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"Microglia and Acute Pediatric Hypoxic Events."

Pediatric stroke is one of the top ten causes of death in children. Hypoxia is associated with cell damage and cell death. A cellular response to hypoxia is the upregulation of the transcription factor hypoxia inducible factor 1a (HIF). HIF in turn activates genes that deal with metabolism, glucose uptake, apoptosis and angiogenesis to name a few. During stroke, reactive oxygen species form, which leads to build up of hydrogen peroxide. Hydrogen peroxide can act as a chemoattractant for microglia. Microglia, the resident immune cells of the brain, provide both neuroprotective signals and inflammatory signals that can cause neuronal damage and removal. While removing pathogens and ailing neurons is important for neural circuit integrity, overactive microglia can lead to excessive cell death. Recently HDAC inhibitors were shown to be neuroprotective after stroke. We hypothesize that HDAC inhibitors directly act upon microglia by increasing neurotrophin release, altering phagocytosis and motility dynamics following brief hypoxia. This project will lay the foundation of pediatric hypoxic experiments in my lab. Furthermore, these experiments will elucidate fruitful targets to alleviate cell death following pediatric hypoxia which will be the focus of an NIH proposal.