preterm (-) IAI and term groups (P<0.001); **3)** TNXB levels were significantly increased in (-) IAI PTB with intact membranes, when compared to (-) IAI PTB with PPROM (P=0.003); **4)** Amnion, chorion, villous trophoblast, uterine myocytes and cervical fibroblasts constitutively express TNXB.

CONCLUSION: TNXB is expressed by human reproductive tissues and is upregulated in IAI. Increased TNXB levels in (-) IAI PTB with intact membranes suggests that in this preterm birth phenotype, cervical change rather than PPROM may be the predominant factor.

25 Effect of sildenafil citrate on fetal central hemodynamics and placental volume blood flow during hypoxemia in a chronic sheep model

Leena Alanne[1], Jonna Hoffren[2], Mervi Haapsamo[3], Juulia Junno[4], Heikki Huhta[5], Tiina Erkinaro[5], Amarnath Bhide[6], Ganesh Acharya[7], Juha Räsänen[8]

[1]Kuopio University Hospital, Kuopio, Finland, [2]University of Eastern Finland, Kuopio, Finland, [3]Lapland Central Hospital, Rovaniemi, Finland, [4]Kainuu Social and Health Care Joint Authority, Kajaani, Finland, [5]Oulu University Hospital, Oulu, Finland, [6]St George's University Hospital, London, United Kingdom, [7]The Artic University of Norway and University Hospital of Northern Norway, Tromso, Norway, [8]Helsinki University Hospital, Helsinki, Finland

OBJECTIVE: In early onset severe placental insufficiency with fetal growth restriction, maternal sildenafil therapy has been introduced as a new treatment option to safely prolong pregnancy and improve neonatal outcome. We hypothesized that sildenafil would improve placental volume blood flow without any detrimental effects on fetal central hemodynamics during prolonged hypoxemia in a sheep model.

STUDY DESIGN: A total of 24 pregnant sheep underwent surgery approximately 122 days of gestation (term 145 days) for fetal instrumentation. After a 5-day recovery period, experiments were performed under general anesthesia. Fetal carotid artery blood pressure and blood gas values were monitored. By pulsed Doppler ultrasonography, fetal right and left ventricular cardiac outputs, right pulmonary artery pulsatility index values and placental volume blood flows were obtained. After baseline data collection, maternal and fetal hypoxemia were induced. Hypoxemia phase data were collected after 30 minutes hypoxemia. Thereafter, in 12 fetuses sildenafil infusion was started and 12 fetuses served as controls receiving saline infusion. Data were collected 30 and 90 minutes after infusion was started. Then maternal oxygenation was returned back to baseline, while infusion was continued and recovery phase data were collected 30 minutes after maternal normoxemia.

RESULTS: At the baseline fetuses in sildenafil group had lower pH levels ($p<0,0465$). Sildenafil did not improve the placental blood volume, cardiac output or pulmonary flow. There was a significant reduction in pO2 ($p<0,0012$) and in mean arterial pressure ($p<0,0494$) in fetuses treated by sildenafil in a recovery period.

CONCLUSION: Fetuses with sildenafil infusion had lower pO2 and carotid artery mean arterial pressure during recovery phase. This indicates that sildenafil can have potentially detrimental effects on fetal cardiovascular hemodynamics.

Fetal Invasive hemodynamic measurements, arterial blood gas analyses and doppler measurements

Variable	C=ControlS=Sildenafil	Baseline Mean(SD)	30 min Mean(SD)	1 h Mean(SD)	5 h Mean(SD)	2.5 h Mean(SD)
MAP (mmHg)	C	49 (10)	43 (11)	47 (15)	46 (10)	50 (11)
	S	45 (10)	43 (7)	40 (9)	35 (3)	36 (4)*
pH	C	7,31 (0,05)	7,30 (0,03)	7,21 (0,11)	7,15 (0,12	7,18 (0,06)
	S	7,25 (0,04)*	7,25 (0,05)	7,19 (0,08)	7,06 (0,16)	7,09 (0,16)
PaO2 (mmHg)	C	2,8 (0,3)	1,6 (0,4)	1,5 (0,4)	1,5 (0,2)	2,8 (0,4)
	S	2,8 (0,8)	1,7 (0,2)	1,5 (0,3)	1,4 (0,5)	2,0 (0,4)*
LVCO ml/min	C	623 (202)	500 (116)	568 (111)	519 (135)	525 (159)
	S	561 (252)	502 (216)	470 (149)	386 (97)	398 (105)
RVCO ml/min	C	622 (170)	619 (228)	580 (211)	619 (192)	593 (158)
	S	688 (294)	651 (294)	678 (319)	623 (345)	622 (281)
Qplas ml/min	C	198 (80)	162 (98)	160 (83)	148 (58)	159 (33)
	S	205 (92)	180 (66)	132 (53)	120 (33)	136 (66)
Rpa PI	C	33 (52)	49 (29)	66 (29)	52 (27)	69 (57)
	S	17 (13)	44 (20)	51 (25)	50 (52)	52 (35)

26 Profiling of microbiota in second trimester amniotic fluid reveals a distinctive community present in the mid trimester and predictive of the placental microbiome at parturition

Derrick Chu[1], Chris Stewart[1], Maxim Seferovic[1], Melissa Suter[1], James Cox[2], Alex Vidaeff[1], Kjersti Aagaard[1]

[1]Baylor College of Medicine, Houston, TX, [2]University of Utah, Salt Lake City, UT

OBJECTIVE: Contrary to prevailing dogma, recent studies have indicated that the intrauterine environment may harbor commensal bacteria in the absence of adverse outcomes. We and others have profiled the microbiota associated with amniotic fluid and placenta of both preterm and healthy term pregnancies, but these observations have been mostly limited to the time of delivery. To determine if commensal bacteria could be detected earlier in gestation, we sought to profile the commensal microbiota associated with second trimester amniotic fluid samples obtained from genetic amniocentesis, and contrast it with the microbiota of other maternal body sites.

STUDY DESIGN: This was a prospective cohort study (n=95) that included amniotic fluid obtained from a genetic amniocentesis (gestational ages 16-20 wks). DNA from 500 ul of amniotic fluid was extracted (MoBio) and analyzed by 16S rRNA gene sequencing on the MiSeq platform (V4). Taxa identified in a negative kit control processed in parallel were considered contamination and subsequently filtered from downstream analysis. Remaining taxa were compared to previously published data of maternal ante- and intrapartum samples comprising multiple body niches.

RESULTS: After stringent filtering, 1685465 high quality reads were assigned to 635 unique taxa across 95 amniotic fluid samples (μ reads/sample = 17741, σ=11902). Consistent with our previous observations of the placental microbiome, the most prevalent taxa (90/95, 94.7%) belonged to the *Escherichia*, with an average abundance of 15.5% when present (Fig. A). However, the overall community structure of the amniotic fluid microbiome remained distinct from other body sites but bore the greatest similarity to the placenta (Fig. B) and oral cavity and nares (Fig. C, p<0.001).

CONCLUSION: We provide evidence of a distinct microbial community within the amniotic fluid as early as the second trimester, providing further supporting evidence for a non-sterile *in utero* environment. Interestingly, many of the taxa of the AF microbiota in the mid trimester were shared with that of the placenta interrogated at delivery. Further studies are warranted to determine the mechanisms through which microbiota can colonize the intrauterine space and its on obstetrical outcomes and fetal development.

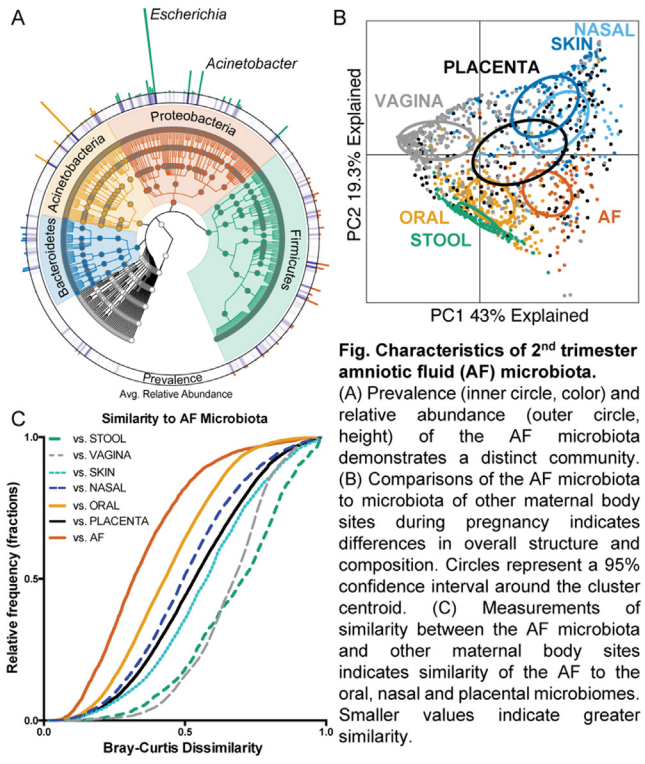

Fig. Characteristics of 2nd trimester amniotic fluid (AF) microbiota.
(A) Prevalence (inner circle, color) and relative abundance (outer circle, height) of the AF microbiota demonstrates a distinct community. (B) Comparisons of the AF microbiota to microbiota of other maternal body sites during pregnancy indicates differences in overall structure and composition. Circles represent a 95% confidence interval around the cluster centroid. (C) Measurements of similarity between the AF microbiota and other maternal body sites indicates similarity of the AF to the oral, nasal and placental microbiomes. Smaller values indicate greater similarity.

27 Single nucleotide polymorphisms in the oxytocin receptor and GRK6 are associated with oxytocin dosing requirements and labor outcomes

Chad A. Grotegut, Emily Ngan, Melanie E. Garrett, Allison E. Ashley-Koch, Geeta K. Swamy
Duke University Health System, Durham, NC

OBJECTIVE: Oxytocin is a potent uterotonic agent widely used for induction and augmentation of labor. Oxytocin has a narrow therapeutic index and the optimal dosing for any individual woman varies widely. The objective of this study was to determine if genetic variation in the oxytocin receptor gene (OXTR) or in the gene coding GRK6, which regulates desensitization of the OXTR, could explain differences in oxytocin dosing and labor outcomes among women being induced near term.

STUDY DESIGN: Pregnant women with a singleton gestation residing in Durham County, NC were prospectively enrolled. DNA was available from 482 women undergoing induction of labor at 36 weeks or greater. 18 haplotype tagging (ht) single nucleotide polymorphisms (SNPs) in the OXTR and 7 htSNPs in GRK6 were genotyped using TaqMan assays. Linear regression was used to examine the relationship between maternal genotype and maximal oxytocin infusion rate, total oxytocin dose received, and duration of labor. Logistic regression was used to test for association of maternal genotype with mode of delivery. For each outcome, backward selection techniques were utilized to control for important confounding variables and additive genetic models were employed. Race/ethnicity was included in all models due to differences in allele frequencies across populations and Bonferroni correction for multiple testing was used.

RESULTS: Five SNPs in the OXTR were significantly associated with maximal oxytocin infusion rate and two SNPs in the OXTR were associated with total oxytocin dose received. One SNP in the OXTR and two SNPs in GRK6 were associated with duration of labor, one of which met the multiple testing threshold (p=0.0014, rs2731664 [GRK6], mean duration of labor 17.7 hours vs. 20.2 hours vs. 23.5 hours for AA, AC and CC genotypes, respectively). Three SNPs, two in the OXTR and one in GRK6, were significantly associated with mode of delivery. (Table)

CONCLUSION: Variation in genes coding the OXTR and GRK6 are associated with the amount of oxytocin required, as well as the duration of labor and risk for cesarean delivery among women undergoing induction of labor near term. Pharmacogenomic approaches may potentially be utilized to improve labor outcomes among women undergoing induction of labor.

Table: Significant associations by outcome and selected OXTR or GRK6 genotype

Outcome	SNP (gene)	p-value (Odds ratio)	Genotype: Mean or Percent outcome
Maximal oxytocin infusion rate (mU/min)	rs1042778 (OXTR)	0.004	GG: 10.9 mU/min GT: 13.8 mU/min TT: 14.0 mU/min
	rs11706648 (OXTR)	0.021	AA: 12.7 mU/min AC: 14.0 mU/min CC: 16.4 mU/min
	rs4686301 (OXTR)	0.016	CC: 12.7 mU/min CT: 14.3 mU/min TT: 17.6 mU/min
Total oxytocin dose (mU)	rs1042778 (OXTR)	0.015	GG: 6,852 mU GT: 10,159 mU TT: 10,425 mU
	rs4686301 (OXTR)	0.034	CC: 8,961 mU CT: 10,874 mU TT: 11,426 mU
Time from start of induction to delivery (hours)	rs2731664 (GRK6)	0.001	AA: 17.7 hours AC: 20.2 hours CC: 23.5 hours
	rs2287694 (GRK6)	0.009	CC: no subjects CT: 26.2 hours TT: 19.7 hours
Cesarean delivery rate (%)	rs2139184 (OXTR)	0.023 (OR 0.55)	AA: 37.5% AC: 31.8% CC: 28.4%
	rs237888 (OXTR)	0.025 (OR 1.68)	CC: 21.3% CT: 26.4% TT: 33.3%
	rs2545796 (GRK6)	0.032 (OR 0.64)	CC: 35.2% CT: 28.1% TT: 29.5%

28 First trimester alcohol exposure alters placental perfusion and fetal oxygen availability affecting fetal growth and development in a non-human primate model

Jamie Lo, Matthias Schabel, Xiaojie Wang, Victoria Roberts, Kathleen Grant, Christopher Kroenke, Antonio Frias
Oregon Health & Science University, Portland, OR

OBJECTIVE: Prenatal alcohol exposure leads to impaired fetal growth, brain development, and stillbirth. The placenta likely contributes to these adverse outcomes, but the mechanisms and specific vasoactive effects of alcohol linking placental perfusion and oxygenation to impaired fetal development are not known. Recently, we developed MRI techniques in non-human primate models to estimate placental oxygen reserve by measurements of T_2^*, and perfusion using dynamic contrast enhanced (DCE) MRI. Our objective was to evaluate the adverse effects of first trimester alcohol exposure on placental outcomes and to characterize fetal brain development *in-vivo*.

STUDY DESIGN: Timed-pregnant Rhesus macaques (n=12) were divided into 2 groups: control (CON, n=6) and ethanol exposed (EE, n=6). Animals were given either 1.5g/kg/day of ethanol (equivalent to 6 drinks/day) or an isocaloric control fluid from preconception until gestational day 60 (G60, term is G168). All underwent Doppler ultrasound (D-US) followed by MRI consisting of