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Editorial

COVID-19 infection and ginseng: Predictive influenza virus strains and non-predictive COVID-19 vaccine strains

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A B S T R A C T

Vaccines help protect people from infections. However, Coronavirus 2019 (COVID-19) vaccinees often still become infected with COVID-19 variants (breakthrough infections) and may go on to suffer from long COVID symptoms due to short-lasting immunity and less-effective protection provided by available vaccines. Moreover, the current COVID-19 vaccines do not prevent viral transmission and ward off only about 15% of breakthrough infections. To prepare more effective vaccines, it is essential to predict the viral strains that will be circulating based on available epidemiological data. The World Health Organization recommends in advance which influenza strains are expected to be prevalent during influenza season to guide the production of influenza vaccines by pharmaceutical companies. However, future emerging COVID-19 strain(s) have not been possible to predict since no sound epidemiological information has been established. Thus, for more effective protection, immune stimulators alone or in combination with vaccines would be preferable to protect people from COVID-19 infection. One of those remedies would be ginseng, which has been used for potentiating immunity in the past.

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2; COVID-19) pandemic has revealed a great deal about the nature of the COVID-19 virus, the efficacies of available vaccines, and potential sequelae of COVID-19 infection. The COVID-19 vaccine was initially expected to provide long-lasting protection from infection but has instead proven to only reliably prevent severe outcomes.

The lack of protection against COVID-19 variants has been ascribed to lower levels of spike (S) protein-specific antibodies generated by currently available vaccines [1]. Frequent S protein mutations in the COVID-19 virus limit the efficacies of neutralizing antibodies elicited by vaccines, prior infections, or treatment with monoclonal antibodies [2–8]. Thus, the limited cross-protectivity of our current vaccines and prior infections has led to many re-infections and breakthrough infections (BTIs). To counteract the current pandemic, vaccines capable of protecting emerging COVID-19 variants with long-lasting immunity will be required. Moreover, the needle-free administration of mucosal (intranasal) vaccines, which induce mucosal IgA and serum IgG as well as cellular T cell responses, could provide protection at the entry point of the virus, thus reducing the prevalence of asymptomatic carriers and/or COVID-19 positive individuals and thereby aborting substantial infection chains. Mucosal vaccines would protect against BTIs, which are caused mainly by new variants along with waning immunity [9,10]. Although both intranasal and intramuscular COVID-19 vaccines protect against pneumonia, intranasal vaccines reduce viral titers in both the nasal passages and the lungs, whereas intramuscular vaccines do not reduce viral titers in the upper respiratory tract [11]. For more effective protection from variant infections at the source, intranasal vaccination should be implemented to block COVID-19 transmission [12]. In addition, there are still severe adverse effects of vaccination with currently available vaccines; mRNA vaccination has been reported to cause myocarditis, mainly in young males. Immunization with nonreplicating adenovirus viral vector vaccines has also induced another serious and potentially life-threatening condition: cerebral venous sinus thrombosis (thrombocytopenia) [9].

Newly emerging variants frequently replace the most prevalent COVID-19 variants around the world. The new variants' S protein has evolved to display a high affinity for the human receptor angiotensin-converting enzyme 2 (ACE2). The rapid spread of new COVID-19 variants may likely be ascribed to antibody evasion along with stronger interaction with the ACE2 receptor than past variants [4]. Globally, two types of COVID-19 strains (Delta and Omicron variants) are currently widespread. Individuals who were vaccinated against the Delta variant have shown less severe lung disease after Delta variant infection and experienced much milder symptoms after Omicron variant infection. Omicron BTI in vaccinated subjects elicited protection against all variants and was superior when compared with the same conditions in unvaccinated subjects [2]. However, because COVID-19 variants can evade antibodies raised by both prior infection or vaccination, the continued emergence of variants may result in attenuated and/or limited

Abbreviations: SARS-CoV-2; COVID-19, Severe acute respiratory syndrome coronavirus-2; BTI, Breakthrough infection.

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protection by vaccination or prior infection [13,14]. It is expected that other variants will become widespread in the future, so a COVID-19 vaccine with cross-variant protection is therefore needed to end the pandemic.

The sequelae that appear after COVID-19 infection are referred to as long COVID, which includes intravascular coagulation and cardiovascular, gastrointestinal, psychological, and neurologic disorders. It is not clear whether the sequelae appear as a result of BTI in people who have been vaccinated against COVID-19. The risk of BTI has been reported at six months after infection, and these BTI patients exhibited a higher incidence of death and post-acute sequelae when compared to those who had protection from a vaccine. However, the current vaccines prevent BTIs in only about 15% of people. Therefore, to prevent primary BTI, it is highly required to optimize strategies continuously [14].

Each year, the World Health Organization (WHO) prepares for influenza season by predicting which specific viral strains of influenza will be present and then recommending their production to pharmaceutical companies for the following season ahead. For the 2022–2023 influenza season, the WHO announced in February 2022 that the northern hemisphere region will require either trivalent (H1N1, H3N2, and B/Victoria lineage strains) or quadrivalent vaccines (trivalent strains and the B/Yamagata lineage) for prevention of the upcoming influenza season (https://www.who.int/news/item/25-02-2022-recommendations-announced-for-influenza-vaccine-composition-for-the-2022-2023-northern-hemisphere-influenza-season). For these influenza vaccines to be effective, the WHO's prediction needs to be closely matched with the most prevalent of the constantly evolving influenza virus strains that are circulating and infecting people. The WHO's recommendation is based on epidemiological surveillance data on influenza virus pandemics for more than several decades; in addition, an accumulated solid understanding of epidemiological and other scientific evidence makes it possible to predict the best composition of influenza vaccines very well, and their composition is periodically updated. Similarly, the pandemic COVID-19 strain is constantly mutating, so effective COVID-19 vaccines should include the predicted strains in much the same manner as the influenza virus vaccines. However, we cannot predict the nature of the COVID-19 variants that may emerge [15]. Therefore, a periodic update of COVID-19 vaccines would not be amenable to the current situation. In conclusion, it will likely not be possible for pharmaceutical companies to produce COVID-19 vaccines that will meet the continuously evolving nature of COVID-19 viruses. Other strategies must therefore be explored.

Recently, ginseng has been shown to be effective for preventing COVID-19 infection. One study examined the clinical effect of Korean Red Ginseng (KRG) on COVID-19 specific antibodies after COVID-19 vaccination and found that the KRG group was better equipped to maintain anti-S and anti-N antibody titers than the non-KRG group [Dong-Hyuk Jung, Personal communication]. Consistently, when ginseng was administered to mice that were susceptible to COVID-19, the ginseng-administered mice showed a 30% chance of survival, whereas the non-ginseng group all died. Thus, the administration of ginseng significantly increased the survival rate and decreased virus titers in the lung by inducing antiviral interferon-gamma (IFN-γ) compared to the non-ginseng administered controls [16]. A dearth of effective and less-toxic vaccines and emerging new variants have led people to doubt the efficiency of currently available COVID-19 vaccines. Therefore, a complementary regimen that includes ginseng should be recommended for potentiation of a vaccine-like effect with long-lasting immunity and fewer side effects.

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References

[1] Collier AY, Yu J, McMahan K, Liu J, Chandrashekar A, Maron JS, Atyeo C, Martinez DR, Ansel JL, Aguayo R, et al. Differential kinetics of immune responses elicited by covid-19 vaccines. N Engl J Med 2021 Nov 18;385(21):2010–2.
[2] Suryawanshi RK, Chen IP, Ma T, Syed AM, Brazer N, Saldhi P, Simoneau CR, Ciling A, Khalid MM, Sreekumar B, et al. Limited cross-variant immunity from SARS-CoV-2 Omicron without vaccination. Nature 2022 Jul;607(7918):351–5.
[3] Dejnirattisai W, Huo J, Zhou D, Zahradník J, Supasa P, Liu C, Duyvesteyn HME, Ginn HM, Mentzer AJ, Tuekprakhon A, et al. SARS-CoV-2 Omicron-B.1.1.529 leads to widespread escape from neutralizing antibody responses. Cell 2022 Feb 3;185(3):467–84. e15.
[4] Mannar D, Saville JW, Zhu X, Srivastava SS, Berezuk AM, Tuttle KS, Marquez AC, Sekirov I, Subramaniam S. SARS-CoV-2 Omicron variant: antibody evasion and cryo-EM structure of spike protein-ACE2 complex. Science 2022 Feb 18;375(6582):760–4.
[5] VanBlargan LA, Errico JM, Halfmann PJ, Zost SJ, Crowe Jr JE, Purcell LA, Kawaoka Y, Corti D, Fremont DH, Diamond MS. An infectious SARS-CoV-2 B.1.1.529 Omicron virus escapes neutralization by therapeutic monoclonal antibodies. Nat Med 2022 Mar;28(3):490–5.
[6] Cao Y, Wang J, Jian F, Xiao T, Song W, Yisimayi A, Huang W, Li Q, Wang P, An R, et al. Omicron escapes the majority of existing SARS-CoV-2 neutralizing antibodies. Nature 2022 Feb;602(7898):657–63.
[7] Hoffmann M, Krüger N, Schulz S, Cossmann A, Rocha C, Kempf A, Nehlmeier I, Graichen L, Moldenhauer AS, Winkler MS, et al. The Omicron variant is highly resistant against antibody-mediated neutralization: implications for control of the COVID-19 pandemic. Cell 2022 Feb 3;185(3):447–56. e11.
[8] Planas D, Saunders N, Maes P, Guivel-Benhassine F, Planchais C, Buchrieser J, Bolland WH, Porrot F, Staropoli I, Lemoine F, et al. Considerable escape of SARS-CoV-2 Omicron to antibody neutralization. Nature 2022 Feb;602(7898):671–5.
[9] Soraci L, Lattanzio F, Soraci G, Gambuzza ME, Pulvirenti C, Cozza A, Corsonello A, Luciani F, Rezza G. COVID-19 vaccines: current and future perspectives. Vaccines (Basel) 2022 Apr 13;10(4):608.
[10] Feikin DR, Higdon MM, Abu-Raddad LJ, Andrews N, Araos R, Goldberg Y, Groome MJ, Huppert A, O'Brien KL, Smith PG, et al. Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease: results of a systematic review and meta-regression. Lancet 2022 Mar 5;399(10328):924–44.
[11] van Doremalen N, Purushotham JN, Schulz JE, Holbrook MG, Bushmaker T, Carmody A, Port JR, Yinda CK, Okumura A, Saturday G, et al. Intranasal ChAdOx1 nCoV-19/AZD1222 vaccination reduces viral shedding after SARS-CoV-2 D614G challenge in preclinical models. Sci Transl Med 2021;13(607). Aug 18 eabh0755.
[12] Lund FE, Randall TD. Scent of a vaccine. Science 2021 Jul 23;373(6553):397–9.
[13] Vora SM, Lieberman J, Wu H. Inflammasome activation at the crux of severe COVID-19. Nat Rev Immunol 2021 Nov;21(11):694–703.
[14] Al-Aly Z, Bowe B, Xie Y. Long COVID after breakthrough SARS-CoV-2 infection. Nat Med 2022 Jul;28(7):1461–7.
[15] Callaway E. Fast-evolving COVID variants complicate vaccine updates. Nature 2022 Jul;607(7917):18–9.
[16] Seo SH. Ginseng protects ACE2-transgenic mice from SARS-CoV-2 infection. Front Biosci (Landmark Ed) 2022 Jun 6;27(6):180.

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