Author’s response to reviews

Title: Identification of a Myometrial Molecular Profile for Dystocic Labor

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Version: 2 Date: 19 September 2011

Author’s response to reviews: see over
Dear Doctors,

Please find attached our manuscript “Identification of a Myometrial Molecular Profile for Dystocic Labor” We have addressed the reviewers comments as outlined below. We have also addressed the editorial concerns outlined in the initial response.

We look forward to hearing your response

Kind regards

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Minor essential revisions:

*Page 11, second paragraph, line 4; the use of the word “inducation”. It's a word I'm not familiar with.*

This was a typographical error and has been corrected.

*Page 13, second paragraph, line 9; “dytocic”, should be dystocic*

This has been corrected.

*In references: Ref 6 and 11 is the same article.*

Thank you, this has been corrected.

Major Compulsory Revisions:

1. *The main limitation of this study is a small number of samples analyzed. It is especially important in view of a very large number of comparisons maderesulting in substantial false positive rate. This is a common problem in high throughput gene expression profiling. This weakness could be address by external validation. The methods section does not state if the results were deposited in one of data repositories. If they were, this would enhance contribution to knowledge on genomics of pregnancy labor and dystocia, allowing for metaanalysis of multiple studies and external validation of presented findings.*

We agree with this point and have deposited the data in the Gene Expression Omnibus as outlined in the text.

2. *Other limitations of this study relate to sampling of myometrium. The methods section does not state if the decidua was included in the samples. This should be clarified to allow interpretation of the findings.*

Decidua was removed, this has been clarified in the methods section.

3. *The lower segment samples have been shown to have a different transcriptomic profile than fundus of the uterus and thus the findings may represent a part of the mechanism of dystocia.*

We take the reviewers point, and have included this in the discussion. We did not feel it was ethical to take a fundal biopsy from a nulliparous patient in labour, as this could complicate future pregnancies increasing the risk of uterine rupture.

4. *Additionally, samples of lower segment in labor dystocia and in the second stage of labor, after complete cervical dilatation and effacement occurred,*
may not be comparable. A discussion of those points would enhance the manuscript.

We feel this is unlikely, as a general surgical principle we aim to perform a “high” transverse uterine incision during cesarean section at full dilatation. All full dilatation cesareans were performed by the same surgeon. In addition all samples were obtained from the upper margin of the hysterotomy.

5. Were the changes in gene expression confirmed by PCR? There are no significant differences noted on the m/s in either the figures or the legend or the text.

Figure 4 shows changes in four genes, as the sample number is small these are not statistically significant but they do confirm the microarray findings.

6. Please comment in the discussion on the issue that the women in the “non dystocia” group were all at 10cm of cervical dilatation. The “lower segment” biopsy in these women is likely to have been composed of more cervix than the lower segment biopsy in those in earlier labour, which will have been composed of a higher proportion of muscle tissue - this is inevitable as labor progresses.

See comment 4 above.

7. Please justify the use of a t test to compare PCR data - were they normally distributed.

We did not use a t-test to compare PCR data, we used a t-test to identify differentially expressed genes.