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Meeting Abstract

Functional signatures of protective antiviral T-cell immunity: A guide to the development of vaccine strategies

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Abstract

At present, we only have indirect knowledge of the protective role of antigen-specific T cells in human virus infections and it has been difficult to demonstrate a correlation between quantitative and qualitative measures of T-cell immunity and the activity of virus-associated diseases. However, recent advances in the characterization of T-cell functions and in the development of standardized T-cell assays have identified distinct functional signatures of T-cell responses that correlate with levels of virus replication and disease activity. The analyses of antigen-specific CD4+ and CD8+ T-cell responses in the virus infections that differ in terms of antigen persistence or exposure and antigen load, indicate that the functional heterogeneity of both CD4+ and CD8+ T-cells is substantially influenced by the antigen load. As the antigen load is a direct reflection of the levels of virus replication, the functional changes observed can be correlated with the activity of virus-associated disease. Therefore, we believe that distinct functional signatures of CD4+ and CD8+ T-cell responses correspond to different levels of virus replication/disease activity. Furthermore, certain functions such as the proliferation capacity and the secretion of IL-2 appear to be associated with effective T-cell response. On the basis of the analysis of IL-2 and IFN-γ, three functionally distinct (single IL-2, dual IL-2/IFN-γ and single IFN-γ) populations of Ag-specific CD4 T-cells and two of CD8 T-cells (dual IL-2/IFN-γ and single IFN-γ) have been identified. The presence of IL-2 secreting CD4 and CD8 T-cells was consistently associated with the Ag-specific proliferation capacity. With regard to CD8 T-cells, both dual IL-2/IFN-γ and single IFN-γ cell populations were found to be cytotoxic as measured by perforin expression and/or degranulation activity. Recently, the term polyfunctional has been used to define T-cell responses that, in addition to typical effector functions such as secretion of IFN-γ and cytotoxic activity, comprise distinct T-cell populations also able to secrete IL-2 and IFN-γ and retaining proliferation capacity. The term monofunctional has been used to define T-cell responses with only effector function. Of interest, several studies have demonstrated that polyfunctional and not monofunctional T-cell responses were associated with protective antiviral immunity.