Hilton Pavilion, Reno Hilton

1 **METABOLOMICS IN PREMATURE LABOR: A NOVEL APPROACH TO IDENTIFY PATIENTS AT RISK FOR PRETERM DELIVERY** ROBERTO ROMERO[1], RICARDO GOMEZ[2], JYH KAE NIEN[1], BO HYUN YOON[3], R. LUO[4], CHRIS BEECHER[4], MOSHE MAZOR[5], [1]Perinatology Research Branch, NICHD, NIH, DHHS, Bethesda, Maryland, [2]CEDIP, Sotero del Rio Hospital, Puente Alto, Chile, Chile, [3]Seoul National University College of Medicine, Department of Obstetrics and Gynecology, Seoul, Korea, South Korea, [4]Metabolin, Inc., Biochemistry and Technology, Durham, North Carolina, [5]Soroka University Medical Center, Beer Sheva, Israel, Israel

OBJECTIVE: Biomarkers for preterm labor and delivery can be discovered through the analysis of the transcriptome (genomics) and protein composition (proteomics). Characterization of the global changes in low molecular weight compounds which constitute the "metabolic network" of cells (metabolome) is now possible by using "metabolomics". Metabolomic profiling has special advantages over genomics and proteomics since the metabolic network is downstream from gene expression and protein sythesis, and thus more closely reflects cell activity at a functional level. This study was conducted to determine if metabolomic profiling can identify women with preterm labor (with and without infection) at risk for preterm delivery.

STUDY DESIGN: The study included patients with premature contractions with intact membranes in the following groups: A) premature contractions without intraamniotic inflammation (IAI) who subsequently delivered at term (n = 16); B) premature contractions without IAI who delivered premature neonates (n = 19); and C) preterm labor/delivery with IAI (n = 20). Amniotic fluid metabolic profiling was performed by combining chemical separation (with gas and liquid chromatography) and mass spectrometry. Compounds were identified by using authentic standards. The data were analyzed using Random Forest and Discriminant Analysis.

RESULTS: Metabolomic profiling was able to identify patients as belonging to the correct clinical group with a 96.3% precision (53/55); 15 of 16 patients with premature contractions who delivered at term (group 1) were correctly classified; all patients with preterm labor without infection and inflammation who delivered preterm neonates were correctly clustered (19/19). Among patients with infection/inflammation, 19/20 were correctly classified.

CONCLUSION: Metabolic profiling can be used to assess the risk of preterm delivery in the presence or absence of infection/inflammation.

2 **DETECTION OF DOWN SYNDROME BY PROTEOMIC PROFILING OF MATERNAL SERUM** MARY D'ALTON[1], DAVID LUTHY[2], FERGAL MALONE[1], JACOB CANICK[3], MICHAEL GRAVETT[4], GERALYN LAMBERT-MESSERLIAN[3], MARK TOMLINSON[5], RON ROSENFELD[6], SRINAVASA NAGALLA[6], [1]Columbia University, Obstetrics & Gynecology, New York, New York, [2]Obstetrix Medical Group, Seattle, Washington, [3]Brown University, Pathology and Laboratory Medicine, Providence, Rhode Island, [4]Oregon Health & Science University, Obstetrics & Gynecology, Portland, Oregon, [5]Northwest Perinatal Associates, Portland, Oregon, [6]Oregon Health & Science University, Pediatrics, Portland, Oregon

OBJECTIVE: To identify sensitive and specific protein profiles in maternal serum for the prenatal detection of Down syndrome in the 1st and 2nd trimesters.

STUDY DESIGN: Maternal sera from 50 patients (25 in the 2nd trimester and 25 in the 1st trimester, range 11–20 weeks) with Down's affected pregnancies were matched for gestational age and fetal sex with maternal sera from 50 unaffected pregnancies. Proteomic profiling was performed on unblinded maternal sera by fluorescent 2-dimensional gel electrophoresis and MALDI-TOF mass spectrometry.

RESULTS: Proteomic profiling identified the differential expression of 6 proteins in Down's affected pregnancies that were differentially expressed in both the 1st and 2nd trimester. A proteomic profile utilizing these differentially expressed proteins correctly identified all 50 cases of Down syndrome, and in all cases distinguished them from unaffected controls in the matched pair samples. No control had a proteomic profile suggestive of Down syndrome. The presence of the differential protein expression between cases and controls in both 1st and 2nd trimester cases indicates the presence of common markers for Down syndrome across a broad range of gestational ages.

CONCLUSION: Differential expression of proteins in maternal serum detected by proteomic profiling detected Down syndrome with 100% sensitivity and specificity in both 1st and 2nd trimester unblinded specimens.

Supported by NIH 1U24DK5860, HD 38652, and by ProteoGenix, Inc.

3 **MINIMALLY INVASIVE MANAGEMENT OF RH ALLOIMMUNIZATION: CAN AMNIOTIC FLUID DELTAOD450 BE REPLACED BY DOPPLER STUDIES? A PROSPECTIVE MULTICENTER TRIAL** DICK OEPKES[1], GARETH SEAWARD[2], FRANK VANDENBUSSCHE[1], JOHN KINGDOM[2], RORY WINDRIM[2], JOSEPH BEYENE[3], HUMPHREY KANHAI[1], ARNE OHLSSON[3], GREG RYAN[2], FOR THE DIAMOND STUDY GROUP[1], [1]Leiden University Medical Center, Dept. of Obstetrics, Leiden, Netherlands, [2]Fetal Medicine Unit, Mount Sinai Hospital, Toronto, Ontario, Canada, [3]Dept. of Paediatrics, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, Canada

OBJECTIVE: In pregnancies complicated by red cell alloimmunization, the fetus may suffer from progressive hemolytic anemia, leading to hydrops and death if untreated. The standard management is to select at risk patients on the basis of obstetric history and maternal serum antibody levels. Evaluation is done by ultrasound for signs of hydrops, and serial amniocentesis for bilirubin (ΔOD450) values. Recently, middle cerebral artery (MCA) peak systolic velocity measurements have been reported to reliably predict fetal anemia. Our aim was to compare the performances of MCA Doppler and amniotic fluid ΔOD450.

STUDY DESIGN: Prospective, international multicenter study of a cohort of consecutive Rh-D, c, E and Fy^a alloimmunized pregnancies with titers of ≥ 64 and antigen-positive fetuses. Both tests were performed simultaneously in all patients, and compared with the "gold standard" of fetal or cord blood sampling (at birth) to assess the actual hemoglobin (Hgb). Abnormal ΔOD450 was defined as a value on Liley's chart in zone 2c or 3. Severe anemia was defined as Hgb of ≥ 5 SD below the mean for gestational age.

RESULTS: In a total of 164 pregnancies with 165 fetuses (one set of twins), 74 fetuses were found to be severely anemic. MCA Doppler correctly predicted severe anemia in 65/74 (88%, 95% confidence interval: 83-93), with a specificity of 82% (77-88), positive predictive value 80% (74-86), NPV 89% (85-94), likelihood ratio pos. 5.00 (3.18-7.90), LR neg. 0.15 (0.08-0.27). Amniotic fluid ΔOD450 had a sensitivity of 76% (69-82), specificity 77% (70-83), PPV 73% (66-80), NPV 80% (73-86), LR pos. 3.28 (2.21-4.88), LR neg. 0.32 (0.21-0.48).

CONCLUSION: MCA peak velocity measurement showed better test characteristics in the prediction of severe fetal anemia than traditional amniotic fluid ΔOD450 assessment. In addition, MCA Doppler is a noninvasive technique. This study shows that MCA Doppler can safely replace amniotic fluid ΔOD450 in the management of Rh-alloimmunized pregnancies.

4 **DEXAMETHASONE PREVENTS LONG-LASTING IMPAIRMENT FOLLOWING THE COMBINATION OF LIPOPOLYSACCHARIDE TREATMENT AND HYPOXIA–ISCHEMIA IN NEONATAL RATS** TOMOAKI IKEDA[1], KENICHI MISHIMA[2], NAOYA AOO[2], NOBUAKI EGASHIRA[2], KATSUNORI IWASAKI[2], MICHIHIRO FUJIWARA[2], TSUYOMU IKENOUE[1], [1]Miyazaki Medical College, Obstetrics and Gynecology, Miyazaki, Japan, [2]Fukuoka University, Physiology and Pharmacology, Fukuoka, Japan

OBJECTIVE: There are no established therapies to prevent or rescue perinatal infection- or inflammation-induced perinatal brain damage. We administered dexamethasone (DEX), a synthetic corticosteroid anti-inflammatory drug, to neonatal rats in a model of such damage induced by the combination of lipopolysaccharide (LPS) and hypoxia–ischemia (HI), which produces characteristic abnormalities both histologically and behaviorally.

STUDY DESIGN: Four hours after the injections of LPS (1 mg/kg, i.p.), 7-day-old Wistar rat pups were subjected to unilateral HI for 1 h according to Levine's procedure. Injections of 0.5 mg/kg of dexamethasone (DEX-treated group, n = 15) or saline (saline-treated group, n = 15) were given 4 h before HI. A sham-control group received neither LPS nor HI (n = 15). We chose rats of this age because their stage of brain maturation is similar to the human neonate. Over 7–16 weeks after treatment in each group, a choice reaction time (CRT) task was employed for assessment of attention processes, an eight-arm radial maze task was used to test short-term memory, and a water maze task was used to test long-term memory. At 19 weeks, the rats were euthanized, the brain was removed, sectioned coronally, and the volume of each part was measured.

RESULTS: The striatum, cortex, and hippocampus showed reductions in volume in the saline-treated group (42.7%, 49.2%, and 34.9% decreases compared with the sham controls, respectively), but this was not observed in the DEX-treated group. All learning and memory processes were impaired in the combination of LPS and HI treatment, but these deficits were almost completely prevented by DEX treatment, except for incorrect lever pressing in the CRT task.

CONCLUSION: Dexamethasone is a promising candidate for prevention against infection- and inflammation-induced perinatal brain damage, and it is widely used for patients with threatened premature delivery. Control of intrauterine infection needs to be considered, because corticosteroids are known to exacerbate such infections.