Project Title

Influence of early life microbiome maturation on head circumference growth and neurodevelopment in premature children

Investigators

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Statement of Purpose

The project will determine if the microbiome immaturity in preterm infants contributes to head circumference growth and neurodevelopmental delay.

Project Summary

In Canada and globally, premature infants (born before 37 weeks of gestation) are much more likely to develop neurodevelopmental disorders impacting cognitive, neuro-motor and behavioural abilities, resulting in poor health outcomes, healthcare and socioeconomical burdens. Every year, 8.0% of Canadian infants are born prematurely in intensive care units (NICU), representing more than 29,000 Canadian infants, resulting in an estimated cost of $8 billion to the health care system and immense socioeconomic cost to families. Globally, premature birth results in 74 million years of life lost due to premature mortality and 3 million years lost to suboptimal health. Enhanced premature infant survival has not resulted in a decrease in neurodevelopmental outcomes, leaving preterm infants at higher risk to develop neurodevelopmental life-long disorders. Thus, there is an urgent need to decipher the biological and environmental determinants to improve early detection and treatment of neurodevelopment outcomes in this fragile population of babies.

Our group and others have made promising clinical and animal findings that implicate the large community of microbes in the human gut (gut microbiome) as a factor contributing to neurodevelopment and behaviour. We recently demonstrated that administration of probiotics containing bifidobacterial strains to extremely premature infants shortly after birth promoted a transition to a term-born, more stable and resilient microbiome composition, a phenomenon defined as microbiome maturation. Importantly, premature infants whose microbiome starts resembling that of healthy, term-born by the age of term, displayed improved head circumference growth compared to infants whose microbiome remained immature. Head circumference growth is a commonly-used marker of neurodevelopment and cognitive function in infants, with poor postnatal head growth in preterm infants being strongly associated with deficient neurodevelopmental outcomes. Thereby, we hypothesized that microbiome maturation in premature infants is independently associated with increased head circumference growth (z-scores) at term age and improved neurodevelopment at ages 2 and 3. If corroborated, this potentially ground-breaking discovery could lead to new microbiome-based strategies to mitigate and/or resolve the risk of neurodevelopmental disorders in this at-risk population of infants.

In this proposal, we aim to determine whether microbiome maturation in premature infants is independently associated with increased head-circumference growth at term-age and improved neurodevelopment at ages 1 and 3. To do so, we will leverage an existing longitudinal cohort of premature infants designed to meticulously monitor the microbiome and health outcomes in this

population. We will apply advanced predictive and causal inference models to microbiome and clinical data from our existing cohort study to first determine correlations and directionality between gut microbiome maturation and head circumference growth trajectories. We will also determine if gut microbiome maturation mediates the association between head circumference growth and neurodevelopment at ages 2 and 3.

Our work will determine if the well-established link between head circumference growth and neurodevelopmental delay can be explained by microbiome immaturity in preterm infants. This would open new perspectives for pre-clinical and clinical microbiome-based therapeutics aimed at decreasing the risk neurodevelopmental disabilities in thousands of premature children.