

March 31, 2017

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 33271-Prospective study.doc).

Title: Association of adiponectin gene polymorphisms with knee osteoarthritis

Author: Dong Zhan, Suthimon Thumtecho, Aree Tanavalee, Pongsak Yuktanandana, Wilai Anomasiri, Sittisak Honsawek

Name of Journal: *World Journal of Orthopedics*

ESPS Manuscript NO: 33271

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) This paper investigated the role of adiponectin in the pathogenesis of osteoarthritis(OA). In particular, Zhan et al explored the effects of polymorphism of adiponectin in the development of OA among Thai population. Although the results show that there is no significant difference in the gene polymorphism between the healthy and OA patients, the authors demonstrated that the levels of plasma adiponectin significantly differ between these groups. The findings are very interesting and provide promising clinical strategy in the diagnosis and treatment of osteoarthritis. This article may garner remarkable readership in your journal. Hence, I recommend that this manuscript be considered for publication after minor typographical revisions will be completed.

Comments:

The paper is well written except for some typographical errors. For instance;

Page 3, last line: Change the word decreaseing to decreasing

Page 10, 2nd paragraph should be this way- The genotype distribution and allele frequency of the +45T/G polymorphism were not significantly different among different groups of OA severity.

*please observe these changes all throughout the manuscript

Response: We have improved our manuscript as the reviewer's suggestion and correct all typographic errors and have checked all throughout the manuscript.

"In chondrocytes, adiponectin could modulate cartilage destruction through increasing tissue inhibitor of metalloproteinase-2 and decreasing interleukin-1 β [7]. Accumulating evidence suggests that adiponectin might play a protective role in the development of OA."

"The association between genotypes of the +45T/G *ADIPOQ* gene polymorphism and radiographic severity of OA patients was shown in Table 3. The genotype distribution and allele frequency of the +45T/G polymorphism were not significantly different among different groups of OA severity. According to the genotypes of the +276G/T *ADIPOQ* gene polymorphism, however, there were significant differences between KL grade 2 and KL grade 3 at +276G/T genotypes ($P=0.037$), as

well as between KL grade 2 and KL grade 4 ($P=0.046$) (Table 4). The allele frequency of +276G/T polymorphism was not significantly different. "

(2) Thank you for inviting me to review this interesting research study on the association with knee arthritis. The study is interesting, however, its results are not important. Moreover, I doubt that the accumulation of cases as in this series might lead to a change in current practice. I cannot see how excluding these polymorphisms from the etiology of knee arthritis might be useful. It will need a lot more for important conclusions to be made on the topic; this is obvious from the authors' own conclusions.

Response: Thank you for your suggestion.

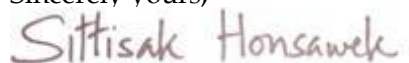
(3) Title: Main idea is clear and understandable. Abstract: Abstract is accurate, coherent and readable. Introduction: Previous pertinent literature cited and discussed. Therefore, introduction is adequate. The necessity for the study is clearly indicated. Methods: Study design is appropriate to achieve study aim. Study population clearly and adequately described. Statistical analyses are appropriate and used appropriately. Overall methodology is valid, replicable and understandable. Results: Results are clearly presented and comprehensible. Text did not duplicate the tables. Discussion: Previous pertinent literature was critiqued. The authors demonstrated continuity between present study and previous studies. Similarities and differences to other studies were noted. Discussion is sufficient, future studies, strengths of study and limitations are indicated. References: References are updated and accurate. Also references are relevant and comprehensive. Tables and Figures: Tables and figures are definite, clear and understandable.

Response: Thank you very much for valuable advice.

3 We provide audio core tip and the required documents. We also delete Reference#18. References and typesetting were corrected.

Thank you again for publishing our manuscript in the *World Journal of Orthopedics*.

Sincerely yours,



Sittisak Honsawek, MD, PhD

Faculty of Medicine

Chulalongkorn University

Patumwan, Bangkok 10330

Thailand

Fax: +66-2-256-4482

E-mail: sittisak.h@chula.ac.th