POSTER

BET PROTEIN INHIBITION ATTENUATES MICROGLIAL ACTIVATION AND OXIDATIVE STRESS IN A CELLULAR MODEL OF PARKINSON'S DISEASE

E. Bisesto[1], D. Pensabene[1], M. Colardo[1], M. Varone[1], M. Segatto[1]

[1]*Dept. of Biosciences and territory, University of Molise, Pesche (IS), Italy*

Microglia are the resident immune cells of the central nervous system (CNS) and play a pivotal role in neuroinflammatory processes associated with neurodegeneration. In Parkinson's disease (PD), microglial activation contributes to disease progression through the release of pro-inflammatory mediators and reactive oxygen species (ROS). Among the emerging epigenetic regulators, bromodomain and extra-terminal (BET) proteins have gained attention as potential therapeutic targets. Nonetheless, their role in microglial reactivity in PD remains elusive. This study aimed to investigate the effects of BET protein inhibition in a microglial in vitro model of Parkinsonian-like neurotoxicity induced by rotenone. Cells were pre-treated with the BET inhibitor JQ1 and subsequently exposed to rotenone to evaluate changes in microglial activation, inflammatory response, and oxidative stress. The collected data suggest that BET inhibition attenuates microglial reactivity. Notably, JQ1 treatment reduced the upregulation of pro-inflammatory cytokines and oxidative stress markers induced by rotenone administration, while partially restoring the expression of key regulators of cell homeostasis. Furthermore, BET inhibition did not significantly affect NF-κB expression, a master regulator of inflammation and a central mediator of oxidative stress-related signaling in microglia, suggesting the involvement of alternative regulatory pathways. Overall, these findings highlight a modulatory role of BET proteins in microglial activation and suggest that their pharmacological inhibition may represent a promising strategy to counteract neuroinflammation and oxidative damage in PD. Further studies in more complex models are warranted to dissect the specific contribution of individual BET family members and to validate their therapeutic potential in vivo.