44 A FUNCTIONAL ROLE FOR THE NOVEL SOLUBLE TOLL-LIKE RECEPTOR- (STLR2) IN MODULATING INTRA-AMNIOTIC IMMUNE RESPONSES ANTONETTE T. DULAY[1], CATALIN S. BUHIMSCHI[1], GUOMAO ZHAO[1], EMILY A. OLIVER[2], AYANDA MBELE[3], SHICHU JING[1], IRINA A. BUHIMSCHI[1], [1]Yale University, Ob./Gyn.&Reprod.Sci, New Haven, Connecticut, [2]King's College London, Women's Health, London, United Kingdom, [3]University of Pretoria, Ob./Gyn., , South Africa

OBJECTIVE: TLRs are pattern recognition transmembrane receptors that play a key role in innate immunity by mediating inflammatory responses to pathogens via release of chemokines, such as IL-8, and cytokines. The recently discovered soluble truncated form of TLR2 (sTLR2) acts as a decoy receptor thereby down-regulating the host response to a microbial attack. This study was conducted to investigate the existence and function of sTLR2 in human amniotic fluid (AF).

STUDY DESIGN: AF was retrieved by amniocentesis in 33 women with normal pregnancy outcomes stratified as follows: 1) genetic midtrimester (GA: 17±1 wks, n=12); 2) rule-out infection (GA: 26±1 wks, n=12); 3) lung maturity (GA: 37±1 wks, n=14). The expression of sTLR2 was determined by western blot, immunoprecipitation and immunohistochemistry (IHC). Specificity was confirmed with neutralizing peptides. The functional role of sTLR2 was assessed in vitro using a villous explant system (term CS, n=4) through the ability of AF to inhibit the release of IL-8 in response to Pam3CSK4 (bacterial lipopeptide analogue and specific TLR2 agonist). Pseudo-amniotic fluid was used as control. IL-8 was assessed by ELISA and tissue viability was confirmed by LDH release. Data was normalized to total tissue protein.

RESULTS: 1) Human AF contains two sTLR2 forms: 42kDa (dominant) and 30kDa. Both forms are immunoreactive with an N- (extracellular domain) but not a C-terminus (intracellular domain) TLR2 antibody; 2) Expression of sTLR2 is gestational age-regulated: term AF has lower sTLR2 immunoreactivity (of both forms) compared to the earlier GA groups ($P<0.001$); 3) The bacterial analogue, Pam3CSK4, induced a significant IL-8 response from villous explants known to express the full-length TLR2 by IHC; 4) Preincubation of Pam3CSK4 with midtrimester AF, but not term AF or pseudo-amniotic fluid, significantly inhibited its ability to elicit an IL-8 response ($p=0.008$).

CONCLUSION: This is the first study to provide evidence that a functional sTLR2 is part of the innate immune response system within the amniotic cavity.

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45 MATERNAL AND FETAL TOLL-LIKE RECEPTOR 4 (TLR4) GENOTYPE AND CHORIONIC PLATE INFLAMMATORY LESIONS HYAGRIV SIMHAN[1], TREVOR MACPHERSON[2], STEVE CARITIS[2], MARIJANE KROHN[2], [1]University of Pittsburgh, Ob/Gyn, Pittsburgh, Pennsylvania, [2]University of Pittsburgh, Pittsburgh, Pennsylvania

OBJECTIVE: To explore the relation between maternal and fetal genetic variation in TLR4 and histologic evidence of chorionic plate inflammation

STUDY DESIGN: In this prospective observational cohort of 111 women with singleton gestations DNA was extracted from maternal and cord blood from all subjects. TLR4 genotype assays on all mom-baby pairs were performed on an Illumina® platform. Single nucleotide polymorphism (SNP) selection was made using a linkage disequilibrium (LD) bin approach. LD bins are composed of SNPs that are very highly correlated with each other, where a single tag SNP can be used to predict the genotypes of other SNPs in the bin. Thirteen tagSNPs were selected in the TLR4 gene. All placentae were examined by a single blinded perinatal pathologist. The diagnosis of chorionic plate inflammation was made using the criteria of Redline et al.

RESULTS: After adjustment for multiple comparisons, one maternal SNP (rs10759932) and one fetal SNP (rs1554973) demonstrated highly significant association with chorionic plate inflammation. In a multivariable model with adjustment for maternal race, smoking, and bacterial vaginosis, carriage of these polymorphic alleles was strongly associated with chorionic plate inflammation (maternal rs1554973: odds ratio 5.2, $p=0.006$. fetal rs10759932: odds ratio 4.95, $p=0.005$). There was no evidence of statistical interaction between these two SNPs.

CONCLUSION: Maternal and fetal genetic variation in TLR4 is strongly associated with histologic evidence of chorionic plate inflammation. These maternal and fetal genotypic effects are independent of each other as well as other environmental covariates.

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46 VERTICAL TRANSMISSION OF HEPATITIS C M MCMENAMIN[1], A JACKSON[2], J LAMBERT[2], S COULTER SMITH[2], L JONES[3], F MCAULIFFE[1], [1]UCD School of Medicine and Medical Science, National Maternity Hospital, Dublin, Ireland, Dublin, Ireland, [2]Rotunda Hospital, Dublin, Ireland, , Ireland, [3]University College Dublin, Ireland, , Ireland

OBJECTIVE: To determine vertical transmission rates of hepatitis C over a 5 year period in two tertiary level maternity units

STUDY DESIGN: Retrospective review of all hepatitis C positive mothers and their pregnancy outcomes in two Dublin maternity units over a 5 year period from 2001-2005 inclusive.

RESULTS: During the study period there were 74,629 deliveries. A total of 473 Hepatitis C positive mothers were identified, who were delivered of 559 liveborn infants, rate of hepatitis C infection was 0.75% (559/74629). 458 infants were delivered to Irish mothers (81.9%). Of the 559 liveborn infants, maternal hepatitis C PCR was detected in 294 (52.5%), undetected in 167 (29.8%), not tested in 93 (16.6%), sample unsuitable for analysis in 3 (0.5%), and no data available for 2 (0.33%) In the neonatal period 367 infants tested negative for hepatitis C PCR, 18 positive and 173 infants did not get tested/were lost to follow-up. The vertical transmission rate is thus 18/385 (4.7%). Overall the caesarean section rate was 20.9%, instrumental delivery rate was 9.4%. One intrapartum fetal blood sample was performed (maternal PCR status unknown, baby PCR negative) and 23 babies had fetal scalp electrode applied, none of these infants subsequently were identified as PCR positive; 9 tested negative, 14 did not have infant PCR checked.

CONCLUSION: This study, one of the largest in the literature, reports a vertical transmission rate for hepatitis C of 4.7%. This is lower than the vertical transmission rate of hepatitis B and for HIV, suggesting a lower level of infectivity despite the majority of women having hepatitis C PCR detectable. Education of labour ward staff in the importance of appropriate intrapartum management of pregnancies affected with hepatitis C may improve adherence to that general guidelines regarding avoidance of fetal blood sampling and application of fetal scalp electrodes in labour.

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47 THE ANTENATAL IDENTIFICATION OF FUNISITIS (FETAL INFLAMMATION) WITH A RAPID MMP-8 BEDSIDE TEST CHAN-WOOK PARK[1], SEUNG MI LEE[1], JOONG SHIN PARK[1], JONG KWAN JUN[1], ROBERTO ROMERO[2], BO HYUN YOON[1], [1]Seoul National University College of Medicine, Obstetrics and Gynecology, Seoul, South Korea, [2]National Institute of Child Health & Human Development/National Institutes of Health/Department of Health & Human Services, Perinatology Research Branch, Detroit, Michigan

OBJECTIVE: Fetal inflammation is a powerful predictor of short and long-term adverse outcomes including cerebral palsy. Neutrophils in the amniotic cavity are of fetal origin and can produce matrix metalloproteinase-8 (MMP-8). Therefore, the detection of an elevated MMP-8 in amniotic fluid (AF) may indicate fetal systemic inflammation. The purpose of this study was to determine if bedside test, MMP-8 PTD Check™, can be of value in the antenatal identification of funisitis. This test requires no equipment and can be performed in 15 minutes.

STUDY DESIGN: The relationship between the presence of funisitis and the results of MMP-8 PTD Check™ test was examined in 139 patients who delivered preterm singleton neonates (gestational age <35 weeks) within 72 hours of amniocentesis. AF was cultured for aerobic and anaerobic bacteria and for genital mycoplasmas. AF was analyzed for white blood cell (WBC) count, interleukin-6 (IL-6) and the MMP-8 PTD Check™ test. IL-6 concentration was also determined in umbilical cord plasma collected at birth. Funisitis was diagnosed in the presence of neutrophil infiltration into the umbilical vessel walls or Wharton jelly. Nonparametric techniques were used for statistical analysis.

RESULTS: 1) Funisitis was present in 27% (38/139) of cases; 2) A positive MMP-8 PTD Check™ test had a sensitivity of 97% (37/38), a specificity of 63% (64/101), a positive predictive value of 50% (37/74) and a negative predictive value of 99% (64/65) in the identification of funisitis; 3) Among cases without funisitis, patients with a positive MMP-8 PTD Check™ test had significantly higher median AF IL-6 concentration, AF WBC count, and umbilical cord plasma IL-6 concentration at birth than those with a negative MMP-8 PTD Check™ test ($p<0.05$ for each).

CONCLUSION: The MMP-8 PTD Check™ test is a rapid, simple and sensitive bedside test which allows assessment of the risk of funisitis (fetal inflammation).

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