

Abstract N°: 1854

Lenabasum, a CB2 agonist, inhibits inflammasome activation

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Background:

Upregulation of the innate immune response via the activity of Toll-like receptors and the NLRP3 inflammasome have been suggested as initiating events that can drive fibrosis in systemic sclerosis (SSc) (Pharmacol Ther. 2018;192:163). Lenabasum, a cannabinoid receptor type 2 agonist, is known to activate the resolution phase of acute human innate immune responses triggered through Toll-like receptor activation, favoring production of pro-resolving lipid mediators, reducing inflammatory infiltrates, and increasing bacterial clearance (Clin Pharmacol Ther. 2018;104:675). Given the potential importance of inflammasome activation in the pathogenesis of SSc, the question remained whether lenabasum inhibits inflammasome activation.

Objectives:

Assess effects of lenabasum on IL-1 β and IL-18 production induced by inflammasome activation.

Methods:

Primary human macrophages were derived from monocytes, stimulated with LPS and ATP to active inflammasomes and cultured with lenabasum. Levels of IL-1 β and IL-18 were measured in cell supernatants by ELISA. Separately, human PBMC were activated with 0.1 μ g/ml LPS \pm 10 μ M lenabasum for 24 hours, and effects of lenabasum on the levels of IL-1 β and other pro-inflammatory cytokines were measured.

Results:

Lenabasum significantly inhibited IL-1 β and IL-18 secretion by monocyte-derived macrophages, with IC₅₀ = 66.73 \pm 3.92 nM and 349.23 \pm 21.27 nM, respectively. A control inflammasome activation inhibitor, MCC950, which showed IC₅₀ = 18.33 \pm 1.22 nM for IL-1 β inhibition and IC₅₀ = 21.43 \pm 0.81 nM for IL-8 inhibition.

Conclusion:

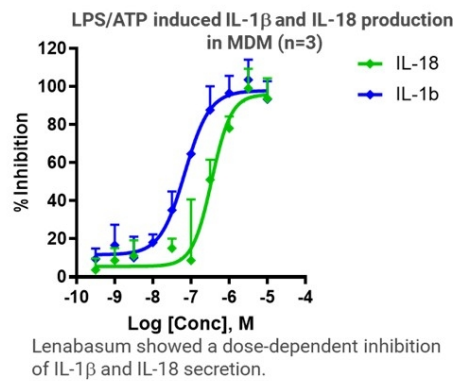
Lenabasum inhibits inflammasome activation, which could contribute to potential therapeutic efficacy in SSc and other autoimmune diseases.

References:

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Figure



Acknowledgments:

Disclosure of interest: Subba Chintalacharuvu Shareholder of: Corbus Pharmaceuticals, Inc., Employee of: Corbus Pharmaceuticals, Inc., Ping Zang Employee of: Corbus Pharmaceuticals, Inc., Barbara White Shareholder of: Corbus Pharmaceuticals, Inc., Employee of: Corbus Pharmaceuticals, Inc., Sergei Atamas Shareholder of: Corbus Pharmaceuticals, Inc., Employee of: Corbus Pharmaceuticals, Inc.