

Reviewer's report

Title: Placental biomarkers of mRNA transcription applied in an epidemiologic setting: methodologic challenges.

Version: 1 **Date:** 26 December 2008

Reviewer: Daniel A Enquobahrie

Reviewer's report:

Thanks for the opportunity to review this work. Adibi et al investigated placental expressions of two genes (CYP19, PPAR#) associated with environmental exposure to evaluate spatial variability of gene expression across placenta, choice and use of internal controls for normalization and effect of sampling characteristics including methods of delivery. The authors also conducted histologic evaluations to confirm cell compositions of samples. This interesting research on placental gene expression and its report may further be strengthened by addressing the following points:

- **Major Compulsory Revisions**

- 1) Title describes a broader concept than the question addressed by the manuscript and needs to be more specific.
- 2) The abstract needs to provide a brief, specific description of the basis and objectives of the research (focus on mRNA biomarkers of exposure to phthalates) including the reasoning behind the choice of the candidate genes and internal controls and a conclusion that is appropriate to the scope of the research work conducted.
- 3) Generalizability of study findings is not adequately addressed. Selection of internal controls for normalization may be dependent on the genes of interest. The suggestion to use 18S may be useful only for the two gene expressions measured and only in comparison with the other two methods that were applied. Spatial, mode of delivery and time since delivery related variability of expressions of the two genes may not be representative of expressions of other genes.
- 4) As pointed by authors, absence of information on other factors related to labor and delivery which may have also influenced gene expression measurements including age may introduce bias to the study and reports should be cautiously interpreted.
- 5) Conclusion of the study is too strong and is not an appropriate interpretation of study findings. For instance, study findings do not resolve any key methodologic challenges as pointed.

- **Minor Essential Revisions.**

- 1) Abstract: Result: It is not clear what 90% and 20% represent. The conclusion of the abstract includes a sentence that is not clear "QPCR-derived biomarkers of placental gene expression are feasible in an epidemiologic setting" and unclear

use of the word “Method” in the second sentence.

2) Background section may be shortened.

3) Background: Page 7, Paragraph 2, Lines 5. The phrase “Time elapsed from delivery” is not clear.

4) Conclusion: What do authors suggest on methods involving pooling after sampling from different regions of the placenta instead of using the mean values?

• Discretionary Revisions

1) Background: Page 6, Paragraph 2, Lines 1-2. More clarification of the nature of the molecular biomarker that was to be identified.

2) Background: Page 6, Paragraph 2, Lines 3-4. What were the other options considered before choosing messenger RNA?

3) Background: Page 6, Paragraph 2. Authors may comment on the specificity and sensitivity of QPCR measurements compared with microarray measures.

4) Applications to microarray studies may be pointed in the discussion and/or conclusion.

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