P15.02 HUMAN HAEMOGLOBIN DERIVED PEPTIDE PREVENTS HIV-1 INFECTION AND PROTECTS CELLS FROM HIV-1 INDUCED INFLAMMATION

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10.1136/sextrans-2015-052270.543

Introduction HIV/AIDS pandemic is one of the leading cause of death worldwide and a matter of serious concern to the scientific world. Most of new HIV infections spread through heterosexual mode and leads to HIV-1 induced immune system activation. This renders infected individuals more susceptible to HIV-1 pathogenesis and opportunistic infections. Hence, preventing HIV infections at early stages and neutralising its effect on host cells is essential in combating AIDS epidemic.
Methods Human haemoglobin derived peptide, named HbAHP-25, was designed *in silico* against CD4 binding domain of gp120 by molecular docking methods. HbAHP-25 was characterised for its inhibitory activity on various strains of HIV-1 in PBMCs in the presence and absence of seminal plasma and vaginal fluid. Specificity of action of HbAHP-25 was determined by HIV-1 pseudotyped assays. Immunofluorescence, Multiplex Cytokine assay and Dual Chamber assays were performed to evaluate safety of HbAHP-25 and its role in modulating immune response to HIV.
Results HbAHP-25 has significant anti-HIV activity against various strains of HIV-1 in a dose dependent fashion. HbAHP-25 binds to a site proximal to CD4 binding site on gp120, has partial epitope similarity with VRC01 on gp120 and inhibits gp120-CD4 interaction. Flow cytometery analysis showed that HbAHP-25 specifically binds to gp120 expressing HL2/3 cells. HbAHP-25 inhibits HIV-1 and doesn't inhibit HIV-1 pseudotyped virus from entering cells. Further, HbAHP-25 didn't affect cell viability even at higher concentrations; nor did it have any effect on epithelial monolayer integrity. HbAHP-25 doesn't elicit any pro-inflammatory response and protects cells from HIV induced inflammation. Results indicate that HbAHP-25 prevents HIV-1 from activating NF-kB pathway, thus limiting its ability to induce cytokines.
Conclusion HbAHP-25 protects cells from HIV-1 entry and HIV-1 induced inflammation by binding proximal to CD4 binding site of gp120. HbAHP-25 maintained good safety profile and can be a potential molecule for pre-clinical development of prophylactic/anti-HIV drug.
Disclosure of interest statement Nothing to declare.

P15.03 DEVELOPMENT OF A NEW CEM REPORTER T-CELLS (GXR-CELLS) VIRAL INHIBITION ASSAY (VIA) FOR ELUCIDATING THE ROLE OF CLASS-I-HLA ALLELES ON THE INHIBITORY CAPACITY OF HIV-1-SPECIFIC CD8$^+$T-CELLS

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Introduction Standard immunogenicity assays, such as ELISpot and intracellular cytokine staining, fail to correlate HIV-1-specific CD8$^+$T-cells responses with HIV-1 replication *in-vivo*. Therefore, it is essential to develop assays that can determine antiviral potential of vaccine elicited CD8$^+$T-cells. The current ELISA-VIA measures HIV-1-p24 production overtime in autologous CD4$^+$T-cells. However, it is not designed to identify the class-I-HLA-allele involved in mediating the response. We developed a new FACS based VIA that can investigate CD8$^+$T-cells antiviral potential in the context of restricting class-I-HLA alleles. The assay measures the ability of CD8$^+$T-cells to kill HIV-1 infected GXR-cells over-expressing class-I-HLA allele of interest. The assay utilises a GXR-cell engineered to express GFP upon HIV-1 infection.
Methods CD8$^+$T-cells were co-cultured with HIV-1 infected GXR-cells for 3 days. Reduction in the infected GXR-cells expressing GFP measured by FACS was used to evaluate the CD8$^+$T-cells killing activity. The assay was validated using a panel of 9 HIV-infected samples and were concurrently assayed with the ELISA-VIA. The tested results on each assay were categorised into four groups namely: true-inhibition (TI ≥50%), doubtful-inhibition (DI ≥20% to ≤49.99%), false-inhibition (FI ≥10% to ≤19.99%) and non-inhibition (NI≤ 9.99%). These results were used in a 2 by 2 table to compute sensitivity (TI/TI+DI) and specificity (FI/FI+NI).
Results True inhibition was observed in 44% of samples analysed using GXR-VIA compared to 33% with ELISA-VIA. 11% with GXR-VIA had doubtful result compared to 33% with ELISA-VIA. 22% with GXR-VIA were categorised as false inhibition compared to 33% with ELISA-VIA. Interestingly, no sample showed non-inhibition with GXR-VIA whereas 22% showed no inhibition by ELISA-VIA. Collectively, GXR-VIA is very specific (100%) but less sensitive (57%) at detecting virus inhibition activity.
Conclusion The specificity of GXR-VIA and its marginal sensitivity indicates that the assay is capable of identifying CD8$^+$T-cells-mediated inhibition of HIV-1 replication. Overall, the GXR-VIA provides a platform to assess the influence of different restricting class-I-HLA alleles on HIV-1-specific CD8$^+$T-cells antiviral function.

P15.04 GENITAL TRACT CELLULAR ACTIVATION AND INFLAMMATION ASSOCIATED WITH HIGHLY PREVALENT SEXUALLY TRANSMITTED INFECTIONS AND BACTERIAL VAGINOSIS IN ADOLESCENT WOMEN AT RISK FOR HIV INFECTION

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10.1136/sextrans-2015-052270.545

Introduction The biological mechanisms underlying HIV risk in younger women is unclear. HIV is primarily transmitted across the genital mucosa and preferentially infects CD4$^+$ T-cells. We investigated the influence of asymptomatic sexually transmitted infections (STIs) and bacterial vaginosis (BV) on CD4$^+$ T-cell