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Interleukin-1 as a Predictor Cytokine SARS-CoV: Article Review

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Abstract

Severe acute respiratory syndrome coronavirus (SARS-CoV) is an etiologic agent of respiratory disease that has a mortality rate of 10%. IL-1 actively participates in the inflammatory response to infection. SARS-CoV-2 appears to act on the activation and maturation of IL-1β, which in turn activates other proinflammatory cytokines, such as IL-6 and TNF-. Therefore, IL-1β is part of the cytokine storm generated by coronavirus infection. Elevated levels of the IL-1 receptor antagonist (IL-1Ra) in severe cases of COVID-19, and this marker have been associated with increased viral load, loss of lung function, lung damage, and risk of death. In addition, there is an increase in IL-1α levels in patients with severe COVID-19, and this is strongly associated with lung injury. IL-1 levels are associated with the virulence of the process, and significantly higher serum levels have been observed in severe symptomatic SARS-CoV-2 cases than in mild cases or in those infected with the 2003 SARS-CoV coronavirus or 2012 MERS coronavirus.

Keywords: cytokines; interleukin-1; severe acute respiratory syndrome coronavirus (SARS-CoV).

Abbreviations: severe acute respiratory syndrome coronavirus (SARS-CoV), IL-1 receptor antagonist (IL-1Ra), interleukin-1 (IL-1), SARS-CoV lacking the E gene (SARS-CoV-ΔE), open reading frame 3a (ORF3a), TNF receptor-associated factor 3 (TRAF3), recruitment caspase domain (ASC)

INTERLEUKIN-1 AND INFECTION

The interleukin-1 (IL-1) family of ligands and receptors plays a central role in the formation and regulation of inflammation as part of the immune response. The IL-1 molecule is best known as a member of a family of proinflammatory proteins called cytokines. They have been shown to play a role, not only during inflammation, but also in influencing additional physiological and pathological functions such as autoimmune diseases, malignancies, and many others. In addition, the biological balance between proinflammatory and inhibitory activity is critical, as any change in the expression of the IL-1 family has the potential to cause disease (Etti, et al., 2018).

Inflammation that occurs as a result of exposure of tissues and organs to noxious stimuli such as microbial pathogens, irritants, or toxic cellular components. The main physical manifestations of inflammation are redness, swelling, heat, pain, and loss of function in the affected area. This process involves the main cells of the immune system, including monocytes, macrophages, neutrophils, basophils, dendritic cells, mast cells, T cells, and B cells. However, examination of various inflammatory lesions reveals the presence of specific leukocytes in certain lesions. That is, the inflammatory process is regulated in such a way as to ensure that the right leukocytes are recruited. These events are in turn controlled by a number of extracellular molecular regulators, including members of the cytokine and chemokine family that mediate immune cell recruitment and the complex intracellular signaling control mechanisms that characterize inflammation. This review will focus on the role of major cytokines, chemokines, and their receptors in the pathophysiology of auto-inflammatory disorders, pro-inflammatory disorders, and neurologic disorders involving inflammation. IL-1 actively participates in the inflammatory response to infection (Turner, et al., 2014), and its main source is activated monocytes and macrophages.

INTERLEUKIN-1 AS A PREDICTOR CYTOKINE SARS-COV

Severe acute respiratory syndrome coronavirus (SARS-CoV) is the etiologic agent of respiratory disease that has a mortality rate of 10%. Previous studies have shown that SARS-CoV lacking the E gene (SARS-CoV-ΔE) is attenuated in several animal model systems. This

suggests that the absence of protein E resulted in reduced expression of proinflammatory cytokines, decreased number of neutrophils in the lung infiltrates, reduced lung pathology, and increased viability of mice, suggesting that lung inflammation contributes to SARS-CoV virulence. Furthermore, SARS-CoV-ΔE infection resulted in decreased NF-B activation compared to levels of wild-type virus. Most importantly, treatment with drugs that inhibit NF-kB activation led to a reduction in inflammation and lung pathology in SARS-CoV-infected cells and mice and significantly improved mouse survival after SARS-CoV infection. These data suggest that activation of the NF-B signaling pathway represents a major contribution to inflammation induced after SARS-CoV infection and that NF-B inhibitors hold antiviral promise in infections caused by SARS-CoV and other potentially pathogenic human coronaviruses (DeDiego, et al., 2014).

Deletion of the SARS-CoV envelope (E) gene attenuates the virus. Gene E encodes a small multifunctional protein that has ion channel (IC) activity, an important function in virus-host interactions. To examine the contribution of the IC activity of protein E in viral pathogenesis, two mouse-adapted SARS-CoV, each containing a single amino acid mutation that suppresses ion conductivity, were engineered. After serial infection, mutant viruses, in general, introduce compensatory mutations in the E gene that create active ion channels. Furthermore, IC activity provided better fitness in competition assays, suggesting that ionic conductivity is an advantage for viruses. Interestingly, virus-infected mice exhibiting IC protein E activity, either with a wild-type protein E sequence or with a revertant that restores ion transport, rapidly lost weight and died. In contrast, mice infected with a mutant lacking IC activity, which did not introduce the mutation in the E gene during the experiment, recovered from the disease and mostly survived. Levels of inflammasome-activated IL-1β were reduced in the lung airways of virus-infected animals lacking IC protein E activity, suggesting that IC protein E function is required for inflammasome activation. The reduction in IL-1β is accompanied by a decrease in the number of TNF and IL-6 in the absence of ion conductivity protein E. All of these key cytokines promote the development of lung damage and ARDS pathology. In conclusion, the IC activity of protein E is a novel determinant for the virulence of SARS-CoV (Nieto-Torres, et al., 2014).

Siu et al. (2019) demonstrated that the open reading frame 3a (ORF3a) accessory protein of SARS-CoV activates the NLRP3 inflammasome by promoting TNF receptor-associated factor 3 (TRAF3)-mediated ubiquitination of an apoptosis-associated spot-like protein containing a recruitment caspase domain (ASC). SARS-CoV and its ORF3a protein were found to be potent activators of pro-IL-1β gene transcription and protein maturation, 2 signals required for NLRP3 inflammasome activation. ORF3a induces pro-IL-1β transcription via NF-B activation, which is mediated by ubiquitination and TRAF3-dependent p105 processing. ORF3a-induced increase in IL-1β secretion is independent of its ion channel activity or is absent in melanoma 2 but requires NLRP3, ASC, and TRAF3. ORF3a interacts with TRAF3 and ASC, localizes with them in discrete mottled structures in the cytoplasm, and facilitates the formation of ASC specks. TRAF3-dependent ubiquitination of K63-associated ASCs was more prominent in cells infected with SARS-CoV or when ORF3a was expressed. Overall, the findings of Siu, et al. (2019) revealed a novel mechanism by which the SARS-CoV protein ORF3a activates NF-B and the NLRP3 inflammasome by promoting p105 and ASC.-Siu-dependent ubiquitination of TRAF3. The severe acute respiratory syndrome coronavirus ORF3a protein activates the NLRP3 inflammasome by promoting TRAF3-dependent ASC ubiquitination (Siu, et al., 2019).

SARS-CoV-2 appears to act on the activation and maturation of IL-1β, which in turn activates other proinflammatory cytokines, such as IL-6 and TNF (DeDiego, et al., 2014; Nieto-Torres, et al., 2014; Siu, et al., 2019). SARS-CoV-infected DCs show low expression of antiviral cytokines (interferon [IFN-α], IFN-β, IFN-γ, and interleukin 12p40 [IL-12p40]), upregulation of proinflammatory cytokines (tumor necrosis). factors [TNF-α] and IL-6) but significant upregulation of inflammatory chemokines (macrophage inflammatory protein 1α [MIP-1α], upregulated on normal-expressed and secreted T cell activation [RANTES]), interferon-inducible proteins from 10 kDa [IP-10], and monocyte chemoattractant protein 1 [MCP-1]). Therefore, IL-1β is part of the cytokine storm generated by coronavirus infection (Law, et al., 2005; Chu, et al., 2016; Hui, et al., 2019; Conti, et al., 2020; Mehta, et al., 2020; Wan, et al., 2020)

Yang, et al. (2020) detected elevated levels of the IL-1 receptor antagonist (IL-1Ra) in 14 severe cases of COVID-19, and this marker has been associated with increased viral load, loss of lung function, lung damage, and risk of death. Liu, et al. (2020) also found elevated levels of IL-1α in patients with severe COVID-19, and this was strongly associated with lung injury. IL-1 levels are associated with the virulence of the process, and significantly higher serum levels have been observed in severe symptomatic SARS-CoV-2 cases than in mild cases or in those infected with the 2003 SARS-CoV coronavirus or 2012 MERS. COVID-19 patients with severe symptoms have elevated levels of IL-1β, which has been associated with SARS, hypercoagulation, and disseminated intravascular coagulation (Zhang, et al., 2020). For this reason, several therapeutic strategies have used IL-1 inhibition in an attempt to avoid cytokine storms (Tanaka, et al., 2016; Kritas, et al., 2020). In this way, mesenchymal stem cells (MSCs) have been used to

inhibit proinflammatory cytokines such as IL-1α and TNF (Chen, et al., 2020).

CONCLUSIONS

The conclusions of the study may be presented in here.IL-1 actively participates in the inflammatory response to infection. SARS-CoV-2 appears to act on the activation and maturation of IL-1β, which in turn activates other proinflammatory cytokines, such as IL-6 and TNF-. Therefore, IL-1β is part of the cytokine storm generated by coronavirus infection. Elevated levels of the IL-1 receptor antagonist (IL-1Ra) in severe cases of COVID-19, and this marker have been associated with increased viral load, loss of lung function, lung damage, and risk of death. In addition, there is an increase in IL-1α levels in patients with severe COVID-19, and this is strongly associated with lung injury. IL-1 levels are associated with the virulence of the process, and significantly higher serum levels have been observed in severe symptomatic SARS-CoV-2 cases than in mild cases or in those infected with the 2003 SARS-CoV coronavirus or 2012 MERS coronavirus.

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