The Effects of Novel Anti-Inflammatory Drugs on LPS-Induced Cytokine Gene Expression BV2 Cells

Ana Herget, Dr. Giridhar Akkaraju
Department of Biology at Texas Christian University Fort Worth, TX 76129

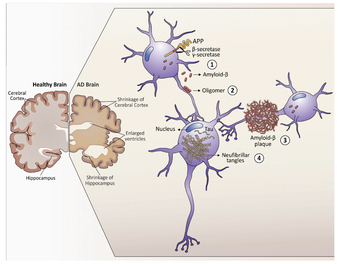
Alzheimer's Disease (AD), the most common form of dementia, currently impacts almost seven million people in the United States over the age of 65. It is predicted that by 2060 over 13 million people in the United States will be affected by AD, which is why there is a growing demand for treatments. Amyloid β plaques and phosphorylated tau proteins are both associated with the progression of the AD pathology since they play a role in the disruption of neuronal integrity. These aggregated proteins along with other molecules, such as lipopolysaccharide (LPS), lead to increased inflammation by activating the NFκB pathway. The NFκB pathway controls the production of proinflammatory cytokines, such as interleukin-1 beta (IL-1β) and tumor necrosis factor-alpha (TNF-α); however, if it is overactive, it can lead to harmful inflammation. The company P2D Biosciences provides novel compounds designed to reduce inflammation, but the exact mode of action of these compounds is unknown. Quantitative reverse transcription polymerase chain reaction (RT-qPCR) can be utilized to measure cytokine mRNA from BV2 cells that have been pretreated with the drugs and then with LPS. In this project we screened multiple compounds provided by P2D Biosciences to evaluate their use as anti-inflammatory agents to treat AD.

I. Introduction

Alzheimer's Markers
-Amyloid β plaques
-Neurofibrillary tau tangles

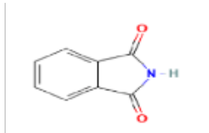
Amyloid β Formation
-BACE1 improperly cleaves the amyloid precursor protein (APP)

Cell Culture
-BV2: mouse microglial cells
-Produce cytokines
-Induced by LPS

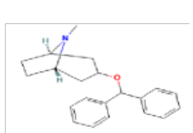


2. P2D Compounds

PD340



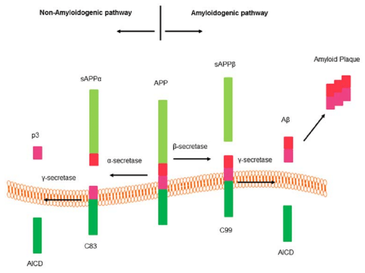
PD2244

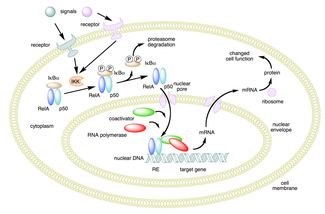


3. Hypothesis

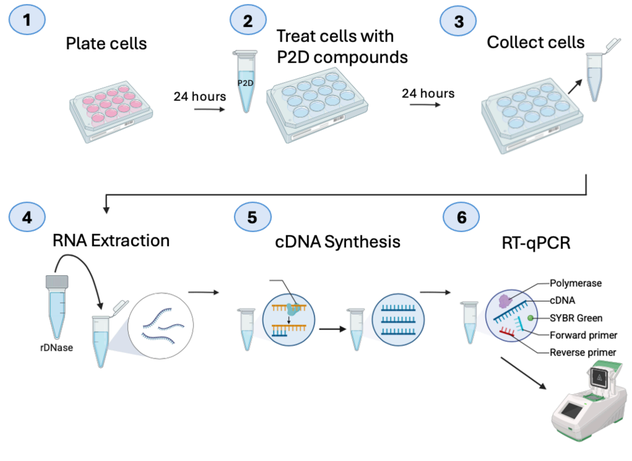
Anti-inflammatory Compounds reduce LPS-induced cytokine gene expression in BV2 cells through NFκB regulation

4. NFκB and APP





5. Methods - RT-qPCR



6. Results

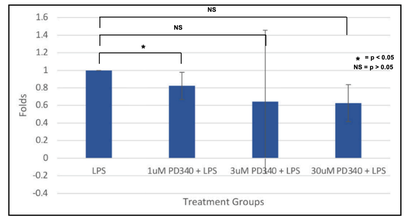


Figure 1 - PD340 - IL-1β

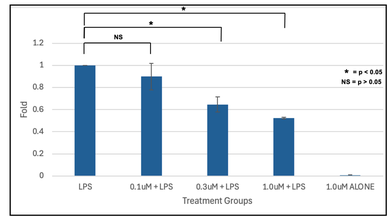


Figure 3 - PD2244 - IL-1β

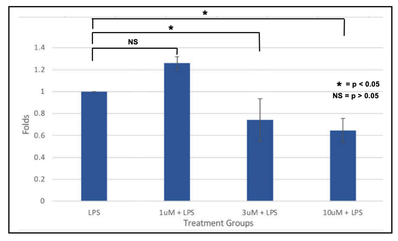


Figure 2 - PD340 - TNF-α

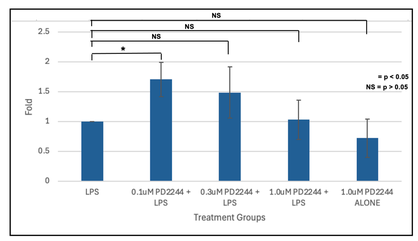


Figure 4 - PD2244 - TNF-α

7. Conclusions

Compounds	IL-1β	TNF-α
PD340	↓	↓
PD2244	↓	↑

- Test PD340 and PD2244 on HT22 (neuronal) and HEK293 (human fibroblasts) cells
- Stimulate the NFκB pathway in HT22 cells with amyloid β
- Test new P2D compounds in BV2, HEK293, and HT22

8. Acknowledgements

Thank you to Dr. Akkaraju for his support, guidance, and leadership!

9. Resources

J. R., Gonzalez, G. A., Barker, W., & Duara, R. (2024). Neuropathology, Neuroimaging, and Fluid Biomarkers in Alzheimer's Disease. *Diagnostics*, *14*(7), 704. https://doi.org/10.3390/diagnostics14070704.
NFKB mechanism of action.png. (2022, May 13). *Wikimedia Commons*. Retrieved 03:49, April 3, 2025 from https://commons.wikimedia.org/ w/index.php?title=File:NFKB mechanism of_ action.png&oldid=655818891.
Zhao, J., Deng, Y., Jiang, Z., & Qing, H. (2016). G Protein-Coupled Receptors (GPCRs) in Alzheimer's Disease: A Focus on BACE1 Related GPCRs. *Frontiers in Aging Neuroscience*, *8* https://app.biorender.com/illustrations/67ecd603297a9c9ae1586d7c