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3rd International AIDS Society Conference on **HIV** Pathogenesis and Treatment

Rio de Janeiro - July 24 - 27, 2005

IMMUNOLOGICAL CORRELATES OF APPARENT PROTECTION IN EXPOSED YET HIV-1 SERONEGATIVE UGANDANS

IAS Conf HIV Pathog Treat 2005 Jul 24-27;3rd: Abstract No. MoOa0402

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INTRODUCTION: It is becoming increasingly evident that sero-conversion may not be the inevitable outcome of repeated exposure to HIV. Apparent protection to HIV-1 infection may be due to a multiplicity of factors including genetic polymorphisms and innate and acquired cellular and humoral HIV-1 specific immune responses.

METHODS: HIV-1 sero-discordant monogamous couples in Uganda with a median duration of union of 10.5 years and a history of unprotected sex were enrolled. The following were evaluated in the seropositive (SP) and exposed seronegative (ESN) partners:

- HIV-1-specific antibodies in mucosal and systemic compartments.
- Expression of CD91 on CD14+ monocytes.
- HLA class I tissue types.
- Recognition by CD8+T cells of HIV-1 peptides quantitating IFN- γ secretion by ELISpot.
- Proliferation coupled to intracellular production of IFN- γ , IL-2, IL-4 and IL-2, perforin in HIV-1 specific CD4+ and CD8+ T cells respectively.

RESULTS:

- In ESN cross-clade HIV-1 gp160-specific IgA and/or IgG antibodies were present in genital secretions but absent in plasma.
- Monocytes of ESN had significantly higher CD91 surface expression than those of SP or unexposed low-risk persons.

- The Cw*06 allele and the B*58-Cw*06 haplotype were over-expressed in ESN compared to SP.
- Quantitation of HIV-1-specific IFN- γ responses suggested preferential HIV-1 peptide recognition between SP and ESN, with ESN recognising peptides previously associated with slow progression of HIV-1 infection, and SP recognising peptides from relatively conserved regions.
- Flow cytometric analysis in showed maintenance of cytokine function in ESN and SPs, but proliferative dysfunction in both CD4+ and CD8+ subsets in SP.

CONCLUSIONS: HIV-1 specific humoral and cellular immune responses in ESN may play an important role in protecting vulnerable persons from HIV-1 infection, and such responses should be induced by prophylactic vaccines.

050724

Basic | MoOa0402 | Frances Gotch

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