Reviewer's report

Title: Genome-wide DNA methylation study of hip and knee cartilage reveals embryonic organ and skeletal system morphogenesis as major pathways involved in osteoarthritis

Version: 2 Date: 27 July 2015

Reviewer: Jose A. Riancho

Reviewer's report:

Authors are to be congratulated for their attempt to gather new information in the field of epigenomics of skeletal disorders. However, some issues need revision or clarification.

Major compulsory revisions.
1. Age has a well known influence on methylation. This is a critical point in the manuscript because of the difference between controls and patients with osteoarthritis. Authors must explore the possible association of methylation with age. Ideally they should repeat the analysis taking age into consideration as a covariate.
2. Authors state that the study is unique in identifying DMRs in developmental pathways. This seems to be an overstatement. In fact, their results are in line with other reports (for example, Delgado-Calle et al, Arthritis Rheum 2013) that should be included in the discussion.

Minor compulsory revisions
1. Please, expand figure legends to make them easier to understand without reading the text. For instance, in figure 1, specify the method used for dimension analysis (also in Methods section), as well as the general meaning of the axes and the figure as a whole, for the benefit of the non-expert reader.

Discretionary revisions
1. Please, provide FDR values

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
'I declare that I have no competing interests'