40 MATERNAL SERUM BIOMARKERS TO DETECT SPONTANEOUS PRETERM BIRTH AMONG WOMEN IN PRETERM LABOR PETER ROBILIO[1], JANE HITTI[1], JODI LAPIDUS[2], XINFANG LU[3], LEONARDO PEREIRA[2], MICHAEL GRAVETT[1], SRINIVASA NAGALLA[3], [1]University of Washington, Seattle, Washington, [2]Oregon Health & Science University, Portland, Oregon, [3]ProteoGenix, Inc., Beaverton, Oregon

OBJECTIVE: To identify potential serum biomarkers to predict spontaneous preterm birth (SPTB) from women in preterm labor by a systematic analysis of the maternal serum proteome.

STUDY DESIGN: This is a secondary analysis of archived serum samples collected prospectively from 138 women in spontaneous preterm labor at 20-34 weeks gestation at the University of Washington. SPTB was defined as spontaneous delivery < 34 weeks. Women diagnosed with intra-amniotic infection were excluded. Sera were immunodepleted for high abundance proteins and analyzed using fluorescence 2D gel analysis, multidimensional liquid chromatography tandem mass spectrometry (2D-LC-MS/MS), and label-free quantification (spectral counting). Pair-wise comparison was performed using ÷2 goodness-of-fit tests. Statistical significance was determined after adjusting for multiple comparisons. Immunodetection was used to confirm potential candidate biomarkers.

RESULTS: Of 138 subjects, 59 (43%) delivered at < 34 weeks (SPTB), while 79 (57%) subjects delivered at term (PTL, term group). There were no significant differences in demographic or reproductive factors between SPTB and PTL term groups. A total of 369 unique serum proteins were identified for label-free quantification. Twenty six proteins were differentially expressed ($p<0.05$) between PTL and SPTB samples. The majority of these proteins are produced in the placenta or decidua and included immunoregulatory, transport, and extracellular matrix proteins.

CONCLUSION: Proteomic analysis identified multiple maternal serum biomarkers that accurately discriminated SPTB from labor without delivery. This may facilitate diagnosis of women in preterm labor destined for delivery from those in false labor and lead to targeted early therapy.

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41 ASSOCIATION OF A SINGLE NUCLEOTIDE POLYMORPHISM AT THE -670 SITE OF THE MATERNAL FAS GENE AND INTRAUTERINE GROWTH RESTRICTION ROYLAND ROBINSON, CHAUR-DONG HSU, ALLYSON CHESEBRO, JOHN NGUYEN, LANCE PARTON, New York Medical College-Westchester Medical Center, Valhalla, New York

OBJECTIVE: The relationship between apoptosis in the maternal/placental interphase and IUGR has been previously reported. The role of Fas gene polymorphisms in IUGR has not been previously reported. In this study, we sought to determine the polymorphism at the -670 site of the Fas gene in pregnant women with and without IUGR.

STUDY DESIGN: Twenty-seven IUGR patients defined as growth percentile less than the 10th percentile and dated by early sonograms or ACOG dating standards and 50 patients with normal uncomplicated pregnancies were studied. DNA was extracted from maternal buccal smears and polymorphism of the DNA samples were determined by real time PCR using specific taqman probes. Maternal SNPs for the -671 site were analyzed. The demographic data was tested for statistical significance by use of the t-test. The genotype data was analyzed by Chi-square testing. A p value <0.05 was considered statistically significant.

RESULTS: There were no differences with respect to maternal age, race or parity between the IUGR and control patients. IUGR patients expressed significantly more GG genotypes (0.41) and less AA genotypes (0.18) than the controls, with GG (0.14) and AA (0.32), [p value =0.028]. The allele frequencies for the IUGR patients were G: 0.62 and A: 0.38 and for the controls were G:0.41 and A:0.59.

CONCLUSION: This study suggests that single nucleotide polymorphisms in the maternal Fas gene may play a significant role in the development of IUGR. In our study, the IUGR patients expressed significantly more GG Polymorphism at the -670 site on the Fas gene, than those without IUGR. Homozygosity for the G polymorphism at the -670 site may reflect less Fas expression, less apoptosis and increased cytotoxicity of maternal immune cells. Consequently this may lead to more placental apoptosis in pregnancy complicated by IUGR. .

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42 TRANS-ABDOMINAL UTERINE ELECTROMYOGRAPHY (EMG) VS. CLINICAL PARAMETERS AS PREDICTORS OF PRETERM DELIVERY SANGEETA JAIN[1], WILLIAM MANER[1], LYNETTE MACKAY[2], GARY D.V. HANKINS[3], ROBERT GARFIELD[4], [1]University of Texas Medical Branch, Obstetrics & Gynecology, Galveston, Texas, [2]University of Texas Medical Branch at Galveston, Obstetrics and Gynecology, Galveston, Texas, [3]University of Texas Medical Branch at Galveston, Department of Obstetrics and Gynecology, Galveston, Texas, [4]University of Texas Medical Branch, Obstetrics and Gynecology, Galveston, Texas

OBJECTIVE: EMG correlates strongly with strength of uterine contractions & can predict true labor. Cervical dilation and contraction frequency are not good predictors of true preterm labor (PTL). Our aim was to compare EMG to clinical parameters in predicting delivery time in PTL.

STUDY DESIGN: EMG was recorded from patients (n=16) with PTL. Data sampling was set at 100Hz, with analog & digital band-pass filtering (0.3 to 1.0 Hz - uterine specific electrical frequency range). Patients were admitted if they had regular uterine contractions accompanied by cervical change. Patients able to give consent, singleton pregnancy, no fetal anomaly, no obstetrical/ medical indication for urgent delivery, were included. Time from EMG measurement to delivery (MTD) was recorded. Maternal demographic data was recorded.Frequency of contractions (FC), estimated using Toco, cervical dilation (CD), and effacement (CE) at admission were noted. EMG signals were analyzed using power spectrum analysis (PDS) on whole records (EMG1) and using the burst-by-burst method (EMG2) to find frequency at which dominant power peaks occurred in the uterine electrical spectrum. Mean values were compared between patients delivered < 6 days (group 1, n=8) vs. those who did not (group 2, n=8) using Student's t-test. Correlation analysis was performed on using Pearson product moment. P value < 0.05 was significant.

RESULTS: The patients in group 1 and 2 were comparable in age & mean gestational age. EMG 2 variable (PDS peak frequency) correlated well with MTD ($p<0.01$, $R=0.996$). The PDS analysis showed power peaks with higher electrical frequencies in group 1 than 2 ($p=0.02$). Though there was correlation between CD and MTD, there was no difference in the mean CD between the 2 groups. FC and CE showed poor correlation to MTD ($p=0.91$, $R=0.03$; $p=0.89$, $R=0.04$).

CONCLUSION: EMG is a better predictor of delivery time in PTL than clinical parameters. EMG is useful to monitor patients with potential PTL. The identification of true PTL could contribute to better treatments.

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43 RECURRENT PREGNANCY IS ASSOCIATED WITH VISCERAL ADIPOSITY AND INSULIN RESISTANCE, BUT NOT BETA-CELL DYSFUNCTION IN A RODENT MODEL FRANCINE H. EINSTEIN[1], LEWIS W. LO[1], RADHIKA H. MUZUMDAR[2], SIGAL FISHMAN[3], GIL ATZMON[3], NIR BARZILAI[3], [1]The Albert Einstein College of Medicine, Obstetrics & Gynecology and Women's Health, Bronx, New York, [2]Albert EInstein College of Medicine, Department of Pediatrics, Bronx, New York, [3]Albert Einstein College of Medicine, Department of Medicine, Bronx, New York

OBJECTIVE: To determine the effect of recurrent pregnancy on fat deposition, insulin resistance and pancreatic beta-cell function.

STUDY DESIGN: Chronically catheterized, unrestrained 10-month old Virgin (V; n=6) and Retired Breeder (RB; at least 9 pregnancies; n=6) Sprague Dawley rats were studied with two-step hyperglycemic clamps. A 25% dextrose solution was infused to raise plasma glucose to 11mM from 0-90 min and 18mM from 90-240 min. We examined AUC of the first-phase insulin release, second phase insulin release and used metabolic clearance of glucose (MCRg=GIR/plasma insulin) as an index of insulin sensitivity. Because insulin resistance is associated with a higher capacity for insulin secretion, we used prolonged maximal hyperglycemic stimulation as a tool to uncover functional defects in insulin secretion independent of insulin sensitivity.

RESULTS: RB were moderately heavier than V (317 ±18.4 vs 274.6 ±28.1g; $p<0.05$) and had twice as much visceral fat (7.0 ±1.0 vs 3.3 ±1.6g; $p<0.01$). RB had significantly decreased insulin sensitivity (MCRg in RB 9.0 ±1.1 vs V 17.6 ±4.0, $p<0.05$) and greater first phase (3.4 ±0.8 vs 1.6 ±0.7 ng/mL) and second phase insulin secretion (4.9 ±0.5 vs 2.0 ±0.3 ng/mL) compared to V ($p<0.01$). No beta-cell defect was seen with prolonged maximal glucose-stimulated insulin secretion (RB 15.9 ±5.3 vs V 5.2 ±1.1 ng/mL, $p<0.01$).

CONCLUSION: We show that recurrent pregnancy is associated with increased visceral adiposity, insulin resistance, and a compensatory hypersecretion of insulin in a rodent model. Thus, recurrent pregnancy may be a risk factor for increased visceral adiposity and metabolic syndrome, and the chronic demand for increased insulin secretion may confer additional risk for T2DM.

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