



CAPRISA

CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

Newsletter

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Integrin $\alpha_4\beta_7$ expression on peripheral blood CD4⁺ T cells predicts HIV acquisition and disease progression

In this Issue

Our feature story this month focuses on the study led by CAPRISA researchers, which was published in *Science Translational Medicine*, that demonstrate for the first time the importance of $\alpha_4\beta_7$ integrin at the time of HIV exposure in humans.

On page 2, we report on a study led by two CAPRISA Research Associates, published in *Science*, on the discovery of new genetic markers, that increases the progression to AIDS-related illnesses. Also on page 2 we congratulate Prof Lynn Morris on her appointment as acting head of the NICD.

We highlight the inauguration of the Chief Justice of South Africa as UKZN's new Chancellor and the WHO meeting hosted by CAPRISA on page 3.

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In the January 24th issue of *Science Translational Medicine*, CAPRISA researchers Dr. Aida Sivo and Dr. Lyle McKinnon led a study that demonstrated that pre-HIV infection levels of $\alpha_4\beta_7$ expression on peripheral blood CD4⁺ T cells was associated with an increase in rates of HIV acquisition in women from the CAPRISA 004 trial of tenofovir 1% gel.

This association was independent of T cell memory and activation phenotypes and concomitant genital inflammation. Infection by HIV strains containing V2 Env motifs with a preference for $\alpha_4\beta_7$ binding was increased in women with higher $\alpha_4\beta_7$ expression.

In addition to its relationship to acquisition, pre-HIV levels of $\alpha_4\beta_7$ expression on peripheral CD4⁺ T cells predicted a more rapid rate of HIV disease progression, correlating with set point viral load and a >2 fold increased rate of CD4 decline. Increased frequencies of $\alpha_4\beta_7$ CD4⁺ T cells pre-HIV infection were also associated with higher expression of LPS binding protein (LBP), a microbi-

al translocation marker, for up to 3 years post-infection.

These findings suggest that there is a link between gut homing potential, gut mucosal damage, and more rapid disease progression. At the earliest stages of HIV infection CD4⁺ T cells expressing $\alpha_4\beta_7$ were rapidly depleted, particularly from the GI tract, and were not restored by early antiretroviral therapy (ART). This study is the first to link the pre-HIV $\alpha_4\beta_7$ expression with HIV clinical outcomes in humans, supporting the previous observations made in animal models.

Given the availability of a clinically approved anti- $\alpha_4\beta_7$ monoclonal antibody (called Vedolizumab) for treatment of inflammatory bowel disease (IBD), these results suggest that targeting of $\alpha_4\beta_7$ can be readily evaluated as a clinical intervention for HIV prevention and/or treatment.

For further reading

A Sivo et al. Integrin $\alpha_4\beta_7$ expression on peripheral blood CD4⁺ T cells predicts HIV acquisition and disease progression outcomes. *Science Translational Medicine* 2018; 10(425): eaam6354 DOI: 10.1126/scitranslmed.aam6354.





Scientists discover new genetic markers that can lead to the faster progression of AIDS-related illness in people living with HIV

CAPRISA Research associates Dr Veron Ramsuran and Vivek Naranbhai led the international research team that discovered a specific-type Human Leucocyte Antigen (HLA) gene complex that helps HIV infected cells to escape the body's first line of defense, an immune cell known as natural killer (NK) cells. The study published in the prestigious journal *Science* sheds new light on how specific human genes can lead to the faster progression of AIDS-related illness in people living with HIV who are not on treatment.

with HIV in South Africa have this specific HLA type.



Dr Veron Ramsuran



Dr Vivek Naranbhai

The research team comprised scientists from the KwaZulu-Natal Research Innovation and Sequencing Platform (KRISP), the Centre for the AIDS Programme of Research in South Africa (CAPRISA) and the Human Pathogenesis Programme (HPP) – all based at the University of KwaZulu-Natal (UKZN) - together with researchers from the US National Institutes of Health, the Ragon Institute as well as researchers from Harvard, Oxford, Vanderbilt, Northwestern and Stanford Universities, Icahn School of Medicine at Mount Sinai, École Polytechnique Fédérale de Lausanne, MIT, Walter Reed Army Institute of Research, University of California, San Francisco Department of Health, and Microsoft.

Most of the laboratory research for this study, led by Ramsuran, a scientist at KRISP and Naranbhai, a scientist at Harvard University was conducted in three laboratories; at the Frederick National Laboratory for Cancer Research (FNLCR) of the National Institute of Health (NIH), the Ragon Institute of the Massachusetts General Hospital (MGH), Massachusetts Institute of Technology (MIT) and Harvard University in the USA and at the KRISP laboratories at Nelson R Mandela School of Medicine. The study is a culmination of five years of research, which included post-doctoral studies by Ramsuran with Dr Mary Carrington at FNLCR.

In addition to studying HLA in almost 10,000 people, the team conducted laboratory experiments with cells in test-tubes, including those assessing HIV infectivity.

These experiments confirmed that the specific HLA-A expression had a direct effect on NK cells and that blocking the interaction between HLA and NK cells with certain drugs reverses this effect.

“These results open a new door to understanding why some people become sick with AIDS so soon after acquiring HIV infection”, says Professor Salim S. Abdool Karim, Director of CAPRISA and Pro Vice-Chancellor (Research) at the UKZN. “The study’s findings highlight the importance of regular HIV testing, so that people with HIV can get to know their status and start antiretroviral treatment early, well before they become ill with AIDS.”

The study of 9,763 people with HIV in South Africa and the USA showed that individuals with the specific HLA type progress from asymptomatic HIV infection to becoming ill with AIDS faster. In these individuals, their viral load (number of viruses in their blood) was higher and their CD4 immune cells were destroyed more rapidly, before they started antiretroviral treatment. It is estimated that about 2 million of the approximately 7 million people living

The publication can be accessed at: <http://science.sciencemag.org/content/359/6371/86>

Prof Lynn Morris appointed as acting head of NICD

Professor Lynn Morris has been appointed as the interim Executive Director of the National Institute for Communicable Diseases (NICD). A leading NRF A-rated scientist, Morris is a CAPRISA Research Associate and holds a joint appointment as Research Professor in the Faculty of Health Sciences at Wits University and is the Head of the HIV Virology Laboratory within the Centre for HIV & STIs based at the National Institute for Communicable Diseases, a division of the National Health Laboratory Services (NHLS).

She has been at the NICD for the past 25 years where she established a “world-class laboratory dedicated to developing a vaccine against HIV,” said Dr Kamy Chetty, acting CEO of the NHLS. For the past 3 years,

Morris is listed on the Highly Cited Researcher list which honours scientists globally.

“I feel very honoured to have been asked to lead the NICD during this transition period. The NICD is a superb and highly functioning organization responsible for pathogen research and surveillance of communicable diseases affecting public health. I am committed to maintaining this high level of scientific excellence in order to best serve the people of South Africa”.





Chief Justice inaugurated as UKZN Chancellor



Professors Salim and Quarraisha Abdool Karim congratulate South Africa’s Chief Justice, Mogoeng Mogoeng following his installation as the new Chancellor of the University of KwaZulu-Natal.

The academic ceremony attended by the legal elite in South Africa was held at the UKZN campus on 13th December 2017. Mogoeng congratulated the University on its Transformation

Charter and encouraged those present to read South Africa’s Constitution.

“Our Constitutional project is about building a united and democratic South Africa founded on human rights, non-racialism, non-sexism, accountability and responsiveness,” he said. He paid tribute to senior UKZN law academics, Professor McQuoid Mason and Managay Reddi for their outstanding contributions to the Law School.

CAPRISA hosts WHO meeting on the public health approach to quality testing



Participants at the WHO meeting held at CAPRISA in Durban.

Dr Rachel Baggaley of the HIV Department, World Health Organisation (WHO) and Professor Quarraisha Abdool Karim, CAPRISA’s associate Scientific Director co-hosted a two-day meeting on the Public Health approach to quality HIV testing. This consultative meeting held on 12 – 13th December 2017 at the CAPRISA headquarters in Durban brought together experts from the health ministries,

academics, researchers, virologists, laboratory specialists, as well as programme experts in treatment, pre-exposure prophylaxis and HIV testing services from across the globe. Key objectives included a review of the latest evidence on HIV testing in the context of ARVs treatment provisions to inform the WHO HIV testing guidelines in 2019



Scientific papers published in 2017

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*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	390	2	229	0	84

for month, ^ since committee initiation

