

How maternal alcohol consumption impacts the intestinal microbiota of breastfed infants

Summary

Regular or heavy alcohol consumption while breastfeeding is associated with negative developmental outcomes in children. It is well-established that alcohol consumption can impact gut microbiota composition of adults by affecting the fitness of specific bacterial species in the gut. However, little is known about how infant microbiota is affected by chronic maternal consumption of alcohol transferred through breastmilk.

Our bodies are permanently challenged by microbial invaders. Some are repelled while others find a niche to stably colonize their host. The human gut microbiota establishes itself as early as birth from a small number of bacterial species. The bacteria infants ingest can stably colonize their gastrointestinal tract, ultimately constituting the gut microbiota. The commensal species that colonize our intestine can have beneficial functions, improving our metabolism, immunity and even influencing our behavior¹⁻³. Animal studies have identified bacterial species and consortia associated with host health and disease, but moving from correlation to causation remains a challenge, thereby limiting the development of therapeutic strategies to beneficially manipulate our intestinal microbiota⁴.

While we know how stable adult microbiota is to perturbations such as moderate alcohol consumption, whether this is true early in life in infants is poorly established⁵. Infant microbiota has reduced diversity due to the standard diet, mainly consisting of oligosaccharides from breast milk or formula. In general, low diversity is associated with poor stability. We thus hypothesize that maternal alcohol consumption can negatively impact the colonization of intestinal commensals in early life. This, in turn, has a potential impact on the development of immune and metabolic functions which will manifest themselves later in life. Consistent with this hypothesis, administration of antibiotics to infants strongly perturbs intestinal microbiota, correlating with obesity and immune dysfunction. Rigorously testing this hypothesis in infants remains however complex. Here, we propose to take an *in vitro* approach to answer this important public-health related question. In particular, we propose to:

- 1. Build an *in vitro* model infant microbiome consortium**
- 2. Characterize infant microbiome stability *in vitro* upon perturbations mimicking maternal alcohol consumption**
- 3. Characterize microbiome robustness upon perturbations mimicking maternal alcohol consumption in a miniGut organoid system**

Altogether, our approach will contribute to a better understanding of the impact of maternal alcohol consumption on infant health and metabolism through the intermediate contributions of intestinal microbiota. This link might have major impacts on health throughout life that have been so far underestimated.