PRESCHOOL CHILDREN GUT MICROBIOTA AND LATER BODY MASS INDEX: RESULTS OF TWO FRENCH NATIONWIDE BIRTH COHORTS

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Objective This study aimed to investigate how the gut microbiota of children at 3.5 years (yrs) is associated with the later body mass index (BMI) at 5 yrs.

Methods Our study included 143 and 369 children from, respectively, the EPIPAGE2 (preterm infants born <32 weeks of gestational age [GA]) and ELFE (infants born >33 weeks of GA) birth cohorts for whom stool samples were collected at 3.5 yrs. Gut microbiota profiling was assessed using bacterial 16S rRNA gene sequencing. Age- and sex-specific BMI z-scores were computed at 2 and 5 yrs. We tested the associations with the gut microbiota at 3.5 yrs and both, BMI at 5 yrs and change of BMI between 2 and 5 yrs, after adjustment for confounding factors. Associations between alpha diversity and *Firmicutes* to *Bacteroidetes* (F/B) ratio and 1) 5-yrs BMI 2) 5-yrs BMI adjusted for baseline (2-yrs) BMI were assessed with linear multivariate regressions. We used Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (PICRUSt2) to predict functional metabolic pathways. To identify specific genera and inferred functional metabolic pathways associated with BMI z-score, we used random forests followed by linear regression models.

Results Our results showed a positive association between F/B ratio and 5-yrs BMI z-score. At 5 yrs, greater abundances of *[Eubacterium] hallii group, Fusicatenibacter,* and *[Eubacterium] ventriosum group* were associated with a higher BMI z-score; greater abundances of *Eggerthella, Colidextribacter,* and *Ruminococcaceae CAG-352* were associated with a lower BMI z-score. Interestingly, some genera were also associated with BMI z-score variations between 2 and 5 yrs. Additionally, some metabolic pathways were associated with the 5-yrs BMI z-score. There was no interaction with preterm status for all the described relationships.

Conclusion Children gut microbiota at 3.5 yrs is associated with later BMI independently of preterm or term birth. Our data support the need of studies in the pediatric population to better understand when the switch to an obese-like gut microbiota may take place and therefore, better comprehend the right timing of possible interventions, including the use of pre/probiotics to improve it.