

Hepatosplenic and Subcutaneous Panniculitis-Like γ/δ T Cell Lymphomas Are Derived from Different V δ Subsets of γ/δ T Lymphocytes

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Gamma/delta T cell lymphomas (γ/δ TCL) represent rare, often aggressive types of T cell malignancy that are clinically and pathologically diverse. Most γ/δ TCL occur as a hepatosplenic or subcutaneous type. To date, analysis of the T cell receptor δ (TCR δ) gene repertoire of hepatosplenic γ/δ TCL (γ/δ HSTCL) and subcutaneous panniculitis-like γ/δ TCL (γ/δ SPTCL) has been reported only in a limited number of cases. In this study we analyzed 11 γ/δ HSTCL and 4 γ/δ SPTCL by polymerase chain reaction and immunostaining to determine their usage of the V δ subtypes (V δ 1–6). It is noteworthy that 10 of 11 γ/δ HSTCL expressed the V δ 1 gene. The remaining case also expressed T cell receptor δ (TCR δ) as determined by flow cytometry and TCR δ rearrangement in Southern blot. However, the V δ gene expressed by this lymphoma could not be determined, which suggests usage of an as yet unidentified V δ gene. In striking contrast to the γ/δ HSTCL, all 4 γ/δ SPTCL expressed the V δ 2 gene. Our data demonstrate that γ/δ HSTCL are preferentially derived from the V δ 1 subset of γ/δ T lymphocytes, whereas γ/δ SPTCL are preferentially derived from the V δ 2 subset. The pattern of V δ gene expression in HSTCL and SPTCL corresponds to the respective, predominant γ/δ T cell subsets normally found in the spleen and skin. This finding suggests that γ/δ TCL are derived from normal γ/δ T lymphocytes which reside in the affected tissues. Furthermore, the selective, lymphoma type-specific V δ gene segment usage may provide a molecular tool to distinguish better among various types of γ/δ TCL lymphoma particularly in the clinically advanced, widely disseminated cases. (*J Mol Diag* 2000; 2:11–19)

Similar to normal T lymphocytes, T cell lymphomas (TCL) may express two different types of T cell receptor (TCR), α/β or γ/δ . Four TCR genes (α , β , γ , and δ) are composed in their germline configuration of noncontiguous segments of variable (V), diversity (D), joining (J), and constant (C) regions. During T cell differentiation, somatic VDJ rearrangements occur and thereby generate variability of the TCR.¹ Only complete in-frame TCR gene rearrangements, consisting of V, D, and J regions, may form a functional TCR. Incomplete rearrangements between two D regions (D-D), between V and D region (V-D), and between D and J region (D-J) are nonfunctional. The majority of normal T lymphocytes express the α/β heterodimer; however, approximately 5% of the T cells express the γ/δ heterodimer.² In contrast to α/β T lymphocytes, development of γ/δ T cells is not dependent on expression of major histocompatibility complex (MHC) I or MHC II molecules.^{3–6} Unlike α/β T cells, which develop almost exclusively in thymus, γ/δ T cells can be generated in extrathymic sites such as intestinal epithelium, skin, spleen, and fetal liver.^{7–9} The exact function of γ/δ T lymphocytes has not been fully elucidated, but some studies suggest a role for these cells in early immune responses to infections, autoimmune disorders, and cancer immune surveillance.⁹ γ/δ T cells share some features with CD8+ α/β T lymphocytes and with natural killer (NK) cells. They show MHC-dependent and MHC-independent cytotoxicity, produce lymphokines, and exhibit NK-like lytic activity.

γ/δ TCL represent a rare type of T cell malignancy. They comprise less than 10% of peripheral T cell lymphomas¹⁰ and occur mostly at extranodal sites in hepatosplenic, subcutaneous, or intestinal form. Hepatosplenic

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