Abstract

Background:
One major challenge in the creation of an HIV-1 vaccine is the extreme genetic diversity of the virus. It is thought that a more cross-reactive T-cell response would be beneficial in circumventing this issue. Despite this, little is known about the characteristics of these responses in nature, and many aspects of the variant-epitope CD8+ T-cell response remain poorly defined. Here, we characterize CD8 + T-cells specific to an immunodominant HIV-1 epitope, IW9, and 2 of its variants, to better understand the level of cross-reactivity between them.

Methods:
Using samples from the Pumwani commercial sexworker cohort in Nairobi, Kenya, individuals positive for either HLA-B*4201 or HLA-B*0702 were screened for binding to tetramers specific for the IW9 epitope and 2 variants. Analysis of epitope specific cytokine expression and proliferation was performed to determine the level of functional cross-reactivity of the variant-specific T-cell pools. Additionally, heteroduplex mobility assays (HDMAs) were performed to determine differences in TCR usage among the T-cells responding to each variant.

Results:
Tetramer co-staining experiments indicate that there is some cross-reactivity among these variants, shown by strong double-positive populations in flow cytometry. However, in some cases, separate cell populations are being recognized by each variant. Proliferation assays show that T-cells stimulated by one variant can be recognized by tetramers specific to another variant. HDMAs revealed that there are differences in TCR usage among variant-specific CD8 + T-cells both at the family and clonotype level. This may suggest a combination of public and private clonotype usage, which could explain the differences in cross-reactivity and functionality.

Conclusion:
In order to create a T-cell vaccine that can target and produce protective immune responses, it will be necessary to fully understand the nature of cross-reactive responses. This study has shown evidence that cross reactivity exists within the IW9 epitope, and that there are several factors that may affect this.