Project Title:

Translational and mechanistic approaches on carbon monoxide as a modulator of neuroinflammation and neuroprotection in the brain

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Summary: (1000 characters)

Exacerbated neuroinflammation and neural cell death are complex process leading to the progressive decline of neuronal activities associated with the development of neurodegenerative diseases but are also key features in the pathogenesis of ischemic stroke (Allaman et al., 2011; Saijo and Glass, 2011) (Eltzschig and Eckle, 2011). Thus, it is crucial and urgent to investigate the cross-talk between neuroinflammation and neuronal cell injury with novel conceptual and methodological approaches that may eventually lead to novel therapies. The heme oxygenase-1 (HO-1) / carbon monoxide (CO) pathway is a plausible novel target that could be explored for such approaches (Motterlini and Otterbein, 2010; Queiroga et al., 2014). The ultimate aim is to identify the cellular and biochemical pathways involved in CO/HO-1 modulation of neuroinflammation and neuroprotection, in particular the role of mitochondria. Astrocyte and microglia functions will be targeted for inducing neuroprotection and modulation of neuroinflammation. This strategy takes advantage of the glial cells natural occurring neuroprotective mechanisms of the physiological role of astrocyte and microglia in maintaining brain homeostasis, metabolism and neuronal functioning. Secondly, the direct effect of CO/HO axis will be studied on neurons.

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