



A and B, Intracellular bacteria in EVTs in placental basal plate. C and D, UPEC and Listeria invading and surviving intracellularly within EVTs in placental basal plate explants (HLA-G+, red).

15 The influence of prenatal smoking status on cervical cytokine distribution

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OBJECTIVE: Maternal tobacco use and cervical immune responsiveness are individually associated with PTB, and the interaction of tobacco use on cervical cytokines requires further study. Our primary aim is to determine whether prenatal smoking impacts cervical cytokine distribution.

STUDY DESIGN: This was a planned secondary analysis of a prospective, longitudinal multi-center trial, pregnant women with singleton gestation underwent cervicovaginal fluid (CVF) sampling during each trimester. Cytokines (IL-1a, IL-1b, IL-2, IL-6, IL-8, IL-10, TNFa) and CRP were measured using a multiplex beadlyte assay on a Luminex IS-100. At each timepoint, smoking status was collected via self report (survey) and validated by preset urine cotinine limits. Cytokine data were log transformed.

RESULTS: Eighty-one women underwent evaluation in the first trimester, 76 in the second and 69 in the third. Thirty-nine of the participants (48%) were smokers and self-report smoking status was strongly correlated with urine cotinine ($p = .68$). First trimester cervical IL-10 was significantly decreased ($p < .01$) in smoking women compared to those who did not admit to smoking (2.3 ± 1.2 pg/mL vs. 3.8 ± 2.1 pg/mL, respectfully). No significant differences were observed in other cytokine concentration of cervical mucus between smoking and nonsmoking women at any other gestational age.

CONCLUSION: Prenatal tobacco use decreases IL-10 concentration in cervical mucus potentially increasing susceptibility to pro-inflammatory mediators. Deregulation of this anti-inflammatory cytokine may alter cervical epithelial structure and immune responsive; potentially impacting cervical length and preterm birth risk.

16 Serum derived exosomes evaluated early in second trimester provide predictive biomarkers of risk for preterm birth before week 34

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OBJECTIVE: The purpose of this study was to confirm in an independent, blinded manner whether a proteomic differentiation exists in maternal blood-derived exosomes obtained from term and preterm patients early in the second trimester. Current methods indicate that circulating microparticles such as exosomes shed from tissue can serve as stable biomarker-harboring vehicles. Placental-derived exosomes freely circulate in high titer in maternal blood and reflect the status of the syncytiotrophoblast maternal-fetal interface. Previous work (Taylor et al., unpublished) has shown that subtle homeostatic changes can be reflected via a unique set of dysregulated exosome-associated proteins when pregnancy complications occur.

STUDY DESIGN: Frozen maternal serum samples (n=48) obtained between 15-17 weeks gestation were analyzed from asymptomatic women (avg. age 28) bearing live birth (excluded: multiple births; systemic disease; known fetal anomalies). Exosomes were isolated using gel filtration, with samples blinded to outcome; proteins were extracted and analyzed using an open proteomic LC-MS differential analysis between term (>37wks) and preterm cohorts (<34wks).

RESULTS: Among 213 proteins identified, a unique pattern was observed in serum derived exosomes isolated from asymptomatic patients that subsequently delivered preterm. Using an ANOVA assessment and rigorous reproducibility, accuracy, and confidence criteria, 21 proteins were characterized across two study phases differentiating the cohorts, with functional analysis implicating inflammatory and cell injury pathways.

CONCLUSION: A novel library of statistically valued exosomal biomarkers has been identified with expected clinical usefulness for the early identification of women at risk for preterm birth, as well as improved understanding of the underlying pathways leading to preterm birth. Priority markers are being further evaluated for commercial deployment in a small-plex assay.

17 Vaginal progesterone as maintenance treatment after an episode of preterm labor (PROMISE Study): a randomized, double blinded, placebo-controlled trial

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OBJECTIVE: To demonstrate if maintenance treatment with vaginal progesterone after an arrested preterm labor reduces the incidence of preterm delivery before 34.0 or 37.0 pregnancy weeks.

STUDY DESIGN: This was a prospective, randomized, double blind, multicenter clinical trial. 12 centers all over Spain were including women with single pregnancy and preterm labor successfully arrested, in whom decision of discharge was made, gestational age between 24.0-34.0 weeks and cervical length < 25mm. Women were randomly