Reviewer's report

**Title:** Quantifying circulating hypoxia-induced RNA transcripts in maternal blood to determine in utero fetal hypoxic status

**Version: 1 Date:** 13 August 2013

**Reviewer:** Zhice Xu

Reviewer's report:

In this study, the authors quantified mRNAs from the tissues and maternal blood using microarray and RT-PCR. They found altered expression of hypoxia-induced genes in maternal blood correlates with degree of fetal hypoxia/acidaemia. It is an interesting and explorative research to measure mRNA in maternal blood for predicting degree of fetal problems in utero. It might provide a novel non-invasive approach potential helpful to clinical application.

However, the data in this study is insufficient to support the conclusion and the following issues should be addressed:

1. All the results of this study only demonstrate that hypoxia changed mRNA of hypoxia-induced gene in maternal blood and placenta tissue. There is very limited data that can support the altered expression of hypoxia-induced genes in maternal blood was caused by fetal hypoxia and correlated with degree of fetal hypoxia/acidaemia.

2. Is the hypoxia-induced genes expression change a common response to hypoxia? Was the similar study conducted to test non-pregnant woman under conditions of hypoxia? Did the authors check oxygen or lactate levels in maternal blood? In addition, the authors should exclude other possible mRNA changes caused by maternal hypoxia itself.

3. Is there a co-relationship between maternal oxygen levels and the fetal hypoxia condition? Checking oxygen levels is convenient and affordable.

4. In Fig7, please explain how to generate a gene hypoxia score?

5. In qPCR analysis, the result should be representative of at least 3 individual experiments, as the data varies so much for each experiment.

6. 30/20 women have selected for this study. Is the sample size big enough?

7. In line 166, “200ng of tRNA”? Does this mean total RNA?

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**
I declare that I have no competing interests