Reviewer's report

Title: Prostaglandin pathway gene expression in human placenta, amnion and choriodecidua is differentially affected by preterm and term labour and by uterine inflammation

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Reviewer: Bryan F Mitchell

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Phillips et al present data regarding expression of proteins that are involved with pathways of prostaglandin synthesis metabolism and action in amnion, choriodecidua and placental tissues from several groups of women in late gestation around the time of delivery at term or preterm. Their objectives are clearly stated. The methods are appropriate but the analyses require further description as described below. The background and rationale are well referenced and the discussion balanced. The abstract and the paper in general are well written. There is a large amount of data presented and this presents difficulty in following the analyses and interpretations. However, I have no suggestions as to how this could be improved.

The following points are major concerns:

1. The relationship between these findings and those of the previous publication (reference 13) needs clarification. The previous publication presented data regarding myometrial gene expression of many of the same genes as this paper. Are the present data a subgroup of the previous paper or entirely new groups. If the former, how were the samples chosen for the current study, since the group sizes are considerably smaller? This information would be important for comparing the data in this paper to those for myometrial tissue in the previous paper.

2. There is confusing terminology between inflammation and infection, which are entirely distinct processes. The authors place special emphasis on the importance of the data from the ‘infection’ group. This group needs to be strictly defined. The only reference is to ‘pyrexia’ and this is very tenuous. In the “Presence of inflammation” section, they describe their comparisons as “women with uterine inflammation” and “women with no inflammation.” Yet the very crux of the rationale for this study (first paragraph of the Background section) is that all labour, term or preterm, infected or non-infected, is associated with an inflammatory process, the effects of which might be mediated by PGs. The reader needs to know the difference between the terms ‘infection’ and ‘inflammation.’ This is of particular importance in the “Influence of inflammation….” Section of the results.

3. In the methodology section, there is no attempt to justify the
immunohistochemistry technique as quantitative. Indeed the difference between ‘colour development’ with some antibodies more so than others may be due to factors (Ab affinity, for target or detector, etc) completely unrelated to concentrations of target protein present. Even for the same antibodies, there have been no description of attempts to validate anything except a grossly qualitative assessment. Thus, the use of quantitative terms such as “weak”, “intermediate” and “intense” throughout the “immunolocalization” sections of the results is perhaps inappropriate without further justification/validation. This issue is compounded by what appears to be a discrepancy between the discussion (the labeling of panels i-iv) in the ‘immunolocalization – gestational membranes’ section of the results and the actual Figure 6.

4. There should be more detail provided in the “Data analysis” section regarding the statistical analyses performed. To this non-expert, it is not clear why a correlation coefficient was used to assess the ‘continuous clinical variables’. Did these analyses use individual data or group data and were all patients used in the analyses? If the latter, wouldn’t ANOVA be more appropriate. In addition, using Student t tests for pair-wise comparisons of all the subgroups would lead to a large number of comparisons. Were corrections made for this to avoid type 1 statistical errors?

In addition, this reviewer would suggest discretionary revisions as follows:

1. Figure 1 appears somewhat ‘cluttered.’ It would be improved and more helpful to the reader if it were designed as a graphic similar to Figure 1 of their prior publication (reference 13).

2. In the final paragraph of the ‘Conclusions’ section, it is unclear what the authors are suggesting. Do they not believe that the ‘inflammatory changes’ accompanying normal parturition are ‘physiological?’ Perhaps this is an extension of the lack of clarity between the terms ‘inflammation’ and ‘infection.’ Are they suggesting that, if chosen properly, ‘appropriate’ tocolytics should be used in the face of intrauterine infection? Or did the ‘appropriate pharmacological intervention’ refer to antibiotics and labour induction in the case of infection?

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.