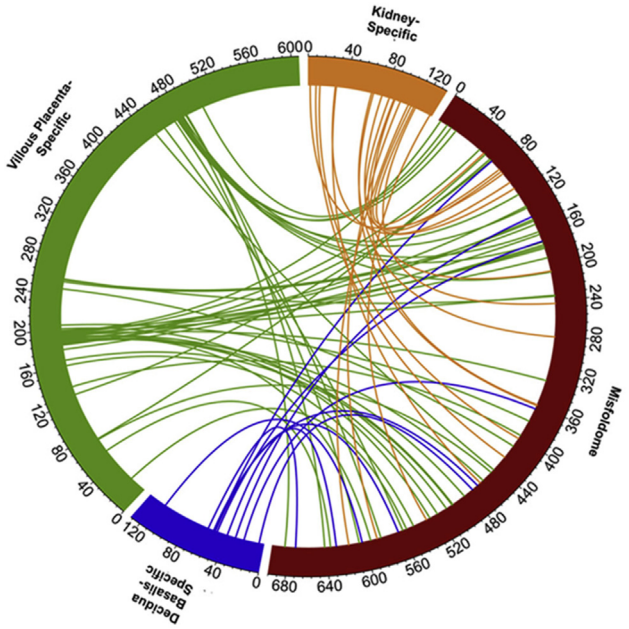
the potential contribution of kidney and placental transcripts to the urine misfoldome in PE.

STUDY DESIGN: Urine from 92 pregnant women was classified by strict clinical criteria in 6 groups: pregnant controls (CRL, n=11, GA: 30±5 wks), mild PE (mPE, n=15, GA: 33±4 wks), severe PE (sPE, n=21, GA: 32±4 wks), superimposed PE (spPE, n=16, GA: 32±6 wks), atypical PE (HELLP±IUGR, n=16, GA: 30±5 wks), and non-PE isolated proteinuria (n=13, GA: 28±6 wks). Misfoldome proteins were enriched by Congo Red precipitation and subjected to UPLC/MS/MS. Deep RNA sequencing (RNA-seq) was performed on decidua basalis (n=5) and villous trophoblast (n=5) of women with preterm severe PE (GA: 32±1 wks). These reads, together with RNA-Seq data from the Illumina Human BodyMap 2.0 database (n=16, adult tissues including kidney), were used to intersect specific transcripts that may contribute to aberrant proteinuria in PE.

RESULTS: 646 unique proteins IDs comprised the urinary misfoldome of PE women. Our intersection analysis showed a potential contribution of villous trophoblast, decidua and kidney to the misfoldome (Figure). Villous trophoblast was a larger contributor than either kidney or decidua (Table). Kidney-specific transcripts such as solute carrier family 22 (SLC22A12, a urate transporter), SMIM24 (an uncharacterized small integral membrane protein), MMP7 (matrilysin), and CALB1 (calbindin 1, a protein linked to Huntington disease) mapped to distinct PE subphenotypes.

CONCLUSION: The urinary misfoldome harbors a considerable number of peptides of placental and kidney origin which may interact to play key pathogenic roles in various PE subphenotypes.



Circos plot showing shared IDs among the urine misfoldome (red) and transcripts specific to the villous trophoblast (green), kidney (orange) and decidua basalis (blue). The size of each sector is proportional to the number of unique IDs in each group, and connecting chords represent shared IDs.

The Number of Villous Trophoblast, Decidua, and Kidney Transcripts Contributing to the Misfoldome

Transcripts Mapped to Misfoldome per Condition	sPE, Villous Trophoblast-Specific	sPE, Decidua-Specific	Kidney-Specific
CRL (n=230)	23	4	3
Non-PE Proteinuria (n=265)	31	2	4
mPE (n=368)	30	5	9
sPE (n=437)	37	4	8
Atypical PE (n=332)	21	3	5
spPE (n=351)	36	5	7

183 Interleukin 1 beta is increased in the hippocampus and posterior cortex of rats with hypertension and systemic inflammation during pregnancy

Cynthia Bean, Shauna-Kay Spencer, Jacob Gibbens, Teylor Bowles, Michelle Owens, Kedra Wallace

[1]University of Mississippi Medical Center, Jackson, MS

OBJECTIVE: HELLP syndrome is a severe form of preeclampsia. We have previously shown that both women and animals with HELLP have an increase in T cells, inflammatory cytokines and blood brain barrier (BBB) permeability. Our objective was to determine if rats with HELLP have evidence of BBB permeability and increase in inflammatory cytokines within the brain.

STUDY DESIGN: On gestational day (GD) 12 we infused sEndoglin and sFlt-1 (7 and 4.7ug/kg/day respectively) via a mini-osmotic pump into timed-pregnant rats. Rats not infused served as normal pregnant (NP) controls. On GD19, MAP was measured via carotid arterial catheters placed on GD18, tissues collected, animals euthanized. The brain was weighed, dissected and frozen until assay prep. The cerebellum, hippocampus, frontal and posterior cortex were defrosted on ice. Tissue was homogenized on ice in ice-cold Tris buffer (pH7.4) with protease inhibitor cocktail. Homogenates were centrifuged and supernatants aliquoted. Samples were run using a Milliplex Kit (EMD Millipore) assaying for these cytokines: IL-4, IL-1β, IL-6, IL-10, IL-17A, and VEGFA. All samples were normalized to total protein using the bicinchoninic acid assay. Data was analyzed with a repeated measures two way ANOVA with a Bonferroni post-hoc analysis if applicable. $P<0.05$.

RESULTS: MAP was significantly increased in HELLP rats compared to NP rats ($p=0.04$; n=4-5/group) on GD19. Infusion of Texas Red dextran on GD19 led to higher dye leakage in the posterior cortex and brainstem of HELLP rats compared to NP rats when viewed by in vivo imaging (IVIS Lumina), indicative of BBB permeability. IL-1β was significantly increased in the posterior cortex ($p=0.03$) and hippocampus ($p=0.01$) of HELLP rats compared to NP rats. There were no significant differences in the frontal cortex ($p=0.996$) between the groups. In the cerebellum IL-1β was significantly decreased ($p=0.002$) compared to NP rats as was IL-6 ($p=0.03$). There were no significant differences between HELLP and NP rats in any other cytokines measured.

CONCLUSION: These findings suggest that levels of inflammation in the posterior and hippocampal regions of HELLP rats may indicate increased anxiety or cognitive disorders such as changes in learning and memory or reflective of the posterior reversible encephalopathy syndrome.

184 Pre-eclampsia, diabetes, and the placenta: a study in differential gene expression & molecular clues to disease states

Diana A. Racusin, R. Alan Harris, Melissa Suter, Maxim Seferovic, Min Hu, Cynthia Shope, Kjersti M. Aagaard

[1]Baylor College of Medicine, Houston, TX

OBJECTIVE: While the exact etiology of pre-eclampsia remains a mystery, the role of the placenta in the pathophysiology of pre-eclampsia continues to be implicated, making the placenta a prime