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Citation

Schaefer, M, J Carlson, D Claiborne, J Prince, W Kilembe, J Tang, P Farmer, et al. 2012. Dynamics and frequency of Gag transmitted polymorphisms in Zambia. *Retrovirology* 9(Suppl 2): P156.

Published Version

doi:10.1186/1742-4690-9-S2-P156

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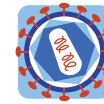
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POSTER PRESENTATION

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Dynamics and frequency of Gag transmitted polymorphisms in Zambia

M Schaefer^{1*}, J Carlson², D Claiborne¹, J Prince¹, W Kilembe³, J Tang⁴, P Farmer¹, R Shapiro⁵, T Ndung'u⁶, J Frater⁷, P Goulder⁷, R Kaslow⁸, S Allen¹, P Goepfert⁸, D Heckerman², E Hunter¹

From AIDS Vaccine 2012
Boston, MA, USA. 9-12 September 2012

Background

HIV immune escape is not random and follows a predictable mutational path in response to the HLA alleles carried by an individual.

Methods

Using 143 epidemiologically linked transmission pairs from a Zambian cohort we assessed: (1) the frequency of Gag polymorphisms circulating in the population, (2) if the polymorphisms could be associated with the infected individual's HLA alleles, (3) the frequency at which polymorphisms are transmitted, and (4) the relevance of the transmitted polymorphisms (TP) to the newly infected individual's HLA-I alleles.

Results

We observed a median of 35 (range 23-66) polymorphisms per chronically infected individual in Gag and 42% of these polymorphisms could be associated with the individual's HLA (16% statistically linked, 26% epitope analysis). When transmission of these polymorphisms was assessed, we observed that the majority of these polymorphisms (84%) are transmitted to the epidemiologically linked partner and, of these TP, an equivalent fraction (43%; 11% statistically linked, 32% epitope analysis) were relevant to the newly infected individual's HLA-I alleles. In 81 transmission pairs observed during the first two years of infection, we observed a very low overall reversion rate (4%/year) of the TP. Reversion was not uniform and when p17, p24, p2, p7, p1, and p6 are examined individually, TP in p17 and p2 exhibited the highest frequency (2.5x) of reversion events based on amino acid length. Four CTL-targeted positions were identified where a majority of TP reverted

to consensus over the two years of follow up, consistent with a reduction in fitness following transmission.

Conclusion

These data indicate: (1) HLA-I associated polymorphisms are stable and circulating frequently in the Zambian population, (2) individuals are acquiring HIV-I variants with a high frequency of polymorphisms relevant to their HLA-I alleles, and (3) reversion is slow and not evenly distributed across Gag.

Author details

¹Emory University, Atlanta, GA, USA. ²Microsoft Research, Redmond, USA. ³Zambia Emory HIV Research Project, Lusaka, Zambia. ⁴University of Alabama-Birmingham, Birmingham, USA. ⁵Harvard School of Public Health, Boston, USA. ⁶University of KwaZulu-Natal, Durban, South Africa. ⁷Oxford University, UK. ⁸University of Alabama-Birmingham, USA.

Published: 13 September 2012

doi:10.1186/1742-4690-9-S2-P156

Cite this article as: Schaefer et al.: Dynamics and frequency of Gag transmitted polymorphisms in Zambia. *Retrovirology* 2012 **9**(Suppl 2):P156.

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¹Emory University, Atlanta, GA, USA
Full list of author information is available at the end of the article