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Role of microglial metabolism in perinatal neuroinflammation (MICRO-MET)

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Infants born preterm are at a markedly increased risk of perinatal brain damage. Birth at less than 28 weeks gestation bears an 80-fold increased risk of developing brain injury and cerebral palsy (CP) the most common cause of severe disability in children.

A leading cause of brain damage in preterm infants is exposure to systemic inflammation, a maternal/foetal infection normally contracted during their hospital stay, which induces inflammation in the brain (neuroinflammation).

Neuroinflammation impairs the development of oligodendrocytes, the cells responsible for enabling high-speed transfer of information between neurons. Microglia (MG), the brain's immune cells orchestrate the inflammatory response. These cells can promote both beneficial and detrimental functions in developing brains; however, the cellular mechanisms governing these contrasting functions are poorly understood. Novel insights are needed to prevent the deleterious functions regulated by MG and alter them into neurosupportive functions. The metabolic features of MG have yet to be investigated, although it is increasingly clear that in several cell types metabolic activity has a key impact on cellular function.

The objectives of MICRO-MET are to understand the links between MG metabolism and MG function and to identify the genes responsible for these mechanisms. We will selectively block key metabolic pathways and assess the consequences on MG function and will manipulate key metabolic MG pathways in a mouse model relevant to perinatal brain damage. Our research will help unravel the complex MG functions to combat perinatal brain injury.