Effects of lipopolysaccharide-induced neuroinflammation on proliferation, survival, and differentiation of adult neural stem/progenitor cells

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Adult neurogenesis is the process of generating new neurons from neural stem/progenitor cells (NPCs) that occurs during adult life in discrete regions of central nervous system (CNS) (*i.e.*, the subventricular zone of the lateral ventricle and the subgranular zone of the dentate gyrus of the hippocampus). NPCs may be useful as an endogenous or transplantable source of newly generated cells, with a potential therapeutic use in many pathological conditions of the CNS, particularly in neurodegenerative diseases. A prerequisite for this is an appropriate sequence of NPC proliferation, differentiation, survival, and progressive maturation into fully functional and integrated neurons. Since most CNS disorders are associated with inflammatory processes, it is important to understand NPC development under inflammatory conditions. In the CNS, the inflammatory process is initiated by microglial cell activation. The latter respond rapidly to pathological changes in the brain by producing and releasing various pro- and anti-inflammatory cytokines, chemokines, neurotransmitters, and reactive oxygen and nitrogen species, in turn modulating the different steps of adult neurogenesis.

In the present study we used lipopolysaccharide-activated microglial cells as an *in vitro* model of neuroinflammation to analyze the effects of conditioned medium on proliferation, survival, and differentiation of NPCs obtained from the subventricular zone of adult mice. Activated microglial cells significantly decreased proliferation and neuronal differentiation of NPCs, without affecting glial differentiation. Furthermore, lipopolysaccharide-activated microglia induced an abnormal NPC-derived cellular phenotype characterized by a simultaneous expression of neuronal and glial markers, indicating a molecular or functional dysregulation.

A better understanding of the mechanisms modulating inhibition of neuronal differentiation and the generation of cells expressing neuronal and glial markers during neuroinflammation could help to develop pharmacological strategies for promoting stem cell therapies which target neurodegenerative diseases with a strong inflammatory component.