IMMUNE SYSTEM, TROPHOBLAST APOPTOSIS AND PREECLAMPSIA?

OBJECTIVE: Toll-like receptors (TLRs), discovered to regulate patterning during embryonic development, were subsequently found to play a role in innate immunity. TLRs recognize microbial ligands as well as host products released during tissue damage or "danger signals." (Science 2002;296:301). Engagement of TLR-4 can induce trophoblast cells to produce pro-inflammatory cytokines. Such cytokines may promote trophoblast cell apoptosis, which is increased in preeclampsia. This study was conducted to explore expression patterns in the extravillous trophoblasts (EVT) in the placental bed of women with and without preeclampsia.

STUDY DESIGN: Placental bed biopsies were obtained from patients with: (1) normal pregnancy at term (n = 40); (2) severe preeclampsia (n = 15); and (3) preterm delivery and intact membranes (PTD) with and without histologic chorioamnionitis (n = 15 for each group). The expression pattern of TLR-4 in EVT was examined by double immunohistochemistry. Image analysis was conducted and non-parametric statistics were employed for analysis.

RESULTS: (1) The median percentage of TLR-4 positive EVT in the placental bed was significantly higher in patients with preeclampsia than in those with PTD with histologic chorioamnionitis (p = .0015). (2) The median percentage of TLR-4 positive EVT was significantly higher in patients with preeclampsia than in those with PTD with histologic chorioamnionitis (p = .0017). (3) The median percentage of TLR-4 positive EVT in the placental bed was significantly higher in patients with PTD and histologic chorioamnionitis than in those without these conditions (p = .037).

CONCLUSION: TLR-4 expression is increased in the extravillous trophoblasts in women with preeclampsia. We propose that "danger signals" may increase the expression of TLR-4 by EVT in the placental bed, which might lead to trophoblast apoptosis and defective hemochorial placentaion in preeclampsia.

TOLL-LIKE RECEPTOR 4: A LINK BETWEEN "DANGER SIGNALS", THE INNATE IMMUNE SYSTEM, TROPHOBLAST APOPTOSIS AND PREECLAMPSIA? YEON MEE KIM1, SEYOUNG OH2, JHY KAE NIE3, RICCARDO GOMEZ4, CHONG JAI KIM5, MOSHE MAZO4, VIKKI ABRAHAM5, GIL NOK6, SHIGERU SATO7, ROBERTO ROMERO8, WALTER STATE UNIVERSITY SCHOOL OF MEDICINE, Department of Pathology, DETROIT, Michigan, 2PERITONALIZE RESEARCH Branch, NICHD, NIH, DHHS, Bethesda, Maryland, 3CEDIP, Solero del Rio Hospital, Puentz Alto, Chile, Chile, 4Seoul National University, Seoul, Korea, 5Soroka University Medical Center, Beer Sheva, Israel, Israel, 6Yale University, Department of Obstetrics and Gynecology, New Haven, Connecticut, 7Toyama Medical and Pharmaceutical University, Department of Obstetrics and Gynecology, Toyama, Japan

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THE EFFECTS OF TREATMENT WITH N-ACETYLCYSTEINE (NAC) IN A RAT MODEL OF PREECLAMPSIA EUGENE CHANG1, ERNEST BARBOSA2, INDERJIT SINGH3, AVTAR SINGH4, MANJEET PAINTILIA3, AVTAR SINGH4, MANJEET PAINTILIA3, MEDICINE, Obstetrics and Gynecology, Cincinnati, Ohio

OBJECTIVE: Preeclampsia may be caused by an imbalance of angiogenic factors. We previously demonstrated that high serum levels of sFlt1 (an anti-angiogenic protein) and low levels of PGF (a pro-angiogenic protein) predict subsequent development of preeclampsia. While sFlt1 is too large a molecule (110 kD) to be filtered into the urine, PGF is much smaller (30 kD) and readily filtered. We hypothesized that urine PGF is altered prior to hypertension and proteinuria and may predict preeclampsia.

STUDY DESIGN: Nested case-control study within the CPEP cohort of healthy nulliparas. Each woman who developed preeclampsia was matched to one normotensive control. 120 pairs were randomly chosen. Concentrations of PGF and creatinine were determined in 704 urine specimens obtained before labor. They were sacrificed and brain weights were determined. Placental tissue and

Parameter | Sham | RUPP | RUPP + NAC
---|---|---|---
Number of animals | 5 | 5 | 5
Average BP | 72.24 mm Hg | 85.78 mm Hg* | 65.58 mm Hg*
Average litter size | 11.2 | 8.8 | 10.4
Average pup weight | 4.37 g | 3.09 g* | 4.58 g
Average pup brain weight | 0.175 g | 0.149 g* | 0.183 g