

SCAF/16/03 - Early-life effects on host-microbiome interactions: identification of ecological drivers that are key to short- and long-term respiratory problems in pre-term born children

Respiratory health problems such as infections and asthma are leading causes of morbidity and mortality worldwide in young children, and responsible for a majority of doctor's visits and health care costs. Prematurely born children are especially at risk of recurrent and severe respiratory infections in the first years of life. They also have a significantly increased risk of developing asthma in the following years. Respiratory infections are actually caused by pathobionts, i.e. bacteria and viruses that are common members of the respiratory microbiome. Interestingly, early presence of these pathobionts is also associated with development of asthma over time. In recent years it has become clear that the human microbiome plays an important role in pathogen-resistance, immune-maturation and –modulation/inflammation and mucosal barrier function. We recently identified in infants/toddlers distinct microbiota profiles, each associated differently with pathogen overgrowth and containment, as well as with development of acute infections and wheezing episodes over time. Moreover, my work and that of others has shown that 'beneficial' microbiota, associated with reduced risk of infections and wheezing, were also associated with vaginal delivery and breastfeeding. These beneficial profiles, however, were quickly eradicated by early antibiotic treatment. Moreover, it has been shown in separate studies that early-life infections lead to epigenetic modifications of immunomodulating genes, and in other studies that epigenetic modifications of immunomodulating genes are associated with asthma. What is lacking is knowledge on how accumulating harmful early-life events drive the microbiome composition in preterm infants. Furthermore, no single study has investigated the individual links A. early environmental effects, B. microbiome development, C. development of acute/recurrent respiratory infections in the first years of life, D. epigenetic modifications and E long-term development of preschool wheeze in premature and term infants in a single cohort, although this would be the most sensible approach to unravel cause-effect relationships and to determine the independent contribution of each link to the proposed chain of events