COMMENTARY

The potential of developing a protective peptide-based vaccines against SARS-CoV-2

Ahmed O. Shalash1 | Istvan Toth1,2 | Mariusz Skwarczynski1

1School of Chemistry and Molecular Biosciences, The University of Queensland, St. Lucia, Queensland, Australia
2School of Pharmacy, The University of Queensland, Woolloongabba, Queensland, Australia

Correspondence
Istvan Toth and Mariusz Skwarczynski, School of Chemistry and Molecular Biosciences, The University of Queensland, St. Lucia, QLD 4072, Australia. Email: i.toth@uq.edu.au and m.skwarczynski@uq.edu.au

Funding information
National Health and Medical Research Council, Grant/Award Number: APP1132975

Abstract
COVID-19 pandemic has been the deadliest infectious disease outbreak since Spanish flu. The emerging variant lineages, decay of neutralizing antibodies, and occurrence of reinfections require the development of highly protective and safe vaccines. As currently approved COVID-19 vaccines that utilize virus-related genetic material are less than ideal, other vaccine types have also been widely investigated. Among them, peptide-based vaccines hold great promise in countering COVID-19 as they may overcome most of the shortcomings of RNA/DNA and protein vaccines. Two basic types of potential peptide vaccines can be developed. The first type are those which rely on cytotoxic T-cell (CTL) responses to kill infected host cells and stop the replication via employing CTL-epitopes as vaccine antigens. The second type of peptide vaccines are those that rely on B-cell peptide epitopes to trigger humoral response via generating SARS-CoV-2-specific antibodies to neutralize and/or opsonize the virus. We propose that combining both cellular and humoral immune responses would be highly protective. Here we discuss opportunities and challenges in the development of an effective and safe peptide-based vaccine against COVID-19.

Keywords
efficacy, genetic vaccines, peptide vaccines, safety, SARS-CoV-2

As of October 2021, severe acute respiratory syndrome coronavirus 2 (SARS-2), causative agent of COVID-19, has resulted in over 240 million infections worldwide and 5 million deaths (Dong et al., 2020). In addition to the overall infection rate, the rapid decay of neutralizing antibodies (Abs) in convalescent patients' (CP) serum ( Bölke et al., 2020), reinfection occurrence (Iwasaki, 2021), increased virulence of emerging lineages, and future virus spillover from animal reservoirs necessitate urgent development of an effective and safe vaccine (Shalash et al., 2021b). The virus infects lower airway tissues, where pneumocytes-II bearing angiotensin converting enzyme-2 receptor (ACE2) are located. The virus surface protein, spike protein (SARS-2-S), binds to host ACE2 receptors via the receptor binding domain (RBD), which allows virus entry into host cells to replicate.

Design of peptide vaccines against COVID-19 has been greatly inspired by vaccine development against SARS-CoV (SARS-1), the causative agent of SARS pandemic in 2003. For example, Wang et al. studied SARS-1-S RBD-derived peptide vaccines which reduced viral lung titers by 20 folds and decreased pneumonia (Wang et al., 2016). In addition, mice immunized with SARS-1-S-derived cytotoxic T-cell (CTL) epitopes were protected from lethal SARS-1 infection challenge (90–100%) and had reduced viral titers...
Thus, T-helper and CTL epitope antigens should be explored further in coronavirus vaccine development.

In the case of SARS-2, the vaccine development has relied mainly on genetic vaccines. RNA-based vaccines typically encode SARS-2-S. In vivo expression in host cells of SARS-2-S ensures its proper folding/conformation and glycosylation. RNA vaccines also trigger cytoplasmic pathogenic recognition receptors that help trigger Th1 responses, such as retinoic acid-inducible gene I and toll-like receptors (Pulendran et al., 2021). In contrast, DNA vaccines trigger considerable side effects and change transfected cells’ genetic material content (Ramasamy et al., 2021). RNA vaccines do not carry this risk, and the possibility of reverse transcription of vaccine RNA has been disproven (Parry et al., 2021). The selection of specific immunogenic and neutralizing subdomains within SARS-2-S sequence could minimize side-effects through omission of dangerous sequences, e.g., BNT162b1 RNA vaccine only encodes the RBD sequence (Sahin et al., 2020). However, genetic vaccines are expensive and pose critical hurdles in terms of stability, cryostorage and transport, and side effects from live, or nonlive cationic, vectors (Ramasamy et al., 2021; Sahin et al., 2020; Shalash et al., 2021b). Furthermore, it has been demonstrated that most broadly used RNA-vaccine (BNT162b2) protection is short-lived; initial efficacy against SARS-2 infection (88%) has been reduced to just 47%, 5 months post-immunization (Long et al., 2020; Tartof et al., 2021).

As SARS-2 genetic vaccines are less than ideal, other vaccines types have been also widely investigated, including SARS-2-S protein vaccines. When the immunogenicity of SARS-2-S adjuvanted with alum/CPG was investigated in a clinical study against SARS-2, severe systemic and local side effects were reported (Richmond et al., 2021). In contrast, Novavax®, a matrix-M-adjuvanted recombinant full-length SARS-2-S vaccine, demonstrated good efficacy (89%) and better tolerability in phase 3 clinical trials (Heath et al., 2021). However, full-length SARS-2-S might still not be the ultimate antigen due to difficulties in stabilizing its desired prefusion conformation, and the presence of immunopathological sequences (Mortaz et al., 2020; Shalash et al., 2021b). In addition, off-target dose loss of SARS-2-S due to ACE2 binding in non-immune cells has also been overlooked (Figure 1) (Shalash et al., 2021b).

Currently approved subunit vaccines rely only on SARS-2-S, or its fragments, and are expected to trigger mostly humoral immunity, thus neutralizing and opsonizing antibody-based protection, rather than CTL-based immune responses. However, many of the CTL epitopes recognized by human MHC-I alleles were identified in proteins other than SARS-2-S (Shalash et al., 2021b; Shomuradova et al., 2020). Unfortunately, these highly protective, conserved,
Peptide-based vaccine against SARS-CoV-2 can be designed by combining B- and T- cell epitopes from different viral proteins, including non-structural proteins. For example, B-cell epitopes can be derived from the receptor binding motif (RBM), while T-cell epitopes can be chosen from variety of already identified SARS-CoV-2 T-cell epitopes (Shomuradova et al., 2020). The relative efficiencies of T-cell and B-cell epitopes have recently been reviewed (Shalash et al., 2021b). Unfortunately, determination of the correlation between T-cell immunity and protection against SARS-CoV-2 is progressing slowly compared to the correlation of neutralizing B-cell responses with protection. Hopefully, humanized mice infection challenge can reveal the protective efficacy of these epitopes.

One crucial source of B-cell epitopes is the RBM—the fragment of the RBD that is in close contact with ACE2. Several of the highly potent neutralizing Abs, IC_{50} = 5–10 ng/ml (Liu et al., 2020), obtained from CP sera were directed against epitopes within the RBM sequence, especially residues S^{445–500} (Shalash et al., 2021b). In contrast, most of the neutralizing Abs in CP sera that were directed against N-terminus terminal domain (NTD) epitopes were of lower potency (Liu et al., 2020). Further, several neutralizing Abs that were directed against RBM remained potently neutralizing against emerging SARS-CoV-2 variant lineages (Stamatatos et al., 2021), as only four RBM residues, R^{452}L, K^{478}T, K/Q^{88}E, and N^{501}Y, were altered in emergent variant lineages (Figure 1c). The RBM-derived epitopes were also found to be neutralizing (e.g., SARS-CoV-2 S^{451–470} and S^{491–510}) in mice when conjugated to diphtheria toxoid and adjuvanted with alum or emulsion-based adjuvants (Pandey et al., 2021; Shalash et al., 2022). When sera of mice immunized with two different epitopes were combined, synergistically inhibited RBD/ACE2 binding when examined using competitive ELISA (Pandey et al., 2021; Shalash et al., 2021a). Furthermore, 14–24-mer peptides were used as vaccine antigens to identify neutralizing epitopes in BALB/c mice. NTD-epitopes (SARS-CoV-2 S^{63–85} and S^{92–106}), and RBM-derived epitopes (SARS-CoV-2 S^{439–454}, S^{455–469}, and S^{475–499}) were found to be strongly neutralizing against the original and D614G SARS-CoV-2 strain (Lu et al., 2021). Short RBD-derived epitopes were considered to be of insufficient length to produce potently neutralizing nAbs, which have only been observed with protein/ RNA subunit vaccines so far. Therefore, longer peptides could be employed to provide the highly discontinuous epitopes needed to trigger the production of potently neutralizing Abs (Shalash et al., 2022; Shalash et al., 2021b). Furthermore, recently complete Freund (CFA)-adjuvanted, long RBD-derived, peptide epitope (S^{444–483}) demonstrated potent neutralization (serum nAb titers >300), against S-protein pseudotyped-virions, which was equivalent to CFA-adjuvanted RBD protein in BALB/c mice (Shalash et al., 2022). EpiVacCorona (Vektor State Research Centre, Russia) is a peptide vaccine composed of three short peptides derived from SARS-CoV-2 (S^{454–478}, S^{1181–1202}, and S^{1191–1213}) conjugated to SARS-CoV-2 nucleocapsid protein. The vaccine induced the production of nAb titers of about 40, following immunization in ferrets. Despite modest neutralizing Ab titers, the efficacy was attributed to the synergistic protection offered by T-cell immunity and strong opsonic Abs (Ryzhikov et al., 2021a, 2021b). EpiVacCorona induced seroconversion in all volunteers and moderate nAb titers approximately 20 in phase 1/2 clinical trials (Ryzhikov et al., 2021b). There are currently no approved peptide vaccines against SARS-CoV-2, however, several peptide vaccine candidates are currently undergoing clinical trials (Table 1).

Vaccine antigen selection should not only focus on original SARS-CoV-2 lineage sequences, but also consider new mutant variant sequences; especially, as several mutations have increased the virulence and also have compromised the efficacy of approved vaccines. Several in vitro methods have been employed to evaluate

| TABLE 1 Peptide vaccines in clinical trials on healthy adult volunteers |
|-----------------|-----------------|-------------------|-------------------|
| **Vaccine**     | **Status**      | **Outcomes**       | **Trial number**  |
| CoVePit 3 (OSE Immunotherapeutics, Belgium) Antigen: Conserved CTL-epitopes from 11 SARS-CoV-2 proteins | Phase 1 Recruiting | N/A               | NCT04885361       |
| EpiVacCorona (Vector Institute, Russia) Antigen: RBD-derived neutralizing peptide epitopes conjugated to N-protein | Phase 1/2 Completed | About 79% of volunteers seroconverted. However, neutralization efficacy assay results were not reported. | NCT04527575       |
| naNO-COVID (Emergex Vaccines, Switzerland) Antigen: SARS-CoV-2-derived T-cell epitopes loaded onto gold nanoparticles | Phase 1 Recruiting | N/A               | NCT05113862       |
| pVAC/CoVac-1 (University Hospital Tuebingen, Germany) Antigen: SARS-CoV-2-derived T-cell epitopes Adjuvant: TLR1/2 ligand XS15 and Montanide ISA 51 | Phase 1 Completed | Highly tolerable and safe. IFN-γ ELISPOT assay showed stronger activation of CD4+ and CD8+ T-cell responses in all participants, compared to those reported by mRNA vaccine (Heitmann et al., 2022). | NCT04546841       |

Abbreviations: mRNA, messenger RNA; RBD, receptor binding domain; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
SARS-2-S neutralization efficacy (Shalash et al., 2021a, 2021b; Shalash et al., 2022), and these methods can be adapted to evaluate vaccine efficacy against emerging variants. Further, since the immune correlates of protection of several approved vaccines were evaluated in animal infection challenge models (e.g., ferrets and non-human primates) and in humans, validation of a translation model is possible to infer higher confidence in the relevance of animal infection challenge outcomes to efficacy in humans (Shalash et al., 2021b). An example of such valuable relationships and their applications include the reported relationship between nAb titers and anti-RBD IgG titers in the sera that was generated by BNT-621 messenger RNA (mRNA) vaccines in adult volunteers (Mulligan et al., 2020; Shalash et al., 2021b). Log_{10} Anti-RBD IgG = 1.53 + 0.94 × Log_{10} Anti-RBD IgG - This relationship shows that neutralization essentially begins after exceeding a minimum threshold of serum log_{10} anti-RBD IgG titers of about 1.53, and then neutralization increases with anti-RBD titers with a slope of about 0.94 beyond this threshold value. Therefore, to achieve similar or higher neutralization values to those of convalescent COVID-19 patients, who have nAb titers of about 100, the minimum target level of immunogenicity for the mRNA vaccine would be above log_{10} anti-RBD IgG titers of 2.6 in healthy adult serum. Similar approaches that rely on reported efficacy outcomes can be employed to obtain similar relationships. Additional valuable relationships could be established via correlation of efficacy results among different animal infection challenge models and humans, thus establishing a translational model that could potentially predict cross-species efficacy for future vaccine development. Furthermore, Immune correlates of "cellular response-based" protection have been overlooked, thus, similar inter- and intra-species, efficacy evaluations of cellular responses to immunization should be established in the future.

Peptide-based vaccines hold great promise in countering SARS-2 infections. They inherently overcome most of the shortcomings of RNA and protein vaccines. By selecting minimally immunogenic and neutralizing component(s), we (a) avoid immunopathological sequences; (b) focus the immune response on neutralizing humoral responses; and (c) prevent off-target loss of antigen dose and promotion of lung injury due to downregulation of ACE2 (Shalash et al., 2021b). Moreover, the RBD secondary structure is predominately random coil, which can be easily adopted by peptides. Other advantages of the peptide-based approach include ease of chemical synthesis at massive scale, avoidance of biological contaminants, and stability as dry powder under normal storage conditions (M. Skwarczynski & Toth, 2016). The only drawbacks to peptide-based vaccines are difficulty in generating highly discontinuous neutralizing Abs that are directed against two-neighboring RBDs, such as those generated against native trimeric SARS-2-S (Shalash et al., 2021b). In addition peptide vaccines have lower immunogenicity compared to protein vaccines (M. Skwarczynski & Toth, 2016). However, low immunogenicity, and even restoration of native conformation, have been overcome in peptide vaccine formulations through combination with approved commercial adjuvants or conjugation to adjuvanting moieties (M. Skwarczynski & Toth, 2016). Conjugation of hydrophobic adjuvanting moieties, such as peptides (Mariusz Skwarczynski et al., 2020) and polymers (Nevagi et al., 2019) to peptide antigens have been proven to greatly improve vaccine efficacy, even when delivered via oral and intranasal routes (Faruck et al., 2020; M. Skwarczynski & Toth, 2016), thus mimicking natural infection and easing the logistics of vaccine distribution and immunization. Although little investigation has gone into developing peptide vaccines against SARS-2 to date, they may yet show great potential to provide high prophylactic or even therapeutic efficacy.

ACKNOWLEDGMENTS

This work was supported by the National Health and Medical Research Council (NHMRC Program Grant: APP1132975). Open access publishing facilitated by The University of Queensland, as part of the Wiley - The University of Queensland agreement via the Council of Australian University Librarians.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ORCID

Ahmed O. Shalash http://orcid.org/0000-0003-3819-4798
Mariusz Skwarczynski http://orcid.org/0000-0001-7257-807X

REFERENCES

Channappanavar, R., Fett, C., Zhao, J., Meyerholz, D. K., & Perlman, S. (2014). Virus-specific memory CD8 T cells provide substantial protection from lethal severe acute respiratory syndrome coronavirus infection. Journal of Virology, 88(19), 11034–11044. https://doi.org/10.1128/JVI.01505-14

Dong, E., Du, H., & Gardner, L. (2020). An interactive web-based dashboard to track COVID-19 in real time. The Lancet Infectious Diseases, 20(5), 533–534. https://doi.org/10.1016/S1473-3099(20)30120-1

Faruck, M. O., Zhao, L., Hussein, W. M., Khalil, Z. G., Capon, R. J., Skwarczynski, M., & Toth, I. (2020). Polycrylate-PEptide antigen conjugate as a single-dose oral vaccine against group A streptococcus. Vaccines (Basel), 8(1), 1. https://doi.org/10.3390/vaccines8010023

Heath, P. T., Galiza, E. P., Baxter, D. N., Boffito, M., Browne, D., Burns, F., Chadwick, D. R., Clark, R., Cosgrove, C., Galloway, J., Goodman, A. L., Heer, A., Higham, A., Iyengar, S., Jamal, A., Jeans, C., Kalra, P. A., Kyriakidou, C., McAuley, D. F., … Study, G. (2021). Safety and efficacy of NVX-CoV2373 Covid-19 vaccine. New England Journal of Medicine, 385(13), 1172–1183. https://doi.org/10.1056/NEJMc2107659

Heitmann, J. S., Blich, T., Tandler, C., Neldé, A., Maringer, Y., Marconato, M., Reusch, J., Jäger, S., Denk, M., Richter, M., Anton, L., Weber, L. M., Roerden, M., Bauer, J., Rieth, J., Wacker, M., Hörber, S., Peter, A., Meisner, C., … Walz, J. S. (2022). A COVID-19 peptide vaccine for the induction of SARS-CoV-2 T cell immunity. Nature, 601(7894), 617–622. https://doi.org/10.1038/s41586-021-04232-5

Iwasaki, A. (2021). What reinfections mean for COVID-19. The Lancet Infectious Diseases, 21(1), 3–5. https://doi.org/10.1016/S1473-3099(20)30783-0
Liu, L., Wang, P., Nair, M. S., Yu, J., Rapp, M., Wang, Q., Luo, Y., Chan, J. F., Sahi, V., Figueroa, A., Guo, X. V., Cerutti, G., Bimela, J., Gorman, J., Zhou, T., Chen, Z., Yuen, K. Y., Kwong, P. D., Sodroski, J. G., ... Ho, D. D. (2020). Potent neutralizing antibodies against multiple epitopes on SARS-CoV-2 spike. *Nature*, 584(7821), 450–456. https://doi.org/10.1038/s41586-020-2571-7

Long, C., Chen, W., Yang, R., & Yao, D. (2020). Ratio estimation of the population mean using auxiliary information under the optimal sampling design. *Probability in the Engineering and Information Sciences*, 36(2), 449–460. https://doi.org/10.1017/s0269964820000625

Bölke, E., Matuschek, C., & Fischer, J. C. (2020). Loss of anti-SARS-CoV-2 antibodies in mild Covid-19. *New England Journal of Medicine*, 383(17), 1694–1698. https://doi.org/10.1056/NEJMmc2027051

Lu, S., Xie, X.-X., Zhao, L., Wang, B., Zhu, J., Yang, T.-R., Yang, G. W., Ji, M., Lv, C. P., Xue, J., Dai, E. H., Fu, X. M., Liu, D. Q., Zhang, L., Hou, S. J., Yu, X. L., Wang, Y. L., Gao, X. H., Shi, X. H., ... Liu, R. T. (2021). The immunodominant and neutralization linear epitopes for SARS-CoV-2. *Cell Reports*, 34(4), 108666. https://doi.org/10.1016/j.celrep.2020.108666

Mortaz, E., Tabarsi, P., Varahram, M., Folkerts, G., & Adcock, I. M. (2020). The immune response and immunopathology of COVID-19. *Frontiers in Immunology*, 11, 3037. https://doi.org/10.3389/fimmu.2020.02037

Mulligan, M. J., Lyke, K. E., Kitchin, N., Abaslon, J., Gurtman, A., Lockhart, S., Neuzil, K., Raabe, V., Bailey, R., Swanson, K. A., Li, P., Koury, K., Kalina, W., Cooper, D., Fontes-Garfias, C., Shi, P. Y., Türeci, Ö., Tompkins, K. R., Walsh, E. E., ... Jansen, K. U. (2020). Phase 1/II study of COVID-19 RNA vaccine BNT162b1 in adults. *Nature*, 586(7830), 589–593. https://doi.org/10.1038/s41586-020-2639-4

Nevagi, R. J., Skwarczynski, M., & Toth, I. (2019). Polymers for subunit vaccine delivery. *European Polymer Journal*, 114, 397–410. https://doi.org/10.1016/j.eurpolymj.2019.03.009

Pandey, M., Ozberk, V., Eskandari, S., Skhalash, A. O., Joyce, M. A., Saffran, H. A., Day, C. J., Lepletier, A., Spillings, B. L., Mills, J. L., Calcutt, A., Fan, F., Williams, J. T., Stanisic, D. I., Hattingh, L., Gerrard, J., Skwarczynski, M., Mak, J., Jennings, M. P., ... Good, M. F. (2021). Antibodies to neutralising epitopes synergistically block the interaction of the receptor-binding domain of SARS-CoV-2 to ACE 2. *Clinical & Translational Immunology*, 10(3), e1260. https://doi.org/10.1002/cti2.1260

Parry, R., Gifford, R. J., Lytras, S., Ray, S. C., & Coin, L. J. M. (2021). No evidence of SARS-CoV-2 reverse transcription and integration as the origin of chimeric transcripts in patient tissues. *Proceedings of the National Academy of Sciences*, 118(33), e2109066118. https://doi.org/10.1073/pnas.2109066118

Pulendran, B., S. Arunachalam, P., & O’Hagan, D. T. (2021). Emerging concepts in the science of vaccine adjuvants. *Nature Reviews Drug Discovery*, 20(6), 454–475. https://doi.org/10.1038/s41573-021-00163-y

Ramasamy, M. N., Minassian, A. M., Ewer, K. J., Flaxman, A. L., Folegatti, P. M., Owens, D. R., Vossey, M., Aley, P. K., Angus, B., Babbage, G., Belij-Romelaerstor, S., Berry, L., Babi, S., Bittaye, M., Cathie, K., Chappell, H., Charlton, S., Cicconi, P., Clutterback, E. A., ... Oxford COVID Vaccine Trial, G. (2021). Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV022): a single-blind, randomised, controlled, phase 2/3 trial. *Lancet*, 396(10267), 1979–1993. https://doi.org/10.1016/S0140-6736(20)32466-1

Richmond, P., Hatchuel, L., Dong, M., Ma, B., Hu, B., Smolenov, I., & Clemens, R. (2021). Safety and immunogenicity of S-Trimer (SCB-2019), a protein subunit vaccine candidate for COVID-19 in healthy adults: a phase 1, randomised, double-blind, placebo-controlled trial.
MacCamy, A. J., Feng, J., Mize, G., De Rosa, S. C., Finzi, A., Lemos, M. P., Cohen, K. W., Moodie, Z., McElrath, M. J., & McGuire, A. T. (2021). mRNA vaccination boosts cross-variant neutralizing antibodies elicited by SARS-CoV-2 infection. Science, 372(6549), 1413–1418. https://doi.org/10.1126/science.abg9175

Tartof, S. Y., Slezak, J. M., Fischer, H., Hong, V., Ackerson, B. K., Ranasinghe, O. N., Frankland, T. B., Ogun, O. A., Zamparo, J. M., Gray, S., Valluri, S. R., Pan, K., Angulo, F. J., Jodar, L., & McLaughlin, J. M. (2021). Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study. Lancet, 398, 1407–1416. https://doi.org/10.1016/S0140-6736(21)02183-8

Wang, Q., Zhang, L., Kuwahara, K., Li, L., Liu, Z., Li, T., Zhu, H., Liu, J., Xu, Y., Xie, J., Morioka, H., Sakaguchi, N., Qin, C., & Liu, G. (2016). Immunodominant SARS coronavirus epitopes in humans elicited both enhancing and neutralizing effects on infection in non-human primates. ACS Infectious Diseases, 2(5), 361–376. https://doi.org/10.1021/acsinfecdis.6b00006

AUTHOR BIOGRAPHIES

Ahmed O. Shalash MSc, PhD Candidate, Ahmed received his BSc in pharmaceutical sciences in 2009. After graduation, he joined the R&D drug formulation and development unit in the European Egyptian pharmaceutical industries and Medizen pharmaceutical Industries (8 years). He is an expert in pre-clinical development of pharmaceutical products, including nanopharmaceuticals design and formulation, analytical and characterization techniques development, and establishing in vitro–in vivo correlations and mathematical models. He obtained his MSc degree in pharmaceutics at Alexandria University, Egypt, in 2015. His MSc research received several awards, including the USP Global Fellowship award in 2014, and the Pat Burnell, top scientific, award from the Drug Delivery to the Lung 27th conference, UK. He is currently in his third year of PhD studies, at the University of Queensland, Australia.

Istvan Toth PhD, DSc, FRACI, FQA, Professor Toth is a chemical engineer with a research focus on medicinal chemistry. He was awarded his PhD in 1972 and has since worked in Hungary, Canada and the United Kingdom before relocating to Australia in 1998. His major research interests are drug delivery, immunoadjuvants, synthetic vaccines and gene delivery. His research has attracted over $60 million in competitive grants, research contracts and investment funds in the past 10 years. He has over 300 peer-reviewed publications, 43 patents, and an excellent track record in research commercialization as a key founder of Alchemia (ASX listed), Implicit Bioscience Pty Ltd, Neurotide Pty Ltd and TetraQ (the commercial arm of Centre of Integrated Preclinical Drug Development).

Dr. Mariusz Skwarczynski PhD, Mariusz Skwarczynski completed his PhD in Chemistry at Wroclaw University of Technology, Poland. His postdoctoral training began at Tokushima Bunri University and then he joined the laboratory of Professor Yoshiaki Kiso at Kyoto Pharmaceutical University, Japan. In 2004 he was awarded with Japan Society for the Promotion of Science fellowship to conduct research on paclitaxel prodrugs. In 2008 he joined Professor Istvan Toth group at University of Queensland (Australia) to work on drug, gene and vaccine delivery. He received Vice-Chancellor Fellowship at University of Queensland in 2010. Since then his research is mainly focused on nanotechnology-based vaccine delivery strategies.

How to cite this article: Shalash, A. O., Toth, I., & Skwarczynski, M. (2022). The potential of developing a protective peptide-based vaccines against SARS-CoV-2. Drug Development Research, 83, 1251–1256. https://doi.org/10.1002/ddr.21969