Author's response to reviews

Title: Understanding decreased fertility in women carriers of the FMR1 premutation: A possible mechanism for Fragile X-Associated Primary Ovarian Insufficiency (FXPOI)

Authors:

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Version: 2 Date: 30 July 2014

Author's response to reviews: see over
To Whom It May Concern:

MS: 1941692269126471
Understanding decreased fertility in women carriers of the FMR1 premutation: A possible mechanism for Fragile X-Associated Primary Ovarian Insufficiency (FXPOI)

Thank you for providing me with the opportunity to resubmit my manuscript: “Understanding decreased fertility in women carriers of the FMR1 premutation: A possible mechanism for Fragile X-Associated Primary Ovarian Insufficiency (FXPOI)”, by Emmanuel Peprah for consideration of publication in Reproductive Health.

The comments from the reviewers were highly constructive and improved the quality of the manuscript. Also provided, are detailed explanations of how the manuscript was revised to address the concerns of the reviewers. All references have been checked and the revised manuscript meets the editorial standards of Reproductive Health.

I look forward to hearing from the editorial staff of Reproductive Health about the status of this manuscript.

Sincerely,

Emmanuel Peprah
Author’s Responses to Reviewer 1 Comments

MS:  1941692269126471
Title: Understanding decreased fertility in women carriers of the FMR1 premutation: A possible mechanism for Fragile X-Associated Primary Ovarian Insufficiency (FXPOI)

Comment #1 from Reviewer #1 (Randi Hagerman)
1. The title needs to have the - between fragile X-associated primary ovarian insufficiency.

Authors’ response to Comment #1
I want to thank the reviewer for taking time to thoroughly review this manuscript. I acknowledge the value of this and other comments and have updated the title of the manuscript to include the hyphen.

Comment #2 from Reviewer #1
2. They also say that 6% of those with the full mutation have ASD but in the full mutation it is 60% have ASD. Perhaps they meant 6% of premutation carriers have ASD and that would be more reasonable.

Authors’ response to Comment #2
I express my gratitude to Reviewer 1 for this very insightful suggestion. I have updated the manuscript to better reflect this oversight; “6%” has been changed to “60%.”

Comment #3 from Reviewer #1
3. There are several references that are not numbered but just an author and date in the text such as Woad et al 2006 etc. The reference lists have several references repeated with different numbers 2 or 3 times.

Authors’ response to Comment #3
I revised the manuscript adhere to the citation requirements on Reproductive Health.

Comment #4 from Reviewer #1
4. They have also misspelled premutation a few times in the text. This looks like the unedited proof of a paper instead of a final version. All of these mistakes need to be corrected and then it is a reasonable commentary.

Authors’ response to Comment #4
I express my appreciation to Reviewer #1, for a comprehensive assessment of the manuscript. I have updated the manuscript to correct the misspelled premutation. Unfortunately, sometime
autocorrect can be a problem when it comes to premutation.

Author’s Responses to Reviewer 2 Comments

Comment #1 from Reviewer #2 (Kerri Kissell)
1. References listed within manuscript: ‘(Woad et al., 2006, Coulam, 1982, Lu et al., 2012)’. Please adhere to guidelines for this journal for referencing articles and be consistent throughout.

Authors’ response to Comment #1
I thank Reviewer 2 for a rigorous reading this manuscript. I updated the manuscript to adhere to Reproductive Health’s guidelines.

Comment #2 from Reviewer #2
2. This line: “Additionally, the length of the CGG repeat contributes to the variation observed in reaching menopausal age; currently the threshold for the onset of FXPOI is ambiguous [15-17]” is confusing in its reference to ‘reaching menopausal age”. I think what this author means to state is that the “length of the CGG repeat contributes to the variation observed in” age of ovarian dysfunction resulting in loss of reproductive capacity. POI associated with FX is different from typical menopause.

Authors’ response to Comment #2
I have edited the sentence and used the language suggested by Reviewer #2.

Comment #3 from Reviewer #2

Authors’ response to Comment #3
As suggested by Reviewer #2, I consulted the publication; after reviewing it I updated the manuscript to better reflect the language used in the Nelson publication.

Comment #4 from Reviewer #2
4. “One interesting case report described premutation monozygotic twins discordant for the FXPOI phenotype in which the woman with the FXPOI phenotype also had elevated FSH”. I fail to find the elevation in FSH interesting as this rise in gonadotropin is
expected with ovarian failure associated with POI. Please revise this commentary.

Authors’ response to Comment #4
Reviewer #2 has a salient point. The sentence was not meant to emphasize FSH levels but the discordance of the premutation monozygotic twins. I have edited the sentence removing FSH as a point of emphasis because it seems to distract from the overall conclusion.

Comment #5 from Reviewer #2
5. The word interesting is stated three times in the last sentence of first paragraph under conclusions and significance.

Authors’ response to Comment #5
Again, I express my gratitude to reviewer #2 for an exhaustive examination of the manuscript. I have edited the sentences removing the word interesting and using other synonyms when appropriate.