Letter to the Editor

Stem Cell INVESTIGATION

# Deletion with 25 nucleotides of *TCRζ* gene in T cells from a case with chronic myeloid leukemia

**Yan Li[1,2*], Jing Lai[1,2*], Ziwei Liao[2], Lixin Guo[2], Bo Li[2], Kanger Zhu[1], Yangqiu Li[1,2,3]**

[1]Department of Hematology, First Affiliated Hospital, Jinan University, Guangzhou 510632, China; [2]Institute of Hematology, Jinan University, Guangzhou 510632, China; [3]Key Laboratory for Regenerative Medicine of Ministry of Education, Jinan University, Guangzhou 510632, China

*These authors contributed equally to this work.

*Correspondence to:* Yangqiu Li. Key Laboratory for Regenerative Medicine of Ministry of Education, Jinan University. Email: yangqiuli@hotmail.com.

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TCRζ is a transmembrane protein, a component of the T cell receptor (TCR)/CD3 complex, and plays a crucial role in T cell activation (1,2). Previous studies showed that T cell immunodeficiency might be related to decreased expression of *TCRζ*. The alternatively spliced isoforms of *TCRζ* 3' untranslated region (3' UTR) in patients with chronic myeloid leukemia (CML) was related to change of T cell activation gene expression pattern, and may be as a novel immunological marker for the evaluation of the CML immune status (3). Recently, we found that polymorphisms/mutations in the *TCR ζ* 3' UTR can regulate the expression level of *TCR ζ* (unpublished data). However, little is known the genetic alteration of *TCRζ* 3' UTR in T cells from patients with CML who showed T cell immunodeficiency. In this study, we investigated the mutations in the *TCRζ* 3' UTR in peripheral blood mononuclear cells (PBMCs) from 10 patients with *de novo* CML by RT-PCR, cloning and nucleotide sequencing (All human peripheral blood samples were collected with informed consent, and ethical approval was obtained from the Ethics Committee of the Medical School of Jinan University). Significant finding is that a deletion with 25 nucleotides located on 725–751 bp of *TCRζ* 3' UTR (727–751 del ACAGACTGTTGTCCCTGCACTCTTT) in a case with CML (Figure 1). According to TargetScan analysis, there are nine miRNA binding sites on the *TCRζ* 3' UTR, in which miR-132-3p/212-3p binding site is located between 730–736 bp of *TCRζ* 3' UTR, this binding site is included in the deleted segment with 25 nucleotides in the case (*Figure 1*). We further compared the expression level of *TCRζ* gene between this case and the control group including 9 cases with CML without *TCRζ* deletion by quantitative real-time PCR. The expression level of *TCRζ* in PBMCs from this case (median: 0.76) seemed high than that from control group (median: 0.25, n=9). Suggesting that miR-132-3p/212-3p may be one of the regulators for *TCRζ*, and the deletion may affect its function in T cells from this case. The genetic alteration of *TCRζ* gene was firstly reported in patients with systemic lupus erythematosus (SLE), which was thought to be related to the susceptibility for SLE. It was also firstly reported a 36 bp deletion of *TCRζ* gene (lacking exon 7), which might alter the signal transduction via TCR in T cells resulting aberrant T cell activation in SLE (2). Moreover, functional study indicated that mutations/polymorphisms and aberrant splicing of the downstream 3' UTR might affect the stability of *TCR ζ* mRNA, leading to TCRζ downregulation in T cells (4,5). In this study, we firstly identified the 25 bp deletion of *TCRζ* gene from patient with CML, the results may contribute for characterizing the T cell immune dysfunction in CML patients. It would be worth to further characterize the mutation, polymorphisms or splice variants in T cells from different hematological malignancies with T cell dysfunction, which might provide the information for reversing the immune dysfunction.

In conclusion, to our best knowledge, we firstly identified a 25 bp deletion of *TCRζ* 3' UTR in CML patient, which involved in a predicted miRNA binding site, and might be related to the increased expression level of *TCRζ* gene as compensatory. However, the functional alteration in T cell activation is needed to further investigation.

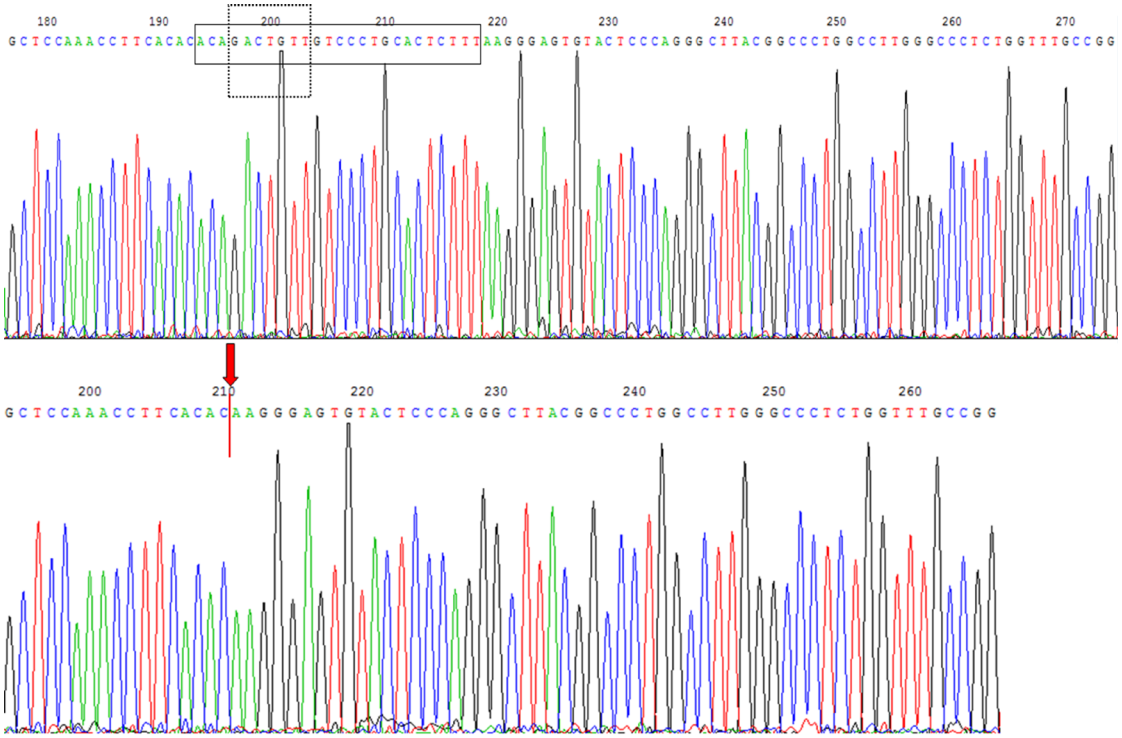


**Figure 1** The deletion of 25 bp segment between 725–751 bp of TCRζ 3' UTR locus in a case with CML. (A) Wild type sequence of TCRζ 3' UTR segment including 725–751 bp (solid line frame) from control sample, dotted line frame showed the miR-132-3p/212-3p binding site; (B) sequence with 25 bp deletion in sample from a CML case, arrow indicated the site of deletion, red line showed the fusion point. 3' UTR, untranslated region; CML, chronic myeloid leukemia.

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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