

The Effect of Novel P2D Anti-Inflammatory Compounds on TNF- α Induced NF κ B Activation

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



Abstract

Chronic inflammation is a major contributor to neurological damage in diseases such as Alzheimer's, which currently affects nearly 7 million Americans. The NF- κ B signaling pathway plays a critical role in mediating inflammatory responses, as it regulates the expression of several pro-inflammatory cytokines, such as TNF- α , that exacerbate neuroinflammation. This study investigates the effectiveness of P2D compounds in regulating TNF- α induced NF κ B activation, using a luciferase reporter assay.

Methods

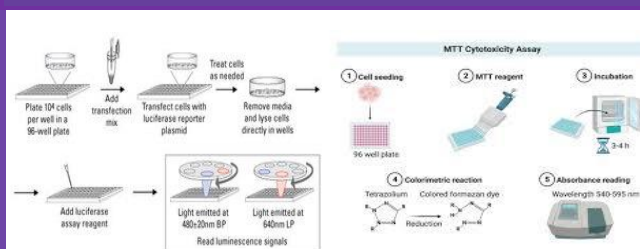


Fig. 1 Luciferase Assay

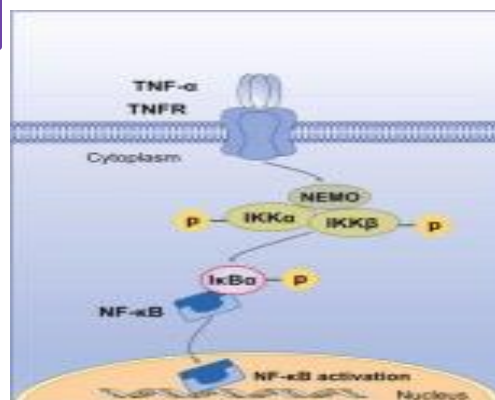
Fig. 2 MTT Assay

Hypothesis

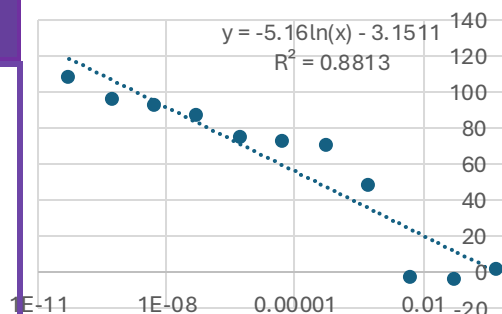
Novel P2D compounds inhibit inflammation by blocking TNF-induced activation of NF κ B in HEK293 cells.

Background

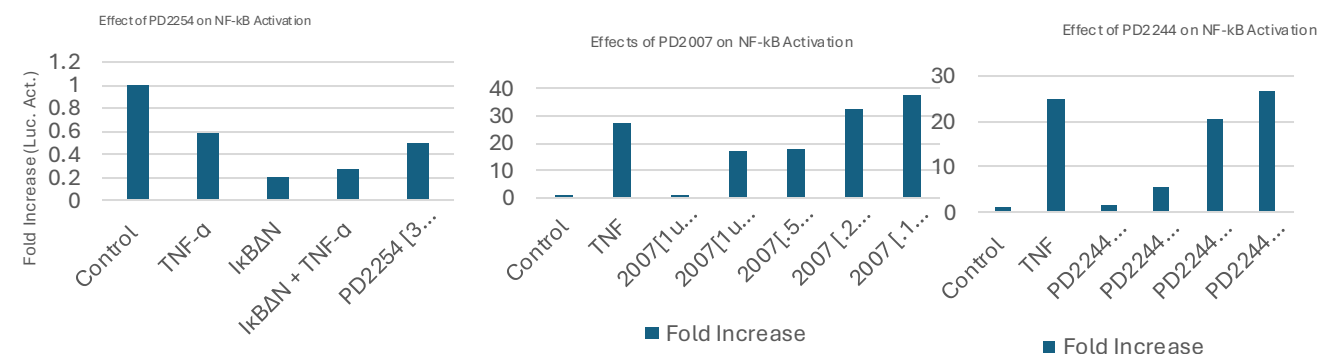
NF κ B is a key transcription factor that regulates immune responses. In its inactive state NF κ B is held in the cytoplasm and bound by I κ B; once active, NF κ B translocates to the nucleus and undergoes transcriptional activity where it drives the production of pro-inflammatory cytokines. Over-stimulation of this pathway contributes to chronic inflammation, due to the cytokines (like TNF- α) ability to stimulate the NF κ B pathway, contributing to inflammatory diseases such as Alzheimer's disease and Rheumatoid Arthritis.



Cytotoxicity



Results



- PD2254 did not inhibit TNF- α induced activation exhibited on NF κ B
 - As the concentration of PD2244 increase, we expect to see a decrease in NF- κ B activation, which is not present here
 - TNF induced activation decreased as the concentrations of 2007 increased
- Further studies need to be tested on 2007 to determine its efficacy in animal models

Acknowledgements

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