The impact of novel Alzheimer's Disease therapeutics on the activation of the pro-inflammatory transcription factor NF-κB

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Abstract

Inflammation is a natural and beneficial response to injury and pathogen invasion. However, chronic inflammation is linked to the progression of various neurodegenerative diseases. Although the exact etiology is unknown, Alzheimer's disease is associated with the overactivation of the NF-kB inflammatory pathway. NF-kB is a transcription factor that, in an unstimulated cell, is sequestered in the cytoplasm as a complex with its inhibitor, IκBα. When the pathway is activated by an external signal, IκBα is phosphorylated and subsequently degraded in the proteasome. Liberated NF-κB translocates to the nucleus, where it acts as a transcription factor for pro-inflammatory genes, highlighting its potential as a therapeutic target. Our research investigates the exact point of interference of novel anti-inflammatory drugs (provided by P2D Biosciences) with the NF-kB pathway through Western blotting and immunofluorescence.

The NF-κB Pathway

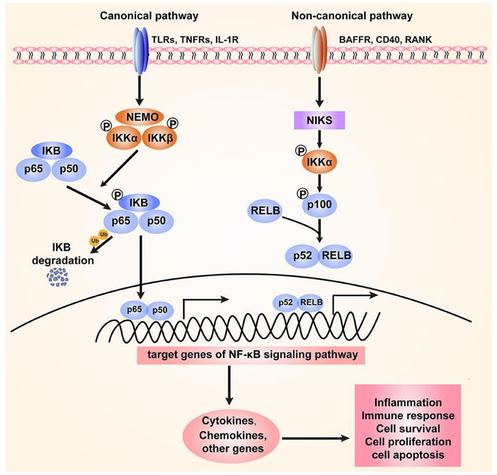

Figure 1. The canonical and non-canonical NF-κB signaling pathway.

PD2244 Inhibits NF-κB Translocation to the Nucleus

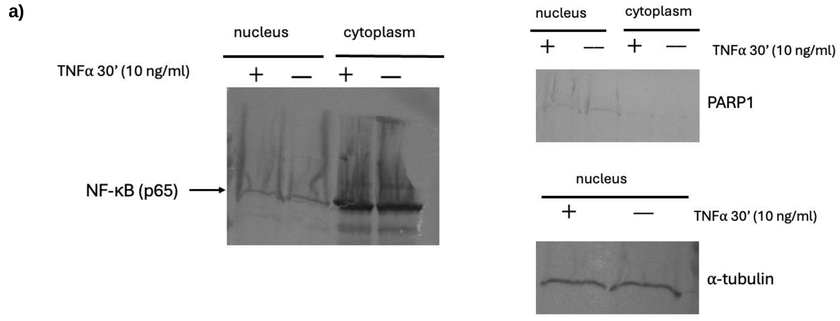

Figure 2. Inhibition of NF-κB translocation in TNFα activated HeLa and 293HEK cells. (a) Western blot of 293HEK treated with TNFα. (b) Confocal microscopy after immunofluorescence staining with anti-NF-κB p65 antibody

Methods

- HeLa and 293HEK cell culture
- Drug treatment followed by TNFα stimulant
- Sample preparation followed by Western blotting
- Immunofluorescence and confocal microscopy

PD2024 Inhibits IκBα Degradation

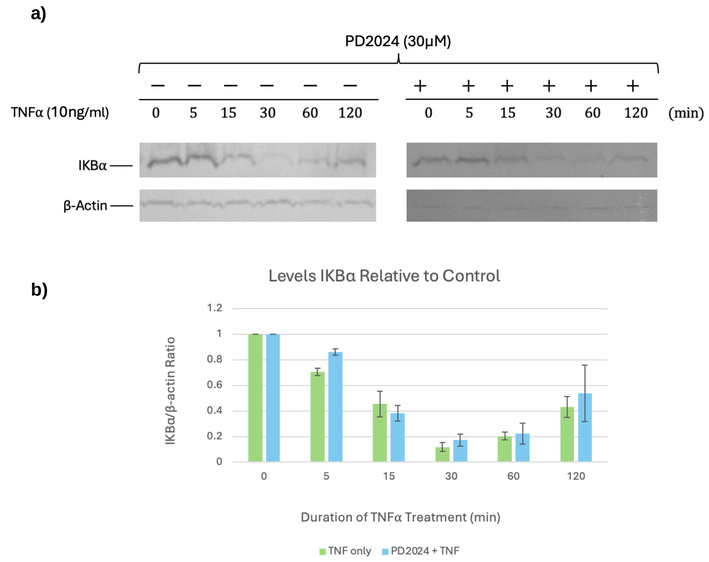

Figure 3. Inhibition of IκBα Degradation by PD2024 in TNFα activated 293HEK cells. (a) Time course of IκBα Degradation detected by Western blot of 293HEK treated with TNFα. (b) Quantification of Western Blot using ImageJ.

Conclusion

PD2244 significantly reduces IκBα degradation and NF-κB translocation to the nucleus.

References

Peng, Chao, et al. "The NF-KB Signaling Pathway, the Microbiota, and Gastrointestinal Tumorigenesis: Recent Advances." *Frontiers in Immunology*, vol. 11, June 2020, https://doi.org/10.3389/fimmu.2020.01387.

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