



Category: Miscellaneous

Full Scholarship Award Winner

Inhibition of cornifins and up-regulation of protease inhibitors in cervicovaginal lavage imparts resistance to heterosexual HIV transmission

Sushama Rokade¹, Hrishikesh Pandit¹, Poonam Gautam², Manoj K. Gupta³,
Bharti Dhaka³, Ravi Sirdeshmukh³, Uday Khopkar⁴, Padmaja Mavani⁴,
Preeti Mehta⁴ and Taruna Madan^{1*}

¹Innate Immunity, National Institute for Research in Reproductive Health (ICMR), Mumbai, INDIA

²Central Proteomics Facility, National Institute of Pathology (ICMR), New Delhi, INDIA

³Institute of Bioinformatics, Bangalore, INDIA

⁴KEM Hospital and Seth G S Medical College, Mumbai, INDIA

*Corresponding author: taruna_m@hotmail.com

Abstract

HIV-exposed seronegative individuals (HESNs) are persons who remain seronegative despite repeated exposure to HIV, suggesting an *in vivo* resistance mechanism to HIV. Elucidation of endogenous factors responsible for this phenomenon may aid in the development of new classes of microbicides and therapeutics. The genital mucosal secretions of both men and women are known to contain a spectrum of antimicrobials and immune mediators that may contribute to resistance against HIV-1. Existence of HIV serodiscordant couples is a testimony to mucosal factors in the genital tract that prevent sexual transmission of the virus. We attempted to map such mucosal factors in female genital secretions of the serodiscordant couples in comparison with HIV infected and healthy participants using quantitative proteomics. The cervico vaginal lavage (CVL) samples were collected from three groups of study participants (HIV infected, n=30; Un-infected Controls, n=10; Serodiscordant, n=24). Abundant proteins, albumin and globulins were removed from the pooled samples using multiple affinity removal spin cartridge (Agilent) to enhance the sensitivity of iTRAQ proteomics analysis. Initial analysis identified a total of 135 proteins and associated 497 peptide matches. Serodiscordant females showed significantly down regulated levels of Cornifin A, B and C, Neutrophil gelatinase, myeloperoxidase and eosinophil peroxidase. Cornifins are cross-linked envelope protein of keratinocytes and are upregulated during inflammation. Downregulation of oxidative stress inducing enzymes and cornifins suggests immune-quiescence in serodiscordant females. CVL of these women showed significantly upregulated levels of Mucin 5B, S100A7, Alpha-2-macroglobulin, Cystatin A (protease inhibitor), Lacto-transferrin, SLPI (anti-leukoproteinase inhibitor) and SERPIN G1 (protease inhibitor). Significantly elevated levels of Cystatin B and Elafin in the CVL of serodiscordant females were confirmed by ELISA. These results suggest that HIV resistance against the sexual transmission of HIV is the result of immune-quiescence contributed by two complementary mechanisms: downregulation of immune activators and upregulation of their inhibitors.

Citation: Rokade, S., Pandit, H., Gautam, P., Gupta, M.K., Dhaka, B., Sirdeshmukh, R., Khopkar, U., Mavani, P., Mehta, P. and Madan, T. Inhibition of cornifins and up-regulation of protease inhibitors in cervicovaginal lavage imparts resistance to heterosexual HIV transmission [Abstract]. In: Abstracts of the NGBT conference; Oct 02-04, 2017; Bhubaneswar, Odisha, India: Can J biotech, Volume 1, Special Issue (Supplement), Page 274. <https://doi.org/10.24870/cjb.2017-a258>