RELATIONSHIP BETWEEN BACTERIAL VAGINOSIS AND VAGINAL PROTEOMIC PROFILES OF SOUTH AFRICAN ADOLESCENT GIRLS AND ADULT WOMEN AT HIGH RISK OF HIV ACQUISITION

Authors:
Abrahams AG[1,2], Radzey N[1,2], Ganief T[1], Mehou-Loko C[2], Harryparsad R[2], Meyer B[2], Manhanzva MT[2], Humphries H[3,4], Gumbi P[5,6], Busakwe F[7], Samsunder N[5], Abdool Karim Q[5,8], Bell L[9,10,11], Du Plessis M[1,10], Ahmed N[7], Fortune F[7], Bekker LG[2,7], Passmore JS[2,5,12], Jaspan HB[2,13], Blackburn J[1,10*], Masson L[2,5,14,15*]

[1]Division of Chemical and Systems Biology, Department of Integrative Biomedical Sciences, University of Cape Town, South Africa, [2]Institute of Infectious Disease and Molecular Medicine, Department of Pathology, University of Cape Town, Cape Town, South Africa, [3]Centre for Community Based Research, Human Sciences Research Council, Pietermaritzburg, South Africa, [4]Department of Psychology, School of Applied Human Sciences, University of KwaZulu-Natal, Pietermaritzburg, South Africa, [5]Centre for the AIDS Programme of Research in South Africa, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, South Africa, [6]School of Life Sciences, University of KwaZulu-Natal, Pietermaritzburg, South Africa, [7]Desmond Tutu HIV Centre, South Africa, [8]Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA, [9]Distributed Platform in Omics (DIPLOMICS), Cape Town, South Africa, [10]D-CYPHR, Department of Integrative Biomedical Sciences, University of Cape Town, South Africa, [11]Centre for Proteomic and Genomic Research (CPGR), Cape Town, South Africa, [12]National Health Laboratory Service, South Africa, [13]Seattle Children's Research Institute, University of Washington, Department of Biochemistry, USA, [14]Life Sciences Discipline, Burnet Institute, Melbourne, VIC, Australia, [15]Central Clinical School, Monash University, Carlton, VIC, Australia
*Co-senior authors

Background:
Bacterial vaginosis (BV), characterised by a non-optimal vaginal microbiome, has been associated with increased inflammation in the female genital tract (FGT), both of which predicts later HIV acquisition. The aim of this study was to evaluate the impact of BV on the vaginal proteomic profiles of South African adolescent girls and adult women, to understand its role on the high rates of HIV infection seen in young women in this setting.

Methods:
Vaginal swabs were collected from 168 adolescents (14-19 years old) and 85 adults (25-35 years old) in Cape Town and KwaZulu-Natal, South Africa, enrolled in the Mucosal Injury from Sexual Contact study. Vaginal smears were Gram-stained for BV diagnosis by Nugent scoring. Vaginal swabs were analysed by liquid chromatography tandem mass spectrometry (LC-MS/MS). The R/Bioconductor limma package and DAVID Bioinformatics were used for differential protein expression and functional analyses.

Results:
Of the 2114 host proteins detected, 583 were significantly differentially expressed in women who had BV (n=108) compared to BV negative women (n=91, FDR adj.

p<0.05), with 214 overexpressed and 369 underexpressed proteins. Overexpressed proteins mapped to several inflammatory functions, including innate (adj. p=0.026) and adaptive (adj. $p=8x10^{-11}$) immunity and NIK/NF-kappaB signalling (adj. $p=3.3x10^{-6}$). Underexpressed proteins mapped to cytoskeleton (adj. $p=3.1x10^{-4}$) and cell junction (adj. $p=4.7x10^{-4}$) cellular components, and the actin-binding molecular function (adj. $p=9.9x10^{-4}$). Protein profiles did not differ between adolescents (n=69) and adults (n=39) who had BV, with both groups having similar inflammatory and epithelial barrier signatures compared to BV negative women.

Conclusion:
BV prevalence is high among South African young women and is associated with protein signatures of inflammation and epithelial barrier disruption in the FGT. Strategies such as point-of-care screening for FGT inflammation and BV, as well as improved treatment, are needed to reduce associated HIV susceptibility in this population.

Disclosure of Interest Statement:
This study was funded by the National Institute of Health.