The Effects of Resveratrol on Neuroinflammation

Lucine Devejian[1], Avisankar Chini[1], Prarthana Guha, Ashcharya Rishi, Nagashree Bhat and Subhrangsu Mandal*

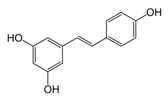
Department of Chemistry and Biochemistry, University of Texas at Arlington, Arlington, TX

Abstract

Neuroinflammation and immune signaling pathways involve various genomic and protein-based factors, such as cytokines, interferons, and long noncoding RNAs (lncRNAs). Our study is focused on understanding the regulatory mechanisms underlying the complexity of this prevalent disease and developing advanced therapeutic approaches. Resveratrol is a polyphenolic compound naturally occurring in many plants such as grapes, berries, and peanuts, known for its antioxidant, anti-inflammatory, and anticancer activity. The goal of this study is to perform an *in vitro* analysis of the effects of resveratrol on mouse microglia cells to determine its effectiveness at reducing neuroinflammation. In this study, we investigated the effect of resveratrol on known biomarkers and protein-based factors, along with lncRNAs which have been reported as crucial players in neuroinflammation. The analysis is performed by quantifying RNA and protein levels of inflammatory genes and cytokines. Analyzing the expression of lncRNAs under neuroinflammation reveals new aspects of gene regulation in neurodegenerative disorders. Our results indicate that resveratrol could potentially hold implications as a preventative and therapeutic candidate for Alzheimer's and other neuroinflammatory diseases.

Introduction

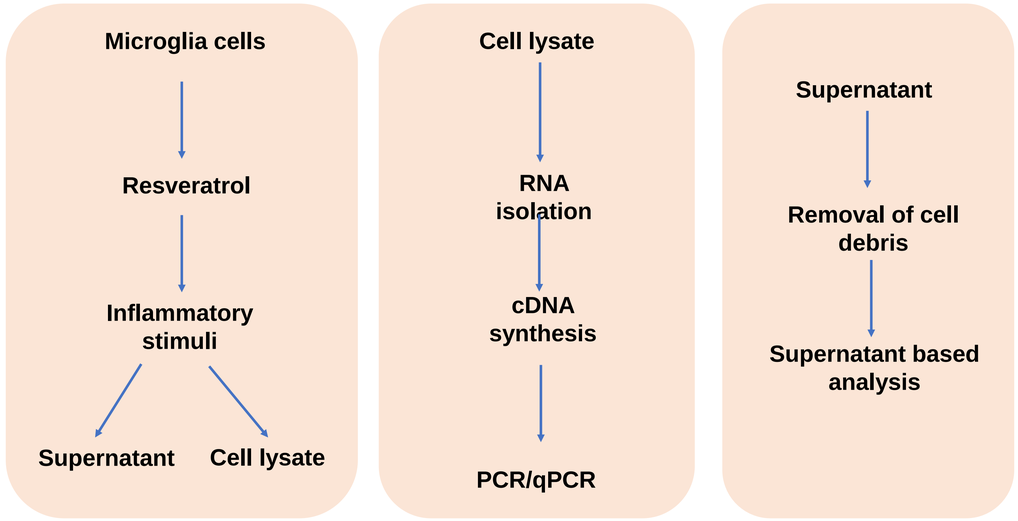
- Neuroinflammation is known to be one of the main causes of neurodegenerative diseases.
- Microglial cells are brain resident macrophages. This study uses BV2 cell line, which is mouse microglial cells to perform *in vitro* analysis.



Resveratrol

- Along with many protein-coding genes, long noncoding RNAs (LncRNAs) are found to be involved in regulation of neuroinflammation and inflammatory signaling pathways.
- Lipopolysaccharide (LPS, a gram-negative bacterial cell wall component, an endotoxin) is known to induce inflammation by activating the NF-κB signaling pathway.
- Resveratrol is a naturally occurring polyphenolic compound, which is reported as having antioxidant, anti-inflammatory, and anticancer activity.
- Here we aim to explore its potential regulation of known inflammation-associated factors such as cytokines.

Materials & Methods



Discussion

- RT-qPCR analysis shows Resveratrol downregulates cytokines such as IL-6 and IL-1β.
- Resveratrol downregulates Nitric Oxide (NO) release levels and suppresses microglial activation.

Future Work

- In the future, protein content of cells will be analyzed to determine how resveratrol affects the NF-κB inflammatory signaling pathway.
- Additionally, the effects of resveratrol on lncRNAs associated with neuroinflammation will be analyzed using PCR and qPCR, such as HOTAIR and BACE1-AS.
- The study will also be extended towards the effect of resveratrol in Aβ-peptide induced neuroinflammation in human cultured microglia cells (HMC3) and to reveal the potential new players in neuroinflammation.
- This finding could lead to strategize inflammation-associated disease diagnosis and potential therapeutics.

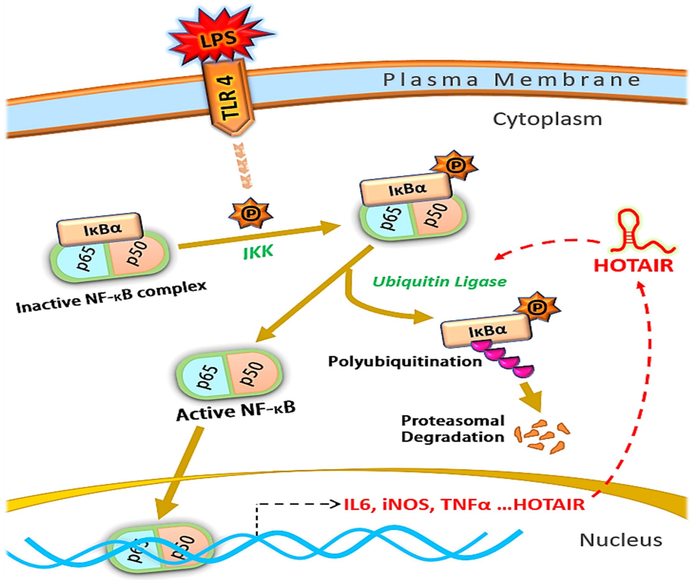
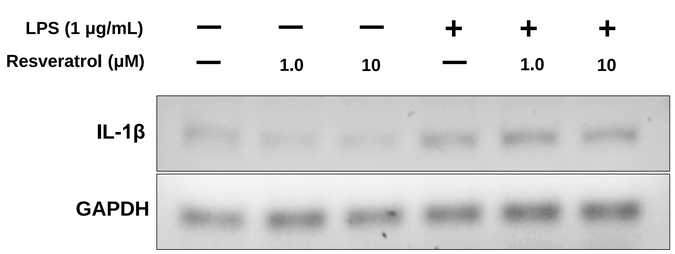
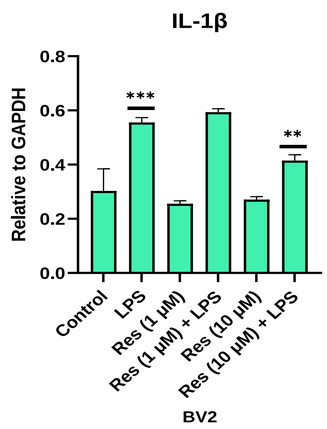


Fig: NF-kB signaling pathway

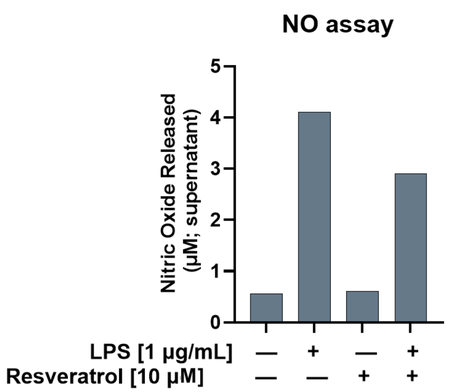
Results

PCR analysis shows Resveratrol downregulates cytokines

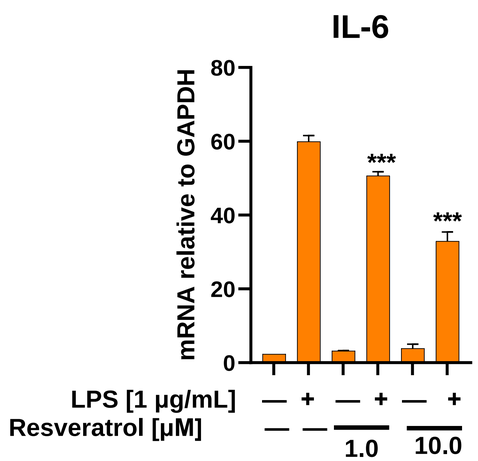


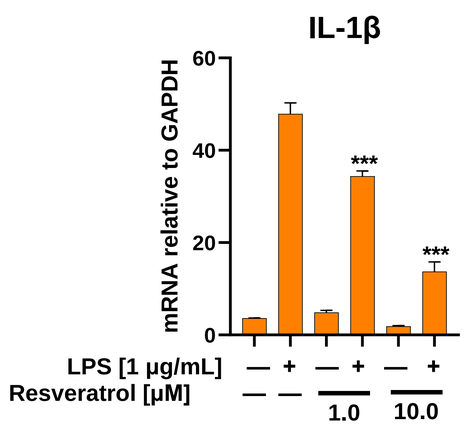


Resveratrol downregulates Nitric Oxide release



RT-qPCR analysis shows Resveratrol downregulates cytokines





References

- Chini *et. al.*, Novel Human Long-noncoding RNAs associated with Inflammation and Macrophage Activation. Sci Rep 13, 4036 (2023).
- Obaid *et. al.*, LncRNA HOTAIR regulates lipopolysaccharide-induced cytokine expression and inflammatory response in macrophages. Sci Rep 8, 15670 (2018).

Acknowledgement

NIH National Institutes of Health *Turning Discovery Into Health*

1 R15 HL170257-01

- **National Science Foundation (NSF AGEP Award - 2243017)**
- **The Schwartzberg Companies**