Pamela J. Fink, Ph.D.  
Editor-in-Chief,

Rheumatology

Dear Prof. J M van Laar,

We would like to submit the enclosed manuscript entitled “Copy number variation of *HLA-DQA1* and *APOBEC3A/3B* contribute to the susceptibility of systemic sclerosis in Chinese Han population”, which we wish to be considered for publication in “Rheumatology “.

Systemic sclerosis (SSc) is a systemic connective tissue disease caused by complex genetic aberrant. A number of SNPs has been identified to be associated with the susceptibility of SSc, while the role of the copy number variations (CNVs) on susceptibility of SSc was not clear yet. In our present study, genome-wide CNV screening was performed in twenty-four SSc patients and hundreds of common CNVs were found in SSc genome. Five common CNVs, which were speculated to be related to the pathology of SSc with biological meaningful, including *HLA-DRB5*, *HLA-DQA1*, *IRGM*, *CDC42EP3* and *APOBEC3A/3B,* were validated in 365 SSc patients and 369 matched healthy samples from Chinese Han population with AccuCopy technology, which were designed for CNV detection in middle-throughput level. It was found that the copy number variations of *HLA-DQA1* and *APOBEC3A/3B*, two of immune system relevant genes, were significantly associated with SSc. The study demonstrated that *HLA-DQA1* and *APOBEC3A/3B* contribute to the susceptibility of systemic sclerosis. Thus, we need pay attention to the variation from copy number variations in human genome which would provide with the opportunity to find more missing heritability for complex diseases. We believe that the results described in this manuscript have addressed an important phenomenon in the susceptibility of scleroderma and will have a broad interest to the readers. We wish this paper is suitable for “Rheumatology”.

All authors have read and approved this version of the article, and due care has been taken to ensure the integrity of the work. The manuscript is approved by all authors for publication. No part of this paper has been published or submitted previously, and not under consideration for publication elsewhere, in whole or in part. We deeply appreciate your consideration of our manuscript, and we look forward to receiving comments from reviewers. If you have any queries, please do not hesitate to contact me.

Sincerely,

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