American Journal of Medical Sciences and Medicine, 2015, Vol. 3, No. 1, 8-10
Available online at http://pubs.sciepub.com/ajmsm/3/1/3

DOI:10.12691/ajmsm-3-1-3

A Short Comment to Ten Reports: Possible "Keys" of TCR VB Exist in the Peripheral Blood of Patients with Leukemia

Jianwei Zhou[1,*], Yinfeng Jia[1], Li Wang[2], Cui Kong[3]

[1]Clinical Laboratory, Affiliated Hospital of Jining Medical College, Jining, PR China
[2]Department of Pharmacology, the First People's Hospital of Jining City, Jining, PR China
[3]Nursing Department, Affiliated Hospital of Jining Medical College, Jining, PR China
*Corresponding author: immunolife@126.com

Received March 14, 2015; Revised March 16, 2015; Accepted March 17, 2015

Abstract In this paper, we reanalyzed the data of ten reports related to variable region of beta chain (Vβ) of T cell receptors (TCR) of patients with leukemia, and attempted to further find their respective characters from a different point of view. In the results, we found that there were different predominant usages of TCR Vβ gene families. According the predominant usage frequencies (PUFs) of TCR Vβ, the histograms were drawn and analyzed. The columns of different heights represented the PUFs of TCR Vβ gene families. The combination of the columns looked like a key, and every column was as same as the kit of the key. The kits were different in different leukemia. In our opinions, the key probably represented the total characterization of TCR Vβ for the patients with leukemia, and these results maybe pose a new idea for analyzing the skewness of TCR for the researchers of the relative study field.

Keywords: *Leukemia, key, peripheral blood, short comment, T cell receptor*

Cite This Article: Jianwei Zhou, Yinfeng Jia, Li Wang, and Cui Kong, "A Short Comment to Ten Reports: Possible "Keys" of TCR VB Exist in the Peripheral Blood of Patients with Leukemia." *American Journal of Medical Sciences and Medicine*, vol. 3, no. 1 (2015): 8-10. doi: 10.12691/ajmsm-3-1-3.

1. Introduction

The analysis of T cell receptor (TCR), especially the variable region of TCR beta chain (Vβ), is one of the sensitive methods to identify the clonal expansion T cells which response to tumor associated antigens. Clonally expanded T cells can recognize tumor cells in patients with leukemia. Leukemia-associated clonal expansion of TCR Vβ gene families were detected in the past fifteen years, including the predominant usages of TCR Vβ gene families. In this paper, we extracted and reanalyzed the data related to the predominant usages of TCR Vβ, and hoped the finding could present new ideas for the researchers in future studies.

2. Review of the Literature

In the present study, ten reports [1-10] were selected as the references for reanalysis, and the including criteria was that the predominant usage TCR Vβ genes were clearly stated in the reports; or it would be excluded. The diseases contained acute promyelocytic leukemia (APL), T cell-acute lymphoblastic leukemia (T-ALL), B cell-acute lymphoblastic leukemia (B-ALL), acute monoblastic leukemia (AML), acute myelogenous leukemia (AMOL) and chronic myeloid leukemia (CML).

In the analysis progress, we found that there were Vβ subfamilies in some reports, for example, Vβ5 contained Vβ5.1 and Vβ5.2, Vβ13 contained Vβ13.1 and Vβ13.2. This probably caused by the different classification standards, but the main Vβ gene families were consistent with each other. Therefore, we took the numbers of Vβ subfamilies together as total of the main Vβ gene family. Besides, a concept of predominant usage frequency (frequencies) (PUF or PUFs) was applied, and the formula was as following:

$$PUF\left(\%\right)=\Sigma n/\Sigma p\times 100$$

Σn: the summary of the times for certain a Vβ gene; Σp: the summary of the patients with certain a disease or all the patients in the study.

As shown in Table 1, the TCR Vβ genes with the highest PUFs in APL were Vβ12, Vβ21 and Vβ23, which PUFs were all 19.1%; Vβ1, Vβ3, Vβ10, Vβ15 and Vβ18 were next to them with the same PUFs of 14.3%. The predominant expression gene in T-ALL was Vβ15 with PUF of 42.9%; Vβ1, Vβ5 and Vβ10 were the second usage genes which PUFs were all 28.6%. In B-ALL, the gene of the highest PUF (28.6%) was Vβ2; Vβ3 was next to it (19.2%). In AML, Vβ3 was the highest clonal gene (16.7%), which followed by Vβ9 and Vβ23 (Both PUFs were 13.9%). PUF of Vβ2 was high to 66.7% in AMOL, and that of Vβ7 was only 22.2%. The highest usage gene

in CML was Vβ3 which PUF was 18.5%; those of Vβ13 and Vβ21 were both 14.8%.

According to PUFs of 24 TCR Vβ gene families specific to the different diseases, the histograms were designed (Figure 1). The *x* axis represented the PUF of every the TCR Vβ gene, and the y axis represented the 24 TCR Vβ gene families.

Table 1. The summary for the PUFs of 24 Vβ gene families in PBMC of the patients with leukemia (%)

TCR Vβ	APL	T-ALL	B-ALL	AML	AMOL	CML
Vβ1	14.3	28.6	0	5.6	0	11.1
Vβ2	9.5	0	0	5.6	66.7	0
Vβ3	14.3	14.3	19.2	16.7	0	18.5
Vβ4	4.8	0	0	0	0	0
Vβ5	9.5	28.6	4.8	11.1	0	0
Vβ6	4.8	0	0	8.3	0	7.4
Vβ7	0	0	0	0	22.2	0
Vβ8	9.5	14.3	0	11.1	0	7.4
Vβ9	0	14.3	4.8	13.9	11.1	7.4
Vβ10	14.3	28.6	4.8	5.6	0	11.1
Vβ11	0	14.3	0	0	0	3.7
Vβ12	19.1	14.3	0	0	0	3.7
Vβ13	9.5	14.3	4.8	2.8	0	14.8
Vβ14	0	0	4.8	2.8	0	3.7
Vβ15	14.3	42.9	14.3	2.8	0	11.1
Vβ16	0	0	0	8.3	0	3.7
Vβ17	9.5	14.3	0	5.6	0	11.1
Vβ18	14.3	0	0	2.8	0	0
Vβ19	0	14.3	9.5	5.6	0	7.4
Vβ20	4.3	0	0	2.8	0	0
Vβ21	19.1	0	28.6	0	11.1	14.8
Vβ22	4.8	0	0	2.8	0	7.4
Vβ23	19.1	0	14.3	13.9	0	0
Vβ24	0	14.3	5.6	2.8	0	0

PUF, predominant usage frequency; APL, acute promyelocytic leukemia; T-ALL, T cell-acute lymphoblastic leukemia; B-ALL, B cell-acute lymphoblastic leukemia; AML, acute monoblastic leukemia; AMOL, acute myelogenous leukemia; CML, chronic myeloid leukemia.

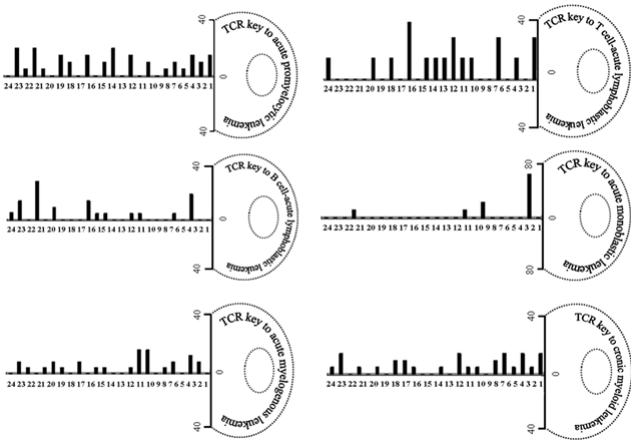

Figure 1. Different "keys" specific to different diseases formed with the predominant usage frequencies of TCR Vβ genes in PBMC of the corresponding patients

According to the reports relates to the predominant usage frequencies of TCR Vβ specific to different diseases, the features of TCR Vβ were reanalyzed with histograms. The columns with different heights represent different predominant usage frequencies of Vβ subfamilies (including the monoclonal, biclonal and oligoclonal gene families), and the polyclonal and low-expression genes are ignored in this analysis. It is easy to see that each merged gram likes a big key, which probably reflects the characteristics of the skewness of T cell receptor (TCR) specific to the corresponding disease. (A) The TCR key to acute promyelocytic leukemia; (B) The TCR key to T cell-acute lymphoblastic leukemia; (C) The TCR key to B cell-acute lymphoblastic leukemia; (D) The TCR key to acute monoblastic leukemia; (E) The TCR key to acute myelogenous leukemia; (F) The TCR key to chronic myeloid leukemia.

3. Discussion

In all the six leukemia, the TCR Vβ gene families with the highest PUFs were different to a certain extent. For example, The TCR Vβ genes with highest PUFs were Vβ12, Vβ21 and Vβ23 in APL, while that was Vβ15 in T-ALL, Vβ21 in B-ALL. These different or similar highest predominantly used genes combing the other predominant expression genes formed a combination of Vβ genes. In APL, the combination was Vβ1-Vβ2-Vβ3-Vβ4-Vβ5-Vβ6-Vβ8-Vβ10-Vβ12-Vβ13-Vβ15-Vβ17- Vβ18-Vβ20-Vβ21-Vβ22-Vβ23; in B-ALL, it was Vβ3-Vβ5-Vβ9-Vβ10-Vβ13- Vβ14- Vβ15-Vβ19-Vβ21-Vβ23-Vβ24; in AMOL, those were Vβ2-Vβ7-Vβ9-Vβ21. There were different complications in different types of leukemia, and in our opinions, the complications probably represent the different features specific to the corresponding diseases.

In order to directly observe the characters consisted of the advantageously clonal genes, the histograms were made up according to PUFs of TCR Vβ specific to the different diseases. The columns with different heights represented the PUFs of Vβ subfamilies, which contained monoclonal, biclonal and oligoclonal expression. Obviously, the histogram for each of the leukemia looked like a key, and every column liked its kit. Thus there were different kits for different leukemia, and the kits for a key liked the combination of different TCR Vβ genes mentioned in the above paragraph. Except the combination, the height of the column determined by PUF also could reflect the characters of the TCR Vβ specific to certain a disease. The higher the frequency of the TCR Vβ gene family was, the higher the kit of the key would be. Therefore, to some extent, the key represented the total characterization of TCR Vβ for the patients with leukemia. In anther words, the key was specific to the corresponding leukemia. Of course, the studies on the skewness of TCR Vβ of the patients with leukemia were little, and the key found in this paper could not exactly show the complete specificity of TCR Vβ for each of leukemia. However, through such a reanalysis of the data, we think that there should be a key specific to every disease, including various pathogen infections, type I diabetes, colorectal cancer, and so on. Once the keys of TCR Vβ specific to the diseases are found through the studies on lots of cases in future, in our opinions, it will be benefit to the diagnosis and the exposure of the mechanism for the diseases.

4. Conclusion

Through the reanalysis of the data in the articles related to TCR Vβ predominant usage, we found the features of the usage in each of the disease. The histogram, drawn with the predominant usage frequencies of the TCR Vβ, like a key which specific to the corresponding disease. These results probably pose a new idea for analyzing the skewness of TCR for the researchers of the relative study field.

5. Financial Disclosure

The work is supported by the Provincial Science and Technology Development Project (No. 2012YD18054),

the Provincial Nature Science Foundation (No. ZR2012HL29), the Project of Shandong Province Higher Educational Science and Technology Program (No. J11LF18), the Population and Family Planning Commission (No. [2011]13), and the Development Plan Project of Jining Science and Technology Bureau of Shandong Province (No. [2011]57, 2014jnjc12 and 2014jnyx14).

References

[1] Yang LJ, Li YQ, Chen SH, Zhou YB, Tang Y, Wu XL, "The feature of clonal expansion of TCR Vβ T cell s from peripheral blood in patients with APL", *Journal of Leukemia & Lymphoma*, 14 (4): 205-214, 2005.

[2] Li Y, Chen S,Yang L, Zhou Y, Wu X,. Huang M, "Geng S. Clonal expanded TCR Vbeta T cells in patients with APL", *Hematology*, 10 (2): 135-139, 2005.

[3] Huang MJ, Li YQ, Chen SH, Zhou YB, Yang LJ, Han SF, "Clonality and gene repertoire analysis of T-cell receptor Vβ associated with T-ALL and T cell strains", *Immunological Journal*, 20 (6): 439-442, 2004.

[4] Sun YP, Shi B, Zhu HQ, Tang XY, Ma R, Yao XS, "Analysis of TCR CDR3 spectratyping of αβ T cells in peripheral blood mononuclear cells with leukemia by using FQ-PCR DNA melting curve technique", *Journal of Zunyi Medical University*, 37 (1): 39-47, 2014.

[5] Huang MJ, Li YQ, Chen SH, Yang LJ, Zhou YB, Zhang T, "Analysis of T-cell receptor Vβ gene repertoire and clonality in patients with B-ALL", *Cancer research on prevention and treatment*, 31 (6): 320-322, 2004.

[6] Li YQ, Yang LJ, Chen SH, Li RF, Zhang YP, Lu YH, Luo GX, "Clonal expansion T cells identified in acute monoblastic leumia by CDR3 size analysis of TCR Vβ repertoire using RT-PCR and genescan", *Chin Med J*, 115 (1): 69-71, 2002.

[7] Chen SH, Li YQ, Yang LJ, Yu Z, Luo GX, "Analysis of clonal expansion of TCR Vβ subfamily T cells associated with AML-M1", *Immunological Journal*, 18 (5): 353-356, 2002.

[8] Li FR, Li YQ, Yang LJ, Chen SH, Zhang XL, Zhang YP, Wang Z, "Analysis of the clonal expansion of TCR Vβ subfamily genes and T cell clonality in AML-M2a using genescan", *Journal of modern clinical medical bioengineering*, 7 (4): 241-243, 2001.

[9] Mao P, Luo CR, Zhang YP, Wang CX, Xu YP, Ying Y, Du QX, Xie JJ, "Expression and clonal proliferation of TCR Vβ subfamilies of peripheral T-cells in acute myeloid leukemia patients", *Journal of Experimental Hematology*, 17 (2): 431-436, 2009.

[10] Li YQ, Yang LJ, Chen SH, Zhang YP, Zhang XL, Luo GX, "T cell receptor Vβ repertoire usage and clonal expansion of T cells in chronic myelogenous leukemia", *Chin Med J*, 117 (6): 840-843, 2004.