Reviewer's report

Title: Evidence for ACTH and androgen receptor roles in the development of giant bilateral myelolipomas in patients with congenital adrenal hyperplasia

Version: 1 Date: 3 March 2014

Reviewer: Ashwini Mallappa

Reviewer's report:

Interesting article which adds to the current literature on myelolipoma etiology.

Minor Essential Revisions

1. Title. The current title is misrepresentative. In the study, one only patient with CAH had evidence of MC2R and AR overexpression. Suggest editing the title.

2. Page 3, Abstract: Expand abbreviations - ACTH, MC2R, SF1. Conclusion section needs to be reworded as only one CAH patient had evidence of overexpression of MC2R and AR.

3. Page 4, Background: Recommend including a sentence about MC2R and ACTH in adrenal cortex in this section. MC2R needs to be expanded.

4. Page 1: Paragraph 2: last line - the authors are interested in the role of ACTH and Androgens hyperstimulation in the pathogenesis. This sentence needs minor correction.

5. Page 6: Expand abbreviations- ACTB, GAPDH.

6. Page 8: Suggest including Hounsfield units from CT studies for all patients.

7. Page 8: Need a space after description of patient 1 and 2.

8. Page 8: Suggest including ACTH and androgen values for patient 3 and 4 (if available) as MC2R expression was high in these 2 individuals. Also suggest including their ages.

9. Please clarify if CAH (was ruled out by clinical and/or genetic testing) and or other cause of ACTH and androgen excess was ruled out in patients 3 and 4.

10. Page 10, Line 2: Sentence on accepted mechanism- needs minor grammatical correction.

11. Discussion: This manuscript provides evidence supporting the hypothesis of chronic ACTH stimulation and myelolipoma pathogenesis, but given that MC2R overexpression was documented in only one CAH patient, it is premature to conclude that the evidence in fact proves it. This sentence needs to be reworded.

12. It is interesting that patient 1 with CAH did not show MC2R and AR
overexpression inspite of elevated lab findings. ACTH exposure was not long enough? Authors to discuss this finding.

13. Inclusion of a histopathology figure highlight the components of myelolipoma will be a nice addition to this manuscript.

14. Spacing error: Throughout the manuscript
Page 3, paragraph 1, line 1-2, paragraph 2, line 2-3, paragraph 3, line 5-6.
Page 4, Paragraph 1: line 5 -6, Paragraph 2: line 2-3.
Page 5, first paragraph, line 5 and 6,
Page 6, paragraph 2, 10-11, 13-14.
Page 8, Paragraph 1, line 1 and 2, Paragraph 2, line 2-3.
Page 9, paragraph 2, line 3-4., paragraph 3, line 1-2.
Page 10, paragraph 1, line 1 -2, paragraph 2, line 1-2, paragraph 3, line 2-3.
Page 11, paragraph 2, line 3-4.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests