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COMMENTARY

DRUG DEVELOPMENT RESEARCH WILEY

CB2 receptor-selective agonists as candidates for targeting infection, inflammation, and immunity in SARS-CoV-2 infections

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Abstract

The COVID-19 pandemic caused by SARS-CoV-2 is a deadly disease afflicting millions. The pandemic continues affecting population due to nonavailability of drugs and vaccines. The pathogenesis and complications of infection mainly involve hyperimmune-inflammatory responses. Thus, therapeutic strategies rely on repurposing of drugs aimed at reducing infectivity and inflammation and modulate immunity favourably. Among, numerous therapeutic targets, the endocannabinoid system, particularly activation of cannabinoid type-2 receptors (CB2R) emerged as an important one to suppress the hyperimmune-inflammatory responses. Recently, potent antiinflammatory, antiviral and immunomodulatory properties of CB2R selective ligands of endogenous, plant, and synthetic origin were showed mediating CB2R selective functional agonism. CB2R activation appears to regulate numerous signaling pathways to control immune-inflammatory mediators including cytokines, chemokines, adhesion molecules, prostanoids, and eicosanoids. Many CB2R ligands also exhibit off-target effects mediating activation of PPARs, opioids, and TRPV, suggestive of adjuvant use with existing drugs that may maximize efficacy synergistically and minimize therapeutic doses to limit adverse/ side effects. We hypothesize that CB2R agonists, due to immunomodulatory, antiinflammatory, and antiviral properties may show activity against COVID-19. Based on the organoprotective potential, relative safety, lack of psychotropic effects, and druggable properties, CB2R selective ligands might make available promising candidates for further investigation.

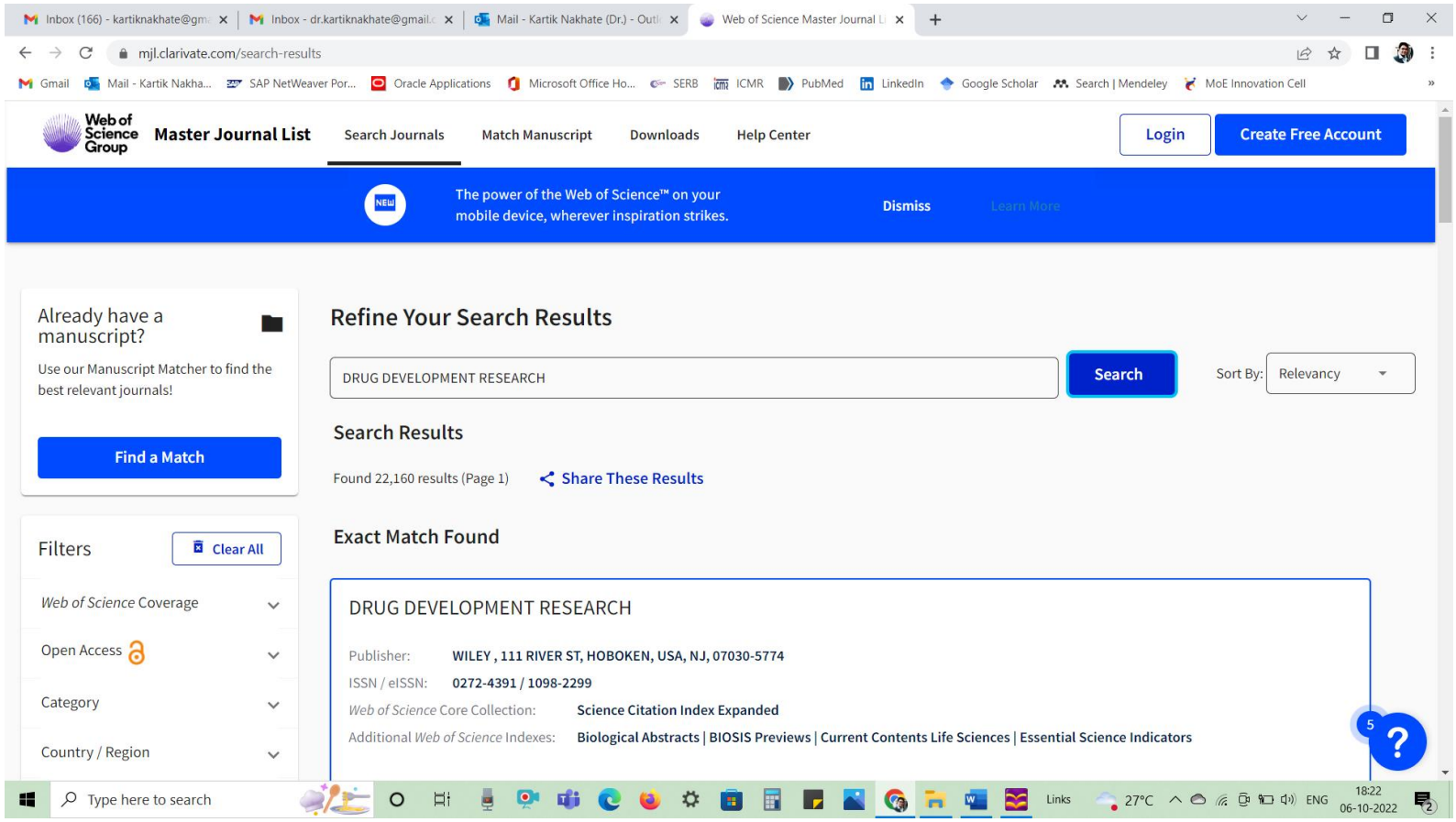
KEYWORDS

cannabinoids, COVID-19, immunomodulators, inflammation

1 | INTRODUCTION

The pathogenesis and complications of COVID-19 infection mainly involve immune-inflammatory cascade. Therapeutic strategies currently rely on the repurposing of antivirals and immunomodulators to reduce infectivity and inflammation, and favorably modulate the immune system (Wu et al., 2020). In principle, immune responses and resultant inflammatory processes work simultaneously to abolition of viral infections, but this may significantly influence pathogenesis of viral infections, similar believed to take place in infections with SARS-CoV-2 and contribute to the clinical spectrum of COVID-19 (Song et al., 2020).

Identifying candidate drugs to ameliorate infectivity, severity, mortality, and improve the prognosis, are needed, given the rapid emergence of COVID-19 (Altay et al., 2020). Use of antiviral agents alone are insufficient for preventing the cytokine storm and related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