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Opinion

# Potential Applications of Plant Biotechnology against SARS-CoV-2

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**Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel coronavirus responsible for an ongoing human pandemic (COVID-19). There is a massive international effort underway to develop diagnostic reagents, vaccines, and antiviral drugs in a bid to slow down the spread of the disease and save lives. One part of that international effort involves the research community working with plants, bringing researchers from all over the world together with commercial enterprises to achieve the rapid supply of protein antigens and antibodies for diagnostic kits, and scalable production systems for the emergency manufacturing of vaccines and antiviral drugs. Here, we look at some of the ways in which plants can and are being used in the fight against COVID-19.**

## COVID-19: How Can Plant Biotechnology Help?

An outbreak of potentially lethal **coronavirus** (**SARS-CoV-2**; see Glossary) in Wuhan, China, in December 2019, has created a pandemic (**COVID-19**) that has provoked governments across the world to introduce emergency containment and control measures. The aim of these measures is to delay the spread of infection, thus reducing the acute pressure on hospital beds, front-line medical staff, and resources. Slowing down the rate of infection and thereby reducing the total number of acute cases at any one time can help to prevent the collapse of national healthcare systems. These tactics also give researchers more time to develop effective testing assays to identify carriers, treatments that reduce the severity of symptoms and resolve infections more quickly, and vaccine candidates to protect the unexposed segment of the population. Researchers working on the applications of plants can have a key role during this critical time by using their knowledge and infrastructure as a means to develop and produce new diagnostics and therapeutics. Indeed, plants may offer the only platform that can be used to manufacture such reagents at scale in a timeframe of weeks, compared with months or even years for cell-based systems. Here, we look at three areas where plants could make major contributions: diagnostic reagents to identify infected and recovered individuals, vaccines to prevent infection, and antivirals to treat symptoms.

## Why Plants?

Plants have been used as a platform for the production of diagnostic reagents and pharmaceutical proteins for more than 30 years, an approach often described as '**molecular farming**' [1,2]. Several molecular farming companies specialize in the development of plant-derived proteins as diagnostic reagents, for example Agrenvec (Madrid, Spain), Diamante (Verona, Italy), ORF Genetics (Kópavogur, Iceland), and Ventria Bioscience/Invitria (Fort Collins, CO, USA). Furthermore, multiple products have been tested in clinical trials, with a small number reaching the market as medical devices and, more recently, pharmaceuticals [1,2]. For example, a chimeric secretory IgA/G produced in transgenic tobacco plants was marketed as a medical device (CaroRX) for topical use to prevent dental caries [3], whereas a recombinant form of the human enzyme glucocerbrosidase

### Highlights

The current COVID-19 pandemic has created an immediate massive demand for diagnostic reagents based on SARS-CoV-2 RNA/proteins and corresponding antibodies, placing immense strain on the supply and distribution chain.

Transient expression in plants could address the shortage by achieving rapid, larger-scale production, complemented by longer-term higher-volume production in transgenic plants.

The same technology used to produce diagnostic reagents could also be used to produce vaccine candidates (SARS-CoV-2 subunits and virus-like particles) as well as therapeutic antibodies and antiviral proteins.

It will be necessary to pool the international resources of molecular farming research groups and industry to capitalize on expertise, although distributed production using local infrastructure is the key to reaching all parts of the world.

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produced in plant cell suspension cultures is marketed as a pharmaceutical (taliglucerase alfa, Elelyso) for patients with Gaucher's disease [4]. The pioneers of molecular farming originally considered the main advantages of plants to be economy, scalability, and safety, because plants can be cultivated inexpensively on a large scale and do not support the growth of human pathogens [5]. However, these advantages have generally not been persuasive enough to displace the major production platforms used in the biologics manufacturing industry. These established platforms utilize the bacterium *Escherichia coli* and a few other microbes, and various mammalian cell lines, mainly due to the robust regulatory framework that exists for these systems and the historic industry investment in corresponding production technologies [6]. However, plants have carved a niche in a small number of cases because they can produce biologics with favorable glycan configurations (such as taliglucerase alfa) [4,7], they allow production on a massive scale (as required for HIV microbicides) [8,9], and, most relevant to the current situation, when **transient expression** systems are used, they can be scaled up rapidly to meet sudden and unforeseen demand [10]. This is ideal for the production of diagnostic reagents, vaccine candidates, and antiviral drugs in the face of a rapidly spreading pandemic disease (Figure 1).

## Diagnostic Reagents

The rapid spread of COVID-19 has generated a sudden and huge demand for diagnostic kits, revealing a critical shortage in the corresponding reagents and the means to produce them. Two major diagnostic assays are required: one to detect the virus itself and, thus, identify the infected population and potential spreaders of the disease, and one to detect antibodies against the virus and, thus, identify the currently infected as well as convalescent and (potentially) immune population.

Assays for the detection of the virus itself fall into two categories: those based on the detection of virus genomic RNA and those based on the detection of virus proteins. The RNA-based assay was developed soon after the sequence of SARS-CoV-2 was deposited in GenBank (NCBI Reference Sequence: NC_045512.2) because the virus is detected by **RT-PCR** and the only specific assay components are the **primers**, which are easy to synthesize. However, one problem with this assay is the absence of a universal positive control, which would allow standardization across different testing laboratories. A group at the John Innes Centre (JIC, Norwich, UK), led by George Lomonossoff and Hadrien Peyret, is developing a diagnostic control reagent for COVID-19 based on **virus-like particles** (VLPs) derived from Cowpea mosaic virus (CPMV). VLPs have the same structure as the parent virus but lack the native genome and, therefore, are unable to replicate. Using an approach first developed for an outbreak of Foot and mouth disease virus [11], the JIC group has packaged artificial RNA containing all of the SARS-CoV-2 genome regions detected by the WHO testing kits inside CPMV-derived VLPs, which are then produced and assembled in plants. The VLPs are thermostable, highly reproducible, and scalable standard reagents that can be used as a source of positive control RNA in the RT-PCR assays (George Lomonossoff and Hadrien Peyret, personal communication, 2020).

The development of kits for the detection of virus proteins requires specific ligands, and this is usually achieved by the identification of corresponding antibodies. The mature SARS-CoV-2 particle contains four structural proteins known as the envelope (E), membrane (M), nucleocapsid (N), and **spike** (S) proteins, but the S protein is the most important in terms of antibody-based detection because it projects from the surface of the virion and exposes the receptor-binding domain (RBD) to the immune system (Figure 2). The injection of whole SARS-CoV-2 preparations or the isolated or recombinant S protein/RBD into mice can be used to generate **hybridoma** clones, or the S protein/RBD can be used to screen phage antibody display libraries or similar platforms. Ultimately, this yields the sequences of antibodies with high affinity for the S protein, and the

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scaled-up production of such antibodies would allow the stockpiling of kits for virus detection using faster and more convenient formats, such as **ELISAs**, lateral flow assays, or assays based on protein chips [12,13]. As with the recombinant virus proteins, transient antibody expression in plants provides a rapidly scalable expression platform to ramp up production in the short term, with transgenic plants fulfilling the need for a longer-term high-volume supply.

The history of molecular farming kicked off with the publication of a *Nature* paper describing the production of antibodies in tobacco (*Nicotiana tabacum*) more than 30 years ago [14] and this remains the product class that has been expressed most often, and with the greatest diversity in terms of antibody format, expression strategy, and host species/platform. Therefore, the production of diagnostic SARS-CoV-2 antibodies in plants can take advantage of the extensive knowledge and knowhow that has accumulated to ensure that plant-derived antibodies are stable and functional and produced at high yields.

The publication of the SARS-CoV-2 sequence also provided the information required to generate recombinant viral proteins as diagnostic reagents. The availability of such proteins allows the immediate development of assays to detect serum antibodies in convalescent patients, particularly antibodies against the S protein. Plants provide the means to produce these proteins within a few weeks on a massive scale so that the kits can be manufactured and stockpiled for distribution to testing centers. By contrast, it would take months to establish cell lines expressing the same reagents, and possibly years to ramp up production capacity to the necessary levels. Therefore, we envisage a scenario in which transient expression systems are used to address the pressing need for large quantities of this reagent in the short term (2–6 months), complemented by transgenic plants to achieve even larger-scale production on a longer-term basis. As an example of the former approach, the Italian biotechnology company Diamante is using tobacco to express antigens based on the SARS-CoV-2 RBD for use in ELISA tests for the detection of serum antibodies.

## Vaccine Candidates

A conventional approach to vaccine development would be based on **inactivated** or **attenuated** strains of SARS-CoV-2, but these approaches take a long time to produce sufficient material and the vaccines have many disadvantages and adverse effects, including the risk of reacquired virulence [15,16]. A quicker and safer alternative is the production of subunit vaccines based on individual proteins, which could be presented either as individual SARS-CoV-2 antigens in a **prime–boost** schedule with a suitable adjuvant, or as VLPs with multiple copies of SARS-CoV-2 antigens arrayed on the surface. Both strategies are currently being developed as a means to address the COVID-19 pandemic. All four structural proteins of SARS-CoV-2 could elicit **neutralizing antibodies** and CD4+/CD8+ T cell responses [17]. However, research on the original SARS-CoV strain indicated that the N protein is unsuitable because it is highly conserved among CoV families (including those that we often encounter in the form of the common cold). Antibodies raised against N proteins do not provide protective immunity, whereas the M and E proteins elicit only weak protective responses [18]. Unusually among coronaviruses, the SARS-CoV-2 S protein is proteolytically cleaved into an **S1 subunit** (685 amino acids) and an S2 membrane-spanning subunit (588 amino acids), the latter being highly conserved (99%) among CoV families. By contrast, S1 shows only 70% identity to other human CoV strains and the differences are concentrated in the RBD, which facilitates virus entry by binding to **angiotensin-converting enzyme 2** (ACE2) on the cell surface [19]. Blocking viral entry is a successful strategy to control infection, and most vaccine candidates for the original SARS-CoV targeted the S protein for this reason, inducing neutralizing antibody responses or **antibody-dependent cell-mediated cytotoxicity** (ADCC)/ **cross-presentation** to achieve protective cellular immunity [20].

## Glossary

**Angiotensin converting enzyme 2 (ACE2):** an enzyme that projects from the surface of certain human cells, including pulmonary epithelial cells, and appears to be the major receptor for SARS-CoV-2.

**Antibody-dependent cell-mediated cytotoxicity (ADCC):** the process by which cells of the immune system actively lyse a target cell the surface antigens of which have been bound by specific antibodies.

**Attenuated vaccine:** a live vaccine that has been passaged multiple times to reduce its virulence, while retaining the antigenic properties of the more aggressive original strain.

**Complex glycans:** oligosaccharide molecules containing diverse sugar residues, which are formed by the extension of high-mannose glycans in the Golgi body.

**COVID-19:** the disease caused by SARS-CoV-2.

**Coronavirus:** a group of related viruses that infect mammals and birds and tend to cause respiratory tract infections in humans.

**Cross-presentation:** ability of antigen-presenting cells to take up, process, and present extracellular antigens with MHC class I molecules to CD8+ T cells.

**ELISA:** an assay format in which an immobilized target protein is detected by an antibody, which either carries a label for direct detection or is in turn detected by another antibody that carries a label.

**Good manufacturing practice (GMP):** the set of regulations that govern the production of approved pharmaceutical products.

**High-mannose glycans:** mannose-rich oligosaccharide molecules with terminal mannose residues, which are the form of glycan attached to proteins in the secretory pathway primarily before they reach the Golgi body.

**Hybridoma:** a cell line created by fusing an antibody-secreting B cell to an immortal myeloma cell line, resulting in hybrid cells that are immortal and secrete a single form of antibody (monoclonal).

**Inactivated vaccine:** a vaccine based on a live pathogen that has been killed or inactivated by heat or chemical treatment.

**Lectin:** a plant-derived protein that binds carbohydrates.

**Molecular farming:** the use of plants for the production of a protein that is

Many subunit vaccine candidates have already been produced in plants, including several for seasonal or pandemic strains of influenza virus produced by transient expression in tobacco. The vaccines were manufactured within 3 weeks of receiving the hemagglutinin and neuramini- dase sequences [21], and were produced using deconstructed vectors based on Tobacco mosaic virus delivered by agroinfiltration with *Agrobacterium tumefaciens* (the basis of this tech- nological approach was developed 20 years ago) [22]. Up to 200 mg of protein was produced per kg of fresh leaves [23]. At least one company is thought to be developing a COVID-19 vaccine based on the expression of SARS-CoV-2 protein subunits in tobacco plants, namely Kentucky BioProcessing (Owensboro, KT, USA), a subsidiary of British American Tobacco [24]. Although the details are not publicly available, the target is likely to be the S1 protein sequence as a com- plete polypeptide or the smaller RBD within it. The S1 proteins of SARS-CoV and SARS-CoV-2 are heavily glycosylated [25,26] and the glycans are a mixture of complex and high-mannose con- figurations, making it necessary to express the recombinant S1 and RBD with N-terminal signal peptides, ensuring that the proteins are secreted to the endomembrane system [27]. It is unclear whether the differing structure of **complex glycans** in humans and plants will make a difference to the effectiveness of a plant-based SARS-CoV-2 vaccine, although the structure of **high- mannose glycans** is fully conserved across higher eukaryotes so at least these epitopes will be consistent. The only previous report of a coronavirus S protein expressed in plants was the S1 ectodomain of swine Transmissible gastroenteritis coronavirus (TGEV) expressed in trans- genic *Arabidopsis thaliana* lines. This recombinant antigen elicited TGEV-specific antibodies in mice, demonstrating that immunogenic coronavirus antigens can be produced in plants [28].

The development of VLPs displaying SARS-CoV-2 antigens as vaccines has multiple advantages because the particles are taken up efficiently by antigen-presenting cells due to their size, trigger- ing the adaptive immune system, and the ordered proteinaceous structures are recognized as danger signals, which can stimulate strong cellular and humoral responses [29]. VLPs based on plant viruses provide an additional layer of safety because even the native particles cannot rep- licate in humans, and they can be produced in massive quantities by molecular farming in plants [30]. A VLP platform using tobacco plants as the production host has been developed by Medicago Inc. (Québec, Canada) and achieved the important milestone of producing more than 10 million doses of vaccine against H1N1 influenza in 1 month, as part of the DARPA Blue Angel program [31]. Medicago recently announced their intention to use their platform for the rapid production of VLP-based vaccines against SARS-CoV-2, although the precise nature of the VLPs remains confidential [32]. Similarly, iBio (Bryan, TX, USA) are developing a VLP-based vaccine in tobacco plants based on their proprietary FastPharming system [33].

Whereas virus subunit antigens and VLPs are designed to elicit an immune response against the pathogen when it is encountered in the wild, the injection of recombinant antibodies against SARS-CoV-2 could help to slow down the infection and give the body time to raise its own anti- bodies before the patient succumbs to the disease. This strategy is supported by the recent find- ing that serum from convalescent patients can reduce the severity of disease symptoms and accelerate recovery [34,35]. Therefore, plants could be used to produce antibodies not only as virus detection reagents, but also as a form of **passive immunotherapy**. The blueprint for this approach was established by Mapp Biopharmaceutical (San Diego, CA, USA) and its commercial arm LeafBio during the 2014 outbreak of Zaire ebolavirus in West Africa. The company manufactured a cocktail of three neutralizing antibodies known as ZMapp [36], which was approved for compassionate use due to its life-saving potential and the lack of any alternatives [37,38]. Large doses (up to 10 mg per patient) of the antibody were required, which would mean that transgenic plants grown on a massive scale would be the only economical route for the manufacture of such a product. Similarly, potential for the large-scale production

usually extracted and purified (or at least used as part of a crude extract) rather than fulfilling a function within the plant.
**Neutralizing antibody:** an antibody that interrupts the life cycle/replication cycle of a pathogen, for example, by preventing interactions with a receptor.
**Passive immunotherapy:** the administration of antibodies that target a particular pathogen or molecule rather than the administration of antigens that cause the body to generate its own antibodies against the target.
**Prime–boost:** a vaccination strategy in which an initial (prime) dose must be complemented by one or more subsequent (booster) doses to elicit a strong immune response.
**Primer:** a short oligonucleotide that anneals to a DNA or RNA template and is used to initiate DNA synthesis in PCR and RT-PCR experiments.
**RT-PCR:** a method used to detect (and in some cases quantify) RNA by first reverse transcribing it into cDNA and then amplifying the latter by PCR.
**S1 subunit:** the exposed N-terminal subunit of the SARS-CoV-2 spike protein, which is proteolytically released from the full-size spike protein during the assembly of viral particles.
**Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2):** a novel coronavirus that is responsible for the current pandemic disease COVID-19.
**Spike protein (S protein):** a protein that projects from the surface of a virus particle.
**Subunit vaccine:** a vaccine based on a single polypeptide derived from a pathogen.
**Transient expression:** an expression strategy in which plants are infiltrated with *Agrobacterium tumefaciens* carrying an expression construct as a T-DNA. Many cells are initially transfected with the T-DNA but are not stably transformed. The genes carried by the episomal T-DNA are expressed for a short time (days) before degradation.
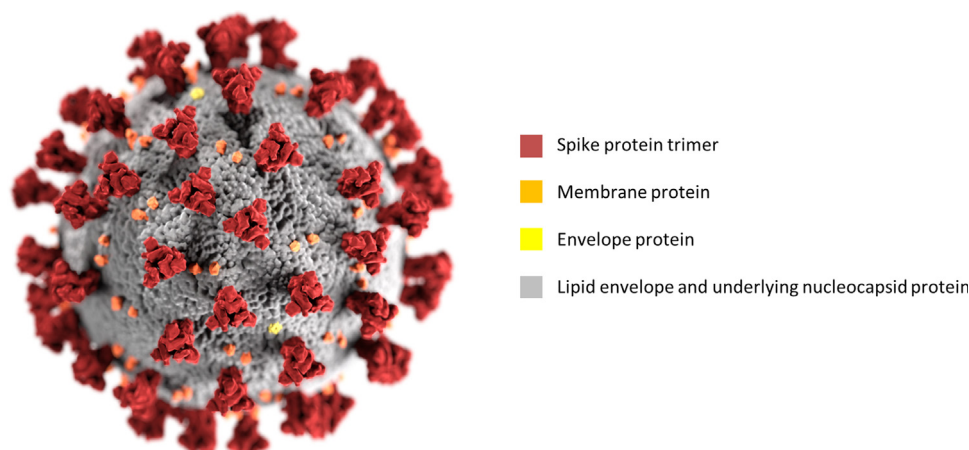**Virus-like particle (VLP):** a structure that is identical or near identical to a virus but lacks the original genome, rendering it unable to replicate. VLPs based on plant viruses can be produced by expressing the capsid proteins in plants because the ability to assemble virus particles is, in many species, dependent on the proteins but not the nucleic acid.

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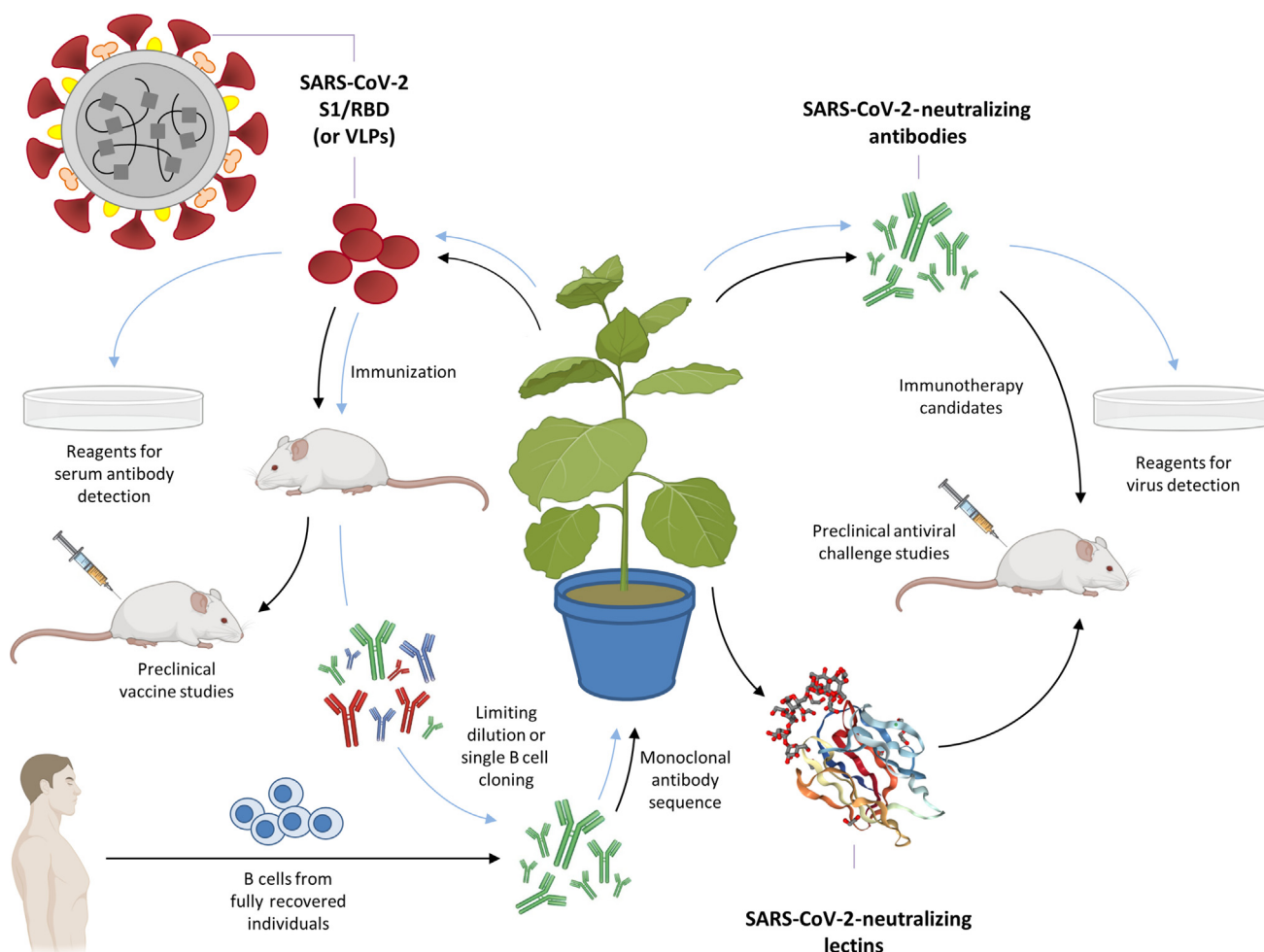


Figure 1. The Applications of Plants for the Production of Diagnostic Reagents, Vaccine Candidates, and Antiviral Proteins to Address the COVID-19 Pandemic. Blue arrows show potential routes for diagnostic reagents. Black arrows show additional routes for vaccines and therapeutics for human use. A tobacco plant is shown, representing both transient expression and stably transformed transgenic plants as production platforms. The figure includes images from Biorender (https://biorender.com/). The structure of griffithsin bound to high-mannose glycans was generated using NGL viewer based on Protein Data Bank file 3LL2. Abbreviations: RBD, receptor-binding domain; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; VLP, virus-like particle.

of broadly -neutralizing HIV-specific antibodies, such as 2G12 and 2F5, has been demonstrated in transgenic tobacco [39], maize (*Zea mays*) [40,41], and rice (*Oryza sativa*) [42]. The German Government issued a **good manufacturing practice** (GMP) license to the Fraunhofer IME for the production of 2G12 in tobacco for testing in a first-in-human Phase I clinical trial, and a similar model could be used for neutralizing antibodies against SARS-CoV-2. Furthermore, rice has recently proven versatile as a means to produce 2G12 along with two antiviral **lectins** (see next section), which could reduce the costs of preformulated cocktails of active ingredients [43]. In addition to the production of antibodies that neutralize the virus directly, plants could also be used to produce large amounts of therapeutic antibodies that inhibit the cytokine storm that follows SARS-CoV-2 infection in many of the most severe and fatal cases. Two antibodies that could be repurposed for the treatment of COVID-19 are sarilumab/Kevzara and tocilizumab/Actemra, both of which bind the interleukin-6 receptor (IL-6R) and are indicated for the treatment of rheumatoid arthritis. They are both undergoing clinical trials for COVID-19 [44,45].

Spike protein trimer

Membrane protein

Envelope protein

Lipid envelope and underlying nucleocapsid protein

**Figure 2. Structure of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), Showing the Prominent Position of the Trimeric Spike Protein.** Public domain image originally produced by the Centers for Disease Control, Atlanta, GA, USA.

## Antivirals

Antiviral drugs inhibit the viral replication cycle and, therefore, slow down the infection, giving the immune system more time to respond. Many antiviral drugs are small chemical entities produced efficiently using synthetic or semisynthetic processes, and it is unlikely a switch to plant-based production would be beneficial or even practical. However, some proteins can also be used as antivirals, including carbohydrate-binding proteins (lectins) from plants. Lectins are known to bind and inactivate a broad range of viruses by blocking the glycan structures present on the virus surface [46]. For example, griffithsin is a 121-amino-acid lectin produced by red algae of the genus *Griffithsia*. It acts as an entry inhibitor against multiple viruses for which no vaccine is currently available, including HIV [47], Zaire ebolavirus [48], and the coronaviruses responsible for the original SARS outbreak (SARS-CoV) [49] and the subsequent outbreak of Middle East respiratory syndrome (MERS-CoV) [50]. Griffithsin has potent activity against these viruses but low toxicity toward human cells, offering a broad and effective therapeutic window. It is not yet clear whether griffithsin inactivates SARS-CoV-2, but the surface-exposed S protein of SARS-CoV and SARS-CoV-2 are highly conserved, with some conserved and some unique glycan positions [25,26]. Therefore, cross-reaction is likely. Similarly, scytovirin is a 95-amino-acid lectin from the cyanobacterium *Scytonema varium* [51] that is also active against multiple viruses, including HIV, Zaire ebolavirus, Marburg virus, and SARS-CoV [52]. A study of 33 additional plant lectins revealed that 20 of the candidates showed some activity against SARS-CoV, with $EC_{50}$ values in the middle nanomolar range and no toxicity at concentrations of up to 100 µg/ml [53]. Mannose-binding lectins typically showed the strongest activity against SARS-CoV, suggesting that high-mannose glycans are the most effective targets. However, lectins specific for galactose, *N*-acetylgalactosamine, glucose, and *N*-acetylglucosamine also showed antiviral effects, although the $EC_{50}$ values varied over a greater range. Interestingly, the lectins appeared to target two different stages of the viral replication cycle, indicating a built-in mechanism for the prevention of escape mutants. Plants have been used to produce a range of antiviral lectins, including griffithsin [54,55], cyanovirin-N [56–59], and cyanovirin-N fusion proteins [60], as well as transgenic rice lines expressing griffithsin and cyanovirin-N simultaneously in the seeds, with or without the antibody 2G12 [43]. Transient expression in plants would provide rapid access to antiviral proteins and the process can be scaled up to provide gram amounts within a few weeks. Transgenic plants could then be used to provide a more permanent resource for even larger-scale production.

## Concluding Remarks: The Future

Transient expression in plants is an excellent platform to provide diagnostic proteins, vaccine candidates, and antiviral proteins in response to emerging pathogens, such as SARS-CoV-2. Whereas diagnostic proteins, such as viral antigens or virus-specific antibodies, can be used immediately as components of assays and kits (following evaluation and approval), the development pipeline for vaccines and therapeutics is longer due to the need for preclinical and clinical testing. Moreover, pharmaceutical proteins must be produced under GMP conditions, adding to the development time and costs. Even so, transient expression in plants is faster than in traditional platforms based on microbes and mammalian cells because there is no requirement to establish stable cell lines producing the final product; neither is there any need for the development of a scaled-up processes because the scalability of transient expression systems is hardwired and requires only the cultivation of more plants. Therefore, transient expression allows the provision of material for clinical testing within a few weeks and the large-scale production of clinical-grade material is feasible with minimal investment. The unique challenge of COVID-19 is the need for universal testing of the entire human population, which is unprecedented in terms of demand. The world needs to go from zero production to making available multiple billions of tests in developed and developing country settings, which is where transgenic plants could provide a solution. Tobacco, legumes, or cereal plants can be grown in many environments and, therefore, the products, be they antigens, antibodies, or antivirals, could be produced using local infrastructure, the same distribution networks that already exist for food and, in the case of cereal seeds, without the need for a cold chain. This approach, established in the EU Pharma-Planta project for humanitarian applications in the context of HIV prophylaxis [39], could facilitate the inevitable rollout of SARS-CoV-2 testing to all sectors of the global population [61,62]. The Pharma-Planta project also examined the regulatory aspects of molecular farming over international boundaries, and similar principles could be applied for COVID-19 [63].

The molecular farming community is extremely active in establishing plant-based processes for the production of diagnostic and therapeutic proteins to fight against COVID-19. Two current EU consortia focusing on molecular farming are proposing to divert their efforts to help with the production of such proteins. These are the two major H2020 projects Pharma-Factory[i] and Newcotiana[ii], both of which are developing plant-based platforms for industrial applications. Cooperation with companies that manufacture diagnostic kits and therapeutic products will be crucial to move the products along the pipeline toward commercialization. We have the opportunity not only to help address the current COVID-19 pandemic, but also to create a model that allows a rapid and targeted response to future pandemics (see Outstanding Questions).

### Outstanding Questions

The molecular farming community has addressed previous epidemics and pandemics, but the scale of the challenge has never been so great and meeting the demand will be an unprecedented test.

One major aspect of this challenge is the need to organize the international response within a matter of months or even weeks.

If coronavirus outbreaks recur, we need to ensure that the infrastructure remains in place for the molecular farming community to meet future pandemics.

The molecular farming community must team up with clinicians and diagnostic and pharmaceutical companies to ensure the translation of plant-based protein products into commercial diagnostic kits and therapeutics.

Current molecular farming strategies to mitigate COVID-19 focus on transient expression systems and, subsequently, transgenic crops grown under containment. Current regulations adequately cover their use, but, to address future pandemics, it will be necessary to re-evaluate genetically modified organism (GMO) regulations, particularly those in Europe, which stifle the development of beneficial technologies.

### Resources

[i] https://pharmafactory.org/
[ii] https://newcotiana.org

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