Diagnostic Pathology

Oral presentation

Molecular and functional analysis of γδ T cell expansions in immunodeficient patients

Paul Fisch*[1], Petros Christopoulos[2], Elisabeth Nikolopoulos[1], Hendrik Veelken[2] and Stephan Wehl[3]

Address: [1]Institut für Pathologie, Universitätsklinikum Freiburg, Germany, [2]Abteilung Hämatologie/Onkologie, Universitätsklinikum Freiburg, Germany and [3]Zentrum für Kinderheilkunde und Jugendmedizin Universitätsklinikum Freiburg, Germany

* Corresponding author

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Aims

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

Methods and results

Two adult patients with thymoma and γδ 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 γδ T cell proliferation while another patient with a benign thymoma and CMV reactivation had a persistent oligoclonal amplification of γδ T cells. In one pediatric patient with incomplete RAG-1 deficiency, we found a restricted variability of the expressed Vδ3, versus Vδ1 and Vδ2 chains and a seemingly monoclonal usage of the Vγ4 element. Sequencing revealed that these γδ T cells showed significant junctional diversity. These data suggested selection of the γδ 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 TNFα in response to CMV infected allogeneic fibroblasts.

Conclusion

Overall, studies of human γδ T cells under the conditions of a limited immune system imply two non-exclusive explanations for the γδ T cell predominance in immunodeficiencies: a) a developmental advantage of γδ T cells, possibly by a less stringent T cell development than for αβ T cells and b) a proliferative response caused by infectious or autoantigen-driven peripheral stimulations, such as CMV infections.