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*Anesthesia-Induced Developmental Neurotoxicity: the Role of Immature Microglia*

**Abstract**

My goal is to understand the role of the neural immune system in anesthetic-induced neonatal neurotoxicity, and eventually to identify therapeutic targets to ameliorate it. Studies have demonstrated the neurotoxic effects of anesthetics in neonatal animal models with implications for abnormalities in both neurocognition and behavior. Although the exact mechanism is unknown, multiple factors have been implicated including neuroapoptosis, impaired synaptogenesis, and suppressed neurogenesis. Because microglia promote neurogenesis, are vital for phagocytosis of apoptotic debris, and participate in synaptic pruning, it is critical to evaluate whether microglia play a role in anesthetic-induced neurotoxicity. At present, microglial contributions remain largely unexplored. I present preliminary evidence that exposure to sevoflurane on postnatal day 7 leads to altered development of murine microglia. Sevoflurane-exposed microglia undergo premature ramification, exhibit decreased proliferative capacity, and up regulate expression of the GABAB receptor on ramified microglia. Based on these findings, we hypothesize that exposure to sevoflurane impairs the normal development of microglia by promoting their premature ramification through activation of the GABAB receptor. To test this hypothesis, the project will address the following aims: 1) Characterize microglial morphology and phenotype after sevoflurane as measured by flow cytometry, immunohistochemistry, and immunofluorescence. 2) Evaluate the potential role of the GABAB receptor in this process. The information gathered through this research will lead to the development of a K08 grant and will help promote Dr. Christine Zanghi as an independent physician-scientist.