

**Modern Rheumatology: Manuscript review result**

"Modern Rheumatology Editorial Office" <em@editorialmanager.com>

收件人: "Dongyi He" <shicheng.guo@hotmail.com>

时 间: 2016-2-23 10:13:31

附 件:

Ref.: Ms. No. MORH-D-16-00071

Genome-wide DNA methylation patterns in CD4+ T cells from Chinese Han patients with rheumatoid arthritis  
Modern Rheumatology

Dear Dr. He,

Reviewers have now commented on your paper.

You will see that they are advising that you revise your manuscript.

If you are prepared to undertake the work required, we would be pleased to reconsider our decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript.

**\*\*Corrections should be indicated in different color.**

Your revision is due by 22-04-2016(dd-mm-yyyy).

To submit a revision, go to <http://morh.edmgr.com/> and log in as an Author.

You will see a menu item call Submission Needing Revision.

You will find your submission record there.

Yours sincerely

Takayuki Sumida  
Editor-in-Chief  
Modern Rheumatology

Reviewers' comments:

Reviewer #1:

Comments to the author with the manuscript MORH-D-16-00071

The present study showed significant DNA methylation change in CD4+ T cells from patients with rheumatoid arthritis (RA) according to the genome-wide DNA methylation profiling. The re

1. Page 4, paragraph 2: It would be better to explain why the authors have focused their attention on the CD4+ T-cells in the genome-wide DNA methylation study in the introduction.
2. Page 4, paragraph 3: Please include the information on smoking status and medication including glucocorticoids, because these have been reported to regulate DNA methylation levels.
3. Page 4, last paragraph: Please provide the more detailed information on the specific antibodies for determination of CD4+ T cells.
4. Page 6, paragraph 2: The authors should confirm and state that the confounding factors including age, gender, and smoking were comparable in their frequencies between the groups.
5. Table 1: It is difficult to understand the data of Table 1. Please add the column that indicates the RA and control groups, respectively, in the top stage. Please also include the p-values.
6. Page 8, last paragraph: It is recommended to indicate the correlations between DNA methylation levels and disease characteristics in additional new figures to improve readability.
7. Discussion: Please explain briefly what is novel in comparison to other similar studies in the first part of discussion. In addition, it would be appreciated to address the potential limitations of the study.
8. Page 10, paragraph 2: Please add the reference number in the place of 'Jeffries' (lines 242, 245, and 249).

Reviewer #2:

In this article, authors identified differential DNA methylation sites in RA CD4 T cells. They also showed the association between DNA methylation and disease characteristics. Because

Major comments;

1. Because they identified differentially methylated genes, such as HDAC4, NXN, TBCD, TMEM61, ITIH3, TCN2, PRDM16, SLC1A5 and GALNT9, in CD4 T cells, they should clarify the function of these genes.
2. They mentioned the reason why they did not examine the gene expression in the discussion section. However, it would be interesting to investigate gene expression of differentially methylated genes.

Minor comments;

1. In line 200, does DAS28 mean DAS28-CRP or DAS28-ESR?
2. In line 226-227, they compared DNA methylation between FLS and CD4 T cells. Because DNA methylation profiles as well as gene expression profiles are different in different types of cells.

