



# Immunodominance and Viral Ditness in Gag May Contribute to Differential Viral Control in HLA-B\*7 Supertype Individuals Acutely Infected with HIV-1C

## Citation

Gounder, K., M. Leshwedi, J. Wright, M. van der Stok, F. Chonco, N. Padayachee, B. Ndimande et al. 2012. Immunodominance and viral ditness in Gag may contribute to differential viral control in HLA-B\*7 supertype individuals acutely infected with HIV-1C. Poster Presentation. *Retrovirology* 9(Suppl 2): P160.

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POSTER PRESENTATION

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# Immunodominance and viral fitness in Gag may contribute to differential viral control in HLA-B\*7 supertype individuals acutely infected with HIV-1C

K Gounder<sup>1\*</sup>, M Leshwedi<sup>1</sup>, J Wright<sup>1</sup>, M van der Stok<sup>1</sup>, F Chonco<sup>1</sup>, N Padayachee<sup>1</sup>, B Ndimande<sup>1</sup>, M Mokgoro<sup>1</sup>, M Jaggernath<sup>1</sup>, P Goulder<sup>2</sup>, BD Walker<sup>3</sup>

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

## Background

HLA-B\*7 supertype alleles are common among people of African descent and are associated with viral control. In particular, HLA-B\*81 has been previously associated with reduced viral fitness. We analyzed the immunodominance of CD8+ T cell responses targeted by the B\*7 supertype alleles, viral evolution and fitness dynamics over 1yr in acutely infected patients.

## Methods

Six HLA-B\*7 supertype participants [HLA-B\*81 (n=2), HLA-B\*4201 (n=3) and HLA-B\*4202 (n=1)] identified with acute HIV-1 infection (antibody negative, vRNA positive) in KwaZulu-Natal, South Africa were studied. CD8+ T cell responses were measured by the IFN- $\gamma$  ELISpot assay. Replication capacities of viruses encoding Gag-protease were measured. Full-length HIV-1 Gag clonal sequencing of plasma was performed at ~14 days post infection and 1yr later.

## Results

The average viral set point of the 4 HLA-B\*42 individuals was higher than the 2 HLA-B\*81, 4.89 vs 4.16 respectively. Approximately 28 days after viral infection, CD8+ T cell responses were directed to an average of 2/5 (range 2-4) HLA-B\*42 Gag-specific epitopes, median magnitude of 490 (range 170–2,480 SFC/million PBMCs). None of these 4 individuals had selected for escape mutations in the immunodominant TL9 epitope at 1yr post-infection. Interestingly, CD8+ T cell responses were only against the TL9 epitope for the 2 HLA-B\*81 patients with a median

magnitude of 950 (range 300–1780 SFC/million PBMCs). One patient had a single wild type epitope in the transmitted virus, compared to 4/5 wild type epitopes in the second patient. However, CD8+ T cell responses were only elicited at the TL9 epitope with a low magnitude against T186S in the 1 patient with a much lower viral fitness.

## Conclusion

Strong, rather than broad immunodominant responses in HLA-B\*7 individuals is desirable in viral control. Furthermore, this study emphasizes the advantage of early dominant CD8+ T cell immune responses and an attenuated virus in conferring clinical benefit among HLA-B\*7 supertype individuals.

## Author details

<sup>1</sup>University of KwaZulu-Natal, Durban, South Africa. <sup>2</sup>University of Oxford, Oxford, UK. <sup>3</sup>Ragon Institute of Massachusetts General Hospital, MIT and Harvard, Boston, MA, USA.

Published: 13 September 2012

doi:10.1186/1742-4690-9-S2-P160

Cite this article as: Gounder *et al.*: Immunodominance and viral fitness in Gag may contribute to differential viral control in HLA-B\*7 supertype individuals acutely infected with HIV-1C. *Retrovirology* 2012 **9**(Suppl 2):P160.

<sup>1</sup>University of KwaZulu-Natal, Durban, South Africa  
Full list of author information is available at the end of the article