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INDUCTION OF MICROGLIA M2 POLARIZATION IN MALE AND FEMALE MICE AND IN RESPONSE TO ESTROGENS USING ICV INJECTION OF IL4

Microglia have the unique property to sense any pathological event and to immediately undergo biochemical and morphological transformations that destroy the damaging insult and trigger tissue repair. The alternatively activated M2 phenotype is associated with anti-inflammatory and regenerative activities, although the ability of microglia within specific brain regions to respond to polarizing signals is not understood yet. We have since long been interested in studying the neuroimmunomodulatory activity of the female steroid hormones, estrogens, and analyzing their role in the sexual dimorphism observed in the pathophysiology of selected neurodegenerative and inflammatory diseases. We previously showed that estrogens can reduce the M1 pro-inflammaotry response of microglia in vivo and in vitro. The aim of the present study is thus to optimize an animal model of M2 polarization by using intracerebroventricular (icv) injections of interleukin-4 (IL4)[1] and to compare microglia polarization among males and females and in response to circulating estrogen levels. The expression of M2 genes and proteins was evaluated in mouse brain areas at different time points following icv IL-4. Our data show that only a subpopulation of microglia is able to respond to icv IL-4 which may translate into physiologically and pathologically relevant region-specific differences in the regenerative potential of microglia against brain insults. Our preliminary results also show a sex and estrogen-dependent dimorphism of microglia responsiveness to M2 activating signals, suggesting a relevant role for this hormone on microglia reactivity in acute and chronic neuroinflammation.

[1]Pepe G. et al, J Neuroinflammation 2014