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MICROBIOME

Baby steps towards the microbiome

> “further insights into the links between the parental and neonatal microbiota... are crucial”

Newborns transition from a relatively stable and sterile fetal life *in utero* to an environment with highly variable factors after birth, including postnatal interactions with commensal and pathogenic microorganisms. However, it is unclear what factors shape the development of the infant microbiota or how they influence the susceptibility of infants to infection. Now, two new studies show that the maternal microbiota affects the development of the immune system of infants and that exposure to pathogens can present a great challenge for infants that are born extremely prematurely.

In healthy infants, the development of protective innate and adaptive immune responses against pathogens is affected by the microbiota; however, how the microbiota of the mother shapes the neonatal immune system is unclear. To study this, Gomez de Agüero *et al.* transiently colonized the gut of germ-free pregnant mice with an engineered *Escherichia coli* strain that does not persist in the intestine, so that mothers revert back to a germ-free state before term. Pups from these ‘gestation-only colonized’ mothers had increased numbers of intestinal innate lymphoid cells and mononuclear cells compared with pups born to germ-free control mice. This increase in leukocytes persisted until at least 8 weeks after birth and weaning, which suggests that temporary colonization of the mother has long-term effects on the immune system of the offspring. In agreement with this, RNA sequencing analysis revealed that the offspring of gestation-only colonized mothers have increased levels of expression of genes that are implicated in intestinal and immune function, including genes encoding antimicrobial peptides. Furthermore, transferring serum from gestation-only colonized mice to pregnant germ-free mice was sufficient to increase leukocyte numbers in their offspring and, importantly, this effect was dependent on the presence of maternal antibodies. Finally, the authors showed that maternal antibodies retain microbial molecules from the mother and transmit them to the offspring, thereby demonstrating a crucial role for the maternal microbiota in the development of the immune system of infants.

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A second study investigated the links between susceptibility to necrotizing enterocolitis (NEC), which is the leading cause of morbidity and mortality in preterm infants, and the microbiota. Bacterial colonization of the infant gut contributes to NEC, and there is evidence for both nosocomial outbreaks or, alternatively, a microbial imbalance (dysbiosis) contributing to disease. In most cases of NEC, a causative agent is not identified. Ward *et al.* used metagenomic sequencing in combination with computational approaches to analyse the early intestinal microbiome of preterm infants and term infants and found that *E. coli* and *Klebsiella* spp. were among the most prevalent members of the Enterobacteriaceae in samples from preterm infants. Furthermore, the authors functionally subtyped *E. coli* strains and identified colonization by uropathogenic *E. coli* (UPEC) lineages as a risk factor for the development of NEC and infant death. Therefore, early identification of colonizing subtypes could facilitate the rapid assessment of the risk of NEC and inform effective treatment strategies.

Considering that bacterial infections are one of the major causes for mortality in preterm and newborn children, further insights into the links between the parental and neonatal microbiota, and the development of the infant immune system are crucial.

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ORIGINAL ARTICLES Gomez de Agüero, M. *et al.* The maternal microbiota drives early postnatal innate immune development. *Science* http://dx.doi.org/10.1126/science.aad2571 (2016) | Ward, D. V. *et al.* Metagenomic sequencing with strain-level resolution implicates uropathogenic *E. coli* in necrotizing enterocolitis and mortality in preterm infants. *Cell Rep.* http://dx.doi.org/10.1016/j.celrep.2016.03.015 (2016)