yumna Moosa, Debbie Stewart, Mike Sathegke, Veron Ramsuran, Wendy Burgers. Front Row: Glaudina Loots, Melissa-Rose Abrahams, Carolyn Williamson, Ron Swanstrom, Nigel Garrett, Michelle Mulder*

**T**he first South African 'Advancing HIV Cure Research Workshop' took place in Stellenbosch on the 6-7<sup>th</sup> October 2016. The workshop was chaired by Professor Carolyn Williamson and Dr Melissa-Rose Abrahams from the Division of Medical Virology at the University of Cape Town (UCT) and Dr Nigel Garrett from CAPRISA, and was supported by the South African Medical Research Council and the Department of Science and Technology (DST). The workshop assembled key stakeholders and representatives involved in HIV cure research and related fields from institutions across the country and abroad with the goal to discuss the latest findings in the field - to identify gaps, and to set priorities for clinical translational cure research in South Africa.

Presentations included advancements in potential interventions to deplete or silence the latent viral reservoir such as the use of broadly neutralizing antibody therapies and gene silenc-

ing through targeted stem cell therapy, CRISPR/Cas9 or gene methylation, and the use of targeted radionuclide therapy (conventionally a cancer treatment) for visualizing and targeting anatomical reservoir sites using radioisotopes, and its potential use for assessing efficacy of reservoir clearance in cure trials. The UCT team presented new technologies for characterizing the size and sequence composition of the latent reservoir, including next-generation sequencing and digital droplet PCR, in women from the CAPRISA 002 Acute Infection cohort. This was followed by a presentation on the Females Rising through Education, Support, and Health (FRESH) acute infection cohort, and the proposal of future clinical studies using therapeutic vaccinations. Glaudina Loots (DST), a board member of the IAS Towards an HIV Cure Initiative, stressed the need for collaboration and inter-disciplinary research in particular, between early career HIV and cancer researchers.

### CAPRISA trio participate in Nickelodeon Genius

**T**hree CAPRISA colleagues judged the Nickelodeon's Genius Kwa-Zulu Natal's regional competition on 13<sup>th</sup> October. Dr Sinaye Ngcapu, Mr Ross Cromarty and Ms Chéli Kambaran judged the three rounds of the competition aimed at young school learners passionate about maths and science. There were 15 teams of

3 students from a range of schools in Kwa-Zulu-Natal. The two winning teams progressed into the national Nickelodeon Genius competition and walked away with R50000 cash reward for the team and a selection of text books from Cambridge University donated to their respective schools.

"This competition provided a fantastic platform for young students to showcase their mathematic and scientific skills and enthusiasm for these fields. The teams that progressed to the later rounds showed strong team ethic and quick thinking, said Ross Cromarty. The competition will be screened on the Nickelodeon TV channel.



## Dialogue on DataFax Clinical Trial Data Management Systems

Data management staff had the opportunity to interact with leading experts on DataFax Clinical Trial Management systems over four days in October and gain insights into the latest developments in the field. The co-founders of DF/Net Research, Inc., Lisa Ondrejcek and Darryl Pahl delivered training workshops and a presentation on the DataFax Clinical Trial management system used by CAPRISA and global organisations. CAPRISA hosted the DataFax User Group (DFUG) 2016 training workshop on 17<sup>th</sup>- 18<sup>th</sup> October at which DF/Net staff from the US and Canada conducted intensive training sessions over two days showcasing new features of DataFax software. On 19<sup>th</sup> October CAPRISA's Director Professor Salim Abdool Karim opened the 22<sup>nd</sup> Annual DataFax User Group Conference held at the Maha-



From L-R: Dr Kogie Naidoo, Ms Nonhlanhla Yende, Ms Lisa Ondrejcek, Dr Leila Mansoor, Mr Darryl Pahl and Prof Quarraisha Abdool Karim who welcomed delegates to the presentation on 21<sup>st</sup> October

rani hotel and on 21<sup>st</sup> October CAPRISA PIs and UKZN researchers had an opportunity to attend a presentation of the system which included several international case studies.

## Opinion: Who do you love? Finding treasure at the last day of R4P

The Global Advocacy for HIV Prevention (AVAC) compiled five "Treasures" taken from R4P on the final day of conference.

The CAPRISA 256 antibody is listed as treasure 3 described aptly by Prof Penny Moore as "a South African national treas-

ure". The article can be accessed at: <http://www.avac.org>

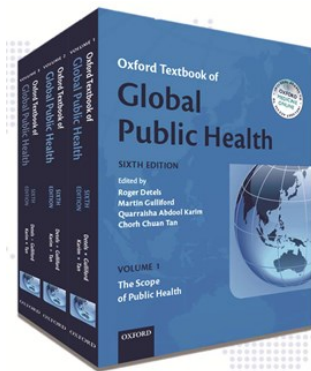
## Public Health textbook lauded by the British Medical Association

Professor Quarraisha Abdool Karim associate Scientific Director at CAPRISA is one of four Editors of the "Oxford Textbook of Global Public Health (6th edition)" acknowledged by the British Medical Association (BMA) at the recent 2016 BMA Medical Book Awards evening. The book received a certificate as a "Highly Commended" textbook in the Public Health category. The textbook, published by Oxford University Press, comprises 1,888 pages bound in 3 volumes was published in February 2015. The four editors of this 6<sup>th</sup> edition textbook are Roger Detels, Martin Gulliford, Quarraisha Abdool Karim and Chorh Chuan Tan.

The BMA Medical Book Awards are held annually to recognise outstanding contributions to

medical literature. Books are awarded prizes and commended in 20 categories. The BMA judging panel assess books for their applicability to audience, production quality and originality. Professor Pali Hungin, BMA President, was guest of honour at the 2016 awards evening held at BMA House in September 2016.

Prof Abdool Karim donated a complete set of the book to the UKZN Research office. The books can be accessed at the EG Malherbe Library at the UKZN Howard College campus.







## Scientific papers published in 2016

- 52\* Selhorst P, **Masson L**, Ismail SD, **Samsunder N**, **Garrett N**, **Mansoor LE**, **Abdool Karim Q**, **Abdool Karim SS**, **Passmore Jo-AS**, Williamson C. Cervicovaginal inflammation facilitates acquisition of less infectious HIV variants. *Clinical Infectious Diseases* 2016 Sept. doi: 10.1093/cid/ciw663 [Epub ahead of print]
- 53 Byrareddy SN, Arthos J, Cicala C, Villinger F, Ortiz KT, Little D, Sidell N, Kane MA, Yu J, Jones JW, Santangelo PJ, Zurla C, **McKinnon LR**, Arnold KB, Woody CE, Walter L, Roos C, Noll A, Van Ryk D, Jelacic K, Cimbri R, Gumber S, Reid MD, Adsay V, Amancha PK, Mayne AE, Parslow TG, Fauci AS, Ansari AA. Sustained virologic control in SIV+ macaques after antiretroviral and  $\alpha 4\beta 7$  antibody therapy. *Science* 2016; 354(6309): 197-202.
- 54 **Daftary A**, **Padayatchi N**. Provider perspectives on drug-resistant tuberculosis and human immunodeficiency virus care in South Africa: a qualitative case study. *International Journal of Tuberculosis and Lung Disease* 2016; 20(11): 1483-88.
- 55 Shaffer JS, **Moore PL**, Kardar M, and Chakraborty AK. Optimal immunization cocktails can promote induction of broadly neutralizing Abs against highly mutable pathogens. *Proceedings of the National Academy of Sciences* 2016 September; [e-pub ahead]. doi: 10.1073/pnas.1614940113
- 56 **Thobakgale C**, **Naidoo K**, **McKinnon LR**, **Werner L**, **Samsunder N**, **Abdool Karim SS**, Ndung'u T, Altfeld M, **Naidoo K**. Interleukin 1-beta (IL-1 $\beta$ ) production by innate cells following TLR stimulation correlates with TB recurrence in ART-treated HIV infected patients. *JAIDS* 2016 Sep 19. DOI: 10.1097/QAI.0000000000001181 [Epub ahead of print].
- 57 Jain P, Weinrick BC, Kalivoda EJ, Yang H, Munsamy V, Vilcheze C, Weisbrod TR, Larsen MH, **O'Donnell MR**, Pym A, Jacobs WR. Dual-Reporter Mycobacteriophages ( $\phi^2$ DRMs) Reveal Preexisting *Mycobacterium tuberculosis* Persistent Cells in Human Sputum. *MBio* 2016; 7(5):e01023-16. doi:10.1128/mBio.01023-16

\*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>
0	367	3	210	0	73

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

## iSpotU and Achievement awards

The CAPRISA iSpotU Innovation Award recognises and rewards employees who contributed in an exceptional manner in respect of innovation, which demonstrate that "There Is a Better Way" of doing a task, process or system. The Achievement Award rewards and recognises employees or teams for accomplishments and achievements which received recognition from an external credible individual and/or organisation. Recipients of the award during October included:

**CAPRISA Innovation Award**  
Zanele Mkhize from the CAPRISA eThekweni Clinic received her award for showing exemplary leadership in engaging with study counsellors and participants alike to achieve a higher quality counselling process, including in depth discussions and consistent and accu-

rate counselling records. Pam Job (HR) and Denolan Naidoo (IT) received their award for initiating a project to implement online completion of certain HR forms with the intention to make greater use of technology and move away from manual completion of forms, resulting in reducing the time taken from req-

uisition to approval. Panji Pillay from the DDMRI Laboratory received her award for taking the initiative to develop the SoftCup Processing work flows and also improved the SOPs and developed troubleshooting scenarios that are user friendly for all lab staff to follow.



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



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

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