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Poster presentation

P16-15. Epitope mapping of HIV-specific CD8+ T-cells responses by polyfunctional and proliferation responses reveal distinct specificity defined by function

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Background

Recent failures of HIV vaccine candidates aimed at inducing protective cellular immunity highlight our need to better characterize responses that are effective in slowing progression to AIDS. Previous work demonstrates that HIV infected subjects who experience slower disease progression maintain better HIV-specific CD8+ T-cell proliferation and polyfunctionality compared with normal progressing controls. While the specificity and breadth of HIV-specific CD8+ T-cell responses have been largely defined by measuring IFNγ, these responses may not be protective, and it is unclear whether the same epitopes would predominate if other functional parameters were considered. A better understanding of the fine specificity of HIV-specific CD8+ T-cells is critical to the design of vaccines intended to elicit protective cell-mediated immunity.

Methods

Peripheral blood mononuclear cells from HIV infected individuals were stimulated overnight and for 6 days with an HIV-1 p24 peptide library. HIV-specific CD8+ T-cell responses were evaluated by polyfunctional flow cytometry measuring a variety of cytokines, cytotoxic potential, and proliferation. Eptiope-specific responses were identified and confirmed at a later time point.

Results

Across the entire data set there were 73 epitope-specific responses, corresponding to 54 unique epitopes. Of the 54 epitopes identified, 42 have not been fully characterized and 12 are considered Best Defined Epitopes (Los Alamos). 74% of epitope-specific responses were IFNγ negative and proliferation was observed in 18% of responses. Polyfunctional responses, characterized by co-expression of 2 or more immunological parameters, were detected in 47% of responses.

Conclusion

These data reveal that the specificity and function of HIV-specific CD8+ T-cell responses differs depending on immunologic readout, and that the measurement of multiple parameters extends the breadth of HIV-specific responses greater than would be detected using IFNγ alone. It is possible to identify epitopes that elicit polyfunctional and proliferation responses, which will result in more effective immune targets for the development of future vaccine candidates.