27 **REGULATOR OF G PROTEIN SIGNALING–2 MESSENGER RIBONUCLEIC ACID TEMPORAL EXPRESSION IN RAT MYOMETRIUM DURING PREGNANCY, INDUCED PRETERM LABOR AND POSTTERM GESTATION** VR SUAREZ[1], ES PARK[1], GDV HANKINS[1], MS SOLOFF[1], [1]University of Texas Medical Branch, Obstetrics & Gynecology, Galveston, TX

OBJECTIVE: To determine whether regulator of G-protein signaling-2 (RGS-2) expression changes during pregnancy, we examined RGS-2 mRNA levels in rat's myometrium during different gestational stages, induced preterm labor and postterm gestation. RGS proteins accelerate GTPase activity of activated G&alpha subunits. RGS proteins thereby negatively regulate responses to activators of G protein signaling, like uterotonic agents such as oxytocin and prostaglandins.

STUDY DESIGN: RGS-2 mRNA was analyzed by Northern blotting, using a full-length cDNA probe. Membranes were reprobed for the constitutively expressed L-19 mRNA for reference. Induction of preterm labor was done by administration of the progesterone antagonist onapristone on day 17 and pregnancy was prolonged by daily administration of progesterone starting on day 19.

RESULTS: RGS-2 mRNA was undetectable in rat myometrium on the first day of pregnancy, but rose sharply by day 5, around the time of implantation, and was maximal around day 10 (time of maximal uterine quiescence). RGS-2 mRNA expression remained elevated almost until the day of parturition, when it fell almost back to basal levels. RGS-2 mRNA levels were low on day 22 whether or not the rats were in labor. Concentrations were low on the first postpartum day, but increased subsequently. Onapristone caused preterm labor on day 19 (instead of day 22), and there was a premature fall in RGS-2 mRNA to levels comparable to those of non-treated rats on day 22. In contrast, progesterone treatment prolonged pregnancy beyond day 25 and resulted in a blunting of the fall in RGS2 mRNA levels.

CONCLUSION: These data suggest that changes in RGS-2 mRNA expression in the myometrium is related to the timing of parturition and that RGS-2 expression may dampen the responsiveness of the uterus to contractile agents, and keep it quiescent until near the end of pregnancy.

28 **PREDICTION OF NEONATAL DEATH FROM PULMONARY HYPOPLASIA BY FETAL PULMONARY DOPPLER AFTER MATERNAL HYPEROXYGENATION** RICHARD BROTH[1], DENNIS WOOD JR[2], JUHA RASANEN[3], JUAN CARLOS SABOGAL[4], STUART WEINER[2], VINCENZO BERGHELLA[2]; [1]Thomas Jefferson University, Maternal Fetal Medicine, Philadelphia, PA; [2]Thomas Jefferson University, Obstetrics and Gynecology, Philadelphia, PA; [3]University of Oulu, Obstetrics and Gynecology, Oulu; [4]Thomas Jefferson University, Obstetrics and Gynecology

OBJECTIVE: To assess the predictive accuracy for death from pulmonary hypoplasia of fetal pulmonary Doppler changes after maternal hyperoxygenation.

STUDY DESIGN: A cohort of women carrying fetuses at ≥30 weeks gestation with congenital anomalies which predispose to pulmonary hypoplasia (congenital diaphragmatic hernia, skeletal dysplasia, congenital cystic adenomatous malformation, etc.) were offered participation into the study. The Doppler flow of the first bifurcation of the branch pulmonary artery was measured before and after administration of 60% humidified oxygen (hyperoxygenation test). A decrease of 30% in the pulsatility index (PI) value was considered a reactive test. Primary outcome was neonatal death caused by pulmonary hypoplasia (ND).

RESULTS: 21 pregnancies met criteria for inclusion and agreed to participate in the study. Of the 10 fetuses that did not have a reactive hyperoxygenation test, 8 (80%) had ND. Of the 11 that had a reactive hyperoxygenation test, only one (9%) had ND. Sensitivity, specificity, positive predictive value, and negative predicitive value were 89%, 85%, 80%, and 91%, respectively with a relative risk of 8.8 (95% CI 1.3-58.0).

CONCLUSION: Fetuses at risk for pulmonary hypoplasia with a nonreactive hyperoxygenation test have an 80% chance of dying from this condition in the neonatal period, while those with a reactive hyperoxygenation test have a 91% chance of neonatal survival. This information may be valuable for counseling and management of these pregnancies.

29 **MONOCYTE CHEMOTACTIC PROTEIN-1 EXPRESSION IS INCREASED IN SPONTANEOUS TERM AND PRETERM LABOR** MICHAEL ESPLIN[1], STEVEN HAMBLIN[1], BARDETT FAUSETT[1], BOB SILVER[2], WARE BRANCH[1], ELI ADASHI[1]; [1]University of Utah, Obstetrics and Gynecology, Salt Lake City, UT; [2]University of Utah, Obstetrics and Gynecology, Salt Lake City, UT

OBJECTIVE: Despite decades of research, the fundamental mechanisms of normal and abnormal labor remain unknown. We, thus, undertook to use new molecular technologies to systematically and comprehensively analyze gene expression during labor.

STUDY DESIGN: cDNA micro-array was used to compare the gene expression patterns of quiescent and laboring lower uterine segments. Several genes expressed during labor were further characterized in various gestational tissues using RT-PCR, Northern blot, ELISA, in-situ hybridization, and immunohistochemistry. One highly up-regulated gene, Monocyte Chemotactic Protein-1 (MCP-1), a potent chemo-attractant and activator of monocytes and macrophages, was characterized in murine models of labor, including a null-mutant mouse for the MCP-1 gene.

RESULTS: We screened > 15,000 micro-arrayed cDNA sequences. Of these, 30 cDNAs were found to be consistently up-regulated during labor. The labor-selective regulation of MCP-1 was confirmed in myometrium using RT-PCR (5-10 fold increase; $P = .001$), in-situ hybridization and immunohistochemistry. Co-localization studies demonstrated MCP-1 expression primarily in smooth muscle of the myometrium. MCP-1 expression was increased in the laboring chorion (2 fold increase; $P = .01$). Amniotic fluid MCP-1 immunoreactivity was increased in patients with preterm delivery compared to controls (3 fold increase; $P = .001$). The length of gestation and the litter size of MCP-1-deficient mice were similar to controls.

CONCLUSION: We have used high throughput techniques to identify and characterize a group of genes involved in labor. MCP-1 expression is significantly increased in myometrium, chorion and amniotic fluid during term labor in the human. Further elucidation of the role of this inflammatory chemokine in labor may improve our understanding of labor physiology and lead to more effective treatments for abnormal labor.

30 **THE EFFECT OF FETAL ACIDEMIA ON FETAL-PLACENTAL VASCULAR TONE AND PRODUCTION OF THE INFLAMMATORY CYTOKINES IL-6 AND TNF-α** BRIAN PIERCE[1], PETER NAPOLITANO[1], LISA PIERCE[1], CHRISTINE KOVAC[1], RODERICK HUME JR[1], BYRON CALHOUN[1], [1]Madigan Army Medical Center, OBGYN, Tacoma, WA

OBJECTIVE: Inflammatory cytokines have been implicated in the pathogenesis of a variety of fetal conditions such as the fetal inflammatory response syndrome and cerebral palsy. We have previously shown elevated cytokines under hypoperfused and hyperoxic placental conditions, implicating both as contributors to fetal morbidity. Our goal is to determine whether the increased rate of cerebral palsy observed following fetal acidemia is caused in part by the inflammatory cytokines IL-6 and TNF-α.

STUDY DESIGN: Using an ex-vivo placental perfusion model, the maternal and fetal circulation of two cotyledons from five human placentas were perfused for four hours. The fetal circulation of one cotyledon was perfused with acidemic (pH = 6.90) Hanks Balanced Salt Solution (HBSS) while the fetal circulation of the other cotyledon was perfused with physiologic (pH = 7.35) HBSS. Fetal venous effluents were collected hourly and IL-6 and TNF-α concentrations were determined by ELISA. Cotyledon perfusion pressures were recorded every 10 minutes.

RESULTS: Fetal-placental vascular perfusion pressure was consistently reduced from baseline under acidemic, but not physiologic, conditions with statistical significance achieved from 20 minutes onward ($P < .05$). IL-6 and TNF-α increased exponentially over time for both conditions ($P < .05$). There was no difference in cytokine production when comparing the acidemic to physiologic conditions ($P > .05$).

CONCLUSION: Fetal-placental vasodilation may be a compensatory mechanism to improve acidemic conditions. Unlike fetal hypoperfusion or fetal hyperoxia, fetal acidemia does not result in elevated placental cytokines. This suggests that the increased rate of cerebral palsy observed in acidemic fetuses is not due to placental production of the inflammatory cytokines IL-6 and TNF-α.