LETTER

Additional maternal and nonmaternal factors contribute to microbiota shaping in newborns

We read, with great interest, the paper by Dominguez-Bello et al. (1). The authors (1) elegantly characterized bacterial communities of 9 mothers and their 10 newborns, looking at diversity associated with delivery modality, caesarean section (C-section) or vaginal delivery, across the different body niches.

The establishment of bacterial diversity early in infancy may affect the individual's risk for adult diseases and particularly for cardiovascular disease (2). Looking at the study from both clinician and microbiologist standpoints, some key aspects may deserve clarification.

Healthy pregnancy was reported in all but two variables, the high birth weight (one child weighting 5 kg) and the poor representation of vaginal *Lactobacilli* in some mothers (V3-Mom6, V4-Mom10, and C2-Mom7 in table S2 in ref. 1) are suggestive of maternal metabolic abnormalities (i.e., excessive weight gain during pregnancy or altered glucose metabolism). Moreover, C-section delivery is, per se, indicative of pathological conditions of the mother, fetus, or both, unless mandatory because of previous C-sections. The authors (1) should explain why C-sections were performed, because any underlying pathological condition could hide determinants of microbiota modulation in newborns. Maternal recto-vaginal rather than vaginal swabs are recommended between the 35th and 37th weeks of gestation. The use of vaginal swabs, as described by the authors (1), does not provide any information on gut microbiota. Nevertheless, the maternal gut microbiota contributes without doubt to microbiota biogenesis of baby habitats, especially in vaginally delivered newborns. Indeed, the UniFrac Global-R (table S1 in ref. 1) for maternal vagina habitat vs. vaginally born babies was poor. This was probably because, in such correlation, the mother's gut microbiota contribution was omitted. Prevalence of anaerobic over aerobic bacteria immediately after birth in vaginally born babies is quite impressive, and it could confirm the contribution from maternal gut microbiota (3). The newborn's skin and oral mucosa swabs should be carried out in the space of a few minutes. If these withdrawals were really performed within a few seconds, it is quite impossible to detect the bacterial contamination from nonmaternal sources. Nevertheless, if such contamination occurred, it was reasonably independent of delivery modality. Timing of sampling and relative results should be better depicted to understand baby niche onset and progression. Additionally, modalities of early breastfeeding may impact the microbiota onset in the first hours of life, and they deserve attention (2).

The authors (1) report on cephalosporin administration "several hours" before the C-section, whereas international guidelines (4) recommend administration during C-section, at skin incision, or after umbilical cord clamping. They claim that cephalosporin "had no apparent effect on the bacterial community structure." Indeed, 6 of 14 genera in C-section babies were Gram-negative, supporting no antibiotic-driven selection against Gram negative. However, the gray bar (figure 1b in ref. 1), representing the abundance of other bacteria, accounts for one half of the taxa distribution and means a grey area of either Gram-negative or Gram-positive bacteria. Pharmacodynamics and cephalosporin generation should be investigated to figure out the real antibiotic activity in a Gram negative to Gram positive ratio (5).

We congratulate the authors on their excellent work; however, by adding the above information, important insights to the topic will be provided.

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