candidate for examining genetic perturbations in gravidae with pre-eclampsia and commonly found co-morbidities such as diabetes.

We previously investigated global placental gene expression among diabetic gravidae, by applying whole transcriptome RNA sequencing (RNA-Seq) and robust computational analysis and found novel changes in placental gene expression by virtue of maternal diabetic status. In this current study we examined a clinically relevant cohort of both diabetic and non diabetic gravidae with the aim of determining placental gene expression changes specific for frequently co-morbid, hypertensive disorders of pregnancies as compared to controls.

STUDY DESIGN: Whole transcriptome sequencing was undertaken with extensively clinically phenotyped, population-based subject placental samples (n=29) on the HiSeq (Illumina), rendering over 150 million reads/sample. RNA Seq computational analysis was used to identify significant placental gene expression differences among our cohort. Two independent, computational platforms (edgeR and DESeq2) were used to verify differential gene expression.

RESULTS: Significant placental gene expression differences were noted in the gravidae with pre-eclampsia as compared to controls (FDR <0.05). Additionally, significant differential gene expression was noted in gravidae with diabetes (both GDM and Type II) and pre-eclampsia when compared to those that had neither, after controlling for subjects with only diabetes or pre-eclampsia (FDR<0.05). Summary data are projected as a heat map (Figure) where values are log2 transformed read counts that have been quantile normalized. Subsequent annotation following control for multiple comparisons revealed significant differences in 782 genes mapping to multiple pathways (p<10-6).

CONCLUSION: Novel placental gene expression differences were seen when stratified by pre-eclampsia and diabetes status. This work in a large population-based cohort further emphasizes the synergistic nature of these conditions, and reveals underlying placental gene pathways which may drive maternal comorbidity.

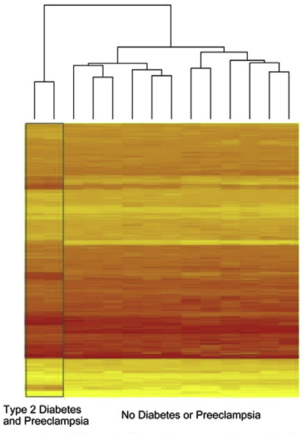

Figure 1. Placental gene expression differs significantly in gravidae with diabetes and pre-eclampsia as compared to controls. Significant differences in expression were noted in 782 genes (FDR<0.05) when comparing gravidae with both diabetes and pre-eclampsia to those without, after controlling for individuals with only diabetes or pre-eclampsia.

185 Serelaxin improves endothelial dysfunction and uterine artery resistance in response to placental ischemia during pregnancy

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OBJECTIVE: Examine the effect of Serelaxin in improving endothelial function and reducing uterine artery resistance index in response to placental ischemia.

STUDY DESIGN: On day 14 of gestation, Sprague Dawley rats entered the RUPP, RUPP+Relaxin or Normal pregnant (NP) control groups. Pregnant rats entering the RUPP and RUPP+Relaxin groups underwent the application of a constrictive silver clip (0.203 mm) to the aorta superior to the iliac bifurcation and ovarian clips (0.100 mm) bilateral uterine arcades at the ovarian ends. Those in the RUPP+Relaxin group received a Serelaxin mini-osmotic pump. Carotid catheters were inserted on GD18. MAP, blood and tissues were collected on GD19.

RESULTS: MAP in normal pregnant (NP) rats (n=5) was 106+5, 128+3 in RUPP rats (n=10) and 110+3 mmHg in RUPP+Serelaxin (n=10), p<0.05. UARI was 0.66+0.01 in RUPP rats (n=6), but was improved to 0.59+0.02 in RUPP+Serelaxin (n=4), p<0.05. Circulating nitrate-nitrite, measured by ELISA, was 16.0+2.4 in RUPP rats (n=9), which increased to 25.4+2.5 μM in RUPP+Serelaxin (n=6), p<0.05. We established that PPET-1 expression increases in RUPP aortas, kidneys and placentas by 20, 3 and 22 fold respectively as compare to NP. Serelaxin reduced PPET-1 expression in aorta, kidneys and placentas by 5, 2 and 3.72 fold as compare to RUPP.

CONCLUSION: Serelaxin improves MAP, UARI and nitric oxide bioavailability, and decreases the expression of PPET-1 in placental, renal cortex and aortic tissue. These data suggest an important role for relaxin in maintaining normal blood pressure and vascular compliance during pregnancy which would be helpful to maintain maternal health and prolong pregnancy in the face of placental ischemia.

186 Sequential angiogenic factor estimation, adverse perinatal outcomes and pregnancy duration among patients admitted for evaluation of preeclampsia

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OBJECTIVE: Angiogenic factors correlate with adverse outcomes when measured in women with suspected preeclampsia in third trimester. No data exists evaluating their sequential levels among admitted patients.

STUDY DESIGN: This was an observational cohort study among women with singleton pregnancies admitted for evaluation of pre-eclampsia <37 weeks gestation in a tertiary hospital in Boston. Plasma samples were collected upon admission and every day for the first three days and then weekly till delivery. Maternal demographics, hospital course, mode of delivery, diagnosis of hypertensive disorder and adverse maternal and neonatal outcomes were collected from patient's charts. Angiogenic factors (sFlt1 and PlGF) were measured on automated platform.

RESULTS: During the study period 100 women were enrolled and 43 had adverse outcomes. Women with adverse outcomes had higher sFlt1 and sFlt1/PlGF ratio on admission and continued to have an increase in levels throughout hospital course. The median (25th-75th) sFlt1/PlGF ratio among patients with adverse outcomes was 205.9 (72.5, 453.1) versus 47.5 (9.7, 87.0) among women without adverse outcomes (P<0.001). The median (25th-75th) absolute change per day in sFlt1 levels (pg/ml) was 491.0 (120.3, 1587.2) among women with adverse outcomes versus 81.3 (-177.9, 449.0) among women without adverse outcomes (P=0.01). Similarly the absolute change per day for sFlt1/PlGF ratio was 15.1 (1.8, 58.1) versus 2.7 (-0.6, 8,3) among the two groups (P=0.004). The mean