accessible biologic surrogate for fetal brain microglia in MATOB and control murine pregnancy.

STUDY DESIGN: C57BL6/J dams were fed either a 60% high-fat diet or 10% fat control diet for 14 weeks pre-breeding and during pregnancy. At e17.5, fetal brain microglia and corresponding placental macrophages were isolated from fresh tissue. We performed single-cell RNA-sequencing on microglia and matched placental macrophages (10x Genomics, N=16, 4 replicates/group).

RESULTS: 77,999 cells were sequenced. Canonical microglial and HBC markers were expressed in both cell types. Unsupervised analyses identified clusters within and across samples that share a significant fraction of "marker genes" (expressed more highly in cells from that cluster than in all other cells). Subsets of HBCs closely resembled subsets of microglia, with overlap analysis of marker genes demonstrating numerous clusters with 80-100% overlap between microglia and HBCs. This was true for both MATOB and CD. ScRNA-Seq elucidated novel shared gene programs and cell states that define HBCs and microglia.

CONCLUSION: Shared gene programs in HBCs and microglia suggest that HBCs may be used as a proxy cell type to assay fetal brain microglial programming, in both MATOB and control mouse pregnancy. This finding may have broader implications for assaying the impact of maternal exposures beyond obesity on fetal brain development.

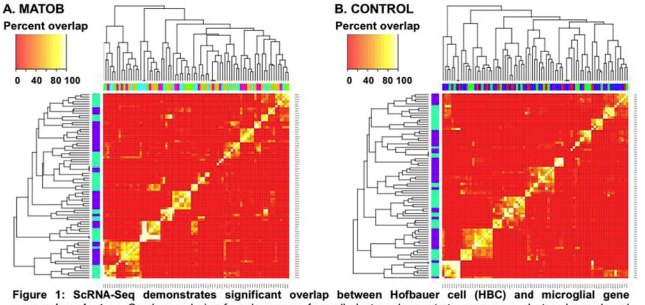

Figure 1: ScRNA-Seq demonstrates significant overlap between Hofbauer cell (HBC) and microglial gene expression clusters. Overlap analysis of marker genes from all clusters demonstrates numerous clusters have shared marker gene expression between HBCs and microglia. Colors oriented horizontally indicate individual microglial and HBC samples; vertically-oriented purple and teal bars represent microglia (purple) or HBCs (teal). Color indicates percentage overlap of marker genes. Yellow to white color indicates clusters with 80%-100% overlap of marker genes; many of these span both HBC and microglial samples. *MATOB:* Maternal obesity.

5 Perinatal and genetic outcomes associated with no call cfDNA results in 18,496 pregnancies

Mary E. Norton[1], Cora MacPherson[2], Bo Jacobsson[3], Melissa Egbert[4], Fergal D. Malone[5], Ronald J. Wapner[6], Ashley Roman[7], Asma Khalil[8], Revital Faro[9], Rajeevi Madankumar[10], Lance Edwards[11], Noel Strong[12], Sina Haeri[13], Robert M. Silver[14], Nidhi Vohra[15], Jon Hyett[16], Kim Martin[4], Pe'er Dar[17]

[1]University of California, San Francisco, San Francisco, CA, [2]George Washington University, Rockville, MD, [3]Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, Gothenburg, Vastra Gotaland, [4]Natera, Inc, San Carlos, CA, [5]Royal College of Surgeons in Ireland, Dublin, Ireland, Dublin, Ireland, [6]Columbia University Irving Medical Center, New York, NY, [7]NYU Langone Health, New York, NY, [8]St George's Hospital University of London, London, England, [9]St Peters Hospital, New Brunswick, NJ, [10]Long Island Jewish Medical Center, Jericho, NY, [11]Suffolk Obstetrics & Gynecology, Port Jefferson, NY, [12]Icahn School of Medicine at Mount Sinai, New York, NY, [13]Austin Maternal Fetal Medicine, Dallas, TX, [14]University of Utah Health, Salt Lake City, UT, [15]Northwell Northshore Medical Center, Syosset, NY, [16]Royal Prince Alfred Hospital, New South Wales, Australia, [17]Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY

OBJECTIVE: Failed or no call cell free DNA (cfDNA) testing confers an increased risk of aneuploidy, but few series include complete obstetric, infant, and genetic outcomes. We hypothesized that failed tests would be associated with aneuploidy and adverse perinatal outcomes.

STUDY DESIGN: Secondary analysis of a multicenter prospective study of SNP-based cfDNA; confirmatory genetic testing was performed in all cases during pregnancy or after birth. Demographics, pregnancy outcomes, and confirmatory genetic results were compared between no call and resulted cases. Univariate analysis compared differences between groups; odds ratios (OR) were calculated after adjusting for BMI, gestational age at draw, and black race. Results applying an updated algorithm after study completion were also compared.

RESULTS: 18,496 women had both cfDNA screening and genetic confirmation. A first draw result was reported in 17,885 while 611 (3.3%) were no calls; 320/435 (73.6%) redraws gave a result, leaving 291 as no calls. No calls were associated with higher BMI, later gestational age, lower fetal fraction, and black race. T13, 18, or 21 was confirmed in 1.6% of no calls vs 0.7% with a result (p=.013). After adjustment for confounders, the aOR for aneuploidy was 2.2 (95% CI 1.1,4.5) after a first no call; this increased to 3.8 (95% CI 1.7, 8.4) after the second. Livebirths occurred in 94.9% with a no call vs 98.8% with a result (p< .001; aOR for livebirth: 0.17 [95% CI 0.10, 0.28]). PTB < 28, 34, and 37wks and preeclampsia were all higher after a no call. All risks were higher after a second no call result (Table). With the updated algorithm, the no call rate decreased to 0.6% and the adverse associations were further increased. The association with perinatal outcomes persisted in euploid pregnancies.

CONCLUSION: Patients with no call cfDNA results are at increased risk for aneuploidy; this risk is further increased with a second no call. The risk of other adverse perinatal outcomes is also increased, including in euploid pregnancies.

Table. Outcomes in patients with no call results

Variable	Results called with 1st draw	No call with 1st draw	No call with 2nd draw	Comparison of call vs. no call with 1st draw
	N=17,885	N=611 (3.3%)	N=291 (1.6%)	
Maternal age (years)	33.7	33.8	33.9	p=0.54
Gestational age (weeks)_	13.2	14.4	13.8	**p<0.001**
BMI kg/m²	26.2	31.2	32.7	**p<0.001**
Fetal fraction	10.0%	5.4%	3.0%	**p<0.001**
Race				**p<0.001**
Asian	8.5%	5.9%	4.5%	
Black	8.3%	13.9%	20.3%	
Caucasian	61.9%	57.9%	51.9%	
Latina	18.0%	19.0%	20.3%	
Other/unknown	3.3%	3.2%	3.1%	
IVF	5.3%	4.9%	5.8%	p=0.69
Nonsmoker	82.7%	81.6%	81.3%	p=0.075
Aneuploidy (T13, 18, 21)	0.7%	1.6%	2.7%	**p=0.013**
Diagnostic testing	2.7%	11.3%	21.0%	**p<0.001**
Fetal anomaly before testing	0.6%	0.2%	0.3%	p=0.27
Livebirth	98.8%	94.9%	90.0%	**p<0.001**
PTB<34 weeks	2.4%	8.3%	13.9%	**p<0.001**
Preeclampsia	3.9%	9.0%	10.0%	**p<0.001**
Small for gestational age	8.7%	11.1%	10.0%	**p=0.049**