TRANSLOCATOR PROTEIN (TSPO, 18 KDA) IN NEUROINFLAMMATION: INVESTIGATION OF ITS FUNCTIONAL ROLE IN PRIMARY HUMAN MICROGLIA

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The mitochondrial translocator protein (TSPO, 18 kDa) is a multifunctional protein implicated in the modulation of several fundamental processes such as steroidogenesis, respiration and production of reactive oxygen species [1]. Recently, it has been proposed to play a pivotal role in neuroinflammation as its expression levels increase in microglia and astrocytes following an inflammatory stimulus, and return to basal levels when the phenomenon is resolved. However, conflicting data have been accumulated mainly due to the use of in vivo and in vitro murine models of neuroinflammation/neurodegeneration [2,3]. Thus, further information are required to propose a TSPO-mediated mechanistic model.

The potential homeostatic role of TSPO during the neuroinflammatory response were evaluated in a model of primary human inflamed microglia (C20 cells). Two different experimental approaches were exploited: i) completely silencing the protein (TSPO knock-out C20 cells) or ii) amplifying the TSPO physiological function by pharmacological stimulation. In the latter case, the effects elicited by synthetic ligands characterized by low and high neurosteroidogenic ability were compared. In basal conditions, the TSPO knock-out C20 cells showed a more inflamed phenotype than wild-type C20 cells. Moreover, they resulted more responsive to the immunogenic stimulus. In parallel, the pharmacological stimulation of TSPO promoted the shift of microglia from pro- to anti-inflammatory phenotype. The blockade of steroidogenic pathway abolished the ligand-induced effects demonstrating the pivotal role of neurosteroids for TSPO action. In conclusion, the results obtained in the present experimental setting suggest that TSPO contributes in maintaining the microglia well-being, exerting a negative regulation on neuroinflammatory mechanisms

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[2] Glia, Choi J et al., 2011, 59:219-30

[3] J Neuroimmune Pharmacol, Bae KR et al., 2014, 9:424-37