influence the susceptibility. In genetic linkage analysis, we identified a linkage peak close to the C-X-C chemokine receptor type 3 (*CXCR3*) gene. CXCR3 is a transmembrane protein present on T cells, natural killer cells, macrophages and airway epithelial cells. In here, the objectives were to elucidate the role of *CXCR3* in singleton SPTB and to analyze the levels of CXCR3 and its ligands in the onset of delivery.
**METHODS:** The only common single nucleotide polymorphism (SNP) within *CXCR3* (rs2280964) was genotyped. The frequency of this SNP in SPTB cases and controls of the discovery and replication populations was compared. Family-based association test was performed. Samples from umbilical cord blood, placental tissue and fetal membranes were collected from preterm and term deliveries. The concentrations of CXCR3 ligands were measured from the cord blood and the expression of CXCR3 in preterm placentas was visualized by immunohistochemistry. RNA and proteins were extracted from the preterm and term placentas for quantitative PCR and Western analyses, respectively. The Mann-Whitney *U* or Kruskal-Wallis tests were used to study the association between the SNP and expression of CXCR3.
**RESULTS:** *CXCR3* SNP rs2280964 associated with SPTB in infants from families with multiple preterm births ($p$=0.009); family-based association test was also significant ($p$=0.007). The minor allele (A) had a protective role. By immunohistochemistry, CXCR3 was detected mostly in cytotrophoblasts, syncytiotrophoblasts and decidual and chorionic trophoblasts. Staining intensity of trophoblasts depended on the fetal rs2280964 allele, with A allele associating with weaker staining. Both at the mRNA and protein level, statistically significant increase in the expression levels of CXCR3 were observed in SPTB placentas. The concentration of CXCR3 ligand (CXCL9) increased in cord blood of SPTB infants, as well.
**CONCLUSIONS:** The genetic, immunohistochemical and quantitative analyses suggest the involvement of CXCR3 mediated signaling in the early onset of labor and preterm birth.

## T-084

**GWAS Identified Inflammatory Polymorphisms Do Not Improve Clinical Markers for Predicting Preterm Birth in an Antenatal Population.** Catherine P James,[1] Juliet Stevens,[1] Oleg Blyuss,[1] Argyro Syngelaki,[2] Kypros Nicolaides,[2] Alexey Zaikin,[1] Donald M Peebles.[1] *[1]Institute for Women's Health, University College London, London, United Kingdom; [2]Harris Birthright Research Centre for Fetal Medicine, King's College Hospital, London, United Kingdom.*
**INTRODUCTION:** The strongest predictive marker for PTB is preterm delivery in a previous pregnancy. These women are offered a different schedule of antenatal care, and may benefit from treatment with either progesterone or cervical cerclage. Identifying women in their first pregnancies who may benefit from these interventions is a pressing challenge.
GWAS studies with PTB as the primary outcome suggest a variety of single nucleotide polymorphisms (SNPs) in inflammatory genes may confer an increased risk of PTB. This study assesses models constructed from combinations of clinical data and TNF-α SNPs rs1800629, rs769178 and rs590368, MTRR SNP rs1801394 and CD74 SNP rs2569094. Although these SNPs individually have a small effect size, we hypothesized that combinations of SNPs, either alone or together with clinical history, may be useful to predict preterm birth.
**METHODS:** This is a retrospective case control study using blood collected (11-13 weeks' gestation) from women attending antenatal screening at King's College Hospital between 2006 and 2010. 50 women with PPROM (preterm prelabor rupture of the membranes) and 50 with sPTL (spontaneous preterm labor) were matched (smoking, ethnicity, BMI) with 300 term controls. SNPs rs1800629, rs2569094, rs590368, rs769178, rs1801394 were genotyped (Taqman, GENPROBE). Data were analyzed by regression analysis and performance of the resulting models was assessed using the Akaike information criterion.
**RESULTS:** Genotyping was successful in 100% (rs769178, rs1801394) and >99% (rs1800629, rs2569094, rs590368) samples. Allele distribution demonstrated Hardy-Weinburg equilibrium. Models with clinical features (ethnicity, BMI, smoking, mode of conception, previous obstetric history) as independent variables performed better to predict PPROM and sPTL than models with SNPs as independent variables (AIC 423.4 vs AIC 445.7 respectively). Including interaction and non-linear terms did not improve model performance, and introducing SNPs reduced the performance of the clinical model.
**CONCLUSIONS:** Polymorphisms identified by GWAS studies with PTB as the primary outcome may provide insight into the inflammatory pathogenesis of PTB, but they are not useful to predict PTB in clinical populations.

## T-085

**Correlation Between DEFB Copy Number and Serum hBD2 Expression Is Disrupted in Pregnancy and DEFB Copy Number Variation Is Not Associated With Preterm Birth.** Catherine P James,[1,2] Razan Abujaber,[3] Argyro Syngelaki,[4] Nigel Klein,[2] Mona Bajaj-Elliott,[2] Kypros Nicolaides,[4] Edward Hollox,[3] Donald M Peebles.[1] *[1]Institute for Women's Health, University College London, London, United Kingdom; [2]Institute of Child Health, University College London, London, United Kingdom; [3]Department of Genetics, University of Leicester, Leicester, United Kingdom; [4]Harris Birthright Research Centre for Fetal Medicine, King's College Hospital, London, United Kingdom.*
**INTRODUCTION:** Increased expression of antimicrobial peptides including human beta defensins (hBD) have been reported in the amniotic fluid and vaginal secretions of women who deliver preterm. We have previously shown these women have increased first trimester serum hBD. The gene encoding hBD2, DEFB4, is part of a cluster on chromosome 8 that is variable in copy number (CN). Increased serum hBD2 is associated with increased DEFB CN. We hypothesized that variation in DEFB CN will be associated with preterm birth.
**METHODS:** In a retrospective, case-control study, genomic DNA (n=378) and serum (n=140) were extracted from blood collected from White European women at 11–13 weeks' gestation attending King's College Hospital between March, 2006, and September, 2010. DEFB copy number was determined by paralogue ratio test. Serum hBD2 concentration was measured by ELISA. Data were analysed using Pearson correlation (Excel) and binary logistic regression (SPSS).
**RESULTS:** DNA was available for 102 women who delivered preterm in the index pregnancy or had a history of preterm delivery; these women were considered cases. 152 women had had at least one previous term delivery and delivered at term in the index pregnancy; these 152 women had no prior history of preterm birth and were considered controls. Modal CN was 4 (range 2-7). Serum was available for 140 women. Median hBD2 concentration was 761.5 pg/mL (IQR 449.6-1232.0). There was no association between DEFB copy number and preterm birth. There was no correlation between copy number and serum hBD2 concentration.
**CONCLUSIONS:** Although variation in hBD2 protein expression in the first trimester may be of use to evaluate preterm birth risk, there is no association between DEFB copy number and preterm birth. Correlation between DEFB copy number and serum hBD2 expression, observed in non pregnant adults, is not present in the first trimester of pregnancy; this may be due to variation in regulatory sequences – some of which are progesterone and oestrogen sensitive – between individual copies.

## T-086

**LPS Elicits Inflammatory Changes in the Fetus Before the Amniotic Fluid in a Chronically Catheterised Ovine Model of Second Trimester Pregnancy.** Matthew W Kemp,[1] Haruro Usuda,[2] Yuichiro Miura,[1] Eleanor Woodward,[1] Matthew S Payne,[1] Judith Bohm,[1] Alan H Jobe,[3] Suhas G Kallapur,[3] Tadashi Matsuda,[2] John P Newnham,[1] Masatoshi Saito.[2] *[1]School of Women's and Infants' Health, UWA, Perth, W. Aust, Australia; [2]Division of Perinatal Medicine, Tohoku University Hospital, Sendai, Miyagi, Japan; [3]Division of Pulmonary Biology, Cincinnati Children's Hospital Medical Centre, Cincinnati, OH, USA.*
**INTRODUCTION:** Infection-derived intrauterine inflammation is associated with early preterm birth and fetal injury. Determining the spatiotemporal nature of intrauterine inflammation is key to our understanding of the pathophysiology of early preterm birth. We aimed