

Table 1. Serum level of fibrosis biomarker (ng/mL)					*P* value
	CTR	HTN	MS	MS-INOs	
TGF-β	60.94±3.3*	87.26±2.4	117.1±2.8#	101.7±8.6	<0.05
PICP	90.86±2.8*	76.28±3.6	75.8±2.8	80.98±2.6	<0.05
PIIICP	1.10±0.1	1.25±0.04	1.41±0.06#	0.72±0.06	<0.001

Transforming growth factor Beta (TGF-β); Procollagen Type 1 C-Terminal Propeptide (PICP); Procollagen Type 3 C-Terminal Propeptide (PIIICP)
Significance in in the table: TGF-β *CTR vs. HTN; #MS vs. HTN; PICP *CTR vs. HTN, MS and MS-INO; PIIICP #MS-INO vs. HTN and MS

87 CD59 and regulation of terminal complement in hypertensive disorders of pregnancy: The COPA II Study

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OBJECTIVE: Terminal complement activation is increased in hypertensive disorders of pregnancy (HDP). CD59 is a glycoprotein that attaches to cells via a GPI anchor and inhibits formation of the terminal complement complex. CD59 may therefore be critical to regulation of terminal complement in HDP. We sought to determine if soluble CD59 concentrations are increased in association with disease severity in preeclampsia (PE)

STUDY DESIGN: COPA, a multicenter case control study, enrolled subjects from 6 centers and 3 cities in Colombia (Nov '15-Jul '16). Subjects enrolled by gestational age and diagnosis: 1. healthy; 2. chronic hypertension (CHTN); 3. gestational hypertension (GHTN); 4. PE and; 5. PE with severe features (PE-SF). COPA was powered for PE-SF (target, n=100); controls enrolled 2:1. Clinical data, blood and urine were collected by trained coordinators. Soluble concentrations of CD59 were determined by enzyme linked immunosorbent assays (MyBioSource). Data analyses by equality of medians test and Spearman's correlation (α=0.05).

RESULTS: COPA enrolled 352 subjects [Healthy (n=54); CHTN (n=50); GHTN (n=87); PE (n=57); PE-SF (n=104)]. Gestational age was similar between groups due to stratified enrollment. Plasma CD59 levels were increased in association with HDP disease severity (P< 0.001), most notably in PE-SF, Table 1. Urine CD59 levels did not vary between groups but fractional CD59 excretion was lower in association with greater disease severity (P=0.003). Increased plasma CD59 levels correlated with decreased platelet count and increased lactate dehydrogenase, creatinine, aspartate transaminase, urine protein/creatinine, and systolic and diastolic blood pressure (P< 0.01, all correlations), Table 2. Urine CD59 levels correlated with decreased systolic and diastolic blood pressure but not laboratory measures

CONCLUSION: This is the first study to describe soluble CD59 concentrations in women with HDP. Plasma CD59 concentrations are increased in association with disease severity in PE and correlate with markers of end-organ injury. There is strong rationale to investigate complement regulation in PE

Table 1. Plasma and urine CD59 concentrations by study group

Measure	Healthy (n=54)	CHTN (n=50)	GHTN (n=87)	PE (n=57)	PE-SF (n=104)	P-Value
Plasma CD59 ng/ml Median (IQR)	23.7 (20-31)	27.5 (24-34)	29.2 (25-35)	28.3* (23-36)	32.0† (27-39)	0.001
Urine CD59 ng/ml Median (IQR)	1.01 (0.7-1.4)	0.96 (0.7-1.1)	0.85 (0.5-1.2)	0.94 (0.6-1.4)	0.77 (0.6-1.1)	0.09
Fractional Excretion CD59†† (%) Median (IQR)	3.89 (2.7-5.5)	3.46 (2.3-4.3)	2.73 (1.8-4.4)	3.19 (2.1-4.3)	2.39** (1.5-3.5)	0.003

CHTN, chronic hypertension; GHTN, gestational hypertension; PE, preeclampsia; PE-SF, preeclampsia with severe features; IQR, interquartile range.

P-value by equality of medians test.

*P=0.02, PE vs. Healthy; †P<0.001, PE-SF vs. Healthy; P=0.002, PE-SF vs. CHTN; **P=0.02, PE-SF vs. Healthy

†† Fractional excretion CD59 = urine CD59/plasma CD59 *100%

Table 2. Plasma and urine CD59 and correlation with laboratory and clinical measures

Laboratory or clinical measure	Correlation with Plasma CD59 (Spearman's rho)	P-value	Correlation with Urine CD59 (Spearman's rho)	P-value
Platelet count (k/μl)	-0.21	<0.001	0.08	0.19
Lactate dehydrogenase (U/L)	0.18	0.003	0.02	0.74
Creatinine (mg/dl)	0.25	<0.001	-0.09	0.17
Aspartate transaminase (U/L)	0.17	0.005	0.01	0.85
Urine protein/creatinine (mg/mg)	0.36	<0.001	-0.07	0.18
Systolic blood pressure (mmHg)	0.28	<0.001	-0.13	0.01
Diastolic blood pressure (mmHg)	0.31	<0.001	-0.14	0.008

88 Mismatch between obesogenic intrauterine environment and low-fat postnatal diet may confer an offspring metabolic advantage

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OBJECTIVE: Mismatch between the in utero and postnatal environments is known to confer an increased risk of cardiovascular disease and metabolic syndrome in offspring. Investigations of this mismatch phenomenon have primarily focused on a nutrient-depleted intrauterine environment and a nutrient-rich postnatal environment. Maternal diet-induced obesity (MATOB) is known to be associated with an increased risk of offspring obesity/metabolic syndrome in the absence of postnatal intervention. We hypothesized that switching offspring of obese dams to a 10% fat control diet (CD) immediately after lactation would ameliorate metabolic morbidity.

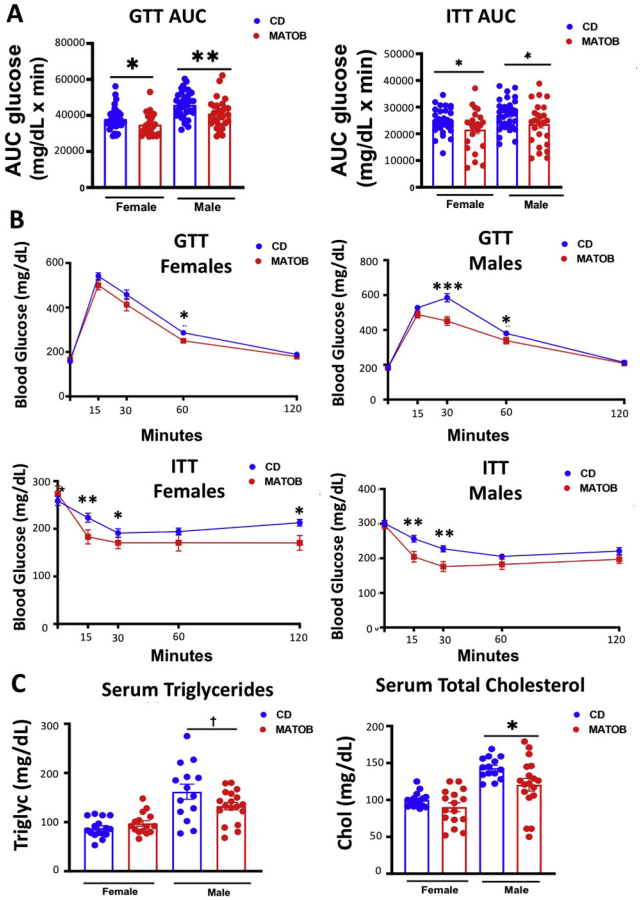
STUDY DESIGN: C57BL6/J female (F) mice were fed either a 60% high-fat diet (HFD) or a 10% fat CD for 14 weeks pre-breeding, and during pregnancy/lactation. Male (M) and F offspring from both groups were weaned to the CD at 3.5 wks. Metabolic parameters were evaluated in adult offspring (16-20 weeks, N=16-36/sex/diet

group). Glucose tolerance and insulin sensitivity were evaluated via GTT and ITT. Fasting triglyceride and total cholesterol were quantified in serum. Resting metabolic rate was evaluated using metabolic cages.

RESULTS: MATOB and HFD during pregnancy and lactation, followed by offspring switch to a 10% fat CD throughout life, was associated with improved glucose tolerance and insulin sensitivity in MATOB-exposed offspring of both sexes, compared to controls (Fig 1A/B). MATOB-exposed Ms also had improved fasting lipids (Fig 1C). Although F MATOB adults were significantly heavier than controls (Fig 2A), there were no differences in basal metabolic rate between MATOB and CD offspring (Fig 2B).

CONCLUSION: A low-fat dietary switch following intrauterine and lactational exposure to MATOB was associated with improved offspring glucose handling and lipid profile in adult life. These findings suggest a mismatch between the intrauterine and postnatal environments, from increased to reduced nutrient availability, may confer a metabolic advantage. Reversal of deleterious metabolic programming by MATOB may be possible with strict offspring adherence to a low-fat diet.

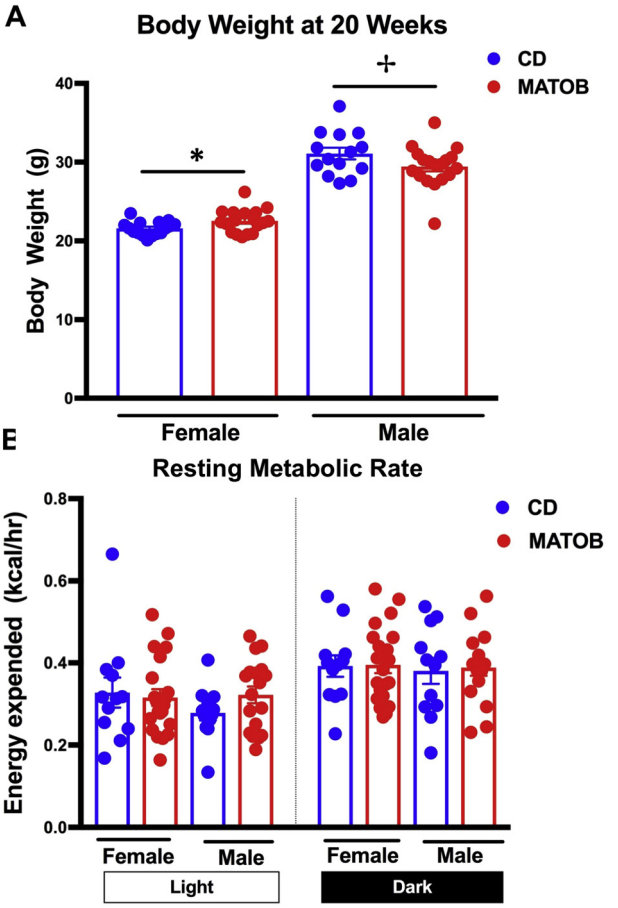
Figure 1: Glucose Tolerance, Insulin Sensitivity, and Lipid Profile in Obesity-Exposed and Control Offspring



A/B: Male and female MATOB adult offspring weaned to 10% fat CD had improved glucose tolerance and insulin sensitivity compared to sex-matched controls. This was true for both AUC analyses (**1A**), and analyses by time (**1B**). MATOB-exposed adult males had significantly lower fasting cholesterol, and a trend toward reduced triglycerides compared to controls (**1C**).

AUC: *area under the curve;* ***CD:*** *control diet;* ***GTT:*** *glucose tolerance test;* ***ITT:*** *insulin tolerance test (glucose is the measured value);* ***MATOB:*** *maternal diet-induced obesity; *p<.05; **p<.01; ***p<.001; † p=0.08.*

Figure 2: Body Weight and Basal Metabolic Rate in Obesity-Exposed and Control Offspring



2A: MATOB-exposed female adults were significantly heavier than controls at 20 weeks.

2B: There were no differences in resting/basal metabolic rate between MATOB and CD offspring of either sex.

CD: *control diet;* ***MATOB:*** *maternal diet-induced obesity;* ***Light cycle:*** *7am-7pm, typical quiet or sleeping period for mice;* ***Dark cycle:*** *7 pm-7am, typical active period for mice. *p<.05; + p=0.09*

89 Longitudinal changes in the cervicovaginal microbiome in high-risk women who experience midtrimester cervical shortening

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OBJECTIVE: Midtrimester cervical length (CL) shortening is a predictor of spontaneous preterm birth (SPTB), especially in women with prior SPTB (high-risk). Evidence suggests that SPTB is associated with pathologic microbial stimuli from the lower genital tract