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Neuroinflammation: Dissecting microglia phenotypes and contributions to injury and repair

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Neuroinflammation is associated with a variety of states within the brain including injury, disease, neurological disorders, and aging. These states have often been associated with a morphological shift in the brain monocyte, the microglia, suggesting an anatomical approach to determining the neuro-inflammatory responses. Of concern is the heterogeneity of the microglia response and the beneficial versus detrimental nature of the response and how this relates to morphological changes in microglia is not clearly characterized. As the primary cellular source for inflammatory factors, microglia serve surveillance, maintenance and repair functions and display varied phenotypes, some beneficial while others require active regulatory control. Dissecting the distinct phenotypes of microglia subsets as associated with various functions (e.g., clearance of debris, synaptic remodeling and neuronal protection) is a critical step in characterizing unique responses contributing to functional differences. Using the trimethyltin mouse model of inflammatory-related hippocampal injury, resident microglia morphological heterogeneity was examined across hippocampal sub-regions and found to be associated with a spatial and temporal elevation of pro and anti-inflammatory cytokines, iNos, and complement expression. These patterns were differentially associated with neuronal death and synaptic loss but were also related to the repair mechanisms initiated. Upon further examination by protein micro-characterization, unique profiles were demonstrated in the distinct hippocampal regions suggestive of phenotypic classifications of microglial and their environmental niches. Further examination of microglia heterogeneity of morphology and associated molecular/biochemical factors will significantly contribute to our understanding of the functional impact of a microglia/neuroinflammatory response following chemical exposure.

Biography

G Jean Harry, PhD, is Head of the Neurotoxicology Group. She obtained an MS in Neuropharmacology from Virginia Commonwealth University with a research focus in drugs of abuse. Her PhD was obtained from VCU in 1981, and bridged the fields of neuropharmacology and neurotoxicology with her research conducted at NIH. Postdoctoral work was conducted in an NIH Training Program in Neuropathology followed by an NIH independent fellowship award in the Biochemistry Department, University of North Carolina. Following a position within the Developmental Disorders Center at UNC, she joined NIEHS as head of Neurotoxicology Group in 1990.

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