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Contribution of technology to human cell properties

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Abstract. After explaining the meaning of SARS-CoV2, the protection rules for the disease caused by this virus are described in order to eradicate the resulting pandemic. Methods to differentiate asymptomatic from symptomatic patients will be mentioned. Human lungs, heart, kidney, endothelium and erythrocyte have specific binding sites for the SARS-CoV2.

The aim of this opinion was to highlight some new disposable technology to identify two cell properties. One of them is the vascular endothelial cell (EC) receptor binding to the SARS-CoV2 and the other is related with red blood cells (RBCs) as SARS-CoV2 carrier.

Keywords: Biotechnology, SARS-CoV 2, endothelial cell, erythrocyte

1. Introduction

Seventeen months have been passed since the world health organization (WHO) announced the state of a pandemic which devastated a huge amount of lives in almost all countries. Starting at China where the first thought about the disease cause was the presence of some kind of virus. Later on it was identified as belong to the family of the corona virus type receiving the name of SARS-CoV2 and consequently the associate disease designation receives the name of Covid-19 [1–4].

All Covid-19 patient's in terminal stage have in common a respiratory deficient syndrome treated by internal physicians, at intensive care units (ICU) tried to surpass the terrible situation submitting them to oxygen therapy machines and to another's for monitories blood parameters continually [2].

SARS-CoV2 rapidly appeared in almost all countries of the world, becoming mandatory to announced rules such as use of face masks, frequently hand disinfection and washing, shoes protection at home and work spaces. Also in the beginning human beings were submitted to home lockdown when necessary according the disease transmission index and number of deaths.

Several scientific studies were undertaken and some scientists started to investigate reliable (consistence) and accurate (validity) methods in order to obtain with confidence the best diagnostic tests for Covid-19 with efficacy, precision and selectivity. Quantitative polymerase chain reaction (qPCR) is nowadays the golden standard test with continue improvements so that it can be used at home as fast test nowadays [5, 6].

Scientists are interested also in the underlying molecular mechanism of the entrance and the replication of SARS-CoV2 on the human body to prevent the transmission between humans and also elimination the spreading of SARS-CoV2 through the entire human body.

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Countless publications appear about the outcomes verified in patients with autoimmune, metabolic, vascular and neurological disease with asymptomatic Covid-19.

A few pharmaceutical industries focus on develop two types pf vaccines producing encapsulate either mRNA or animal Adenovirus encoding by recombinant DNA technology into unilamellar liposomes. The vaccination process is in course with exception of the poor countries.

The aim of this opinion was to highlight some new disposable technology to identify two cell properties. One of them is the vascular endothelial cell (EC) receptor binding to the SARS-CoV2 and the other is related with red blood cells (RBCs) as SARS-CoV2 carrier.

2. How protein spike in SARS COV-2 is recognized by ACE2 receptor for vascular endothelial cell entrance

The SARS-CoV2 is a corona virus which the single strand of RNA is encapsulated by one lipid envelop of embedded proteins in phospholipids. After RNA extraction from samples of patients its composition is almost equal to the first SARS-CoV as verified by sequencing after real time qPCR procedures using the well-known biotechnology by the molecular genomic scientists [4].

One of the corona virus proteins responsible for it recognition by the epithelial cells and vascular endothelial cells present on the respiratory tract, lungs, cardiac, renal and gastrointestinal organs is the glycoprotein transmembrane spike (S) protein composed by two sub-units S1 and S2 [7, 8] The sub-unit S1 containing a receptor like peptide domain (RBD) for the vascular endothelial cell angiotensin converting enzyme 2 (ACE2) receptor which attach to the peptidase of the host cell and the other sub-unity S2 responsible for the corona virus intracellular fusion through ACE2 receptor [8, 9]. Employing the high resolution cryo-electron microscopy it was shown simultaneous binding between two S-glycoprotein trimers and two RBD of the ACE2 dimer [10]. The corona virus fusion by its trimeric glycoprotein into the human EC needs that S2 undergo proteolytic cleavage by a protease of the ACE2 target host cell receptor [10]. This biotechnology gives us a 3,3 angstroms of resolution at the binding interface [10].

For dynamic studies of the interaction between RBD and ACE2 receptor force–distance (FD), curve-based atomic force microscopy (FD-curve-based AFM) was done [11]. These technologies - applied on molecules binding properties allied to advance microscopy identified the participant molecular domains given simultaneously measurements of the force strength stablished and its dynamic like kinetic and bioenergetics properties [11].

3. How red blood cells (RBCs) carrier SARS-COV-2

One of the rules to impaired the SARS-COV2 contamination which was only announced in the beginning of the pandemic state highlight the ban on touch the eyes, but has been overlooked.

The eyes were one of the door entrances of the nanoparticles that fast enter into ocular capillaries vessel and consequently traveling into human blood circulation [12]. The entrance of SARS-COV2 occur through membrane band 3 protein as evidenced using the Resonant Recognition Model (RRM) [13]. The RRM has unquestionable efficacy been currently and successfully used in several scientific fields, for example to the binding of SARS-CoV2 spike protein sub-unit S1 to RBD of ACE2 [8–10, 13].

SARS-CoV2 may also bind to RBCs membrane CD147 protein originating clusters of only RBCs and also between RBCs and white blood cells or with endothelial cells [14, 15].

Previously was verified that the antibiotic ivermectin inhibits the RBC membrane enzyme & receptor acetylcholinesterase (AChE) interfering in the nitric oxide (NO) transduction mechanism [16, 17].

The AChE inhibited state induces increasing the amount of NO derivatives reactive nitrogen species molecules inside RBC originating a beneficial effect on SARS-Co2 damage stopping its spread to all body organs. [16].

After it was verified that ivermectin binds to Spike protein of the SARS-CoV2 impeachment to visualize the transmembrane CD147 protein of blood cells and EC eliminating the binding and consequently the viral action [17].

The experimental work under those data have been possible due to amperometric coupled NO sensor, confocal microscopy fluorescence imaging, flow cytometry, surface plasmon resonance, ELISA assays, pharmacokinetics and toxicity approaches.

Red blood cells are able to be a strong partner in dissemination to all tissues of the human body of the SARS-CoV2 by two ways of transport one external by liaison to the membrane CD 147 and other internal by entrance to the anion exchange chloride and bicarbonate channel protein also known by band3 protein. However, there are several therapeutic drugs which have been employed in countries without or waiting for more vaccines [18, 19].

Conflict of interest

The author has no conflict of interest to report.

References

[1] Chen L, Liu W, Zhang Q, Xu K, Ye G, Wu W, Sun Z, Liu F, Wu K, Zhong B, Mei Y, Zhang W, Chen Y, Li Y, Shi M, Lan K, Liu Y. RNA based mNGS approach identifies a novel human coronavirus from two individual pneumonia cases in 2019 Wuhan outbreak. Emerg Microbes Infect. 2020:9:313-9.

[2] Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, Hu Y, Tao ZW, Tian JH, Pei YY, Yuan ML, Zhang YL, Dai FH,Liu Y, Wang QM, Zheng JJ, Xu L,Holmes CE, Zhang YZ.A new coronavirus associated with human respiratory disease in China. Nature. 2020:579:265-9.

[3] Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, Si HR, Zhu Y, Li B, Huang CL, Chen HD, Chen J, Luo Y, Guo H, Jiang RD, Liu MQ, Chen Y, Shen XR, Wang X, Zheng XS, Zhao K, Chen QJ, Deng F, Liu LL, Yan B, Zhan FX, Wang YY, Xiao GF, Shi Z. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020;579:227-70.

[4] Lu R, Zhao X,Li J, Niu P, Yang B, Wu H, Wang H, Song H, Huang B, Zhu N, Bi Y, Ma X, Zhan F, Wang L, Hu T, Zhou H, Hu Z, Zhou W, Zhao L, Chen J, Meng Y, Wang J, Lin Y, Yuan J,Xie Z, Ma J, Liu WJ, Wang D, Xu W, Holmes EC, Gao GF, Wu G,Chen W, Shi W,Tan W. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020;395:565.

[5] thermofisher.com/covid19

[6] https://www.bionova.es/covid-19-diagnostico.asp

[7] Li F. Structure, Function, and Evolution of Coronavirus Spike Proteins. Annu Rev Virol. 2016;3:237-61.

[8] Moore WL J, Vasilieva N, Sui J, Wong SK, Berne MA, Somasundaran M, Sullivan LJ, Luzuriaga K, Greenough CT, Choe H, Farzan M. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. Nature. 2003:426:450-4.

[9] Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. J Virol. 2020;94(7):e00127-20.

[10] Yan R, ZhangY, Li Y, Xia L Guo Y, Zhou Q. Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2. Science. 2020:367:1444-8.

[11] Yang J, Petitjean SJL, Koehler M, Zhang Q, Dumitru AC, Chen W, Derclaye S, Vincent SP, Soumillion P, Alsteens D. Molecular interaction and inhibition of SARS-CoV-2 binding to the ACE2 receptor. https://doi.org/10.1038/s41467-020-18319-6.

[12] Saldanha C. Erythrocyte a target for COVID-19 infected patients. Mod Appro Drug Des. MADD. 2020;3(1):000555. DOI: 10.31031/MADD.2020.03.000555

[13] Cosic I, Cosic D, Loncarevic J. RRM prediction of erythrocyte band3 protein as alternative receptor for SARS-CoV-2 Virus. Appl Sci. 2020:10:4053. doi:10.3390/app10114053.
[14] von Ungern-Sternberg SNI, Zernecke A, Seizer P. Extracellular Matrix Metalloproteinase Inducer EMMPRIN (CD147) in Cardiovascular Disease. International Journal of Molecular Sciences. 2018;19(2):507.
[15] Jung F, Krüger-Genge A, Franke RP, Hufert F, Küpper J-H. COVID-19 and the endothelium. Clin Hemorheol Microcirc. 2020. 2020;75(1):7-11.
[16] Saldanha C, Silva-Herdade AS. Erythrocyte acetylcholinesterase is a signalling receptor Nov Appro Drug Des Dev. 2018:3(4):555617.
[17] Review and perspective Ivermectin for COVID-19 treatment: clinical response at quasi-threshold doses via hypothesized alleviation of CD147-mediated vascular occlusion. David E. Scheim*(email: E-mail: dscheim@alum.mit.edu.) is a commissioned officer in the US Public Health Service, inactive reserve. He developed the software for the eyeGENE clinical-genetic database, National Eye Institute, US National Institutes of Health. This preprint research paper has not been peer reviewed. Electronic copy available at: https://ssrn.com/abstract=3636557 Preprint
[18] Saldanha C. Therapeutic approaches for COVID-19 patients. Nov Appro Drug Des Dev. 2020;5(3):NAPDD.MS. ID.555664.
[19] Pillay TS. Gene of the month: the 2019-nCoV/SARS-CoV-2 novel coronavirus spike protein. Journal of Clinical Pathology. 2020:jclinpath-2020-206658.