PHYSIOLOGY

# Abstracts 44 – 52

**Moderators: Michal Elovitz, MD; Kjersti Aagaard, MD**

## 44 Maternal diet persistently alters the developing juvenile microbiome in a primate model of obesity

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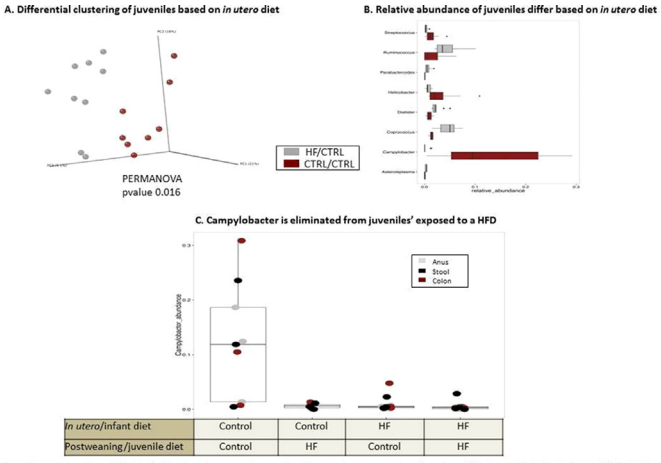
**OBJECTIVE:** Dysbiosis of the microbiome has been previously associated with obesity. Additionally, it has been hypothesized that obesity begets obesity, and our lab has demonstrated that a high fat (HF) maternal diet can alter the fetal epigenome. Therefore, we aimed to determine if, when, and how maternal diet influences the developing fetal microbiome.

**STUDY DESIGN:** Japanese macaque dams (n=26) were fed either a control (13%) or high-fat (35%) diet. Offspring were born vaginally and maintained on a maternal diet until weaning. At weaning (4-6 months of age) offspring were either maintained on the maternal diet (control vs HF) or were switched to the opposing diet (crossover cohort, HF vs control). At one year of age, the microbiome of the juvenile's stool, anus, or colon was examined via deep sequencing (16S V3V5 rRNA; 454FLXTitanium). Data was QC filtered and analyzed using QIIME. Differential Campylobacter abundance was confirmed by bacterial genus and species specific qPCR.

**RESULTS:** Juveniles exposed to a HF diet in utero clustered distinct from those of control diet fed dams. Further, this clustering was maintained when juveniles exposed to a HF diet were switched to a control diet post-weaning (Permanova, p=0.016; panel A). Specifically, upon exposure to a HF diet (be it in utero or post-weaning), Campylobacter was no longer detected in the gut of the offspring (panel B). Switching to a control diet post weaning (crossover cohorts) did not rescue this affect, and was confirmed by targeted analysis (panel C).

**CONCLUSION:** These data suggest that a high fat maternal diet persistently alters the juvenile microbiome out to one year of age. Collectively, our prior findings and these new results make evident that maternal influences occur irrespective of maternal habitus and are seen in dams that are sensitive (obese) or resistant (lean) to a high-fat diet. We speculate that alterations in the maternal diet may propagate their affects long-term through alterations in the offspring microbiome.




Juveniles exposed to a high-fat diet *in utero* have an altered microbiome at one year of age based on (A) differentially clustering and (B) relative abundance. Additionally, the genus campylobacter is eliminated from individuals exposed to a high-fat diet *in utero* and postpartum (C).

## 45 Accelerated aging in the offspring of mothers with pre-pregnancy obesity in a mouse model of developmental programming of metabolic syndrome

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**OBJECTIVE:** Obesity and metabolic syndrome are associated with acceleration of the aging process, characterized by shorter telomeres and low expression of *Klotho* gene. The objective of this was to determine if similar features are present in an established mouse model of developmental programming of metabolic syndrome, characterized by insulin resistance, obesity, hypertension and hyperlidemia.

**STUDY DESIGN:** We utilized an established mouse model where, over 3 months, the dams are fed either high fat diet (34.9% fat, HF group) or standard chow (5.8% fat, SF group). After weaning, offspring from both groups were put on standard chow until sacrifice at 6 months of age. Visceral adipose tissue (VAT) and kidneys were obtained (n = 5-6 per group). Telomere relative length (TRL) was measured using genomic DNA analysis and quantitative real time PCR. Protein expression of *Klotho* was assessed by Western blot. Statistical analysis was performed using Student t- or Mann-Whitney test as appropriate (significance $p<0.05$).

**RESULTS:** TRL in VAT was shorter in both HF female (HF 0.6 ± 0.1 vs SF 1.5 ± 0.4; p=0.02) and male (HF 0.4 ± 0.2 vs SF 0.8 ± 0.2; p=0.25) offspring compared to SF offspring. In kidneys TRL was higher in both HF male (HF 2.4 ± 0.3 vs SF 0.9 ± 0.1, p=0.004) and female (HF 1.8 ± 0.3 vs SF 1.0 ± 0.1; p=0.03) offspring. In contrary, in kidneys *Klotho* gene was significantly lower from HF males (HF 0.1 ± 0.04 vs SF 0.3 ± 0.1; p=0.03) and females (HF 0.09 ± 0.03 vs 0.5 ± 0.1; p=0.02) compared to SF (Figure).