Abstract

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is an enveloped, single-stranded RNA virus, a member of the Coronaviridae family. This virus was declared the cause of a global pandemic in 2019. It is associated with pneumonia and Acute Respiratory Distress Syndrome (ARDS), a condition characterized by lung injury and respiratory failure underlined by uncontrolled hyperinflammation resulting from deregulated immunity. SARS-CoV-2 infects human through the Spike (S) protein, which binds to the human angiotensin-converting enzyme 2 (hACE2), expressed on the membrane of different cell types, including the alveolar epithelial cells. In the lungs, the binding of SARS-CoV-2 to hACE2 triggers the immune cells, increases cytokine production, and activates other inflammatory responses. COVID-19 has been characterized by higher concentrations of IL-2, IL-6, IL-8, TNF-α, and IFN-γ in patients' plasma. The disease severity is correlated with high expression of IL-6 and TNF-α together with a poor type 1 interferon response. Heme arginate is a heme compound that is used for the treatment of acute porphyrias. Previous papers have described that heme and HO-1 induction inhibited the growth and replication of various RNA and DNA viruses. Lately, Dr. Mělková and colleagues have observed that heme arginate inhibited SARS-CoV-2 in tissue culture and modified the course of infection in K18-hACE2 mice. This thesis aims to characterize levels of TNF-α, IFN-γ, IFN-α, IL-6, IL-10, IL-22, IL-1β, IL-17A, IL-2, IL12-p70 and IL-4 cytokines produced in response to SARS-CoV-2 in these mice.

Keywords: SARS-CoV-2, Heme Arginate, Cytokines, K18-hACE2 mice