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RESEARCH ARTICLE

ELECTRICAL CHARGES OF COVID-19 SURFACE AND PROCOAGULANT EFFECT FOR VACCINE PERSPECTIVE. OXIDIZED AND REDUCED CELL IMPLICATION

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ABSTRACT

An electrical charges status has been found in Coronavirus COVID-19 surface. As a result of this research it is possible to look for viral surface properties that may indicate with their electrical feature the possibility to be considered in the prevention as well in the therapy of patients. Vaccine designed strategy has benn already suggested for the ralationship with procoagulated effect due to the spike SARS-CoV-2 protein. Of course other approaches are being valuted as the antiviral activity of cellular glutathione.

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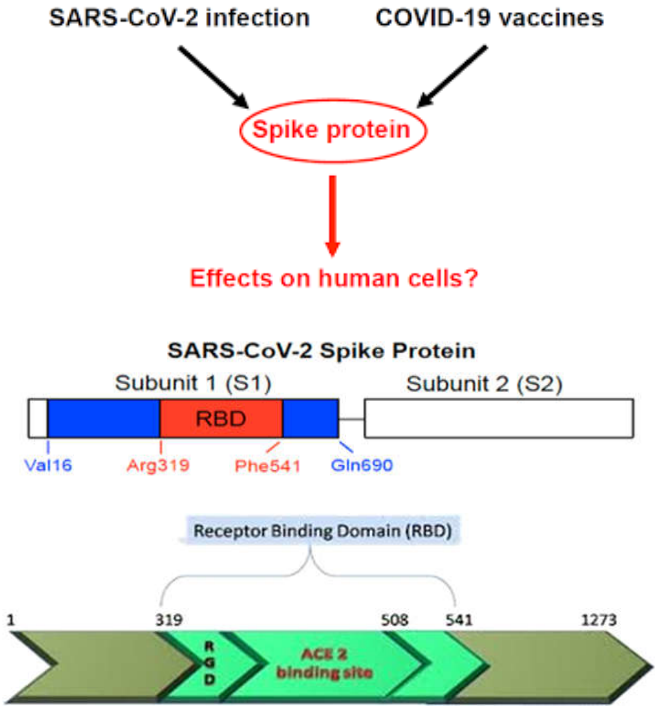
INTRODUCTION

An investigation of the SARS-CoV-2 spike for its electron geometric properties was performed by Anna Kucherova *et al* (2020). The authors reported the electro-geometric properties of the receptor binding domain and its vicinity. Their work opens the way for a new approach, where molecular dynamics simulations are combined with the production of computational maesunements for protein investigations: the electric potential was computed as the solution of the non-linear Poisson-Boltzmann genoma equation. Other authors analyzed the coronavirus COVID-19 surface properties related to the pattern of electrical charges status (Luisetto, Tarro *et al*, 2021a).

The presence of an electrical feature on the viral surface can be an important factor to take in consideration for preventive or treatment measure. The possibility of immune evasion and the different pattern of efficacy towards variants of some vaccines or some antibodies push the need to verify if the electrical feature of viral surface may be an element to be considered for the immune condition. Specific chemo physical factor can influence the electrical charges of the viral surface and its behaviour to hypertonic saline solution, humidity, electrical charge barrier in mask, are an example of the possible effect.

The issue of SARS-CoV-2 protein as procoagulant factor and vaccine class effect hypotesys: The paper was written as research article (Luisetto *et al*., 2021b): some COVID vaccines are under investigation related to some cases of thrombosis. According to the literature it is reported the observation in the first as well in the second-third wawe of COVID-19 epidemy a

relationship with increased thrombosis in the most severe patients. Therefore it is possible to say that there is a procoagulant property of the COVID-19 virus. The question is whether this property is related to all the virus particle or due to the spike protein. Of course in this last circumstance one cannot project a vaccine based on this protein. The virion binding to integrins on endothelial cells might activate angiogenic cell signaling pathways as well as dysregulate integrin mediated signaling pathways controlling developmental processes and finally precipitate endothelial activation to initiate blood clothing (Luisetto at al., 2021b). This procoagulant state, together with enhancement of platelets aggregation by virus binding to them could amplify the production of microthrombi that lead to preliminary thrombosis and embolism as well as strokes and other thrombotic consequences. There is a similarity in thrombosis due to COVID-19 and some rare event after the same virus vaccination. The problem is whether to use spike protein vaccination is really the right solution. Of course before to use this vaccine it is needed to test people for platelet level, coagulation factor level and other tests like protein C and S deficiency, factor V Leiden, D-dimer, antithrombosis abnormality and other relevant factors (smoke, estrogen or progestin pill, chronic inflammatory diseases). In the figures reported in Luisetto, Tarro *et al*, in press. It is possible to look at some figures that explain the effects on human cells of spike protein (Fig. 1) the SARS-CoV-2 spike domain (Fig. 2), RBD and binding effect (Fig. 3) relationship for vaccine design strategy.



Procoagulant effect of the receptor binding domain (RBD) of the spike protein COVID vaccine and the lenght spike in protein vaccine (Luisetto, Tarro *et al*., 2021c). In the AstraZeneca trials the candidate vaccine induced a similar immune response across all age groups, while it was less reactogenic in other adults than in younger adults. Early markers for reactogenicity, as the humoral innate immunity molecule PTX3, may help early assesment of activation of innate immunity and reactogenicity. In a fraction of COVID-19 patients was associated with autoimmune reactions blocking the interferon pathway or causing thrombosis. Also autoimmune disorders might be recalled and further studies are needed to be carried on to know the impact of COVID-19 and vaccines on autoimmunity including myastenia-gravis (Forni and Mantovani, 2021). The use of RBD in vaccines is compromised by its limited immunogenicity due to its small molecular size and more possible with mixed forms of multiple complexes (as nanomers, dimers or trimers). Increasing antigen size has been adopted by fusing the RBD with an Fc domain or by displaying multiple copies or RBD on viral particles (Dai and Gao, 2020). Some vaccine use the spike protein more similar to the spike-protein expressed by natural infection, triggering an immune response that can protect against COVID-19. Therefore the need for the new vaccine to be examined for their influence on the different target that might cause procoagulant effect.

Table 1. COVID-19: the numbers that keep people afraid

	September 13, 2020	September 13, 2021	Difference
Intensive care	187	563	+376
Hospitalized with symptoms	2.042	4.200	+2.158
Home isolation	36.280	121.141	+84.861
Total hospitalized	2.229	4.763	+2.534
Total active cases	38.509	125.904	+87.395

Source: Gimbe Foundation

Antiviral activity of cellular glutathione: Glutathione is present in cells in the form of reduced glutathione (GSH) and oxidized glutathione (GSSG). The antioxidant capacity of the cell is maintained by glutathione reductase (GSSG-r) which regenerates glutathione from GSSG. Glutathione binds to the membrane of the virus-infected cell and repolarizes the membrane so that glutamate returns to the cell and glutathione synthesis begins again. To maintain cell viability and survival, a correct ratio of GSH to GSSG must be maintained. The virus penetrating into the cell depolarizes the cell membrane preventing the entry of glutamate (due to the inhibition of the transport carrier) which is fundamental in the synthesis of glutathione. Glutathione continuously passing from the reduced to the oxidized form generates and maintains the redox state necessary for the cell which avoids the formation of sulfur bridges of the viral proteins which therefore changed into allosterisms and spatial configurations, are completely eliminated by the immune system. All viruses are weakened, HIV, COVID-19, Polio, Ebola, H1N1 Swine Flu (virus) because they have to undergo the passage of protein formation (Ansovini, 2020).

Perspectives: According to Robert Gallo, director of the Institute of Human Virology at the University of Maryland, when a vaccination campaign against polio was conducted in Russia on a large scale in the 1970s, there were hardly any cases of influenza in the following winter season. The same observation was made in Singapore with seasonal flu. COVID-19 exactly like polio and flu, are caused by viruses with an RNA-based genome, it is plausible that a vaccine stimulates the immune system to act not only on one, but also on the other viruses (Tarro, 2020). 90 vaccines developed against SARS-CoV-2 by research groups in companies and universities around the world. Researchers are experimenting with several technologies, some of which have not been used in a licensed vaccine before. At least six groups have already started injecting formulations into volunteers in safety trials; others have begun testing on animals (Nature, 2020).

Conclusion

"In March 2020 Tarro explained that Sars-Cov-2 had already infected tens of millions of Italians, no one believed it, also because the official figures, in order to justify the lockdown, gave it present only in the few patients Covid swabs. The virus is already endemic and it is as if it 'wakes up' within us, thus allowing any tests to intercept it. This 'awakening' almost never produces symptoms. It has become endemic and cannot be eradicated with the vaccine that some temporary protection should guarantee it. On the contrary, see the case of Fasano. 33 guests and 10 members of the health staff are vaccinated, in the social health residence on February 3, receiving the second dose of Pfizer vaccine. But a little later they all turn out positive. It is not the variant. It could depend on whether the messenger RNA, introduced with the Covid-19 vaccine, has 'activated' the latent virus already present in the body, or the one that arrived following a new infection before the antibody response. It is the same spike protein that activates the virus, at least as far as messenger RNA vaccines are concerned " (Amorosi, 2021). What should we expect for autumn-winter? (Table 1). "I think we will be like the English, they without lockdown we with mask and other limits but if we invest more in the treatments ..." (Tarro, 2021). Vaccination in the UK worked effectively. In our opinion, the problem of the Indian variant can be easily solved at most with another reminder. It is useless to look for flaws in the British vaccination policy, which was impeccable. They immediately left with the elderly and the most fragile subjects and in this way they avoided what instead happened to us with the confusion that there was about the age categories. Let's not forget that the 500 victims we had at the beginning of the year were all elderly, so much so that when the new chief of Italian goverment Draghi arrived he immediately gave priority back to those who needed to be vaccinated before the others".

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