Hypoxic inducible miRNAs in placental pathologies

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Preeclampsia and fetal growth restriction (FGR) are the most serious complications of pregnancy, both conditions stem from poor placental development, resulting in persistent hypoxic stress in the placenta. MicroRNAs (miRNA) are small non-coding RNAs that regulate gene expression through mRNA degradation and translational repression. Emerging evidence suggests that microRNAs (miRNA) are altered in preeclamptic and FGR placentas. Thus we hypothesized that hypoxia-inducible miRNAs are dysregulated in preeclamptic and FGR placentas. Previously we identified increased expression of the miRNAs miR210 and miR424 in the maternal circulation of pregnancies complicated by FGR. This study aimed to extend on these findings and aimed to examine the expression of hypoxia-inducible miRNAs and target gene expression in placental tissue collected from 1) preeclamptic and 2) FGR pregnancies. We also aimed to determine whether culturing trophoblast (isolated from the placenta) under hypoxic (1% oxygen) *versus* normoxic (8% oxygen) conditions, or whether silencing hypoxia inducible factor 1α (HIF1α) altered expression in human trophoblast.

We detected significantly elevated expression of miR210 in preeclamptic placenta tissue from both term and preterm tissue. In addition we observed significantly increased miR210 expression preterm FGR placentas, but not term. Furthermore miR424 was significantly increased in placentas complicated with preterm preeclampsia, but not term. Expression of miR210 was significantly increased in primary trophoblasts cultured under hypoxia (around 5-fold). However silencing HIF1α had no effect on the increase in miR210 expression.

These data provide support for a role of the microRNA miR210 in placental pathologies associated with hypoxia (preeclampsia and FGR). However expression of miR210 does not appear to be regulated by the hypoxic transcription factor HIF1α. These data extend our understanding of hypoxia inducible miRNAs in the pathophysiology of placental dysfunction and may provide further targets for diagnostics and treatment for preeclampsia and FGR.