Project Title

Gut microbiota and immune system alterations in children with Fetal Alcohol Spectrum Disorder (FASD): Implications for mental health

Investigators

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Statement of Purpose

To investigate the link between the gut microbiota and peripheral inflammation in children with FASD and whether this is associated with increased susceptibility to mental health problems.

Project Summary

There is extensive, complex, and dynamic communication among the central nervous system, the immune system, and the gut microbiota, collectively referred to as the gut-immune-brain-axis. A healthy gut microbiota is critical for typical brain development and function; however, persistent imbalances in the gut microbial community with its associated inflammation are linked to altered brain and immune system development, and mental health problems. Due to their critical roles in brain development, alterations in the gut microbiota and immune system disturbances have been extensively investigated in the pathophysiology of many neurodevelopmental disorders, such as autism spectrum disorder (ASD) and attention deficit hyperactivity disorder. Fetal Alcohol Spectrum Disorder (FASD) is a neurodevelopmental disorder that occurs following prenatal alcohol exposure (PAE), with an estimated prevalence as high as 5% in North America. Moreover, approximately 90% of individuals with FASD experience mental health problems, with depression and anxiety being most common. Importantly, our preclinical and clinical studies have demonstrated broad impacts of PAE on immune system development and function. However, an important unanswered question remains – whether the gut-immune-brain-axis is involved in the pathophysiology underlying the high prevalence of mental health problems in individuals with FASD. The goal of this proposal is to fill this gap by characterizing the impact of PAE on the microbiota during childhood and to explore the links between microbiota composition, inflammation, and mental health status.

We hypothesize that children with FASD who display signs of mental health problems will differ from their resilient FASD counterparts (i.e., with no/low signs of mental health problems) and unexposed controls in their microbiota composition and immune function. To address this hypothesis, we will collect blood spots and fecal samples from children with FASD and unexposed controls (girls and boys) currently enrolled in longitudinal studies at three sites: 1) the University of Calgary (led by Dr. Lebel); 2) the University of Guelph (led by Dr. McLachlan); and 3) the University of Queensland (led by Dr. Reid).

Children will complete a battery of mental health, neurodevelopmental, and behavioural assessments, with a summary score [emotionality score (ES)] computed from these assessments to identify “at risk” (high ES) and “resilient” (low ES) children. Blood spots will be used to measure 40 cytokines/chemokines levels and fecal samples used to evaluate gut microbiota composition (16s rRNA sequencing) and short chain fatty acids (key metabolites produced by gut microbes that mediate gut-brain-immune interactions). Bioinformatic analyses will be performed with assistance from Dr. Parfrey (UBC).

This study will fill a critical gap in the field by exploring how immune function and the gut microbiota are affected in children with FASD. In addition, understanding how immune function and gut microbiota composition may confer risk for, or resilience to, mental health problems represents a unique approach that could be widely applied to other neurodevelopmental disorders. Finally, as there are currently minimal treatment options for children with FASD, exploring this new area of the gut-immune-brain-axis could lead to development of novel intervention strategies for these individuals.