

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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Table of Contents Vdelta Epopeacutée Cistercienne T

1. Understanding the eBook Vdelta Epopeacutée Cistercienne T
 - The Rise of Digital Reading Vdelta Epopeacutée Cistercienne T
 - Advantages of eBooks Over Traditional Books
2. Identifying Vdelta Epopeacutée Cistercienne T
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Vdelta Epopeacutée Cistercienne T
 - User-Friendly Interface
4. Exploring eBook Recommendations from Vdelta Epopeacutée Cistercienne T
 - Personalized Recommendations

- Vdelta Epopeacutée Cistercienne T User Reviews and Ratings
- Vdelta Epopeacutée Cistercienne T and Bestseller Lists
- 5. Accessing Vdelta Epopeacutée Cistercienne T Free and Paid eBooks
 - Vdelta Epopeacutée Cistercienne T Public Domain eBooks
 - Vdelta Epopeacutée Cistercienne T eBook Subscription Services
 - Vdelta Epopeacutée Cistercienne T Budget-Friendly Options
- 6. Navigating Vdelta Epopeacutée Cistercienne T eBook Formats
 - ePub, PDF, MOBI, and More
 - Vdelta Epopeacutée Cistercienne T Compatibility with Devices
 - Vdelta Epopeacutée Cistercienne T Enhanced eBook Features
- 7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Vdelta Epopeacutée Cistercienne T
 - Highlighting and Note-Taking Vdelta Epopeacutée Cistercienne T
 - Interactive Elements Vdelta Epopeacutée Cistercienne T
- 8. Staying Engaged with Vdelta Epopeacutée Cistercienne T
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Vdelta Epopeacutée Cistercienne T
- 9. Balancing eBooks and Physical Books Vdelta Epopeacutée Cistercienne T
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Vdelta Epopeacutée Cistercienne T
- 10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
- 11. Cultivating a Reading Routine Vdelta Epopeacutée Cistercienne T
 - Setting Reading Goals Vdelta Epopeacutée Cistercienne T
 - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Vdelta Epopeacutée Cistercienne T
 - Fact-Checking eBook Content of Vdelta Epopeacutée Cistercienne T

- Distinguishing Credible Sources
- 13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
- 14. Embracing eBook Trends
 - Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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