

Taming the Cytokine Storm by Modulating the NF- κ B butterfly effect: Repurposing Montelukast for the attenuation and prophylaxis of COVID-19 symptoms.

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The two main complications of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections are the development of acute respiratory distress syndrome (ARDS), as well as the development of complications from a hyperinflammatory cytokine profile (a cytokine storm). NF- κ B (nuclear factor kappa-light-chain-enhancer of activated B cells) is a protein complex involved in cytokine production and inflammation, with attenuation of NF- κ B associated with a reduction in cytokine production. Montelukast, an FDA and Health Canada approved asthma drug, has been shown to inhibit the signalling of NF- κ B, and other proinflammatory mediators, such as interleukin-6,8,10, TNF- α , MCP-1. Herein, we outline the scientific rationale behind our hypothesis that repurposing Montelukast to target suppression of NF- κ B activation in COVID-19 positive patients will result in a corresponding reduction of proinflammatory mediators, thereby attenuating cytokine production, and dampening of the cytokine storm. Additionally, we postulate that a reduction in proinflammatory mediators by Montelukast will result in a mitigation of severe COVID-19 symptoms and serve as a therapeutic for SARS-CoV-2 infections. In this manner, we propose to target attenuation of COVID-19 symptoms, rather than the virus, as an effective therapeutic strategy to improve COVID-19 related clinical outcomes. In support of our hypothesis, we explore the latest clinical reports on COVID-19 and cytokine storm syndrome, as well as the clinical role of NF- κ B in COVID-19 pathogenesis, including results from the literature on Montelukast and its ability to modulate NF- κ B, reduce cytokine production, and mitigate RNA virus infections. Currently, as part of a larger team approach, we are preparing to initiate a clinical trial protocol for the study of the efficacy of Montelukast in patients who are newly identified as COVID-19 positive, The COvid-19 Symptom MOntelukast Trial (COSMO), NCT04389411. Also, we would share some anecdotal evidence from patients who got benefit by adding Montelukast in their drug regimen.