European Review for Medical and Pharmacological Sciences 2020; 24: 11992-11994

Letter to the Editor

CD147 as an alternative binding site for the spike protein on the surface of SARS-CoV-2

Dear Editor,

The status of the patients with COVID-19 reveals that SARS-CoV-2 is more communicable than SARS-CoV and MERS-CoV[1]. There is no specific therapy for COVID-19 but broad-spectrum antivirals namely oseltamivir and remdesivir[2]. ACE2 is considered the main receptor for entry of SARS-CoV-2 into host cells[3]. High transmission rate of SARS-CoV-2 and considering cells with low expression of ACE2 could justify the existence of other binding sites for entry into T lymphocytes including CD147[4], Figure 1.

CD147 is a transmembrane glycoprotein which has been documented to facilitate the entrance of viruses namely measles, malaria and HIV into human host cells. Direct interaction of CD147 with cyclophilin A caused chemotaxis of leukocytes and intensified the inflammation[5,6]. The infection of T cells by SARS-CoV-2 and concurrently low values of ACE2 in T lymphocytes highlight the feasibility of CD147 as an alternative site for the viral entrance[7]. CD147 is also engaged in lymphocytopenia due to expression on T cells and binding to spike proteins which facilitate the invasion to lymphocytes[8]. Studies[9] demonstrated the direct binding between CD147 and SARS-CoV-2. Consequently, inhibition of CD147 might offer an efficient therapy for COVID-19[9].

Humanized anti-CD147 antibody, meplazumab, inhibited the formation of the complex between CD147 and spike protein which prevented the virus from cell entrance in a dose-dependent manner. Additionally, meplazumab binds to CD147 which is the receptor of pro-inflammatory protein cyclophilin A and inhibits the inflammation[9].

Table I describes undergone clinical trials assessing the efficacy of anti-CD147 antibody, meplazumab, for COVID-19. Fast viral clearance, improved respiratory rate, acceptable chest

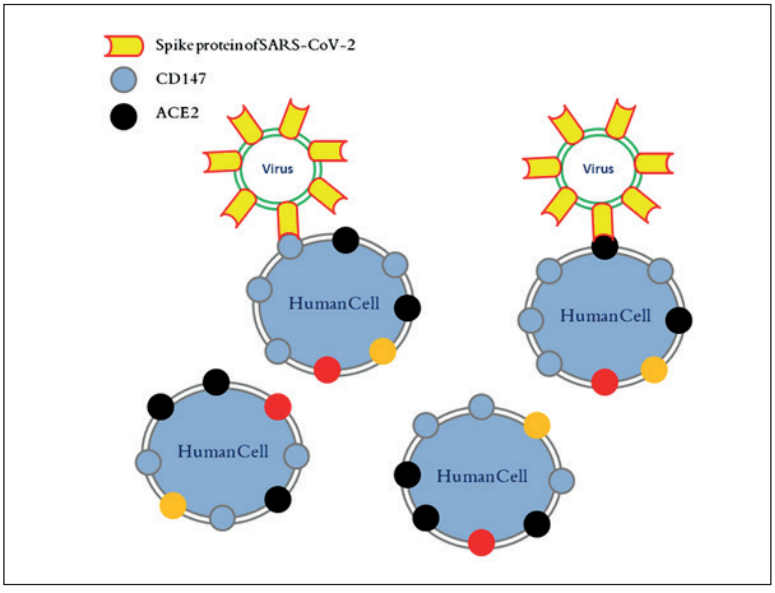

Figure 1. Interaction between CD147 and spike protein of SARS-CoV-2.

Corresponding Author: Homa Faghihi, MD; email: Faghihi.h@iums.ac.ir

Table I. Clinical studies under trial to evaluate the efficacy of meplazumab in patients with COVID-19.

NCT number	Title	Number of cases/design	Location/date
NCT04275245	Clinical Study of Anti-CD147 Humanized Meplazumab for Injection to Treat With 2019-CoV Pneumonia	• 17 patients • 10 mg Meplazumab by iv infusion • Every day for 2 days	• February 2020 • Tang-Du Hospital
NCT04586153	Study to Assess the Effect of Meplazumab on COVID-19	• 456 participants • Interventional • Low, middle and high dose groups • Low dose a: 0.12 mg/kg - Day 1; b: control - Day 8 • Middle dose group: a: 0.2 mg/kg - Day 1;b: 0.2 mg/kg - Day 8 • High dose group: a: 0.3 mg/kg - Day 1; b: 0.3 mg/kg - Day 8	• Jiangsu Pacific Meinuoke Bio Pharmaceutical Co Ltd • October 2020

Abbreviations: SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; MERS-CoV, Middle east respiratory syndrome coronavirus; ACE2, Angiotensin-converting enzyme 2; CRP, C-reactive protein.

radiographic status, normal CRP level and no adverse reactions can introduce CD147 as a target for the treatment of pneumonia in COVID-19[5,9]. To consider the treatment as a valid approach clinical designs at larger scales are required.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

1) Woolf SH, Chapman DA, Sabo RT, Weinberger DM, Hill L. Excess deaths from COVID-19 and other causes. JAMA 2020; 324: 510-513.
2) Kumar R, Gupta N, Kodan P, Mittal A, Soneja M, Wig N. Battling COVID-19: using old weapons for a new enemy. Trop Dis Travel Med Vaccines 2020; 6: 6.
3) Yan R, Zhang Y, Li Y, Xia L, Guo Y, Zhou Q. Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2. Science 2020; 367: 1444-1448.
4) Aguiar JA, Tremblay BJM, Mansfield MJ, Woody O, Lobb B, Banerjee A, Chandiramohan A, Tiessen N, Cao Q, Dvorkin-Gheva A, Revill S, Miller MS, Carlsten C, Organ L, Joseph C, John A, Hanson P, Austin RC, McManus BM, Jenkins G, Mossman K, Ask K, Doxey AC, Hirota JA. Gene expression and in situ protein profiling of candidate SARS-CoV-2 receptors in human airway epithelial cells and lung tissue. Eur Respir J 2020; 56: 2001123.
5) Wang K, Chen W, Zhou YS, Lian JQ, Zhang Z, Du P, Gong L, Zhang Y, Cui HY, Geng JJ, Wang B, Sun XX, Wang CF, Yang X, Lin P, Deng YQ, Wei D, Yang XM, Zhu YM, Zhang K, Zheng ZH, Miao JL, Guo T, Shi Y, Zhang J, Fu L, Wang QY, Bian H, Zhu P, Chen ZN. SARS-CoV-2 invades host cells via a novel route: CD147-spike protein. bioRxiv 2020.
6) Yurchenko V, Constant S, Eisenmesser E, Bukrinsky M. Cyclophilin-CD147 interactions: a new target for anti-inflammatory therapeutics. Clin Exp Immunol 2010; 160: 305-317.
7) Helal MA, Shouman S, Abdelwaly A, Elmehrath AO, Essawy M, Sayed SM, Saleh AH, El-Badri N. Molecular basis of the potential interaction of SARS-CoV-2 spike protein to CD147 in COVID-19 associated-lymphopenia. J Biomol Struct Dyn 2020; 1-11.
8) Chen Z, Mi L, Xu J, Yu J, Wang X, Jiang J, Xing J, Shang P, Qian A, Li Y, Shaw PX, Wang J, Duan S, Ding J, Fan C, Zhang Y, Yang Y, Yu X, Feng Q, Li B, Yao X, Zhang Z, Li L, Xue X, Zhu P. Function of HAb18G/CD147 in invasion of host cells by severe acute respiratory syndrome coronavirus. J Infect Dis 2005; 191: 755-760.

9) Bian H, Zheng ZH, Wei D, Zhang Z, Kang WZ, Hao CQ, Dong K, Kang W, Xia JL, Miao JL, Xie RH, Wang B, Sun XX, Yang XM, Lin P, Geng JJ, Wang K, Cui HY, Zhang K, Chen XC, Tang H, Du H, Yao N, Liu SS, Liu LN, Zhang Z, Gao ZW, Nan G, Wang QY, Lian JQ, Chen ZN, Zhu P. Meplazumab treats COVID-19 pneumonia: an open-labelled, concurrent controlled add-on clinical trial. medRxiv 2020.

H. Faghihi

Department of Pharmaceutics, School of Pharmacy, Iran University of Medical Sciences, Tehran, Iran