**The effect of novel TSPO Ligands 2-Cl-MGV-1 and MGV-1 on LPS-induced microglial activation**

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Previous studies have shown that the 18 kDa translocator protein (TSPO) ligands 2-Cl-MGV-1 and MGV-1 can prevent cell death of astrocyte-like cells (U118MG) and to induce differentiation of neuronal progenitor cells (PC-12), including neurite outgrowth. This suggests that these ligands may have therapeutic effects in several brain diseases. Brain injury and some neurodegenerative diseases leads to microglial activation. Microglial activation is associated with over-expression of TSPO. Neuro-inflammatory response of the central nervous system (CNS) is associated with microglial activation. Lipopolysaccharide (LPS) is a bacterial membrane protein which activates the cellular inflammatory pathways. The response to LPS includes activation of microglia and corresponding release of pro-inflammatory molecules, including cytokines and chemokines, such as, Interleukin-6 (IL-6), IL-1β, Interferon- γ (IFN-γ), inducible nitric oxide synthase (iNOS), cyclo-oxygenase-2 (COX-2), and nitric oxide (NO). In the present study we demonstrate that the TSPO ligands 2-Cl-MGV-1 and MGV-1 can prevent the LPS-induced activation of microglia (BV-2 cell line). Co-administration of the LPS with TSPO ligands (final concentration- 25 μM) can reduce significantly the release of IL-6 by 91%; IL-β by 95%, IFN- γ by 91%; and TNF-α by 94%. Also, we found that 2-Cl-MGV-1 and MGV-1 could decrease NO levels by 100% within 48 hours, when the ligands were administrated with fresh medium every 24 hours. Median fluorescence intensity of cardilipin peroxidase and cell metabolism assay shows significant effects after the administration of these two novel TSPO ligands. No alterations in IL-10 and IL-13 were detected. Thus, it appears that 2-Cl-MGV-1 and MGV-1 can suppress the LPS-induced activation of inflammatory responses of microglia. Such an effect may be relevant to inflammatory diseases. Acknowledgements: The Israel Science Foundation is thankfully acknowledged for their support for this project (Prof. Moshe Gavish 1931/14).