

VIRAL RNA MIMETICS-INDUCED ALTERATIONS IN MICROGLIAL FUNCTION AND MITOCHONDRIAL NETWORK ARCHITECTURE

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Neurodegenerative diseases are a group of neurological disorders that negatively affect the lives of many people worldwide and are associated with progressive loss of neurons in the central nervous system (CNS) or peripheral nervous system (PNS). Treatment of these neurological diseases is limited to symptomatic management, and this is mainly due to the lack of advances in the understanding of the molecular mechanisms underlying neurodegenerative processes.

Some of the main processes associated with neurodegenerative diseases are related to neuroinflammation. Key factors and triggers of neuroinflammatory responses are viral and bacterial infections, which activate innate immune response and innate immune effector cells, primarily microglia, which have a negative impact on neuronal viability and function. Viral components can activate pattern recognition receptors on microglia, such as TLR3 and TLR7, and modulate neuroinflammatory response. Several studies also suggest that changes in mitochondrial function and structure can modulate microglia cell response during neuroinflammatory response, but these molecular mechanisms remain poorly understood.

In this study, we investigated the microglial BV-2 cell line and their mitochondrial response to viral RNA-mimetic compounds Loxoribine and Poly (I:C) by various methods, including fluorescence microscopy, BrdU labeling assay, polymerase chain reaction (PCR) and Oroboros O2k oxygraphic system.

Our findings indicate that loxoribine and Poly (I:C) have no effect on BV-2 microglia cell culture viability and proliferation or mitochondrial content changes. Moreover, Poly (I:C) does not affect oxidative phosphorylation of BV-2 microglia cells. However, loxoribine exerts a concentration-dependent effect – lower concentrations stimulate oxidative phosphorylation and maximum respiratory rate, but higher concentrations of loxoribine inhibit mitochondrial respiration rate. Additionally, Loxoribine and Poly (I:C) have no effect on BV-2 microglia fusion (Mfn1, Mfn2, Opa1) or fission (Drp1, Fis1) marker gene expression change, but significantly increased fission marker (Mff) and tend to alter mitochondrial biogenesis regulatory factor (PGC-1 α) expression.

The present results suggest that viral RNA-mimetic Poly (I:C) does not influence BV-2 microglia cells or their mitochondria, but loxoribine has a concentration-dependent effect and may alter genes related to mitochondrial dynamics and oxidative phosphorylation.

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