Reviewer's report

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

Version: 1  Date: 12 March 2015

Reviewer: W den Hollander

Reviewer's report:

In this manuscript the authors have performed a gene targeted association analysis for OA in 4 genetic variants that are located in either the HIF1a or WISP1 gene. Apart from the rather poor written English throughout the manuscript, I have got the following major points which should be addressed:

1) For a genetic association study the sample size (70 patients vs. 66 controls) is fairly small, the authors should elaborate on this in the discussion.

2) There is a significant difference in BMI between the two groups, as is uric acid for that matter. Could the authors explain why they believe their significant HIF1a SNP would be involved in OA, rather than in BMI or uric acid biology.

3) The discussion about the hypothesized HIF1a polymorphism consequences is hard to follow. People carrying the risk allele were shown to express HIF1a to higher extent, but it is nowhere mentioned in the paper whether this would be good or bad for cartilage homeostasis.

4) Also, the authors state that heterozygous carriers are protected for OA. In what comparison? Compared with homozygous carriers of the risk allele? Please clarify this and point 4 in the main text.

And as a minor point:

1) Please mention the rs identifiers as opposed to the amino acid changes. While the amino acid change is of course of interest for biological interpretation, from the point of view of the reader it is easier to look up rs identifiers in online databases.

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests