Research Article

Trends in General Medicine

Sars Cov-2 Spike Protein- ACE receptor link, Graphene and Electro-Magnetic Field: toxicological aspetcs HYPOTESYS OF WORK

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ABSTRACT

Related the profile of some toxicological aspect of some COVID -19 vaccine and in specifc way to the rare effect like pericarditis or trombosys are reported in this work some relevant literature involved in the effect played by the SPIKE PROTEINS and its link on epithelial tissue ACE receptor, the Graphene (if present) and under some magnetic field or electrical condition. An experimental hypotesys is submitted to the reseacher in order to produce a global conclusion of toxicological interest.

Keywords

Spike protein, Ace receptor, Graphene, ELECTRIC CHARGE, Electromagnetic field, Magnetism, Pathology, Toxicology, Sinergy.

Introduction

Aim of this work is to evaluate the effect played by electro-magnetic field on the complex SARS COV-2 SPIKE PROTEIN-ACE before the epithelial cell intake and also in presence of graphene.

The nature of the inteaction between SPIKE P and ACE: The protein RBD is attracted by the ACE2 due to their opposite net charges at their binding interfaces. And according Ansovini R, Compagnucci L. Use of Polio Vaccine Salk vs SARS- CoV-2E and HIV-1E 2, both as Therapeutic Drug and Effective Vaccine to Make Memory-Cells Able to Stop Reinfections. J Biomed Res Environ.

"Dr. Ansovini began studying the viruses by focusing his attention on HIV-1. Themain discovery he made is that this virus, so difficult

to treat, can be classified as “electrical”: one of its functional proteins, like “p. 24”, actually has an electrical value, in other words it has a charge, and therefore it is not allosterically neutral as proteins usually are.”

Comparative Study J Am Chem Soc. 2008 Jan 23; doi: 10.1021/ja075244z. Epub 2007 Dec 20. Comparison of electrical properties of viruses studied by AC capacitance scanning probe microscopy Robert I MacCuspie , Nurxat Nuraje, Sang-Yup Lee, Anne Runge, Hiroshi Matsui.

“Because those capsid proteins and glyco-proteins are characteristic of the virus strain, this kind of technique could be applied to detect and identify viruses at the single viron level using their distinct capacitance spectra like fingerprints without labeling.”

And according : The SARS-CoV-2 Spike protein has a broad tropism for mammalian ACE2 proteins
Carina Conceicao et al. December 21, 2020 https://doi.org/10.1371/journal.pbio.3001016 was reported:

“Coronavirus entry into host cells is initiated by direct protein–protein interactions between the virally encoded homo-trimeric Spike protein, a class I trans-membrane fusion protein found embedded in the virion envelope, and proteinaceous receptors or sugars on the surface of the host cells”. It is so possible to say that the electrical interaction by the SPIKE PROTEIN and ACE is a crucial factor that Influence the cellular intake with the start of the pathological event related this virus infectious disease.

It is of great interest to observe also the research of P CAMPRA university of ALMEIRA https://www.researchgate.net/publication/355684360_Deteccion_de_grafeno_en_vacunas_COVID19_por_espectroscopia_Micro-RAMAN
Or recent and really interesting new evicence (DISINFECTION ad Natura Docet Darkfield microscope analysis n 1/ 2022 giovannini f et al. and other research works published also by university professors and other professionals YOUNG RO , YOUNG Mi LEE et al., GIOVANNINI F et al.
All work related the presence of graphene derivates in vials of some COVID-19 vaccine or in blood of vaccinated.

The electrical properies of graphene and graphene GO are clearly reportend in scientific literature. But this impurity in some COVID-19 vaccine how can inlfuence the SPIKE-ACE interaction? And electro magnetic field of various intensity and duration can produce acute/ chronic damage vs normal condition?

“The efficiency of delivery of D.N.A. vaccines is often relatively low compared to the protein vaccines. The use of super-paramagnetic iron oxide nanoparticles to deliver genes via magnetofection shows promise in improving the efficiency of gene delivery both *in vitro* and *in vivo*. The duration for the gene transfection especially for in vitro application can be significantly reduced by magnetofection compared to the time required to achieve high gene transfection with standard protocols. SPIONs that have been rendered stable in physiological conditions can be used as both therapeutic /diagnostic agents due to their unique magnetic characteristics. Valuable features of iron oxide nano-particles in bio-applications include a tight control over their size distribution, magnetic properties of these particles, and the ability to carry particular biomolecules to specific targets. The internalization and half-life of the particles within the body depend upon the method of synthesis.Various synthesis methods have been used to produce magnetic nano-particles for bio -applications with different sizes and surface charges. The most common method for synthesizing nanometer-sized magnetite Fe3O4 particles in solution is by chemical coprecipitation of iron salts. The coprecipitation method is an effective technique for preparing a stable aqueous dispersions of iron oxide nanoparticles. Here We describe the production of Fe3O4-based SPIONs with high magnetization values (70 emu/g) under 15 kOe of the applied magnetic field at room temperature, with 0.01 emu/g remanence via a coprecipitation method in the presence of trisodium citrate as a stabilizer. Naked SPIONs often lack sufficient stability, hydrophilicity, and the capacity to be functionalized. In order to overcome these kind of limitations, polycationic polymer was anchored on the surface of freshly prepared SPIONs by a direct electrostatic attraction between the negatively (-) charged SPIONs (due to the presence of carboxylic groups) and the positively charged polymer. Polyethylen-imine was chosen to modify the surface of SPIONs to assist the delivery of plasmid D.N.A. into mammalian cells due to the polymer's extensive buffering capacity through the "proton sponge" effect”.

Nanomaterials (Basel). 2019 Feb; 9(2): 297. Feb 20. doi: 10.3390/nano9020297
Electrical Property of Graphene and Its Application to Electrochemical Biosensing
Jin-Ho Lee, Soo-Jeong Park, and Jeong-Woo Choi

“Graphene, a single 2-dimensional (2D) layer of a hexagonal structure consisting of sp2 hybridized carbon atoms, and its derivatives have received increasing attention in bio-medical fields, due to its unique physico and chemical properties. This feature includes a high surface area, excellent electrical conductivity, strong mechanical strength, unparalleled thermal conductivity, and ease of surface functionalization.”

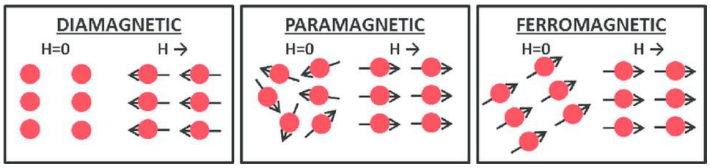

Figure 1: In the absence of a magnetic field, diamagnetic and paramagnetic materials remain non-magnetized on ... [+]LEONADRO RICOTTI / V. IACOVACCI ET AL., 2016, IN LAB-ON-A-CHIP FABRICATION AND APPLICATION.

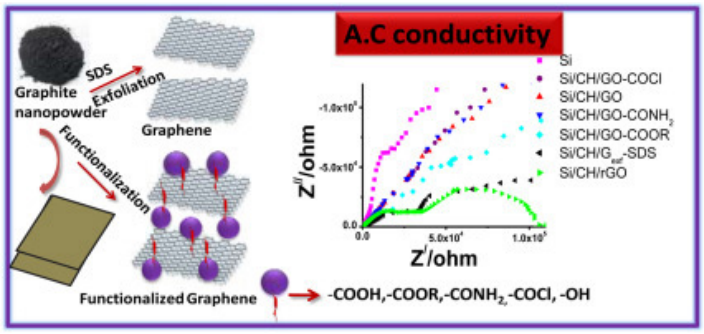

Figure 2: Magnetic field lines, as illustrated by a bar magnet: a magnetic dipole, with a north and south pole ... [+]NEWTON HENRY BLACK, HARVEY N. DAVIS (1913) PRACTICAL PHYSICS.

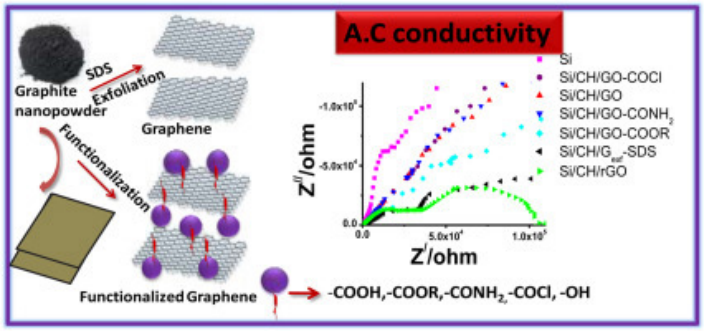

Figure 3: Graphene conductivity from https://doi.org/10.1016/j.matchemphys.2015.07.036.

In scientific reports articles article 07 December 2020
Observation of magnetic domains in graphene magnetized by controlling temperature, strain and magnetic field
Mahsa Alimohammadian & Beheshteh Sohrabi:

"Graphene, as a 2D material1, is an excellent candidate for replacing many conventional materials in various kind of applications due to remarkable electrical, thermal, mechanical, and optical properties. In the honeycomb structure of the graphene, the presence of one free electron per atom is responsible for high electron mobility and the carriers transport is described by Dirac equation.Other electrical properties such as room-temperature quantum Hall effects, unique band structure, and ambipolar electric field effects, covers the electronic application".

From https://www.gov.uk/government/publications/freedom-of-information-responses-from-the-mhra-week-commencing-21-june-2021/freedom-of-information-request-on-reports-of-magnetism-at-COVID-19-vaccine-injection-sites-foi-21-545

"During clinical trials for the vaccines currently deployed in the United Kingdom, no adverse events that match the magnetic phenomenon described were reported. The 'Information for UK Recipients' [Pfizer BioNTech/AstraZeneca vaccines] and 'Patient Information Leaflet' [Moderna vaccine] provide a list of ingredients for each vaccine. None of these ingredients are considered to cause "magnetism" when administered to a vaccine recipient".

And from https://www.gov.uk/government/publications/freedom-of-information-responses-from-the-mhra-week-commencing-20-september-2021/freedom-of-information-request-on-the-authorisation-of-the-COVID-19-vaccines-foi-21992

"I have evidence of someone displaying magnetism at the site of an injection (given in preparation for travel abroad) at a Boots pharmacy in the East of England prior to January 2021. How can this be accounted for? Are the MHRA aware of any other reports of cases of post-injection magnetism prior to the rollout of the COVID-19 vaccines?

During clinical trials for the vaccines currently deployed in the UK, no adverse events that match the magnetic phenomenon described were reported. The 'Information for UK Recipients' [Pfizer BioNTech/AstraZeneca vaccines] and 'Patient Information Leaflet' [Moderna vaccine] provide a list of ingredients for each vaccine. None of these ingredients are considered to cause "magnetism" when administered to a vaccine recipient."

In a NON PUBLISHED ARTICLE: (Study on the Electromagnetism of Vaccinated Persons in Luxembourg, European Forum for Vaccine Vigilance, Goudjil, 2021) CITED BY https://www.gov.uk/government/publications/freedom-of-information-responses-from-the-mhra-week-commencing-20-september-2021/freedom-of-information-request-on-the-authorisation-of-the-COVID-19-vaccines-foi-21992 and this document it is reported that:

The information described as 'Study on the electromagnetism of vaccinated persons in Luxembourg' does not appear to have been published in a recognized scientific journal or subjected to peer review. The article does not state which vaccines were given so little can be derived from this information.

Study on the Electromagnetism of Vaccinated Persons in Luxembourg, European Forum for Vaccine Vigilance,Mamer and Goudjil, 2021
https://www.efvv.eu/images/content/2021/0617/study-on-electromagnetism-of-vaccinated-persons-in-luxembourg_6edfa.pdf

Mr. Amar GOUDJIL, Treasurer of the Association AEFVV and Member in Charge of Demographic and Sociological Issues
That a panel of 200 individuals living or working in Luxembourg would be interviewed. That this panel would be divided into 2 groups. The first would be composed of 100 individuals vaccinated in Luxembourg and the second of 100 unvaccinated individuals for comparison purposes.
"Summary presentation of the results for the study week from 1 June to 5 June 2021:

Only 30 vaccinated and 30 unvaccinated people were finally

interviewed while the target was to interview 100 for the first group and 100 for the second. The condition of gender distribution was met. In each group, 15 women and 15 men were interviewed.

In the non-vaccinated group, out of the 30 individuals interviewed, the number of people showing attraction to the magnet was 0 (zero). Therefore the experiment ended there for this group. In the vaccinated group, on the other hand, 29 of the 30 individuals interviewed showed attraction to the magnet. That is, the magnet adhered to their skin without difficulty." Of these same 29 individuals, 22 have the magnet adhering to only one shoulder and only to the injection area. These 22 individuals are those who received only one injection. The other 7 people in this same group have the magnet adhering on both shoulders.

It is now the responsibility of toxicologists and pharmacologists to discover the origins and causes of these attractive effects on vaccinated subjects, and it is the responsibility of the guarantors of the health of the citizens of this country to very quickly demand the opening of an enquiry into the exact and real composition of these so-called vaccines"

According https://www.globalresearch.ca/study-electromagnetism-vaccinated-persons-luxembourg/5749516 **This survey, of a purely statistical and sociological nature,** on this supposed electromagnetic effect, which is the subject of this report, raises at least three important questions.

And also of interest: OPERATION SECRET 16' by Opérateurs: Dr Julien DEVILLEGER, cardiologue et Jessy Duthil, infirmière libérale (Charente, France) du 11 juin au 27 juillet 2021. as reported in https://www.efvv.eu/images/content/2021/0803/operation-secret-16_f7a17.pdf

(A questionable study, low scientific?)

Magnetization research method:

- Coin held between thumb and index finger, with middle finger bent (safely).
- Person standing, arms swinging, dry skin, little hair on the arms, cream cleaned off with water, then skin dried, sweat absorbed by single-use dry towel.
- Coin held at 20 centimetres below the shoulder, lightly touching the skin, without pressing, and sliding from bottom to top up to about 3 finger-widths below the shoulder.
- Technique to be carried out 2 times in a row, in case of magnetization alternately on the left arm/right arm.
- Magnetization if the coin held for at least 10 seconds.

"Between June 1 to July 7, 2021, 256 subjects were enrolled in the study. In our population, 148 (57.8%) declined the COVID-19 vaccination and 108 (42.2%) received it. As expected, the age of the of the 108 vaccinated subjects was significantly greater than the non-vaccinated patients for obvious reasons (44.2 ± 17.1 vs 34.2 ± 19.3; $p < 0.0001$). Of the vaccinated patients, 68.5% received the Pfizer vaccine, 24.1% Moderna, and 7.4% Johnson & Johnson. Demographics of the study population are noted in Table reported reviews the results of the non-COVID-19 vaccinated group (148) versus the COVID-19 vaccinated group (148 vs 108). Magnet and paper clip attachment to the deltoid muscles occurred in most

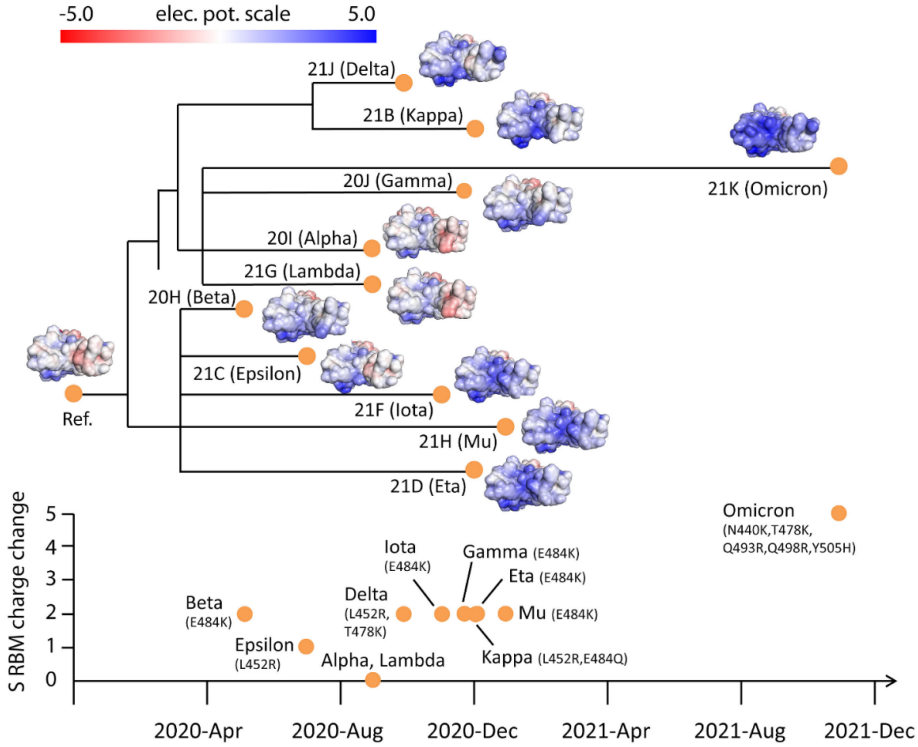

Figure 4: Electrostatic surfaces of Spike RBD variants organized by Nextstrain SARS-CoV-2 phylogeny. Tracking of total charge changes with accompanying mutations in S RBM suggests a gradual increase of positive charges over time. The color scale of the electrostatic potential surface is in units of kT/e at T = 37°C.

subjects regardless of vaccination status. No statistical differences between the COVID-19 non-vaccinated and vaccinated groups were observed. **Comparison of unvaccinated versus vaccinated groups yielded no significant differences (p > 0.1) in the magnet score of 4/4 (62.8% vs 53.7%);** the clip score of 6/6 (54.1% vs 46.5%) and; the field scores of 10/10 (50.0% versus 41.7%)"

"Our findings reveal that the SARS-CoV-2 S protein is slightly more positively (+) charged than that of SARS-CoV since it contains four more positively charged residues and 5 less negatively charged residues"

SARS-CoV-2 spike mR.N.A. vaccine sequences circulate in blood up to 28 days after COVID-19 vaccination.

"In Denmark, vaccination against SARS-CoV-2 has been with Pfizer-BioNTech (BTN162b2) or Moderna (mR.N.A.-1273) mR.N.A. vaccines. Patients with chronic hepatitis C virus (HCV) infection followed in our clinic received mR.N.A. vaccinations according to the Danish roll-out vaccination plan. To monitor H.C.V infection, R.N.A. was extracted from patient plasma and R.N.A. sequencing was performed on the Illumina platform. In 10 of 108 HCV patient samples, full-length or traces of SARS-CoV-2 spike mR.N.A. vaccine sequences were found in blood up to 28 days after the COVID-19 vaccination. Detection of mR.N.A vaccine sequences in blood after vaccination adds important knowledge regarding this technology and should lead to further research into the design of lipid-nanoparticles and the half-life of these and mR.N.A. vaccines in humans."

"During the SARS-CoV-2 pandemic, novel and traditional vaccine strategies have been deployed globally. We investigated whether antibodies stimulated by mR.N.A. vaccination (BNT162b2), including third-dose boosting, differ from those generated by infection or adenoviral (ChAdOx1-S and Gam-COVID-Vac) or inactivated viral (BBIBP-CorV) vaccines. We analyzed human lymph nodes after infection or mR.N.A. vaccination for correlates of serological differences. Antibody breadth against viral variants is lower after infection compared with all vaccines evaluated but improves over several months. Viral- variant infection elicits variant-specific antibodies, but prior mR.N.A. vaccination imprints serological responses toward Wuhan-Hu-1 rather than variant antigens. In contrast to disrupted germinal centers (GCs) in the lymph nodes during infection, mR.N.A. vaccination stimulates robust GCs containing vaccine mR.N.A. and spike antigen up to 8 weeks post-vaccination in some cases. SARS-CoV-2 antibody specificity, breadth, and maturation are affected by imprinting from exposure history and distinct histological and antigenic contexts in infection compared with vaccination. Prolonged detection of vaccine mR.N.A. in LN GCs and spike antigen in LN GCs and blood following SARS-CoV-2 mR.N.A. vaccination.

The bio-distribution, quantity, and persistence of vaccine mR.N.A. and spike antigen after the vaccination and viral antigens after SARS-CoV-2 infection are incompletely understood but are likely to be major determinants of immune responses. We performed in situ hybridization with control and SARS-CoV-2 vaccine mR.N.A.-specific R.N.A.Scope probes in the core needle biopsies of the ipsilateral axillary LNs that were collected 7–60 days after the second dose of mR.N.A.-1273 or BNT162b2 vaccination and detected vaccine mR.N.A. collected in the GCs of LNs on days 7, 16, and 37 post-vaccination, with lower but still appreciable specific signal at day 60. Only rare foci of vaccine mR.N.A. were seen outside of GCs. Axillary LN core needle biopsies of nonvaccinees (n = 3) and COVID-19 patient specimens were negative for vaccine probe hybridization. Immuno-histochemical staining for spike antigen in mR.N.A.-vaccinated patient LNs varied between individuals but showed abundant spike protein in GCs 16 days post-second dose, with spike antigen S.A.still present as late as 60 days post-second dose. Spike antigen localized in a reticular pattern around the GC cells, similar to staining for follicular dendritic cell processes. COVID-19 patient LNs showed lower quantities of spike antigen but a rare GC had positive staining. Immuno-histochemical staining for N antigen in peribronchial LN secondary and primary follicles of COVID-19 patients was positive in 5 of the 7 patients, with a mean percentage of ucleocapsid-positive (+) follicles of more than 25%."

Cutting Edge: Circulating Exosomes with COVID Spike Protein Are Induced by BNT162b2 (Pfizer–BioNTech) Vaccination prior to Development of Antibodies: A Novel Mechanism for Immune Activation by mR.N.A. Vaccines.

A reference has been published: Comment on "Cutting Edge: Circulating Exosomes with COVID Spike Protein Are Induced by BNT162b2 (Pfizer-BioNTech) Vaccination prior to Development of Antibodies: A Novel Mechanism for Immune Activation by mR.N.A. Vaccines".

"SARS-CoV-2 causes severe acute respiratory syndrome. mR.N.A. vaccines directed at the SARS-CoV-2 spike protein resulted in development of Abs and protective immunity. To determine the mechanism, we analyzed the kinetics of induction of circulating exosomes with SARS-CoV-2 spike protein SP and Ab following vaccination of healthy individuals. Results demonstrated induction of circulating exosomes expressing spike protein on day 14 after vaccination followed by Abs 14 d after the second dose. Exosomes with spike protein, Abs to SARS-CoV-2 spike, and T cells secreting IFN-γ and TNF-α increased following the booster dose. Transmission electron microscopy of exosomes also demonstrated spike protein Ags on their surface. Exosomes with the spike protein and Abs decreased in parallel after four months. These results demonstrate an important role of circulating exosomes with spike protein for effective immunization following mR.N.A.-based vaccination. This is further documented by induction of humoral and cellular immune responses in mice immunized with exosomes carrying spike protein".

Persistence of SARS CoV-2 S1 Protein in CD16+ Monocytes in Post-Acute Sequelae of COVID-19 (PASC) up to 15 Months Post-Infection Bruce K. Patterson, Edgar B. Francisco, Ram Yogendra, Emily Long, Amruta Pise, Hallison Rodrigues, Eric Hall, Monica

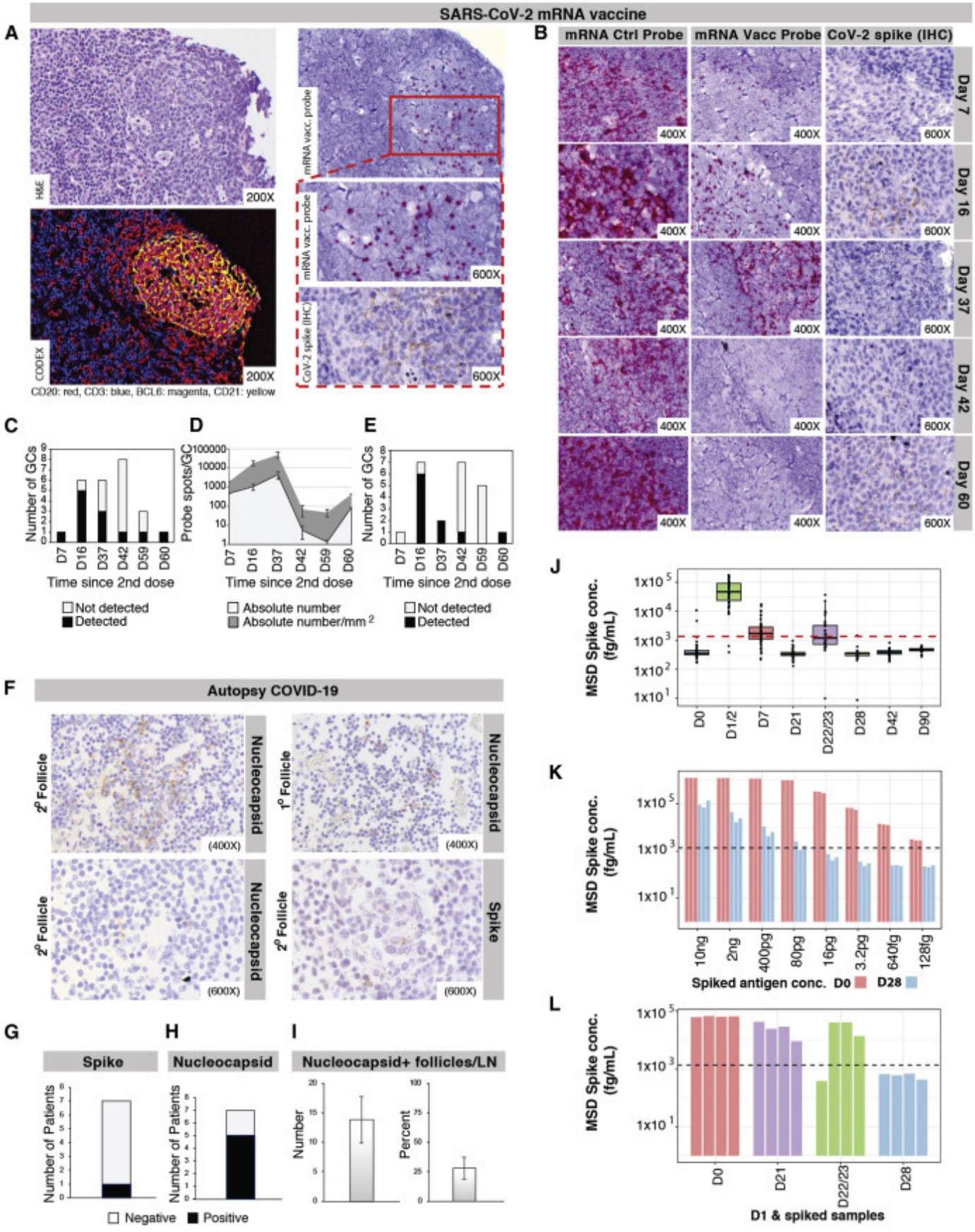

Figure 5: Localization of SARS-CoV-2 proteins and vaccine mR.N.A. in LNs.

Herrera, Purvi Parikh, Jose Guevara-Coto, Timothy J. Triche, Paul Scott, Saboor Hekmati, Dennis Maglinte, Xaiolan Chang, Rodrigo A. Mora-Rodríguez and Javier Mora.

"The recent COVID-19 pandemic is a treatment challenge in the acute infection stage but the recognition of chronic COVID-19 symptoms termed post-acute sequelae SARS-CoV-2 infection (PASC) may affect up to 30% of all infected individuals. The underlying mechanism and source of this distinct immunologic condition three months or more after initial infection remains elusive.

We investigated the presence of SARS-CoV-2 S1 protein in 46 individuals. We analyzed T-cell, B-cell, and monocytic subsets in both severe COVID-19 patients and in patients with post-acute sequelae of COVID-19. The levels of both intermediate (CD14+, CD16+) and non-classical monocyte (CD14Lo, CD16+) were significantly elevated in PASC patients up to 15 months post-acute infection compared to healthy controls (P=0.002 and P=0.01, respectively). A statistically significant number of non-classical monocytes contained SARS-CoV-2 S1 protein in both severe (P=0.004) and PASC patients (P=0.02) out to 15 months post-infection. Non-classical monocytes were sorted from PASC patients using flow cytometric sorting and the SARS-CoV-2 S1 protein was confirmed by mass spectrometry- MS . Cells from 4 out of 11 severe COVID-19 patients and 1 out of 26 PASC patients contained ddPCR+ peripheral blood mononuclear cells, only fragmented SARS-CoV-2 R.N.A. was found in PASC patients. No full length sequences were identified, and no sequences that could account for the observed S1 protein were identified in any patient. That non-classical monocytes may be a source of inflammation in PASC warrants further study."

"We report a case of a patient with a bilateral branch retinal vein occlusion (BRVO) 24h after a booster vaccination with the mR.N.A.-1237 vaccine. Fluorescein angiography, performed at three weeks follow-up, showed vascular leakage and blockage, corresponding to hemorrhage areas associated with ischemic areas in the macula and along the arcades involved in the occlusion. The patient was scheduled for urgent injections of intravitreal ranibizumab and laser photocoagulation of the ischemic areas. To the best of our knowledge, this is the first case described of concomitant bilateral RVO after COVID-19 vaccination. The rapid onset of the side effects in a patient with multiple risk factors for thrombotic events suggests that vulnerable micro-vascular conditions require detailed investigations before administration of a COVID-19 vaccine".

"Current neuromodulation techniques such as optogenetics and deep-brain stimulation are transforming basic and translational neuroscience. These 2 neuromodulation approaches are, invasive since surgical implantation of an optical fiber or wire electrode is required.

We have invented a non-invasive magneto-genetics that combines the genetic targeting of a magneto-receptor with remote magnetic stimulation. The non-invasive activation of neurons was achieved by neuronal expression of an exogenous magneto-receptor, an iron-sulfur cluster assembly protein 1. In the HEK-293 cells and cultured hippocampal neurons expressing this magneto-receptor, application of an external magnetic field resulted in membrane depolarization and calcium influx in a reproducible and reversible manner, as indicated by the ultrasensitive fluorescent calcium indicator GCaMP6s. the magnetogenetic control of neuronal activity might be dependent on the direction of the magnetic field and exhibits on-response and off-response patterns for the external magnetic field applied. The activation of this kind of magneto-receptor can depolarize the neurons and elicit trains of action potentials, which can be triggered repetitively with a remote magnetic field in whole-cell patch-clamp recording. In transgenic Caenorhabditis elegans expressing this magneto-receptor in myo-3-specific muscle cells or mec-4-specific neurons, application of the external magnetic field triggered muscle contraction and withdrawal behavior of the worms, indicative of magnet-dependent activation of muscle cells and touch receptor neurons, respectively. The advantages of the magneto-genetics over optogenetics are its exclusive non-invasive, deep penetration, long-term continuous dosing, unlimited accessibility, spatial uniformity and relative safety. Like optogenetics that has gone through decade-long improvements, magneto-genetics, with continuous modification and maturation, will reshape the current landscape of neuro-modulation toolboxes and will have a broad range of applications to basic and translational neuro-science as well as other biological sciences."

Materials and Methods

Whit an observational point of view some relevant scientific literature are reported and analyzed. All article comes from PUBMED or other database. Figure from 1-10 help in the discussion Additionally also some documents are reported (some study of low level of quality or white paper) in order to Produce hypotesys of work to be verified according the scientific criteria of reproducibility and accurancy. After this phase an esperimental project hypotesys will be produced in order to submit to the researcher a New hypotesys of work.

Results

"Binding of virions to integrins on endothelial cells could activate angiogenic cell signaling pathways; dysregulate integrin-mediated signaling pathways controlling developmental processes; and precipitate endothelial activation to initiate blood clotting. Like a procoagulant state, perhaps together with enhancement of platelet PTL aggregation through virions binding to integrins on platelets, could amplify the production of micro-thrombi that pose the threat of pulmonary thrombosis and embolism, strokes and other thrombotic consequences. "There is a similarity in thrombosis due by COVID-19 and some rare event post some COVID-19 vaccination.

All this evidence requires to submit a relevant question to the researcher : to use spike protein model to produce a vaccine is really the right solution. It is possible that a class effect can be observed? And before to use this vaccine it is needed to test patient for platelet level, coagulation factor level and first level and second level tests like protein C and S deficiency, factor V Leiden, D-dimer,

antithrombin abnormality and other factors that can be relevant (smoke, estrogen - progestin pill, chronic inflammatory disease)" [1].

"Because in toxicology are well known various situation of combined toxic effect by multiple chemical dangerous exposure It is needed to verify the clinical effect of the self-assembling graphene G.O. effect added to spike protein using in vitro sample (Animal model and sample from humans' specimens: subjects volunteers).

The experimental project submitted can help for this scope. It is also of interest to verify if the cumulative effect of this 2 substantia Graphene GO and SPIKE protein. Show and added toxic effect (sinergic) or this is greater than the single molecule acting alone and the kinetic related" [2].

"To assess clinical and cardiac magnetic resonance imaging features of patients with peri-myocarditis following Coronavirus Disease 2019 (COVID-19) vaccination. We retrospectively collected a case series of 27 patients who underwent CMR in the clinical suspect of heart inflammation following COVID-19 vaccination, from 16 large tertiary centers. Our patient's cohort was relatively young (36.6 ± 16.8 years), predominately included males (n = 25/27) with few comorbidities and covered a catchment area of about 8 million vaccinated patients.

CMR revealed typical mid-subepicardial non-ischemic late gadolinium enhancement (LGE) in 23 cases and matched positively with CMR T2 criteria of myocarditis. In 7 cases, typical hallmarks of acute peri-carditis were present. Short-term follow-up (median = 20 days) from presentation was uneventful for 25/27 patients and unavailable in 2 cases. While establishing a causal relationship between peri-myocardial inflammation and vaccine administration can be challenging, our clinical experience suggests that CMR should be performed for diagnosis confirmation and to drive clinical decision-making and follow-up" [3].

"Step III Electrical events link with an emitted electromagnetic radiation: In the biological cell, contains ions (the potassium K+ and chloride anion Cl–) are inside the cell, and ions (Na+, Ca2+ cations, and chloride anion Cl– (at higher concentration) are outside the cell . After the virus enters a host cell leads it to changes the electrical steady state of the virus because the different distribution of electrical charges inside and outside the virus leads to an electrical gradient (voltage) across membrane.

This electrical gradient is a difference across viral membrane that generates a store of potential energy in the form of an electro-chemical gradient, which helps create the electric field or an electrical potential by the movement of ions across the 2 sides of the membrane.

The viral membrane marks the border between the internal and external of the COVID-19 particle, which means, here the difference in electric potential between the inside and outside the COVID-19 particle. The viral membrane is responsible for the

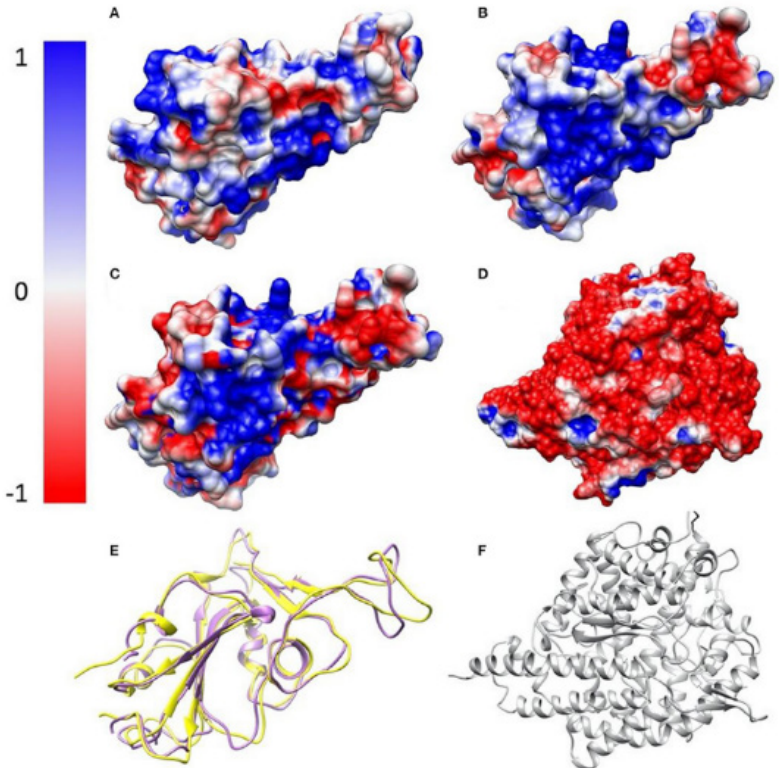

Figure 6: Electrostatic surfaces of SARS-CoV S protein RBD, SARS-CoV-2 S protein RBD and ACE2 RBD. (A) Electrostatic surface of SARS-CoV S protein RBD; (B) Electrostatic surface of SARS-CoV-2 S protein RBD; (C) Electrostatic difference between SARS- CoV and SARS-CoV-2 S protein RBD, by subtracting electrostatic values of SARS-CoV-2 by SARS-CoV, and mapped the values on the surface of SARS-CoV-2; (D) Electrostatic surface of human ACE2 RBD; (E) Structure comparison of SARS-CoV S protein RBD and SARS-CoV-2 S protein RBD, colored with purple and yellow, respectively; (F) The structure of human ACE2 binding domain, colored with gray.

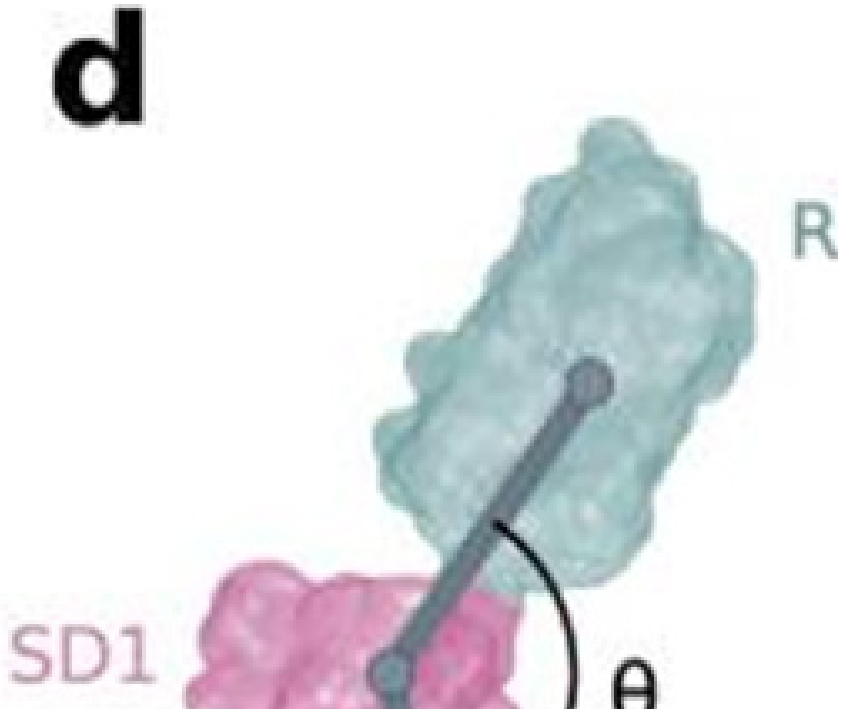

Figure 7: The binding between the S protein and ACE2 can be altered when external electric fields induce drastic conformational changes and damage in the Spike protein. Very strong electric fields (109 V/m) disable the protein by largely deforming its shape, leaving a structure which is unrecognised by ACE2 (NC = 0). Moderate electric fields, which can be induced by available industrial or laboratory devices, strongly reduce NC and are therefore candidates to decrease the affinity of Spike to ACE2 and, consequently, the infectivity of the virus. Electric fields are able to induce global conformational changes in the spike glycoprotein, affecting the stability of folding states. While the structural flexibility of S allows the virus to improve its probability of entering the cell, it is also the origin of the surprising vulnerability of S upon application of electric fields of strengths at least 2 orders of magnitude smaller than those required for damaging most proteins. The secondary structure of the RBM can be irreversibly perturbed by the electric fields, affecting residues that participate in the binding to ACE2. a The recognition loop L3 (Tyr470 to Pro491), exhibits 2 parallel β sheets, which are responsible for a higher affinity to ACE215, 42. The electric field induces a change of the secondary structure of L3 to an un-structured loop (example for EF = 107 V m−1) From nature communications 13 September 2021 The SARS-CoV-2 spike protein is vulnerable to moderate electric fields Claudia R. Arbeitman, Pablo Rojas, Pedro Ojeda-May & Martin E. Garcia.

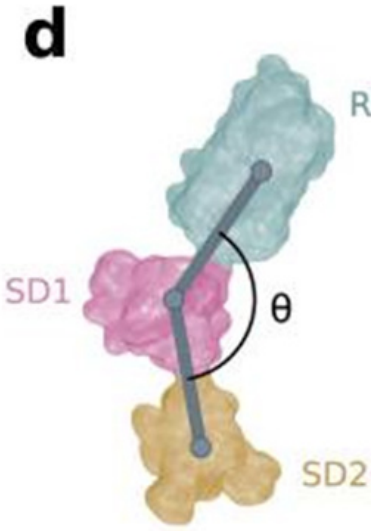

Figure 8: Field-induced conformational states can be characterised by the angles formed by the vectors connecting the centroids of clustered residues.

establishment of the electrical potential and serves as an insulator, all this indicates that there are lost or gained an electron, so there are lost or gained electrical charges" [4].

"Various neurological sequalae have been described following COVID-19 vaccination. Here we describe the first case of untreated post COVID-19 vaccine encephalitis with spontaneous resolution of contrast enhancing hyperintensities on MRI concomitant with clinical improvement.

A 59-year-old woman presented with a 2 day history of unsteady gait, incoordination, visual symptoms, and lethargy. She had received AZD1222 (AstraZeneca AZ) and mR.N.A.-1273 (Moderna) COVID-19 vaccines at 3 months and 12 days, respectively, before presentation. Brain MRI showed no abnormality on the non-enhanced sequences, but numerous enhancing lesions in the cerebral cortex, deep grey matter, brainstem, and in the cerebellum. Treatment was expectant, the patient improved clinically over 10 days, and repeat MRI showed near complete resolution of imaging abnormality.

We describe neurological deterioration 12 days after a second dose of COVID-19 vaccine. There was no evidence of edema or demyelinating lesions in brain on M.R.I, but there was extensive contrast-enhancement indicating loss of blood-brain barrier integrity. This provides a potential *in vivo*, clinical-imaging correlate of the post-mortem evidence that SARS-CoV-2 spike protein may induce loss of the BBB permeability. While this adds to the list of rare adverse neurological reactions to COVID-19 vaccination, the benefits of receiving the vaccine far outweigh these risks." [5].

"Myocarditis is a rare complication of COVID-19 mR.N.A. vaccines.1 Although the short-term prognosis is usually favorable, little is known about the longitudinal follow-up and/or midterm prognosis of patients with COVID-19 vaccine–associated myocarditis. In non–vaccine-related myocarditis, the persistency of nonischemic myocardial injury on cardiac magnetic resonance imaging is associated with an increased risk of adverse cardiovascular events. But it is unknown whether the same occurs in COV19VAM. We present CMR imaging findings, as well as clinical characteristics, of 5 adult patients previously affected by COV19VAM. This is the first systematic longitudinal evaluation of both clinical and imaging data up to 3-month follow-up (median follow-up time from first CMR in this study was 106 days; IQR: 75.5-107.5 days) for patients with previous COV19VAM" [6].

(A to D) Initial CMR of patient 3 demonstrating (A and C) prominent myocardial edema and (B and D) LGE of the basal inferior and inferolateral walls consistent with acute myocarditis. (E to H) Follow-up CMR demonstrating (E and G) resolution of myocardial edema and (F and H) decrease in nonischemic LGE, consistent with the transition from injury or inflammation to replacement fibrosis. 1 and 2 = regions of interest. Abbreviations as in Figure 1.

"SARS-CoV-2 has been widely spread in the world, causing more than 2 million deaths and seriously threatening human life. Effective protection measures are important to prevent the infection and spreading of the virus. To explore the effects of graphene on the virus adsorption and its biological properties, the adsorption process of the receptor binding domain of SARS-CoV-2 on graphene has been investigated by molecular dynamics simulations in this work. The results show that RBD can be quickly adsorbed onto the surface of graphene due to π–π stacking and hydrophobic interactions. Residue PHE486 with benzene ring has stronger adsorption force and the maximum contact area with graphene. Graphene significantly affects secondary structure of RBD area, especially on the three key sites of binding with the human ACE2, GLY476, PHE486 and ASN487. The binding free energy of RBD and graphene shows that the adsorption is irreversible" [7].

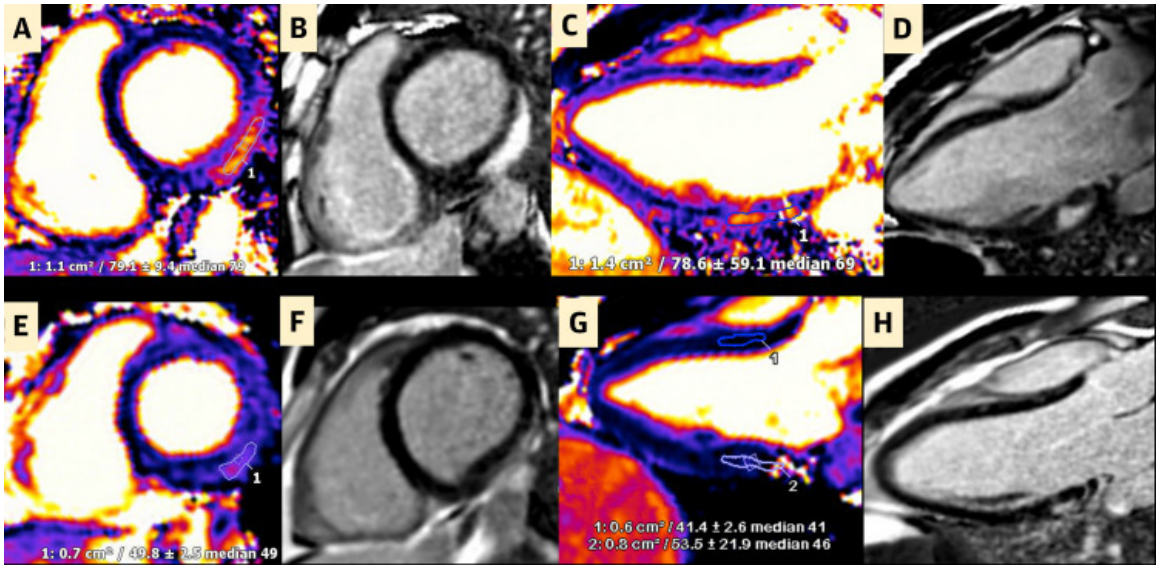

Figure 9: Initial and Follow-Up CMR of Patient 3.

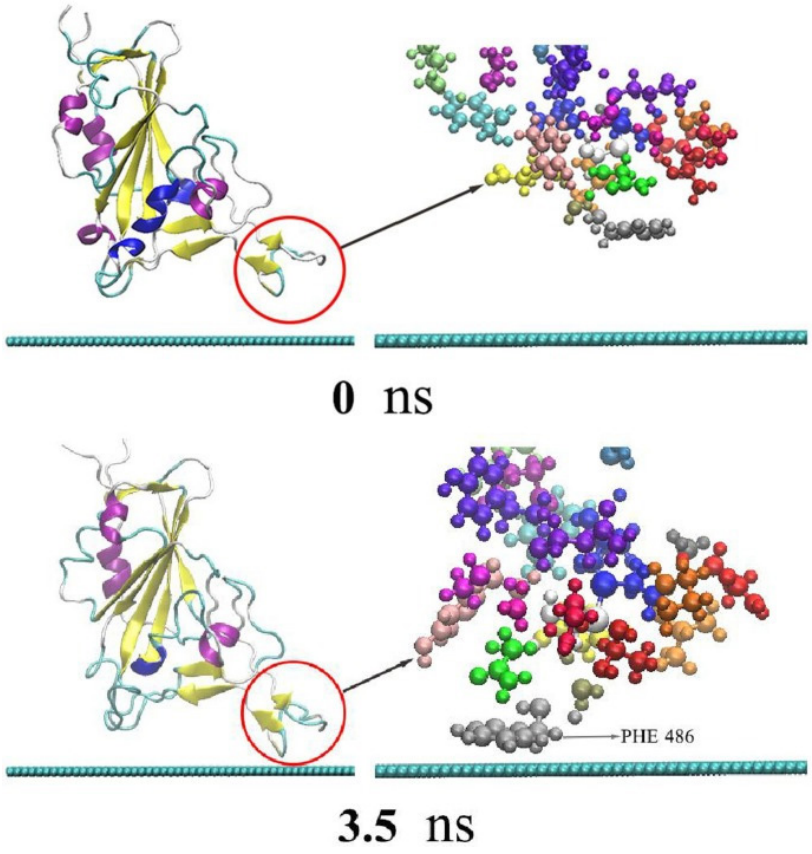

Figure 10: The adsorption process of RBD on the surface of graphene. The left is the secondary structure of RBD presented in newcartoon type, in which the red circle indicates the protein adsorption area. The right is the enlarged CPK type structure of the adsorption area. The blue-green spherical chain below is the side view of 2-dimensional graphene.

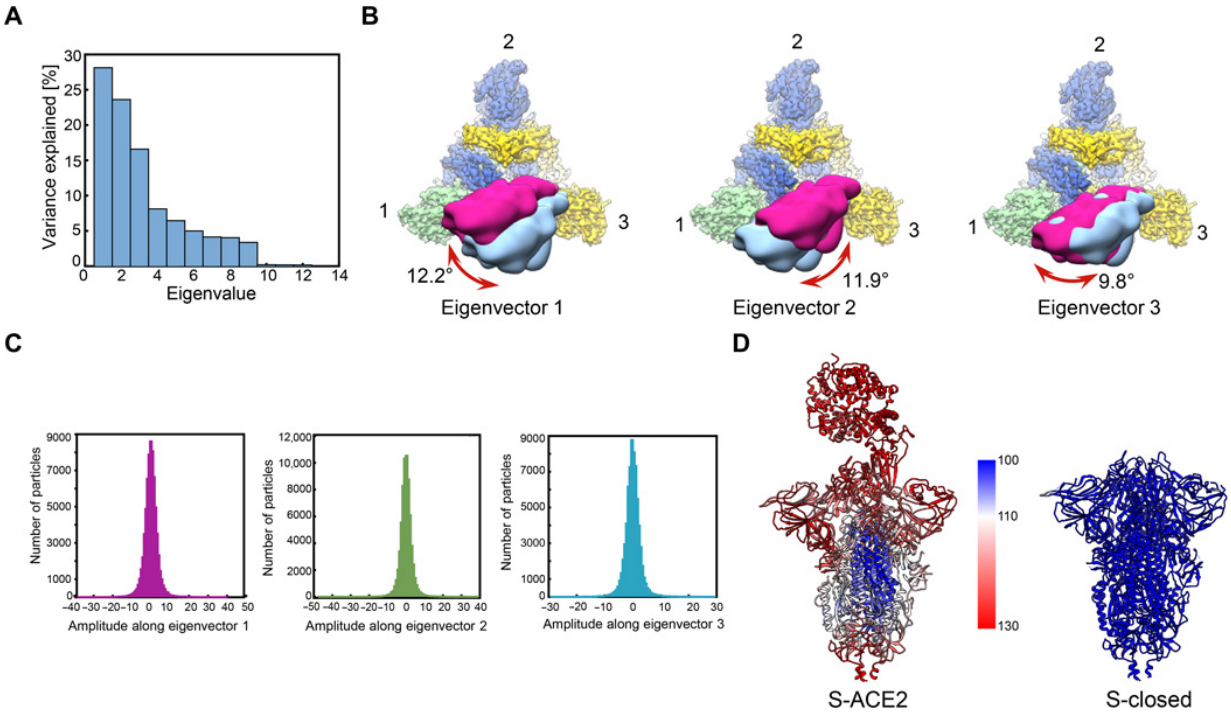

Figure 11: (D) Atomic models of S-ACE2 and S-closed, colored according to the B-factor distribution [ranging from 100 (blue) to 130 Å2 (red)]. **ACE2 binding to SARS-CoV-2 strictly requires the up conformation of RBD.**

"The S protein RBD is attracted by the ACE2 due to their opposite net charges at their binding interfaces. This electrostatic binding force is common in other strong protein–protein interactions, which provides long-range interactions" [8].

Experimental project hypotesys

In order to verify th effect played by various factor in the relationship between spike protenin ad ACE of pulmonary epitelial cell using an artificial system:

1) Cellular colture (pulmonary epitehleal cell) to evaluate the effect of spike protein linked to ACE receptor.
2) Cellular colture spike -ace plus graphene derivates.
3) Cellular colture spike-ace- added graphene under electromagnetic field of various intensity TIME OF OBSERVATION: after 1-2-6-12-24-48-72 hour and more 7 -30- 60 days.

Discussion

the Spike protein RBD is attracted by the ACE2 due to their opposite net charges at their binding interfaces. This link increase the epithelial cell penetration.

In this work are reported the effect played by electric field on the link between spike protein and the tissue ACE receptor. The same is reported the effect observed in CMR in myocarditys by COVID-19 vaccinated. It is possibe to say that electric – magnetic field can influence the interaction of the spike protein (naturals due by infections) or sintetically by a COVID-19 vaccine. But what happen if in this interaction, under electric magnetic umbalance, the graphene molecule and related self assembling propery are present?

The electrical properties of graphene are clear by literature. Even if The presence of graphene reduce aggressivity of the coples spike-ACE receptor by an electrical interference there is an increase the duration of the effect. Graphene can assume charge (conductive property), So It is possible to consider the graphene like a carrier that modulate the spike protein toxicicy? Under a toxicological point of view it is always interesting to observe the toxicicty of the various single molecule of factor but especiallly if acting in the same time in a single body.

What happen if in the same time after a time related episode the self assembling property of graphene added to spike protein toxicity is influenced by a temporary electromagnetic field? (interference in the system) TWO FIXED FACTOR PLUS A VARIABLE ONE. It is possible to divide toxic effect in acute or long term according this situations?

Conclusion

Because toxicity of sars cov-2 virus spike protein can produce clots, pericarditys or other pathologic event It is of interest to evaluate some additional co- factor in the case of COVID-9 vaccine spike based.

What happen in presence of graphene derivates and what happen under determinate condition of external electro-magnetic filed. And what effect is played by various electromagnetic field intensity applied or by the time of application?

Related this topic it is interesting to observe that there are no or few literature about the effepct played by the combination of SPIKE PROTEIN – ACE and graphene under various grade of electro- magnetic field. "It has been theoretically predicted and experimentally demonstrated that static and time-dependent electric fields (EFs) are capable of inducing conformational changes or even irreversible damage in proteins" [9]. And "ACE2 binding to SARS-CoV-2 strictly requires the up conformation of RBD" [10].

"**Electric fields are able to induce global conformational changes in the spike glycoprotein, affecting the stability of folding states". (As written by Claudia R. Arbeitman et al.) So The intensity and duration of the link between SPIKE and ACE is influenced by electric fields (maximum or minimum effect according the intensity of interference)**

The rare effect observed for some m R.N.A. VACCINE like pericarditis in young are currently reported in scientific databaese, the same the procoagulant etc. But because there is a variability in this effect it can be relevant observe the environment around the patient body and the real composition of the vaccine vials. Various independent reseacher finded graphene derivates in some vials of COVID-19 vaccine and the same other reported this substantie in blood of vaccinated. Because electro-magentic field can modify the electrical charge of various molecule it is crucial for the author of this work to invesigate deeply the cumulative affect played by this three independent factor (primary or secondary) in the development of adverse event.

Mainly related the intensity of this relationship and during a wide windows of time. Even if the aggressivity of phenomena is not really high the persistence during time can produce pathological effect.

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