Immunogenetics: Open Access

Hou, et al., Immunogenet open access 2016, 1:2

Commentary Open Access

Composition and Variation Analysis of the TCR -Chain CDR3 Repertoire in Systemic Lupus Erythematosus Using High-Throughput Sequencing by Sui, et al

Xianliang Hou[1], **Yong Dai**[2] **and Hongyan Diao**[1*]

[1]*State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, China*

[2]*Clinical Medical Research Center, the Second Clinical Medical College of Jinan University (Shenzhen People's Hospital), Shenzhen, Guangdong, P.R China*

[*]**Corresponding author:** Hongyan Diao, State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, China, Tel: 0123456789; E-mail: diao.hy@163.com

Received date: March 05, 2016; **Accepted date:** April 01, 2016; **Published date:** April 06, 2016

Commentary

Sui et al. used a combination of multiplex-PCR, Illumina sequencing and IMGT/High V-QUEST for a standardized analysis of the characteristics and polymorphisms of the T-cell receptor β chain Complementarity-Determining region 3 (TCRβ CDR3) genes in T cells from Systemic Lupus Erythematosus (SLE) patients and healthy donors (NC). However, there are several issues which warrant further consideration. Herein, we will discuss this topic.

It's honoured to provide a brief commentary on the brilliant study of Sui et al. concerning the T cell immune repertoire sequencing (IR-SEQ) [1]. IR-SEQ refers to a method to evaluate the diversity of immune system by amplifying the Complimentary Determining Region (CDR) of B-cell Receptor (BCR) or T-cell Receptor (TCR) using multiple-PCR or 5'RACE methods, followed by high-throughput sequencing, which can be used to investigate the association between immune repertoire and diseases. The authors performed high-throughput sequencing of TCR β chain CDR3 regions in SLE patients and healthy donors. They used multiplex-PCR amplification and Illumina sequencing system together with alignment and data analyses based on a program developed by Mi Laboratory. The authors found that there were more expanded clones and more restricted T-cell repertoire in the SLE group compared to the NC group. Also, SLE patients showed different usage frequencies of TRBV and TRBJ segments compared to NC group. In addition, the study was of potential interest in that the authors seem to have identified a few TCRβ CDR3 DNA and amino acid sequences which were common to all SLE patients and could perhaps serve as biomarkers for SLE risk. This was a timely written review article needed for the recent explosion of interest in immune repertoire sequencing used for various research and application. Nowadays, immune repertoire sequencing technology can comprehensively assess the diversity of the immune system, and has been applied to vaccine development and efficacy assessment, biomarker discovery, minimal residual disease detection, autoimmune diseases, transplant rejection and tolerance [2-5].

Overall the manuscript was well written but there were several issues which warrant further consideration. Firstly, the authors identified the degree of CDR3 sequence sharing among subjects. However, the repertoire features of public CDR3 sequences were not analyzed. Recent studies have shown that public sequences in humans are closer to germ-line configurations, and have shorter mean CDR3 length and higher mean abundance. However, there are many secrets have not been found. Understanding the basis of public T cell responses not only is important for our understanding of immune repertoire and diversity and hierarchy, but it also has implications for immune control of pathogens and vaccine design [6]. Secondly, the influence of HLA on shared T cell clones could be explained better. Particularly, there was no information about HLA profile of the study subjects. One well-established mechanism of antigen selection is positive selection for HLA binding affinity during thymic T-cell maturation. Relative proportional TCR gene segment usage and the resulting repertoire may be determined by the HLA make up of an individual. Previous studies have showed a strong association between the sharing of HLA class 1 alleles and the proportion of shared TCRB sequences ($P < 1\times10\text{^}6$) [7]. Thirdly, the authors also analyzed the distribution characteristics of CDR3 length, VD indel length, and DJ indel length, and found that the length distributions were similar between the SLE and NC groups. This point should be analyzed from two aspects, including the distribution characteristics among unique TCRβ nucleotide clonotypes and across the total TCRβ nucleotide repertoires. In a similar study by Venturi et al. [8], they also found that the distributions of CDR3 lengths among unique TCRβ amino acid clonotypes were similar in the memory and naïve pools within individuals and between individuals. However, they found substantial CDR3 length distribution differences between the memory and naive pools across the total TCRβ amino acid repertoires.

Generally speaking, this article gave us a new insight into deeply understanding the human adaptive immune system and the pathogenesis of SLE. This was a scientific and technically applicable study. Unfortunately, more data should be presented and discussion of the methodology was inadequate. For example, technical information about TCR primer selection was missing. If adapted or followed from earlier published report, the reference should be mentioned. In the first paragraph of the results section, the authors gave some numbers of raw reads, but the raw data was not shown, it should be as a supplement for the article, because these data was basis for the article and could give readers more information. In conclusion, we wished to thank Sui et al., for their timely and valuable contribution for initiating this discussion. It was to be hoped that recognition of these issues in the literature will stimulate a revitalized research effort in this area.

Conflicts of interest

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

References

1. Sui W, Hou X, Zou G, Che W, Yang M, et al. (2015) Composition and variation analysis of the TCR β-chainCDR3 repertoire in systemic lupus

erythematosus using high-throughput sequencing. Mol Immunol 67: 455-464.

2. Kim C, Wilson T, Fischer KF, Williams MA (2013) Sustained interactions between T cell receptors and antigens promote the differentiation of CD4+ memory T cells. Immunity 39: 508-520.
3. Klarenbeek PL, de Hair MJ, Doorenspleet ME, Van Schaik BD, Esveldt RE, et al. (2012) Inflamed target tissue provides a specific niche for highly expanded T-cell clones in early human autoimmune disease, Ann. Rheum. Dis 71: 1088–1093.
4. Wu D, Sherwood A, Fromm JR, Winter SS, Dunsmore KP, et al. (2012) High-Throughput Sequencing detects minimal residual disease in acute T lymphoblastic leukemia. Sci Transl Med 4:134-163.
5. Muraro PA, Robins H, Malhotra S, Howell M, Phippard D, et al. (2014) T cell repertoire following autologous stem cell transplantation for multiple sclerosis. J Clin Invest 124: 1168-1172.
6. Venturi V, Kedzierska K, Price DA, Doherty PC, Douek DC, et al. (2006) Sharing of T cell receptors in antigen-specific responses is driven by convergent recombination. Proc Natl Acad Sci USA 103: 18691-18696.
7. Warren RL, Freeman JD, Zeng T, Choe G, Munro S, et al. (2011) Exhaustive T-cell repertoire sequencing of human peripheral blood samples reveals signatures of antigen selection and a directly measured repertoire size of at least 1 million clonotypes. Genome Res 21: 790-797.
8. Venturi V, Quigley MF, Greenaway HY, Ng PC, Ende ZS, et al. (2011) A mechanism for TCR sharing between T cell subsets and individuals revealed by pyrosequencing. J Immunol 186: 4285-4294.