Reviewer's report

**Title:** Comparison of orthopaedic manifestations of multiple epiphyseal dysplasia caused by MATN3 versus COMP mutations: a case control study

**Version:** 3  **Date:** 26 January 2014

**Reviewer:** Barbara Vertel

**Reviewer’s report:**

This study nicely extends the Kim et al 2011 publication by providing important clinical findings and a clinical/orthopedic context for the previous work. The authors note some limitations of this study; nonetheless, it is a worthwhile contribution.

**Major Compulsory Revisions**

1. Fig 1F is shown as a MAT3-MED patient radiograph, but in the previous Kim et al 2011 publication from which it is reproduced, the same image is shown in Fig 3C as a COMP mutation patient radiograph. Please explain and correct this critical discrepancy.

2. Background paragraph 2. Since ethnic differences in the distribution of the causative genes for MED is a major rationale for these studies, it is really important to include the specific distributions (numbers) in Caucasian populations as a comparison for the numbers provided for Korean and Japanese populations so that this key point is properly supported by data.

**Minor Essential Revisions**

3. Discussion Paragraph 2, sentence 5-It is written “the MATN3 mutation results in relatively mild phenotypes as compared with those of COMP mutation. Also written in the Conclusion- “MATN3-MED develops a relatively mild phenotype from an orthopedic point of view.” Are the phenotypes really relatively mild, or relatively milder in comparison to COMP-MED phenotypes? My suggestions are to change “relatively mild” to “relatively milder” in the Discussion, and to add “in comparison to COMP-MED” in the first sentence of the Conclusion.

4. Background- The sentence about severe Fairbank and mild Ribbing is a little distracting, and doesn’t add much to the manuscript. It could easily be deleted.

5. Results Paragraph 1-beginning “In the MATN3 group…” since complaints of knee and joint pain did not differ statistically, it is more reflective of the data to equate them as the most common complaints rather than to include knee joint pain ahead of hip pain.

6. Figure 3 legend- Please provide a more detailed description of the findings, as
has been done for Figure 1 and 2 legends.

7. Discussion Paragraph 4 is rambling and unfocused. Please focus, tighten and clarify this discussion of the clinical findings and their implications. Sentences 1 and 2 are particularly difficult to understand. As written, “more guarded” and the point about MED in relationship to Legg-Calve-Perthes disease lack meaning. Please reorganize and rewrite the paragraph.

8. Although there is a separate Conclusion section, the Discussion would be improved by ending it with a stronger, more specific and focused paragraph.

9. Conclusion, last sentence-Suggest rewriting as follows to better clarify the message- “These differences in clinical manifestation and prognosis justify distinguishing between the COMP or MATN3 molecular subtypes of MED in orthopedic patients.”

The following are spelling, grammar and editorial suggestions and corrections.

10. Background Paragraph 1, sentence 5-Mutations of the genes encoding cartilage
11 & 12. Background Paragraph 2, sentence 1-ethnic differences; last sentence-Type IX collagen
13. Background Paragraph 3, sentence 2-each genotype of
14. Background Paragraph 3, sentence 4-clinical characteristics
15. Methods sentence by itself before last paragraph-Type and purpose…..were categorized
16. Results last line-should refer to Table 4 and not Table 3.
17. Discussion Paragraph 2, sentence 2- should add “and” so that it reads “and early onset osteoarthritis”
18. Discussion Paragraph 2, sentences 4 and 5-corrected as follows: “The MATN3 group demonstrated a significantly lower incidence of gait abnormality throughout the follow-up period, and patients were less likely to have complaints of hip pain and limitation of daily activity at the latest follow-up. Accordingly, our findings suggest.....”
19. Discussion Paragraph 3, sentence 2- angular (spelling)
20. Discussion Paragraph 3, last sentence- better as “Due to the multicenter nature of this study”
21. Discussion Paragraph 3, sentence 4, under 5) compatible (spelling)
22. Discussion Paragraph 3, sentence 5- “abnormal hip development which is not.....”
23. Discussion Last paragraph, sentence 2- should be “on an all-or-none basis”
24. Conclusion, sentence 2- hips not hip
25. Figure 2 legend- Resorption (spelling)
26. Figure 1- major issue queried above under Major Compulsory Revisions; also, remove the random letter “G” on panel D
27. Figure 1- remove the random letter “R” on panel A

**Level of interest:** An article whose findings are important to those with closely related research interests

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

**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