Characterization of CD57+ T-cell subset in Blood, Bone Marrow, and Lymphoid Tissue

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Introduction

T-cells have many subsets playing different immune functions. The CD57+ T-cell subset is particularly interesting to us because of its potential diagnostic and prognostic significance in cancer immunology[1]. According to David's study, this subset constantly demonstrated an increased number of CD57 expression and frequently co-expressed CD4 and CD8 in tissues with nodular lymphocyte predominant Hodgkin lymphoma (NLPHL). This unique flow cytometry pattern could be used to differentiate NLPHL from classic Hodgkin lymphoma (CHL) or reactive lymphoid hyperplasia (RLH)[2]. In terms of prognostic significance, Focosi's study had shown that a reactive microenvironment infiltrated predominantly by CD57+ T cells was associated with a significant increase in adverse clinicobiologic manifestations[3]. Mileshkin's study showed that elevated CD57+ cells predicted a superior progression-free survival in patients with relapsed/refractory myeloma received thalidomide[4]. According to Serrano's study, an elevated frequency of CD4+CD57+ T cells was correlated with a more advanced disease stage in chronic lymphocytic leukemia[5].

Aims and Objectives

To further define the diagnostic and prognostic significance of CD57+ T-cell subset in cancer immunology, we perform this study to examine the frequency and immunophenotypic variation of CD57+ T-cell subsets in three most encountered tissue specimens for diagnostic workup: peripheral bloods (PB), bone marrows (BM), and lymph nodes (LN). The CD57+ T-cell percentages and immunophenotypes were compared among different tissue types with or without neoplastic infiltrate.

Methods

Patients' flow cytometry list mode data were retrieved and re-analyzed on Kazula (a software for flow cytometry). A protocol was designed to identify the frequency of CD2, CD4, CD5, CD7, CD8, CD16, and CD56 expression on CD57+ T cells (Figure 1). The information about the tissue type of samples, age of the patients at diagnosis, and the pathology diagnosis were collected from patients' medical records. The frequency of reactive CD57+ T cells and their expression profile of CD2, CD4, CD5, CD7, CD8, CD16, and CD56 were examined. T-test was used to compare the difference among different specimen types and diagnoses. The demographic of the study subjects were summarized in Table 1. Of 247 specimen studied, 66 specimens had neoplastic infiltrate including myeloid neoplasia (n=16), lymphoid neoplasia (n=44), plasmacytic neoplasia (n=3), and metastatic cancer (n=3).

Results

Figure 1: Flow Cytometry Data Analysis

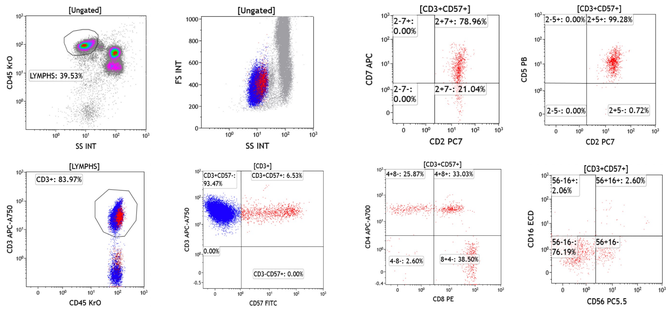

Table 1: Patient demographics

Age	Average (year)	60.5
	Range (year)	1 - 102
Gender	Males (number)	116
	Females (number)	131
Specimen type	LN (number)	56
	PB (number)	78
	BM (number)	113

1. Reactive CD57+ T-cells were significant lower ($p < 0.05$) in LN samples without neoplastic infiltrate when compared with LN samples with neoplasms. However, such difference was not observed in PB or BM.

Table 2: The means and standard deviations of reactive CD57+ T-cells % of total T-cells by specimen type with or without malignancy.

Tissue	With neoplastic	Without neoplastic
LN	17.2 ± 9.5	7.3 ± 7.2
PB	17.6 ± 11.8	17.4 ± 16.0
BM	21.2 ± 13.2	15.3 ± 12.6

2. The expression profiles of CD2, CD5, and CD7 were very similar ($p > 0.05$) between specimens with or without neoplastic infiltrate.

Table 3: CD2, CD5, and CD7 expression patterns (mean % of CD3+CD57+ T-cells).

Tissue	Neoplastic ?	CD2+CD5-	CD2-CD5+	CD2+ CD5+	CD2-CD5-	CD2+ CD7-	CD2-CD7+	CD2+ CD7+	CD2-CD7-
LN	+	3.1	1.7	95.2	0.1	18.5	0.2	79.9	1.4
	-	3.4	2.1	94.4	0.1	21.3	0.6	76.6	1.5
PB	+	9.0	1.4	89.5	0.1	17.4	0.7	81.2	0.6
	-	8.2	0.5	91.2	0.0	19.1	0.1	80.5	0.2
BM	+	8.4	0.5	90.9	0.1	15.0	0.3	84.5	0.2
	-	6.9	0.5	92.5	0.1	16.4	0.3	83.1	0.2

3. The expression profiles of CD4 and CD8 were very similar ($p > 0.05$) between specimens with or without neoplastic infiltrate. However, CD4:CD8 ratio and CD4+CD8+ T-cells were higher ($p < 0.05$) in LN than PB or BM.

Table 4: CD4 and CD8 expression patterns (mean % of CD3+CD57+ T-cells) and ratios of CD4+:CD8-:CD4-CD8+ of CD57+ T cells.

Tissue	Neoplastic?	CD4+CD8-	CD4-CD8+	CD4:CD8	CD4+CD8+	CD4-CD8-
LN	+	45.1	35.4	2.0	12.8	6.6
	-	46.7	33.9	2.8	11.2	8.2
PB	+	21.9	62.9	0.5	6.5	8.6
	-	19.7	66.9	0.5	6.3	7.0
BM	+	16.4	67.5	0.3	7.0	9.1
	-	16.7	64.9	0.3	8.7	9.7

4. The expression profiles of CD16 and CD56 were similar between specimens with or without neoplastic infiltrate and between PB and BM. However, CD57+T-cells had less ($p < 0.05$) CD16+ subset in LN than in PB or BM.

Table 5: CD16 and CD56 expression patterns (mean % of CD3+CD57+ T-cells).

Tissue	Neoplastic?	CD16+CD56-	CD16-CD56+	CD16+CD56+	CD16-CD56-
LN	+	1.4	14.7	1.8	82.1
	-	3.7	16.6	3.4	76.3
PB	+	7.4	18.7	8.9	65.1
	-	11.0	19.2	7.2	62.6
BM	+	5.8	16.4	6.9	70.9
	-	5.6	15.3	8.9	70.2

Conclusions

1. Reactive CD57+ T-cells were highly variable among samples with or without neoplastic infiltrate.
2. CD57+ T-cells showed very similar profiles of CD2, CD4, CD5, CD7, CD8, CD16, and CD56 between the PB and BM specimens. But they had higher CD4:CD8 ratios, more CD4+CD8+ subsets, less CD16+ subsets in the LN samples.
3. CD57+ T-cells in the LN without neoplastic infiltrate were significantly lower than the LN samples with neoplastic infiltrate. However, neoplastic infiltrate did not affect the expression profiles of CD2, CD5, CD7, CD4, CD8, CD16, and CD56 in CD57+ T-cells.
4. This study provided a foundation for future investigation of the role of CD57+ T-cells in cancer immunology.

References

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