Reviewer's report

Title: Polymorphic variation of Hypoxia Inducible Factor-1 A (HIF1A) gene might contribute to the development of knee osteoarthritis

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Reviewer: Won Sang S Park

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General Comments:
The authors have described a clinical study evaluating the relationship between the polymorphisms of the HIF1A and WISP1 genes and development of osteoarthritis in a Mexican population and found that P582S SNP of the HIF1A is associated with knee osteoarthritis. The biggest problem with this study is that it does not have much power. In particular, the authors should genotype a larger group of case and controls. In addition, detailed and careful criteria of the selection of patients and control should be provided.

Comments

1) They analyzed HIF1A and WISP1 polymorphisms in 70 patients with knee OA and 66 healthy controls. However, they found zero frequency genotype in SNPs of HIF1A, suggesting that the number of the patients is not big enough. Making an analysis of the power of the study is completely necessary. The number of both the patients and healthy control must be increased.

2) The authors need to include Kellgren and Lawrence grade (KL grade) or joint space narrowing (JSN) grade of the patients with Knee OA and to analyze the relationship between these clinical grade and these polymorphisms.

3) Clinical information including age, gender, BMI, glucose, cholesterol and uric acid were collected. Did they analyze the relationship between P582S polymorphism of the HIF1A and above clinical information?

4) The p values that are reported in the results (Table 3 & 4) should be the p values adjusted by age and sex.

5) In Table 3 & 4, number of patients and control should be corrected. In addition, allele frequencies of rs2057482 and rs2929970 in control group are not correct.

6) In Table 2, they found a significant difference in BMI and uric acid level between patients and controls. Did they describe this difference in "Discussion" section?