Neurotrophin receptor ligands modulate select immune functions of microglia

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Introduction

Alzheimer’s disease

- Alzheimer’s disease (AD) is a severely debilitating brain disorder characterized by progressive cognitive decline and dementia.
- An accumulation of amyloid beta (AB) protein plaques and neurofibrillary tangles, as well as a state of chronic neuroinflammation, are the main hallmarks of AD pathology.

Hypothesis

LM11A-31 and proBDNF reduce the neurotoxic effect and secretion of ROS and RNS by activated microglia, as well as modulate microglial phagocytic activity.

Methods

- Murine BV-2 microglia: Stimulated with lipopolysaccharide (LPS) 24 hours after NTR ligand treatment
- Human THP-1 microglia-like cells: Stimulated with interferon-gamma (IFN-γ) and LPS 24 hours after treatment with NTR ligands
- SH-SY5Y neuronal cells: Cell viability tested with the MTT and propidium iodide assays 72 hours after treatment with above mentioned THP-1 microglia
- Murine BV-2 microglia: Stimulated with lipopolysaccharide (LPS) 15 min after NTR ligand treatment
- Respiratory burst induced by formyl-methionyl-leucyl-phenylalanine (FMLP) 24 hours later to detect ROS secretion as increased chemiluminescence signal.

Results

- proBDNF upregulates phagocytosis of latex beads by BV-2 microglia

Conclusions

- LM11A-31 and proBDNF do not affect RNS secretion by murine microglial BV-2 cells as shown by the Griess assay.
- LM11A-31 and proBDNF do not affect MCP-1 secretion by human THP-1 microglia-like cells as shown by ELISA.
- LM11A-31 and proBDNF have no effect on the viability of SH-SY5Y neuroblastoma cells following their exposure to cytotoxic THP-1 microglia-like cell supernatants.

Abbreviations

- BDNF: Brain-derived neurotrophic factor
- NGF: Nerve growth factor
- MCP-1: Monocyte chemoattractant protein-1
- TNF: Tumor necrosis factor
- LPS: Lipopolysaccharide
- FMLP: Formyl-methionyl-leucyl-phenylalanine
- ROS: Reactive oxygen species
- RNS: Reactive nitrogen species

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