Investigating the role of DJ-1/LRRK2 and RhoT1 in microglial polarization

https://www.neurodegenerationresearch.eu/survey/investigating-the-role-of-dj-1lrrk2-and-rhot1-in-microglial-polarization/

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Investigating the role of DJ-1/LRRK2 and RhoT1 in microglial polarization

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Research Abstract

Several lines of evidence suggest that different mediators derived from non-neuronal cells could modulate the initiation and/or progression of Parkinson?s disease (PD). Microglial cells are the immune effectors of the central nervous system (CNS) and actively communicate with the neuronal network. Depending on the type of environments they encounter, microglial cells are skewed along a continuum spectrum of activation, the M1 (classical activation) and M2 (alternative activation) states representing its extremes. Although the idea that these cells may play a crucial role in responding to specific cues in the CNS, the functional significance of microglial cell contribution in the establishment of specific responses correlated to

neurodegeneration remains to be defined.Mitochondrial dysfunction has been postulated to play a major role in PD. Exposure to pesticides that are complex I inhibitors, such as rotenone, has been linked to increased risk of developing PD. Different loss- or gain-of-function mutations responsible for rare forms of PD code for mitochondria-associated factors and, among others, DJ-1, LRRK2 and RhoT1 mutations have been associated with early-onset PD. While the damaging effects of mitochondrial dysfunction in neurons have been extensively analysed, we suggest here to investigate its consequences in microglial cells. Mitochondrial impairments will be achieved genetically using DJ-1-KO/LRRK2(R1441C) double mutant mice and RhoT1 KO mice. By coupling in vitro and systems biology/-omics approaches (transcriptomics, metabolomics and high content imaging) we aim to identify specific signalling and metabolic pathways modulated in microglia under mitochondrial dysfunction, thus going one step further on the characterization of microglial cells polarization associated to neurodegenerative processes. Taken together, the results of the present project could lead to the identification of novel targets whose therapeutic modulation could help to promote a specific beneficial microglial cell phenotype in PD.

Further information available at:

https://www.fnr.lu/projects/investigating-the-role-of-dj-1lrrk2-and-rhot1-in-microglial-polarization-2/

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