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The *in utero* environment plays a critical role on health outcomes of the offspring later in life; of which, the placenta is a principal component in this environment. The objective of this study was to assess alterations in miRNA expression by known environmental toxicants measured in placental samples collected from the National Children's Study (NCS) birth cohort. This study analyzed villous samples from 110 term placentas collected within 6 hours of delivery from singleton vaginal deliveries. MicroRNA expression profiling of 654 miRNAs was conducted using the nCounter Analysis System by NanoString Technologies. The organic pollutants dichlorodiphenyldichloroethylene (DDE), bisphenol A (BPA), congeners of polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs), and the toxic metals mercury (Hg) and lead (Pb) were measured in these placentas. A moderated t-test was first used to identify a panel of differentially expressed miRNAs, which was then further analyzed using generalized linear models. Placental miRNA expression levels were highly variable, with 112 miRNAs consistently expressed in >30% of the samples. Out of the top ten most abundant miRNAs (mir-517a, mir-125b, mir-517c/mir-519a, mir-720, mir-181a, mir-126, mir-522, mir-23a, mir-100, and mir-24), four miRNAs (mir-517a, mir-517c, mir-522, mir-23a) are located within the imprinted placenta-specific C19MC cluster. The toxicant levels detected in placenta samples were low, but they fell within the range observed in previous studies in western industrialized countries. A positive association between congener PBDE209 and miR-188-5p and an inverse association between PBDE99 and let-7c were observed. Positive associations were also observed between miR-1537 expression and total PCBs as well as specific congeners 52, and 101. High levels of Hg and Pb were associated with significant changes in multiple miRNAs, many of them belonging to the let-7 family that has been implicated in multiple disease outcomes including cancer. We did not observe any associations between expression of miRNA and placental DDE or BPA levels. This is the first study linking exposure to environmental toxicants and microRNA expression in placentas with normal deliveries. Our results suggest that placental miRNA profiles may function as sensors for *in utero* exposures to toxic environmental chemicals. (Supported in part by NIH-LOI-2-BIO-18.)

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KOLEVA PT[1], KIM JS[2], GUTTMAN DS[3], SEARS MR[4], BECKER AB[5], MANDHANE PJ[1], SUBBARAO P[6], TURVEY SE[7], SCOTT JA[2], KOZYRSKYJ AL[1], INVESTIGATORS CHILD STUDY[8]. [1]Department of Pediatrics, University of Alberta, Edmonton, AB, Canada, [2]Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada, [3]Cell and Systems Biology, University of Toronto, Toronto, ON, Canada, [4]Department of Medicine, McMaster University, Hamilton, ON, Canada, [5]Department of Pediatrics and Child Health, University of Manitoba, Winnipeg, MB, Canada, [6]Department of Pediatrics, University of Toronto, Toronto, ON, Canada, [7]Department of Pediatrics, University of British Columbia, Vancouver, BC, Canada, [8]Canadian Healthy Infant Longitudinal Development Study, Hamilton, ON, Canada. Impact of Maternal Overweight during Pregnancy on the Newborn Gut Microbiome

Introduction: Obesity in pregnancy alters women's gut and breast milk microbiota and potentially interferes with the transmission of maternal bacteria to the infant gastrointestinal tract. Elucidation of the influence of maternal obesity on the development of infant gut microbiota and, in turn, as a modifier of child health is a research priority. The aim of this study was to assess the impact of maternal prepregnancy overweight status on infant meconium and fecal microbiota. Specific emphasis was put on the *Lactobacillales* an order of bacteria whose members become more abundant in intestine and vagina during the third trimester of pregnancy. Methods: This study comprised a subset of 57 mothers and their full-term infants from the Winnipeg site of the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort. Microbiota of meconium and feces collected at 3-4 months were characterized by Illumina sequencing of the hyper-variable V4 region of the 16S rRNA gene. Measures of the mother's anthropometry prepregnancy and infant diet were obtained from standardized questionnaires and hospital records. Wilcoxon test and Spearman's analysis were applied to investigate for any association between taxon abundance and maternal prepregnancy overweight. Results: Of 57 infant meconium samples, sufficient amplification product to permit sequencing was obtained from 13. The prevalence of prepregnancy overweight mothers was 61% (n=8). Abundance of members of the *Lactobacillales* increased from birth to the 3-4 month fecal sample (median 0.22 vs 1.06, p=0.03). These taxa were significantly correlated with the abundance of the genus *Ruminoccocus* (r=0.64 and p=0.02) and the family *Veillonellaceae* (r=0.73 and p=0.01) in meconium and in fecal samples 3-4 months (r=0.81 and p=0.002, and 0.67 and p=0.01, respectively). Significantly higher ratios of *Lactobacillales* to *Bacteroidaceae* (0.04), *Lactobacillales* to *Ruminococcaceae* (p=0.04) and *Lactobacillalles* to *Lachnospiraceae* (p=0.04) were observed in meconium microbiota following prepregnancy overweight compared to normal weight, but not in samples at the 3-4-month time point. Discussion: To conclude, this study highlights the influence of prepregnancy weight on the microbiota of meconium. Members of the order *Lactobacillales* were significantly correlated with the abundance of butyrate-producing gut microbial communities in meconium samples.