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LETTER

CD147 as a novel receptor in the pathogenesis of SARS-CoV-2: Is there any correlation with the risk of COVID-19 in dermatological diseases?

Dear Editor,

The world is currently grappling with a new coronavirus pandemic. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) invades host cells by interacting with cellular receptors, giving rise to the coronavirus disease 2019 (COVID-19).[1] Recent studies have identified two host cell receptors for virus invasion, namely angiotensin-converting enzyme 2 (ACE2) and CD147.[2] The most important structural protein for virus binding to host cells is the spike protein.[3] It has been reported that the structure of the spike protein is similar between SARS-CoV-2 and SARS-CoV; both viruses attack host cells via the ACE2 receptor. Recently, a study showed that the SARS-CoV-2 spike protein also attaches to host cells through the CD147 receptor.[2] CD147 is a transmembrane protein that interacts with several extracellular and intracellular molecules.[4] Two main extracellular ligands that activate CD147 are cyclophilins A and B, which can interact with non-structural protein 1 of SARS-CoV.[4]

The CD147 receptor is expressed in some cells including epithelial, neuronal, lymphoid, and myeloid cells; it is also prominent in several disorders such as some cancers, inflammatory disorders, and microbial infections.[3] It has been mentioned that CD147 fulfills a critical role in the pathogenesis of human immunodeficiency virus, hepatitis B, hepatitis C, and SARS-CoV infections.[3,4] Also, *Plasmodium falciparum* invades erythrocytes through CD147.[1]

Radzikowska et al reported the exclusive expression of ACE2 at the barrier sites, but ubiquitous expression of CD147 and cyclophilins in immune and epithelial cells.[4] Interestingly, these findings may propound the role of CD147 in lymphopenia that occurs in the SARS-CoV-2 infection. Furthermore, ACE2 and CD147 are highly expressed in skin tissues.[4] It has been described that CD147 may have an important role in the pathogenesis of pseudo-chilblain lesions in COVID-19 patients.[1]

Bian et al reported a humanized anti-CD147 antibody as a presumptive treatment in COVID-19 therapy.[5] In addition, Ulrich and Pillat suggested azithromycin as a potential anti-COVID-19 agent that is likely to work through the CD147 protein pathway.[2] Rodrigues-Diez et al proposed that atorvastatin downregulates CD147 in human cells and diminishes viral infectivity; therefore, it could be an option for COVID-19 therapy.[3]

On the other hand, it is noteworthy that the *CD147* gene is located on the PSOR6 locus of chromosome 19P13, an important gene in the pathogenesis of psoriasis. Increased CD147 expression has been found in psoriatic skin lesions in addition to elevated levels of soluble CD147 and greater CD147 expression in the blood neutrophils of psoriatic patients.[6-8] Besides, CD147-related molecules are expressed increasingly in the lesional skin of atopic dermatitis patients.[4]

Given the possible role of CD147 in the pathogenesis of SARS-CoV-2 and its increased expression in some dermatological diseases such as psoriasis and, possibly, atopic dermatitis,[4,6-8] it may be hypothesized that patients with a history of these diseases are more prone to COVID-19.

This is a novel idea that requires not only further clarification of the role of CD147, but also a detailed evaluation of the effect of azithromycin and other drugs that potentially offer anti-SARS-CoV-2 activity,[9,10] especially in COVID-19 patients with a history of dermatological diseases such as psoriasis.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

AUTHOR CONTRIBUTIONS

Fahimeh Abdollahimajd and Mohammad Reza Pourani contributed to the conception of the work. Mohammad Reza Pourani drafted the manuscript. Fahimeh Abdollahimajd critically revised the manuscript. Both the authors gave final approval and agreed to be accountable for all aspects of the work ensuring integrity and accuracy.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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