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

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**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

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**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 ($\mu$ reads/sample = 17741, $\sigma$=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.