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Short Communication

The Risks in Formation of COVID-19 Variants Displaying Multiple Mutations in Environments Polluted with Natural Radionuclides and How to Prevent Them

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Abstract

The Covid-19 Omicron subvariants BA.1, BA.2 and BA.3 which appeared at the end of 2021 in South Africa contain ~50 mutations in comparison to the original Wuhan strain, many of which unique to each subvariant. This number of mutations is much higher than that observed in other Covid-19 variants or in variants of other viruses. Such high number of mutations in genetic material is usually induced in nature by ionizing-radiation. Therefore, this communication aims to raise the concern that Omicron-subvariants could have been formed in SARS-CoV-2 infected individuals that inhaled polluting dust contaminated with Naturally Occurring Radionuclide Materials (NORMs) such as uranium. This NORMs contaminated dust originates in waste ore of some gold mines (called mine-tailing) rich in uranium. Covid-19 infected-individuals, living close to NORMs containing mine-tailings, inhale NORMs contaminated dust-particles blown by winds from nearby mine-tailings. These dust-particles are trapped in mucus coating the airways at very close proximity to infecting virions. Ionizing- radiation emitted by the inhaled radionuclides can cause multiple random mutations in virions close to radioactive dust-particles. Some of these mutations can generate new immune-resistant variants with transmissibility/virulence which may be even higher than that observed with Omicron subvariants. These considerations raise the theoretical possibility that communities which are chronically exposed to pollution by NORMs originating in mine-tailings may become future reservoirs for Covid-19 variants that keep mutating and acquiring immune-resistance to currently used single-antigen gene-based vaccines. These risks may be avoided by vaccination of these communities and of general populations with multi-antigenic highly immunogenic Covid-19 vaccines. It is further suggested that inactivated SARS-CoV-2 whole virus vaccine that is engineered to present α-gal epitopes may serve as an effective highly immunogenic vaccine that induces a protective immune response which prevents infection by the original Wuhan virus as well as by present and future Covid-19 variants.

Keywords: Covid-19 Vaccine; Mine-tailings; Inactivated whole-virus vaccine; Omicron; Radioactive contaminated dust; SARS-CoV-2 Variants

Introduction

The objective of this communication is to draw attention to the concern that highly mutated virulent Covid-19 variants may develop in infected individuals living in environments polluted with dust contaminated by Naturally Occurring Radionuclide Materials (NORMs). The Corona virus SARS-CoV-2 which mediates the Covid-19 pandemic is capable of tolerating multiple mutations without being inactivated. This is exemplified in the recent appearance of Omicron subvariant BA.1 in South Africa, followed by BA.2 and BA.3 which appeared shortly after BA.1 also in South Africa [1]. The BA.1 subvariant (also referred to B.1.1.529) displays ~50 mutations in comparison to the wild-type (Wuhan) strain, BA.2 shares 32 mutations with BA.1 but has 28 distinct ones and BA.3 lost 6 mutations found in BA.1 and acquired 2 mutations found in BA.2 [1-3]. These are variants of concern since BA.1 has ~10-times higher transmissibility than the wild-type strain and it can infect nonvaccinated individuals and those vaccinated with currently used gene-based vaccines, whereas BA.2 can infect patients originally infected by BA.1, nonvaccinated and vaccinated individuals [2,4].

The number of mutations in the three Omicron subvariants is much higher than previously detected in the S-protein gene of other SARS-CoV-2 variants [5,6]. Moreover, the three Omicron subvariants appeared almost simultaneously at the end of 2021 and

many of their mutations are unique to each subvariant. This raises the question of the cause for so many simultaneous different mutations, many of which are not in the S-protein. Previous SARS-CoV-2 variants evolved by a Darwinian-like "natural selection" and display only few mutations which confer higher transmissibility, virulence, or immune resistance [5,6]. A high number of mutations in genetic-material, as that observed in Omicron, is usually expected to be generated in the lab by sub-lethal ionizing radiation of microorganisms or nucleated cells. In nature, multiple mutations have been found in miners working in mines with high concentration of NORMs such as uranium mines [7,8].

Presentation of Concerns

Communities living close to some gold mines may be exposed to NORMs carried by the dust that originates in ore waste (called "mine-tailings") in a proportion of the gold mines. Such dust containing NORMs is occasionally blown by strong winds from the mine-tailings into adjacent residential areas and inhaled by populations in these areas [9,10]. This hypothesis raises the concern that the mutagenesis resulting in multiple mutations in the Omicron subvariants has been caused by inhaled dust contaminated with NORMs which originated in mine-tailings. The concentrations of NORMs in "clean" environments on the Earth surface are low. However, in a proportion of gold mine ores, the concentration of NORMs, including uranium, is estimated to be higher than that of the gold [9,10]. NORMs like uranium and its decay products, such as radium and thorium, pose significant health risks to communities living near the mines because they contaminate the mine-tailings of active and abandoned mines. Such mine-tailings are the source of NORMs containing dust pollution that is blown by the wind into neighboring residential areas. Accordingly, elevated uranium levels were found in hair samples of residents living near mine-tailings [11]. This proximity of residential areas to mine-tailings further raised the possibility of a link between inhaled NORMs and the disproportionately high incidence of hematological malignancies among residents of these areas [12].

NORMs contaminated dust blown from mine-tailings and inhaled by individuals infected with SARS-CoV-2 is likely to affect this virus. SARS-CoV-2 initially infects the respiratory epithelial cells of the airways, replicates in them and is released in large numbers into the mucus lining the airways. In infected individuals, inhaled NORMs containing dust particles may be trapped in the mucus at very close proximity to the virus. The ionizing radiation emitted by the inhaled radionuclides can cause multiple random mutations in virions adjacent to the radioactive dust particles. Although SARS-CoV-2 can tolerate a large number of mutations without being inactivated, as observed in the Omicron subvariants [1,2], many of the radiation induced mutations are likely to be "lethal" to the virus. However, few of the mutations which do not destroy the infective and replicative abilities of the virus may increase transmissibility and/or virulence of SARS-CoV-2. Other radiation induced mutations may be "escape-mutations" conferring immune-resistance to anti-S-protein antibodies, as observed with Omicron subvariants even in immunized individuals [1-3]. Therefore, communities that are chronically exposed to pollution by NORMs contaminated dust may become future reservoirs for Covid-19 variants that keep mutating and acquiring immune-resistance to single-antigen gene-based vaccines such as those that are currently used.

Evidently, it is difficult to prove the hypothesized in vivo mutating mechanism of SARS-CoV-2 by polluting NORMs contaminated dust. Nevertheless, this hypothesis can be tested in vitro by replication of the original SARS-CoV-2 virus in host cells cultured in the presence of sterilized NORMs contaminated dust obtained from mine-tailings and confirmed to be radioactive. If the NORMs in the mine-tailing dust have mutagenizing effects on the virus, then it is expected that the number of mutations in virus isolates evaluated following repeated passages in cell cultures co-incubated with the radioactive dust may be significantly higher than in virus isolates replicating in cell cultures containing "clean" dust lacking NORMs.

Suggested Solutions

Prevention of appearance of Covid-19 variants containing escape-mutations in populations which may inhale NORMs contaminated dust, as well as in general populations, may be feasible by developing future vaccines that contain several SARS-CoV-2 antigens or genes encoding these antigens (i.e., multi-antigenic vaccines). Individuals vaccinated with multi-antigenic vaccines will develop protective humoral and cellular immune response against several viral antigens. The more individuals vaccinated in the at risk populations, the less is the chance for appearance of variants of the virus. The induced immune response will be protective both against "wild-type" virus and against variants containing immune-resistance mutations in their S-protein. Destruction of wild-type virus and of variants will be mediated both by antibodies and by T-cell cytolysis of virus infected cells, all targeting multiple viral antigens, in addition to antibodies and T cells against the S-protein which may not be effective in protection against variants acquiring escape-mutations [13,14].

A practical and relatively easy to produce multi-antigenic Covid-19 vaccine that does not require cloning of various viral genes for vaccinating protein production, is the inactivated SARS-CoV-2 whole-virus vaccine. Such a vaccine includes the full range of the viral antigens for induction of an anti-Covid-19 immune response, provided that the vaccine is highly immunogenic. A Covid-19 inactivated whole virus vaccine has been produced and found to be well tolerated and to induce anti-virus antibody production [15-17]. However, a study of vaccinated individuals infected with the SARS-CoV-2 Gamma variant reported suboptimal efficacy of the inactivated whole-virus vaccine [18]. A major cause for decreased vaccine efficacy is low uptake of vaccinating virions due to electrostatic repulsion between the negative charges of sialic-acid units on the virus glycan-shield and similar charges on Antigen-presenting-cells (APC) [13]. This uptake can be markedly increased by replacing the sialic acid on the virus with a carbohydrate antigen called "α-gal epitope" (Galα1-3Galβ1-4GlcNAc-R) to generate "SARS-CoV-2α-gal vaccine". Such conversion is feasible by enzymatic reactions with neuraminidase and α1,3galactosyltransferase (α1,3GT-the enzyme synthesizing α-gal epitopes in non-primate mammals), propagating SARS-CoV-2 in host-cells transfected with several copies of the

α1,3GT gene (GGTA1), or propagation of the virus in host-cells transduced with replication defective adeno-virus carrying the α1,3GT gene [13]. Immediately following vaccination, the natural anti-Gal antibody, abundant in all humans [19], binds to α-gal epitopes on vaccinating virions and targets them for rigorous uptake by APC via anti-Gal Fc "tail" binding to Fc-receptors on APC. This extensive internalization of vaccinating virions by APC will result in marked increase in processing of the vaccine load transported by the APC to regional lymph nodes and presentation of antigenic viral peptides, compared to uptake, processing and presentation of vaccinating SARS-CoV-2 lacking α-gal epitopes. Ultimately, presentation of the many SARS-CoV-2α-gal peptides by the APC within the lymph nodes is likely to result in a much more effective immune protection against the virus than in individuals vaccinated with inactivated SARS-CoV-2 lacking α-gal epitopes.

Due to safety limitations, engineering of SARS-CoV-2 into SARS-CoV-2α-gal and evaluation of the increase in immunogenicity and efficacy of such vaccines cannot be determined in standard academic research facilities. Nevertheless, the increased efficacy of viral vaccines engineered to present α-gal epitopes could be determined with inactivated influenza-virus vaccine [20] and with gp120 of HIV vaccine [21], studied in transgenic mice lacking α-gal epitopes and producing anti-Gal. Immunization of the mice with inactivated influenza-virus or with gp120 vaccines engineered to present α-gal epitopes resulted in ~100-fold increase in production of anti-viral antibodies in comparison to mice immunized with the vaccines lacking α-gal epitopes [20,21]. In addition, in immunized mice that were challenged with a lethal dose of "live" influenza virus, ~90% of those immunized with the α-gal vaccine survived, whereas only ~10% of those immunized with the inactivated virus lacking α-gal epitopes survived the challenge [20]. Moreover, gp120 vaccine presenting α-gal epitopes elicited antibodies that neutralize HIV whereas the antibodies elicited by gp120 vaccines lacking α-gal epitopes did not display this virus neutralizing activity [21]. These observations suggest that vaccination with SARS-CoV-2α-gal whole virus vaccines that are inactivated may similarly result in induction of very effective production of antibodies and T cell clones against multiple viral antigens. Such an effective immune response may destroy the unmutated virus as well as future SARS-CoV-2 variants which acquire various escape-mutations in their S-protein.

Conclusion

The unusually high number of mutations in the Omicron subvariants which emerged at the end of 2021, strongly suggests that they were caused by ionizing radiation. Some gold mines generate waste ore containing uranium and its decay radioactive products which are present in mine-tailings. The polluting dust contaminated with uranium which is blown from mine-tailings by winds into neighboring residential areas is inhaled by the residents. It is hypothesized that the Covid-19 virus in the airways of infected individuals inhaling this radioactive polluting dust, will be subjected to ionizing radiation emitted by the dust particles and therefore will acquire many mutations. Some of the mutations may result in formation of new detrimental variants. This will convert these at risk communities into future reservoirs for Covid-19 variants that keep mutating and acquiring immune-resistance to single-antigen gene-based vaccines. Formation of such reservoirs may be prevented by vaccination of these populations with multi-antigenic Covid-19 vaccines, such as inactivated SARS-CoV-2 whole-virus vaccine engineered for high immunogenicity by presentation of α-gal epitopes on the glycan-shield of the vaccinating virions.

Highlights

a) The many mutations in Omicron subvariants may be caused by ionizing radiation.

b) Dust of gold mine waste ores contains uranium and pollutes nearby residential areas.

c) Covid-19 infected individuals in these residential areas inhale radioactive dust.

d) The radioactive dust emits radiation that mutagenizes Covid-19 to form new variants.

e) Variants formation can be prevented by immunization with multi-antigenic vaccines.

Conflict of Interest

The author declares no financial conflict of interests or any other conflict of interest with the content of this manuscript.

References

1. Viana R, Moyo S, Amoako DG, Tegally H, Scheepers C, et al. (2022) Rapid epidemic expansion of the SARS-CoV-2 Omicron variant in southern Africa. Nature 603(7902): 679-686.
2. Iketani S, Liu L, Guo Y, Liu L, Chan JF, et al. (2022) Antibody evasion properties of SARS-CoV-2 Omicron sublineages. Nature 604: 553-556.
3. Desingu PA, Nagarajan K, Dhama K (2022) Emergence of Omicron third lineage BA.3 and its importance. J Med Virol 94(5): 1808-1810.
4. Chen J, Wang R, Gilby NB, Wei GW (2022) Omicron (B.1.1.529): Infectivity, vaccine breakthrough, and antibody resistance. J Chem Inf Mode 62(2): 412-422.
5. Kandeel M, Mohamed MEM, Abd El-Lateef HM, Venugopala KN, El-Beltagi HS (2022) Omicron variant genome evolution and phylogenetics. J Med Virol 94(4): 1627-1632.
6. Raman R, Patel KJ, Ranjan K (2021) COVID-19: Unmasking Emerging SARS-CoV-2 Variants, Vaccines and Therapeutic Strategies. Biomolecules 11(7): 993.
7. Schneider J, Philipp M, Yamini P, Dörk T, Woitowitz HJ (2007) ATM gene mutations in former uranium miners of SDAG Wismut: a pilot study. Oncol Rep 17(2): 477-482.
8. Popp W, Plappert U, Müller WU, Rehn B, Schneider J, et al. (2000) Biomarkers of genetic damage and inflammation in blood and bronchoalveolar lavage fluid among former German uranium miners: a pilot study. Radiat Environ Biophys 39(4): 275-282.
9. Kamunda C, Mathuthu M, Madhuku M (2016) An assessment of radiological hazards from gold mine tailings in the province of Gauteng in South Africa. Int J Environ Res Public Health 13(1): 138.
10. The Guardian (2015) Radioactive city: how Johannesburg's townships are paying for its mining past.
11. Winde F, Geipel G, Espina C, Schüz J (2019) Human exposure to uranium in South African gold mining areas using barber-based hair sampling. Plos One 14(6): e0219059.

12. Inamasu T, Patel M, Espina C, Pentz A, Joffe M, et al. (2018) Retrospective case-series analysis of hematological malignancies in goldmining areas of South Africa. S Afr Med J 108(10): 858-864.

13. Galili U (2020) Amplifying immunogenicity of prospective Covid-19 vaccines by glycoengineering the coronavirus glycan-shield to present α-gal epitopes. Vaccine 38(42): 6487-6499.

14. Galili U (2021) COVID-19 variants as moving targets and how to stop them by glycoengineered whole-virus vaccines. Virulence 12(1): 1717-1720.

15. Zhang Y, Zeng G, Pan H, Hu Y, Chu K, et al. (2021) Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18-59 years: a randomized, double-blind, placebo-controlled, phase 1/2 clinical trial. Lancet Infect Dis 21(2): 181-192.

16. Tanriover MD, Doğanay HL, Akova M, Güner HR, Azap A, et al. (2021) CoronaVac Study Group. Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey. Lancet 398(10296): 213-222.

17. Ella R, Reddy S, Blackwelder W, Potdar V, Yadav P, et al. (2021) Efficacy, safety, and lot-to-lot immunogenicity of an inactivated SARS-CoV-2 vaccine (BBV152): interim results of a randomized, double-blind, controlled, phase 3 trial. Lancet 398(10317): 2173-2184.

18. Hitchings MDT, Ranzani OT, Torres MSS, de Oliveira SB, Almiron M, et al. (2021) Effectiveness of CoronaVac among healthcare workers in the setting of high SARS-CoV-2 Gamma variant transmission in Manaus, Brazil: A test-negative case-control study. Lancet Reg Health Am 1: 100025.

19. Galili U (2013) Anti-Gal: an abundant human natural antibody of multiple pathogeneses and clinical benefits. Immunology 140(1): 1-11.

20. Abdel-Motal UM, Guay HM, Wigglesworth K, Welsh RM, Galili U (2007) Immunogenicity of influenza virus vaccine is increased by anti-Gal mediated targeting to antigen presenting cells. J Virol 81(17): 9131-9141.

21. Abdel-Motal UM, Wang S, Lu S, Wigglesworth K, Galili U (2006) Increased immunogenicity of human immunodeficiency virus gp120 engineered to express Galα1-3Galβ1-4GlcNAc-R epitopes. J Virol 80(14): 6943-6951.

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