

Oral presentation

Molecular and functional analysis of $\gamma\delta$ T cell expansions in immunodeficient patients

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Aims

Patients with various forms of immunodeficiencies frequently show expansions of $\gamma\delta$ T cells in their peripheral blood. We attempted to characterize the $\gamma\delta$ T cell subpopulations in these patients and possibly elucidate the cellular mechanisms involved in the $\gamma\delta$ T cell expansions in some of these patients.

Methods and results

Two adult patients with thymoma and $\gamma\delta$ T cell expansions were studied by flow cytometry and T cell receptor γ - and δ -chain spectratyping. One patient suffering from leishmaniasis and thymic carcinoma showed a peculiar polyclonal $\gamma\delta$ T cell proliferation while another patient with a benign thymoma and CMV reactivation had a persistent oligoclonal amplification of $\gamma\delta$ T cells. In one pediatric patient with incomplete RAG-1 deficiency, we found a restricted variability of the expressed V δ 3, versus V δ 1 and V δ 2 chains and a seemingly monoclonal usage of the V γ 4 element. Sequencing revealed that these $\gamma\delta$ T cells showed significant junctional diversity. These data suggested selection of the $\gamma\delta$ T cells by antigens such as CMV infection. Indeed, 4 out of 5 δ T cell clones that could be derived from this patient secreted TNF α in response to CMV infected allogeneic fibroblasts.

Conclusion

Overall, studies of human $\gamma\delta$ T cells under the conditions of a limited immune system imply two non-exclusive explanations for the $\gamma\delta$ T cell predominance in immunodeficiencies: a) a developmental advantage of $\gamma\delta$ T cells, possibly by a less stringent T cell development than for $\alpha\beta$

T cells and b) a proliferative response caused by infectious or autoantigen-driven peripheral stimulations, such as CMV infections.