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Emerging importance of nanotechnology-based approaches to control the COVID-19 pandemic; focus on nanomedicine iterance in diagnosis and treatment of COVID-19 patients

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ABSTRACT

The ongoing outbreak of the newly emerged coronavirus disease 2019, which has tremendously concerned global health safety, is the result of infection with severe acute respiratory syndrome of coronavirus 2 with high morbidity and mortality. Because of the coronavirus has no specific treatment, so it is necessary to early detection and produce antiviral agents and efficacious vaccines in order to prevent the contagion of coronavirus. Due to the unique properties of nanomaterials, nanotechnology appears to be a highly relevant discipline in this global emergency, providing expansive chemical functionalization to develop advanced biomedical tools. Fascinatingly, nanomedicine as a hopeful approach for the treatment and diagnosis of diseases, could efficiently help success the fight among coronavirus and host cells. In this review, we will critically discuss how nanomedicine can play an indispensable role in creating useful treatments and diagnostics for coronavirus.

1. Introduction

Following the identification of severe acute respiratory syndrome coronavirus (SARS-CoV) and middle east respiratory syndrome coronavirus (MERS-CoV), it was predicted that we would encounter another virus from the corona virus family that originates from common human and animal resources [1]. In late 2019, the first human cases of coronavirus (CoV) was identified in Wuhan/China. On March 11, 2020, the World Health Organization (WHO) describe the deployment of coronavirus disease 2019 (COVID-19) as a pandemic [2]. COVID-19 is the third largescale epidemic in human history, and the first pandemic caused by a coronavirus [3]. At the time of writing, September 24, 2021, more than 230,418,451 cases of coronavirus have been confirmed worldwide, of which 4,724,876 million have died (https://covid19.who.int/). With a total of 10,000 cases, the mortality rate of SARS and MERS were reported to be 10 and 37%, respectively. Nevertheless, the incidence of COVID-19 is nearly 90 times higher than that of SARS and MERS in total [4]. Considering the high transmissibility of COVID-19, secondary prevention measures in the form of timely diagnosis may contribute to the containment of the situation [5]. Scientists have made great efforts to propose an effective treatment for COVID-19 [6].

Therefore, considering the increasing prevalence of this disease, it is a good time for all researchers to think about producing a quality detective tests and so new therapies without side effects and methods so they quickly sequenced the SARS-CoV-2 genome [7]. In current years, nanomedicine has provided hopeful solutions to surmount the curbs of

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current diagnostics and treatments [8–11]. Highly sensitive immunological diagnostic assays are particularly efficacious for detection of viral antigens, particularly that of SARS-CoV-2 [12]. The lesser known "nano-based diagnostics" were also investigated in the case of major epidemics such as influenza [13] as reliable alternative solutions to conventional tests [14].

Traditional circulation-based delivery of drugs is not deemed to be an effective intervention, necessitating development of novel platforms for delivery of therapeutics to hard-to-reach tissues in human body. Today, several nanotechnology-based drug delivery platforms are available for experimental use against COVID-19 [15] in hopes of lowering the course of the disease [16].

This review critically argues various diagnostic and therapeutic strategies for CoVs, concentrating on nanomedical applications in COVID-19 and associated pathogenic CoVs (Graphical abstract).

2. COVID-19 characteristics

Coronavirus (CoVs), as a member of the coronaviruses family, has a single-stranded RNA genome of positive polarity that infect humans and animals [17]. Moreover, CoVs are enveloped and non-segmented RNA viruses with an asymmetric shape and surface spikes located so as to look like a crown [18]. Their genome size ranges from 28 to 32 kb, being the largest identified RNA virus. The structural proteins, which are encoded by 3' terminus of SARS-CoV-2), consist of envelope (E), nucleocapsid (N), membrane (M) and spike (S) proteins [19] (Fig. 1. Modified from Ref. [20]).

CoVs are the second most widespread reason of the typical cold in humans and have been isolated from infants, humans, and animals in gastrointestinal infections and gastroenteritis [19]. There are four groups in this family: Alpha-CoV, beta-CoV, gamma-CoV, and delta-CoV. SARS-CoV-2 is classified in the beta-corona group of viruses [21]. COVID-19 was first reported in Hubei province, on December 31, 2019 and quickly outbreak all over China [22]. SARS-CoV was the cause of the Guangdong, china, outbreak in 2002, and MERS-CoV was first revealed in Saudi Arabia in 2012 and circulated along the Arabian Peninsula [23]. In general, these viruses attack the gastrointestinal and respiratory epithelial cells and can cause mild diseases in infants [24]. The virus is stable at low temperatures and at ambient temperatures for some time, but is similar to the Rabdo virus and is sensitive to light [25]. The most general signs contain fever, cough, and shortness of breath, extreme languor, digestive problems, and loss of sense of smell [26]. CoVs are most often transmitted through direct contact with a sick person [26]. The virus can also be spread by touching an infected surface and then touching the eyes, nose, mouth, and respiratory aerosols (droplets) [26,27]. CoVs attaches to host cell surface glycoproteins through connections between viral glycoprotein spikes [21,28]. Several CoVs bind to sialic acid glycoproteins and glycolipids via spike and/or hemagglutinin esterase glycoproteins [29]. Interactions between CoVs and host cell receptors determine the degree of specificity, tissue growth, and pathogenicity of the virus [28,29].

3. Therapeutic approaches

To date, no available methods are available to effectively treat the progression of COVID-19 [30]. Scientists have made great progress in repurposing of therapeutics for successful treatment of COVID-19 that include 1) drugs: old medicine (chloroquine phosphate), antiviral drugs (Lopinavir/ritonavir, leronlimab, galidesivir, and arbidol (umifenovir)), renin–angiotensin-aldosterone system (RAAS inhibitors), 2)

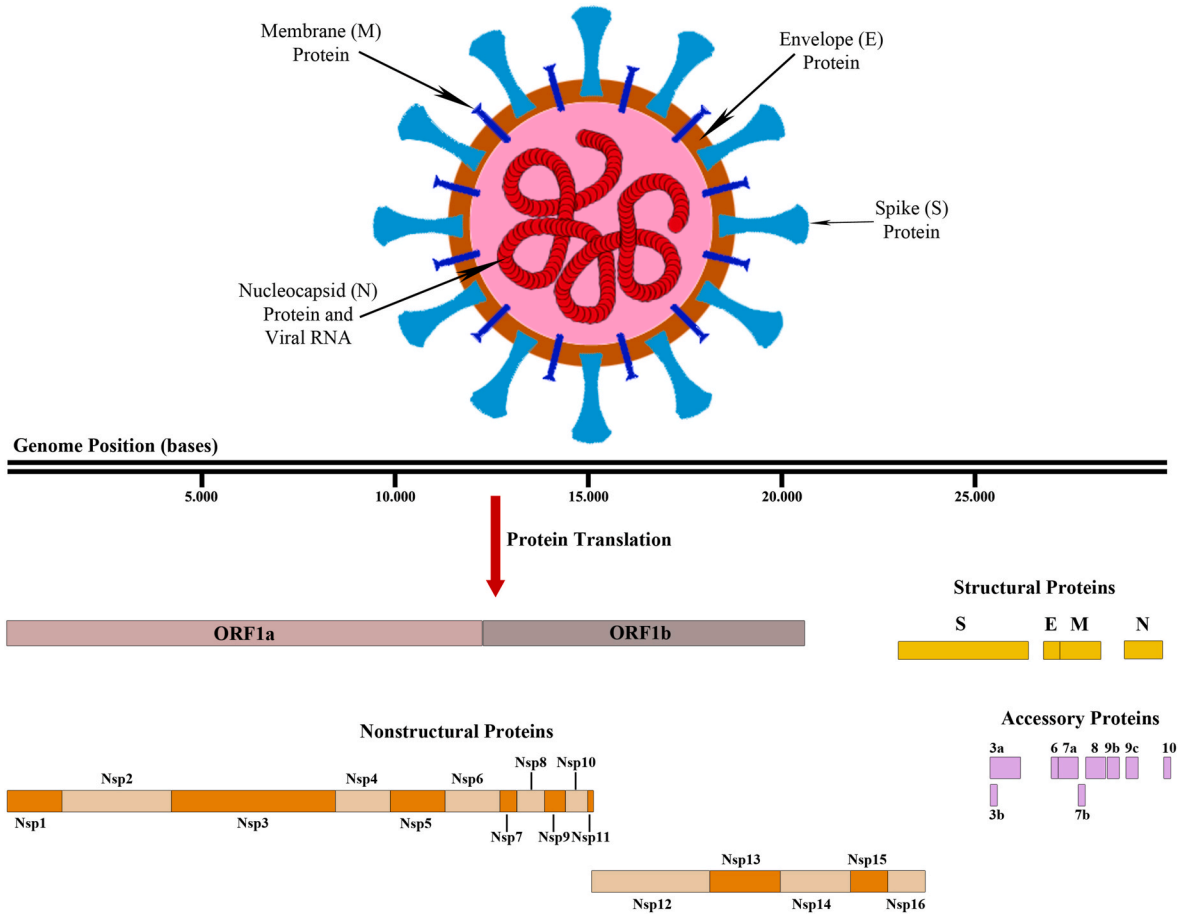

Fig. 1. Schematic representation of a coronavirus structure and genome structure. (modified from Ref [20]).

Combination therapy, 3) Convalescent blood therapy, 4) Mesenchymal stem cell (MSC) therapy, 5) Psychological interventions [6] and 6) vaccines [31].

Owing to a shortage of appropriate vaccines and particular treatments preventive measures are currently effective for control [31]. Experts and governments are emphasizing the need for social distancing and quarantine to stop the spread of this contagious disease [32]. Currently, the most important concern for researchers around the world is to fight the CoVs is to develop a good vaccine [33].

3.1. Vaccines against CoVs

Certainly, the first part of the medicinal intermediation, is the elimination of the virus before it infected target cells or even be distributed throughout the body [34]. To date, the WHO has issued the first emergency authorization to use one of the vaccines against the Covid-19 pandemic [35]. Hence, the United Nations has agreed to make emergency use of Pfizer and BionTech vaccines to prevent CoVs infection. But researchers are still trying to produce an efficient vaccine versus the SARS-CoV-2 to improve safety and decrease associated signs [36]. Table 1 displays various vaccine platforms utilized versus CoVs [37–52].

Vaccines basically introduce antigenic molecules to the body, which is generated in patients who have this illness, which in general can be said to be an assured procedure for the patient [53]. These antigens are present on the surface of dendritic cells and macrophages, known collectively as antigen presenting cells (APCs), as part of the major histocompatibility complex (MHC) I and II [54]. These antigens are pivotal for the function of adaptive immune system, which recognizes such antigens as antagonistic attackers and as well as generates antibodies or activate T cells to destroy the raider [55,56]. Furthermore, memory B cells progress virus particular antibodies on the outer area of the cell prompt a quick immune response to eliminate the infection of viral. Depending on the kind of infection, numerous different kinds of vaccines are presently in use, contain passive vaccines, conjugated vaccines, live attenuated vaccines, more newly DNA or RNA vaccines [57]. In spite of its presence for more than 20 years, because of side effects upon treatment or inadequacy of the vaccine, up to now no efficient vaccine against human CoVs could be developed, representing the need of a new approach to target CoVs. S protein as an important part of Co Vs considered a promising target in the development of vaccines [7]. The recently developed purified inactivated SARS-CoV-2 vaccine termed 'PiCoVacc' by Sinovac Biotech is currently in phase I clinical trials (Fig. 2. Modified from Ref. [20]).

3.1.1. DNA vaccine

A vaccine is a type of medicine that supplies active acquired immunity to a given infectious disease [58]. Nowadays, later than one years the find of SARS-CoV-2, antiviral drugs and vaccines are being established, with numerous treatment opportunities and vaccines in clinical studies around the world [59]. However, antiviral drugs are very important in modulating the existing pandemic disease, but effective vaccines are vital to control it [59,60]. The ability to stimulate the innate and acquired immune responses is the most important advantage of DNA vaccination [61]. A DNA vaccine designed to induce CD4+/CD8+ immune response by inducing the expression of SARS-CoV spike protein inside the host cells is currently being explored in a phase I clinical trial [62]. During antibody-dependent enhancement, in response to vaccines, the virus-specific antibodies facilitate viral entry and thus increase the incidence of infection [63]. Vaccines that stimulate an immune response against the S protein to prevent it's attaching with the host angiotensin-converting enzyme 2 receptor, can be deliberated as efficient vaccines against SARS-CoV-2 [64]. Presently, the INO-4800 structure (Fig. 2) is a DNA vaccine candidate matched to the SARS-CoV-2 S protein and developed by Inovio Pharma in a fashion similar to their previous MERS-CoV vaccine, which is presently undergoing clinical studies [46,65]. Moreover, a recombinant adenoviral vector-based vaccine for COVID-19 was reported to be safe and immunogenic in a first-in-human trial [66]. The vaccine developed by CanSino Biologics is the first candidate to be tested and has entered Phase II medical test [66]. The Shenzhen Immunogenic Medicine Institute of China is ensuing the COVID-19 vaccine and two global vaccine applicants for COVID-19 in the experimental stage, LV- SMENP-DC and pathogen-specific an APC (Fig. 2). Synthetic SARS-CoV-2 minigenes with certain modifications on conserved domains of the polyprotein protease and viral structural proteins and a have been investigated using an effective lentiviral vector system (NHP/TYF) to induce transcription of viral proteins to modulate the activity of dendritic and T cells.

3.1.2. mRNA vaccine

An RNA vaccine or mRNA (messenger RNA) vaccine is a novel kind of vaccine that work via introducing an mRNA sequence encoding a target antigen to incite an immune response [67]. mRNA vaccines are highly effective at inducing cellular immunity, since antigens are expressed inside the cell [68]. Over 150 COVID-19 vaccines are presently under progress via Biopharma Institute and investigation Governments in the globe [69]. Recently, Moderna partnered with researchers at the Vaccine Research Center (VRC) developed vaccine platforms against SARS-CoV-2 encoding for a prefusion fixation form of S protein through the use of mRNA-1273 [70]. Numerous studies are

Table 1
Vaccine platforms for CoVs.

Vaccine Platform	Target	Product by	Virus	Number of candidate vaccine	Ref.
Live-attenuated virus	all proteins of the virus	codagenix/serum institute of india	CoVs	3	[37,38]
Inactivated vaccines/ alum	whole structural protein of the virus	osaka university/sinovac biotech china	CoVs	9	[39,40]
RNA vaccines	SARS-CoV-2 spike protein	Moderna, Inc (USA), BioNTech/fosun pharma/Pfizer (Germany, China, USA), CureVac(Germany)	SARS-CoV-2	16	[41]
virus-like particles	unknown	Doherty institute (Australia) Medicago Inc (Canada) Saiba GmbH Griffith University (Australia)	CoVs	12	[42,43]
DNA vaccines	s glycoprotein and subunit of sars-cov-2	Zydus Cadila(india), Inovio pharmaceuticals (USA), Takara Bio (USA), BARDA and Sanofi pasteur(USA,France)	CoVs containing SARS-CoV-2	11	[44–46]
Protein subunit	s glycoprotein and peptides/unknown	Novavax, and Sanofi pasteur France), University of Queensland, (Australia), Vaxil Bio (Israeli), Emergent BioSolutions Inc(USA)	NVX-(COV2373)/ RSV	49	[47,48]
Recombinant protein vaccines	Spike protein Nucleocapsid protein Membrane protein		CoVs containing SARS-CoV-2		[49–52]

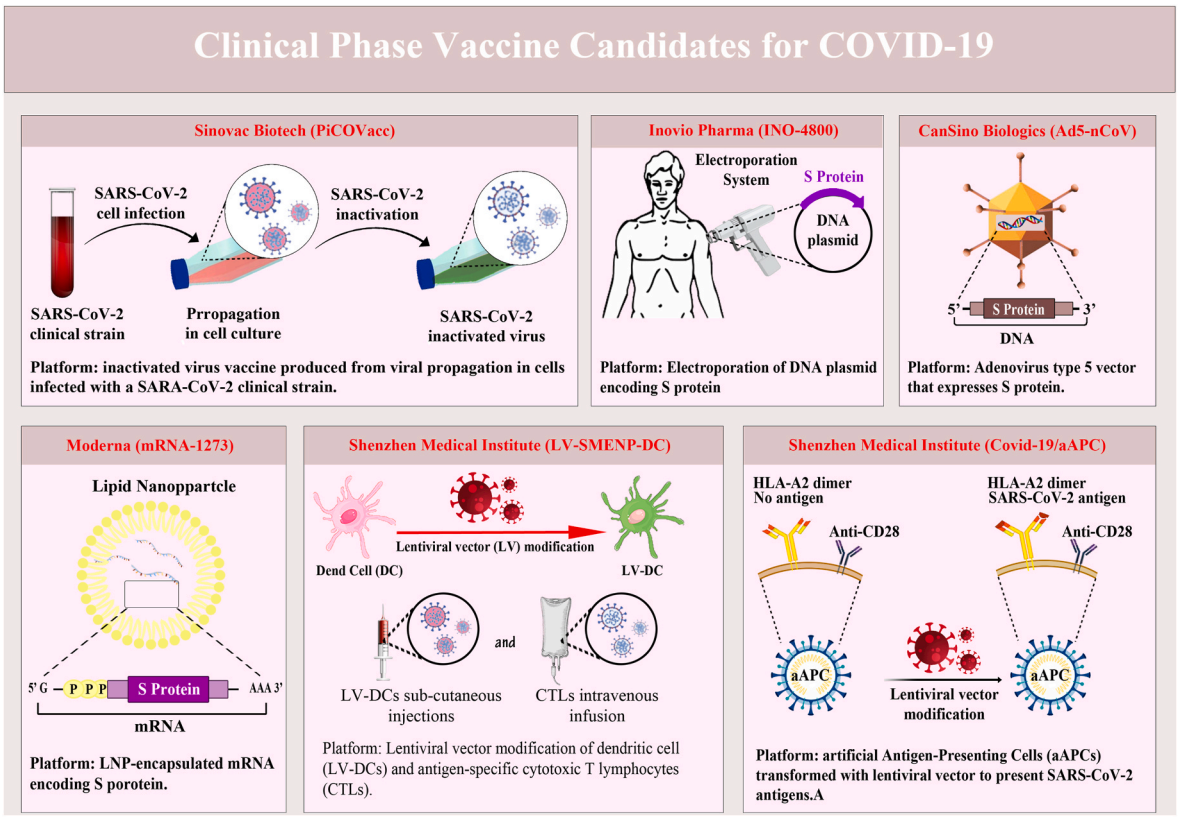

Fig. 2. The COVID-19 treatment by clinical phase vaccine candidates (modified from Ref. [20]).

currently simultaneously underway to improve mRNA vaccine versus SARS-CoV-2 [71]. In addition, administration of mRNA to encode antibody proteins is another similar approach for development of a COVID-19 vaccine.

3.1.3. Viral proteins

Subunit-based vaccines present an antigen lacking other viral elements to immune cells, via a specific, isolated protein of the pathogen [72,73]. Researchers have been able to determine the genetic sequence of the S protein and the baculovirus expression system is commonly used to produce recombinant proteins [74,75]. The foundation on the structure of coronavirus S protein, containing C-terminal, receptor-binding and N-terminal domains [76,77], and or fusion peptide [46], is considered as a vital target for the development of a vaccine versus SARS-CoV and MERS-CoV due to its capability to promote the immune response and deliver neutralizing antibodies [47,78,79]. At present, the most promising treatment Modality against COVID-19 is S-protein-based vaccines and up to now, many organizations and associations are paying close attention to this field. An alternative Covid-19 vaccine was generated via the combination of MERS-CoV-S1 and/or SARS-CoV-2-S1 immunoreactive epitopes with S-fold on trimerization region, reaching 27 lengths of amino acids, which was applicable to naïve viral structure. This complex had a unique affinity to the TLR on the cell surface and could trigger relevant signaling pathways [52]. It has been shown that the local introduction of target antigens could be done via the application of the novel delivery subcutaneous delivery system [52]. For instance, the microneedle patch system is a sophisticated delivery an approach to release target antigens to the subcutaneous areas where local immune cells could appropriately respond to immuno-reactive molecules [80]. Via its patented Trimer-TagC knowledge, Clover Biopharmaceuticals Inc. has produced a vaccine via trimeric S protein that is analogous to the natural trimeric S protein of SARS-CoV-2 [51]. In addition, Dynavax is supplying CpG 1018, the adjuvant used in the FDA-approved HEPLISAV-B vaccine, to mediate the rapid development of COVID-19 Trimeric S protein vaccine [51]. Furthermore, a molecular clamp is a polypeptide used to preserve the shape of proteins in experimental vaccines [81]. According to conducted researches, the pre-fusion proteins available on the covid-19 surface are considered an ideal target for immune response [82]. Of note, it should be administered with other adjuvants' therapy. Investigation of potential interactions among B and T cells and SARS-CoV S and N proteins (as protecting epitopes) in order to study vaccines epitopes are at the center of attention [83]. Due to some limitations including low-molecular-weight-related rare immunogenicity, it takes other adjuvants so as to increase its efficacy [82]. Notwithstanding its plenty in CoVs, N protein immunization did not persuade VN antibodies and provided no safety versus SARS-CoV [49]. However, it has been investigated that full-length M protein can induce effective neutralizing antibodies in SARS patients. Hence, it can be considered a candidate protein for designing SARS-CoV-2 vaccine [84,85].

3.1.4. Neutralizing antibodies

Antibodies can induce passive systemic anaphylaxis (PSA) through the low-affinity IgG receptor FcγRIII and platelet-activating factors in high antigenic environments [86]. The S protein is an important target for developing vaccines against coronavirus infections [31]. The inactivated SARS-CoV vaccine produces copious amounts of S protein-specific antibodies that inhibit receptor binding and viral entry. Fusion inhibitors target cellular receptors or viral epitopes to prevent the triad of binding, fusion, and virus entry [78,87,88]. Undoubtedly, Sui et al. developed a nonimmune human antibody library and recognized an anti-S1 human monoclonal antibody, 80R that can inhibit SARS-CoV entry by inhibiting S1 attachment to ACE2 receptors [78]. Soluble forms of angiotensin-converting enzyme 2 (ACE2) have lately been shown to prevent SARS-CoV-2 infection and could create long-lasting immunity for those who were previously infected [89].

3.2. COVID-19 ongoing vaccines

COVID-19 vaccines are perhaps the most rapidly developed in the history of vaccines [90]. Presently, there are over 180 vaccines being developed and 100 in clinical trials [91]. As of now, 18 different vaccines have been approved for public use against COVID-19 [91,92]. The COVID-19 vaccines can be classified in four major categories: (1) inactivated virus, (2) protein-based, (3) viral vector, and (4) nucleic acid [93]. Table 2 lists the characteristics of COVID-19 vaccines [90,91].

4. Antiviral compounds against CoVs

The manufacture of novel drugs and antiviral targets is time-consuming. To speed up the work process, it is essential to understand viral replication. An urgent demand to generate drugs to treat covid-19 is vital. In this regard, using well-known drugs with approved efficacy and structure can be totally fruitful. Nucleoside and nucleotide analogs are commonly used in the therapy of cancer and viral infections [89,94,95]. They prevent virus replication by interfering with the cellular nucleotide synthesis. Remdesivir, a nucleotide analog prodrug, has broad-spectrum activity against viruses from multiple families. Remdesivir strongly binds the SARS-CoV-2 RNA-dependent RNA polymerase and Main Protease, and was recognized early as a promising therapeutic candidate against COVID-19 because of its capability to inhibit in vitro SARS-CoV infection Several clinical experiments of favipiravir in combination with interferon have been performed in the therapy of COVID-19 in China [94,96,97]. Lopinavir is a new protease inhibitor (PI) established from ritonavir and stops the virus from replicating by attaching to viral proteases. Lopinavir is a new protease inhibitor (PI) developed from ritonavir and stops the virus from replicating by attaching to viral proteases and has been used for the treatment of SARS and MERS coronavirus infections and clinical trial versus SARS-CoVs-2 has been started [98–100]. Antimalarial chloroquine is used for the therapy of immune-mediated diseases and neutralized by activating indolamine (2,3)-deoxygenase in PBMC and has been clinically tested versus COVID-19 the WHO suspends chloroquine-related clinical trials Because of chloroquine' ineffective [94,101–104]. There are also other clinical trials for the therapy of COVID-19 worldwide like the neutralizing antibodies in patient sera، passive antibodies and lastly, blocking factors that present affinity to attach to ACE2 receptor [105–109] and the use of cell-based methods such as mesenchymal stem cells MSCs are between the greatest commonly used cell kinds for regenerative medicine [110].

MSCs are attractive candidates for treating different diseases such as COVID19, largely since these cells showing several precautionary mechanisms to protect and repair pulmonary harm [111]. Besides, MSCs are considered suitable for anti-viral therapy as the safety and effectiveness of these cells have been mentioned in clinical studies of lung infections [112]. As well, that the use of Famotidine use is related to a decreased danger of clinical deterioration leading to intubation or mortality in patients who are hospitalized in COVID-19, according to a study published in Gastroenterology [113,114].

5. Nanotechnology in medicine; nanomedicine

Recently, many researchers have focused on nanomedicine and its advancement in the treatment and diagnosis of a wide range of diseases, such as cancers [115–117], inflammatory diseases [118], bacterial infections [119] as well as COVID19 [120].

Cancer, cirrhosis, viral and bacterial infections stand among the pathologies to have been detected by nanoscale diagnostics [121] before the onset of diseases. Furthermore, *in vivo* and in *vitro* studies demonstrated that drug-loaded nanocarriers are more effective than free drugs to treat such diseases [122–131].

Nanomaterial-based drug delivery platforms have improved efficiency of targeted drug delivery approach through sustained delivery of

Table 2
The COVID-19 vaccines characteristics in advanced stage of clinical development.

Vaccine platform	Type of vaccine	Developers	Phase
Viral vector (Non-replicating)	INO-4800 + EP	International Vaccine Institute + Inovio Pharmaceuticals + Advaccine (Suzhou) Biopharmaceutical Co., Ltd	Phase II/III
	GRAd-COV2 (Replication defective Simian Adeno (GRAd) encoding S)	Univercells + Leukocare + ReiThera	Phase II/III
	Gam-COVID-Vac Adeno-based (rAd26-S + rAd5-S)	Gamaleya Research Institute; Health Ministry of the Russian Federation	Phase III
	Ad26.COV2.S	Janssen Pharmaceutical	Phase III
	ChAdOx1-S - (AZD1222)	University of Oxford + AstraZeneca	Phase IV
	Recombinant nCoV vac. (Adeno type 5 vector)	CanSino Biological Inc./ Beijing Institute of Biotechnology	Phase IV
DNA based vaccine	AG0301-COVID19	Takara Bio + AnGes + Osaka University	Phase II/III
	nCoV vac.	Zydus Cadila	Phase III
Protein subunit	SCB-2019 + AS03 or CpG 1018 adjuvant + alum adjuvant (Native like Trimeric subunit S pro. vaccine)	Clover Biopharmaceuticals Inc./GSK/Dynavax	Phase II/III
	MF59 adjuvanted SARS-CoV-2 Sclamp vac.	Seqirus + University of Queensland + CSL Ltd.	Phase II/III
	UB-612 (Multitope peptide based S1-RBD-protein based vac.)	Vaxxinity	Phase II/III
	SARS-CoV-2 rS/Matrix M1-adjuvant (Full length recombinant SARS CoV-2 glycoprotein NP Vac. + Matrix M adjuvant) NVX-CoV2373	Novavax	Phase III
	Recombinant SARS-CoV-2 vac. (CHO Cell)	Institute of Microbiology, Chinese Academy of Sciences + Anhui Zhifei Longcom Biopharmaceutical	Phase III
	VAT00002: SARS-CoV-2 S protein + adjuvant	GSK + Sanofi Pasteur	Phase III
	FINLAY-FR-2 anti-SARS-CoV-2 vac. (tetanus toxoid + RBD + adjuvant)	Instituto Finlay de Vacunas	Phase III
	EpiVacCorona (EpiVacCorona vac. + peptide antigens against COVID-19)	Federal Budgetary Research Institution State Research Center of Virology and Biotechnology 'Vector'	Phase III
	CIGB-66 (aluminium hydroxide + RBD)	Center for Genetic Engineering and Biotechnology (CIGB)	Phase III
Virus like particle	CoVLP COVID-19	Medicago Inc.	Phase II/III
Inactivated Virus	COVID-19 inactivated vac.	Shifa Pharmed Industrial Co	Phase II/III
	Inactivated SARS-CoV-2 vac. (Vero cell)	Sinopharm + Wuhan Institute of Biological Products + China National Biotec Group Co.	Phase III
	Inactivated SARS-CoV-2 vac. (Vero cell), BBIBP-CoV	Sinopharm + Beijing Institute of Biological Products + China National Biotec Group Co.	Phase III
	SARS-CoV-2 vac. (Vero cells)		Phase III

(continued on next page)

Table 2 (*continued*)

Vaccine platform	Type of vaccine	Developers	Phase
		Chinese Academy of Medical Sciences + Institute of Medical Biology	
	QazCovid-in1-COVID-19 inactivated vac.	Research Institute for Biological Safety Problems, Rep of Kazakhstan	Phase III
	Whole-virion inactivated SARSCoV- 2 vac. (BBV152); covaxin	Bharat Biotech International Limited	Phase III
	Inactivated SARS-CoV-2 vac. (Vero cell)	Shenzhen Kangtai Biological Products Co., Ltd.	Phase III
	VLA2001	Valneva, National Institute for Health Research, United Kingdom	Phase III
	CoronaVac; inactivated SARS-CoV-2 vac. (Vero cell)	Sinovac Research and Development Co., Ltd	Phase IV
RNA based vaccine	CVnCoV vaccine	CureVac AG	Phase III
	SARS-CoV-2 mRNA vac. (ARCoV)	Academy of Military Science (AMS), Walvax Biotechnology and Suzhou Abogen Biosciences	Phase III
	mRNA-1273	Moderna + National Institute of Allergy and Infectious Diseases (NIAID)	Phase IV
	BNT162b2 (3LNP-mRNAs), or 'Comirnaty'	Pfizer/BioNTech + Fosun Pharma	Phase IV

Adeno or Ad: Adenovirus, CoVLP: CoV-like particle, EP: Electroporation, nCoV: novel CoV, NP: Nanoparticle, S pro: Spike Protein, Vac: Vaccine.

therapeutics via nanomaterials without causing significant toxicity [132,133]. Understanding the genetic mechanisms underlying the spread of novel viral outbreaks has mostly been made possible through nanotechnology [134].

Otechnology in medicine finds importance in several overlapping molecular technologies [133,135–138].

5.1. Nanomedicine and CoVs control

Following the emergence of the COVID-19 virus in early 2020, governments worldwide begin to implement measures to impede the expanse of the virus that became a universal pandemic. The application of nanotechnology for medical aims has been called nanomedicine, can be used to develop modern formulations for targeted drug drugs that are potentially safe and therefore can be associated with improved outcomes by reducing drug side effects [139].

It is necessary to advance the expansion of engaged translatable clinical treatments versus different viral infections. The field of Nano medicine has formerly made significant success and activity versus numerous infectious diseases consist of HBV [140], HIV-1 [141,142], respiratory syncytial virus [143], and influenza virus [144]. Also, several CoV-associated proposals have been introduced in the field of nanotechnology [145]. The strategy of using nanoparticles (NPs) against SARS-CoV-2 involves mechanisms that might affect the entry of the virus into the host cell [146]. The Executive capability with a varied variety of functional teams and NPs high-level gives particular physicochemical features, leading to favorable interactions of cell and impressive therapeutic efficacy [147]. These days due to the need for efficient and effective delivery of diagnostic or therapeutic factors in addition to immunogens versus coronaviral infection, NP based delivery systems have been planning and established [139,147].

In summary, nanomaterials can be produced via diverse pathways, each having its own benefit and drawback. Nanoparticles may action a significant impress at different steps of COVID-19 pathogenesis, considering their deterrence potential in the primary sticking and the fusion of the viral membrane entry and infected cell protein fusion. Moreover, nanoencapsulation of antimicrobial drugs may be rather effective in activating intracellular mechanisms and may contribute to the development of safe treatments for COVID-19 and other viral diseases. Table 2. Nanoparticles-based vaccination against.

5.1.1. Therapy

5.1.1.1. NPs-based vaccines against CoVs. Nanotechnology, as an interdisciplinary approach, is the most interesting area for generating novel nanoproducts in biotechnology and biocompatible medicine [148,149]. One of the most important and well-known nanoproducts applied for medical purposes is nanoparticles (NPs) [150,151]. Currently, the ultimate goal for rapid control of the CoVs outbreak is vaccination. Administration of vaccine by NPs delivery systems can improved the efficacy and immunization of vaccine by protection of antigens degradation, controlled and sustained release as well as controlling cellular uptake and processing by APCs [152–154]. Table 3 summarizes the Nano-vaccines produced against the pathogenic CoVs [42,87,89,155–172].

Nanovaccines are made by loading CoVs antigen into nanocapsules or locating them on NPs surface, fabricating NPs of similar immunological conformation. S protein is an important binding factor and immuno dominant antigen in the coronavirus and is the main Nano-based vaccine candidates. The most common process for developing and producing corona viral Nano-based vaccines is structure-based assembly. The assembly pattern is important for controlling the thermodynamic consistency of assembled NPs and for preventing aggregation. S protein trimmers in SARS-CoV can be assembled with the removal of a non-ionic purifier versus the filtration process to form NPs Vaccination of mice through these NPs prompts the production of neutralizing antibodies, which are enhanced by the use of aluminum hydroxide nanoparticles and the development of composite adjuvants. To prompts, a high surface of neutralizing antibodies, vaccinate mice with NPs is also remarkably augmented with adjuvants such as or M1 matrix (68-fold) and aluminum hydroxide (15-fold) [157]. Adjuvants may well also ameliorate safety and immunity with the MERS-CoV vaccine [175]. In addition, virus-like particles (VLPs) have a multi-protein structure and are fundamentally analogous to viral particles, except that they lack a viral genome and are potential candidates for vaccine production [176,177]. MERS-CoV VLPs (MERS-CoV-LPs) are made in insect cells by expressing S, M, and E proteins [178]. With a slight correction of these NPs with S protein SARS-CoV, it causes the NP proteins to bind to the ACE2 receptor, thereby strengthening and stimulating the immune system. The structural gene of VP2 canine parvovirus is integrated with RBD MERS-CoV, it can Self-assemble into chimeric [158]. Therefore, RBD-Dedicated safety responses induced by mice vaccination and antiserum can preserve cells from MERS-CoV entry. Bacterial expression systems due to affordable, fast breeding speed, easiness of culture, and production of high-yield recombinant proteins that can be used in nano-vaccine assembly processes. Using ferritin as a molecular scaffold in bacterial systems, self-assembled NPs of MERS-CoV antigens can be formed. Fusion of RBD with bacterioferritin and RNA-interaction domain to be expressed in a soluble form in *Escherichia coli*. In addition, chaperones immunize mice versus CoV via intervening with RBD binding to the DPP4 receptor. Bacteriophytin (Bfr) is an oligomer protein that contains both dual-core iron centers and Heme B, which prevents accumulation during the assembly of viral antigens. SARS B cell epitopes of HRC1 protein S have been activated with self-assembled polypeptide NPs (25 nm) to produce tridimensional indigenous compounds and to produce highly particular antibodies [179]. Gold nanoparticles (AuNPs) are generally used in Nano-vaccines because by incite antigen-presenting cells and ensuring control of the release of antigen they can be used to increase the quality and effectiveness of vaccines. VLPs can be created via incubating AuNPs as a core with CoVs protein which automatically functionalizes the surface (S-AuNPs).

Table 3
Nanoparticles-based vaccination versus coronaviruses.

Platform	Antigenic component	virus	Approach and result	Ref.
AuNPs	S pro	SARS-CoV	Stimulation of IgG response	[87,89,173]
Ferritin-based NPs	MERS-CoV (RBD antigen)	MERS	Stimulation of $CD4^+$ T cells and IFN-TNF- responses	[155]
VLPs from MERS-CoVs protein	Ad5/MERS, alum	MERS	$CD8^+$ T cell response; IL-2, TNF-a, GM-CSF, and IFN-c responses; higher with Ad5/MERS	[156]
VLPs from SARS-CoV& MERS-CoVS protein (full)	alum, Matrix M1	SARS, MERS	Antibody titers is high against homologous virus virus-specific vaccine	[156,157]
RBD-displaying VLPs	Gene of RBD of S pro	MERS-CoV	Preserving the host cells from CoV infection through persuade RBD-specific immune responses Antisera	[158]
Hollow polymeric NPs	MERS-CoV (RBD antigen)	MERS-CoV	Stimulate more levels of humoral responses and IgG2a antibodies without induction of lung eosinophilic immunopathology	[156,159]
Chitosan NPs	SARS-CoV N pro	SARS	Intramuscular, Intranasal, dendritic cell targeting. Strong $CD4^+$ response. high titers of IFN-γ, IgA and IgG (including IgG1, IgG2a, IgG2b)	[160]
S-AuNPs	S pro	SARS	Tempted potent IgG responses Lung eosinophilic immunopathology, considerable recovery in vaccination potency	[42,87,174]
Lipid NPs	RNA vaccine (Phase III) ModernaTX, Inc.	SARS-CoV-2	Acts as mRNA carrier for efficient/safe transport *in vivo*	[161]
	mRNA vaccine (Phase I/II/III) BioNTech/Fosun Pharma/Pfizer	SARS-CoV-2	mRNA carrier for efficient/safe transport *in vivo*	[162–164]
	RNA vaccine (Phase I/II) Arcturus Therapeutics Ltd	SARS-CoV-2	mRNA carrier for efficient/safe transport *in vivo*	[165,166]
	mRNA vaccine (Phase III) CureVac AG	SARS-CoV-2	mRNA carrier for efficient/safe transport *in vivo*	[166–168]
Novel lipid NPs	RNA vaccine (Phase I) Chulalongkorn University	SARS-CoV-2	mRNA carrier for efficient/safe transport *in vivo*	[166,169,170]
VLNPs	Protein subunit Vaccine (Phase I/II) Novavax	SARS-CoV-2	Thermostable, with higher binding affinity toward the human ACE2 receptor, considerable neutralizing of virus infection	[171,172]

ACE: Angiotensin-converting enzyme, Ad5: Adenovirus serotype 5, AuNPs: gold nanoparticles, CD4+: Cluster of differentiation 4, CD8+: Cluster of differentiation 8, IFN: Interferon, IgA: Immunoglobulin A, IgG: Immunoglobulin G, IL-2, Interleukin-2, GM-CSF: Granulocyte/Macrophage Colony Stimulating Factor, MERS-CoV: Middle East Respiratory Syndrome Coronavirus, N pro: nucleocapsid N, NPs: nanoparticles, RBD: Receptor-binding domain, SARS-CoV: Severe acute respiratory syndrome coronavirus, S pro: Spike protein, S-AuNPs: Spherical gold nanoparticles, TNF: Tumour necrosis factor, VLPs: Virus like particles, VLNPs: Virus like nanoparticles.

S–AuNP-based vaccines which used versus other severe pneumonia-related CoVs can increase lymphatic antigen transmission and humoral and cellular immune responses compared to free antigens. Although, this vaccine prompted an antigen-dependent IgG response, it is defective in stimulating protective antibodies and limiting the infiltration of eosinophils into the lungs. Thus, an in-depth and effective study of the S-AuNPs concentration and size are needed for promising CoVs vaccines [87].

5.1.1.2. NP-based compounds for CoVs. Nanotechnology based medicine is a helpful treatment method that targets the various stages in CoV's lifecycle. Virus entry, into a host cell, is started by sticking to receptors and is followed by significant conformational changes of viral proteins. Thus, NPs are often designed to block S protein and prevent corona viral entry. Fig. 3 illustrates a number of well-known nanosystems preferred by several companies for development of their products. To the evidence indicate that AuNRs-based antiviral factors demonstrate a hopeful method for managing the infectious. Thus, Huang et al. [180] expand PIH-modified gold nanorods (AuNRs) with a poly ethylene glycol (PEG) coating, which has HR1 deterrence activity (IC50 = 1.171 μM). The three domains associated with the S2 subunit are HR1 with HR2 and fusion peptides which MERS-CoV contaminate the host cells via S2 subunit prompted membrane fusion [180]. Compared with PIH alone, PIH-modified gold nanorods Increase inhibitory activity. HR1 inhibitor can prevent membrane fusion as a result of HR1/HR2 complex (6-HB) formation and inhibit MERS-CoV infections [180]. PIH-AuNR with enhanced potential biocompatibility and biostability. Using molecular dynamics simulations, we have shown that a peptide inhibitor, which is elicitation from ACE2 creates very Promising routes for SARS-CoV-2 blockage [181]. The essential method of action of boronic acid-functionalized CQDs is interference with protein S and prevention of HCoV-229E entry, it can also simply enter cells and inhibit the virus from replicating [182].

5.1.2. Diagnosis

5.1.2.1. NPs-based diagnosis of CoVs. Common diagnostic assays for detection of SARS-CoV-2 adopt nucleic acid-based testing procedures, the most prominent of which is the RT-PCR technique [183,184]. Rapid diagnostic tests and identification for infectious diseases is the foremost method to contain epidemics, and this is difficult with common detection manner due to inaccessibility to tool, as well as the requirement for technological experience. Given the importance of prompt, sensitive, and cost-effective COVID-19 detection, nanotechnology holds enormous potential in the identification, treatment, and prevention of COVID-19, and can use NP-based electrical, mechanical, and magnetic attributes. Exact analyses need effective and sufficient isolation of RNA from samples to prevent infection or false-negative results. Table 4 provide a summary of the NPs used in the diagnostic detection of CoVs [185–190].

Magnetic NPs (MNPs) can be adopted for separation of nucleic acids. Fig. 4 represents the nanoparticle-based assays for CoVs (modified from Refs. [20,191]. For example, an investigation [189] reported successful extraction of SARS-CoV-2 RNA by means of specialized MNPs with poly (amino ester) with carboxyl groups (pcMNPs) coatin agent. These purified nucleic acids (NA), in the presence of an external magnetic field, are released from the surface of MNPs. The pcMNP-based rapid extraction of RNA molecules is possible due to the strong interaction between carboxyl groups of these nanoparticles with viral nucleic acids. In addition, silica-coated superparamagnetic NPs prepared with a probe just complement the SARS-CoV target cDNA. The functionalized superparamagnetic NPs were shown to strengthen and detach target cDNA from samples under a magnetic field [192]. Following the amplification of the isolated DNA with polymerase chain reaction (PCR), silica-coated fluorescence NPs (40 ± 5 nm) were incorporated into sandwich hybridization assessment for identification of the target cDNA [192]. AuNPs were checked for creating nano assays for two causes: SPR transfer and alteration in color and the ease of electrostatic surface-plan

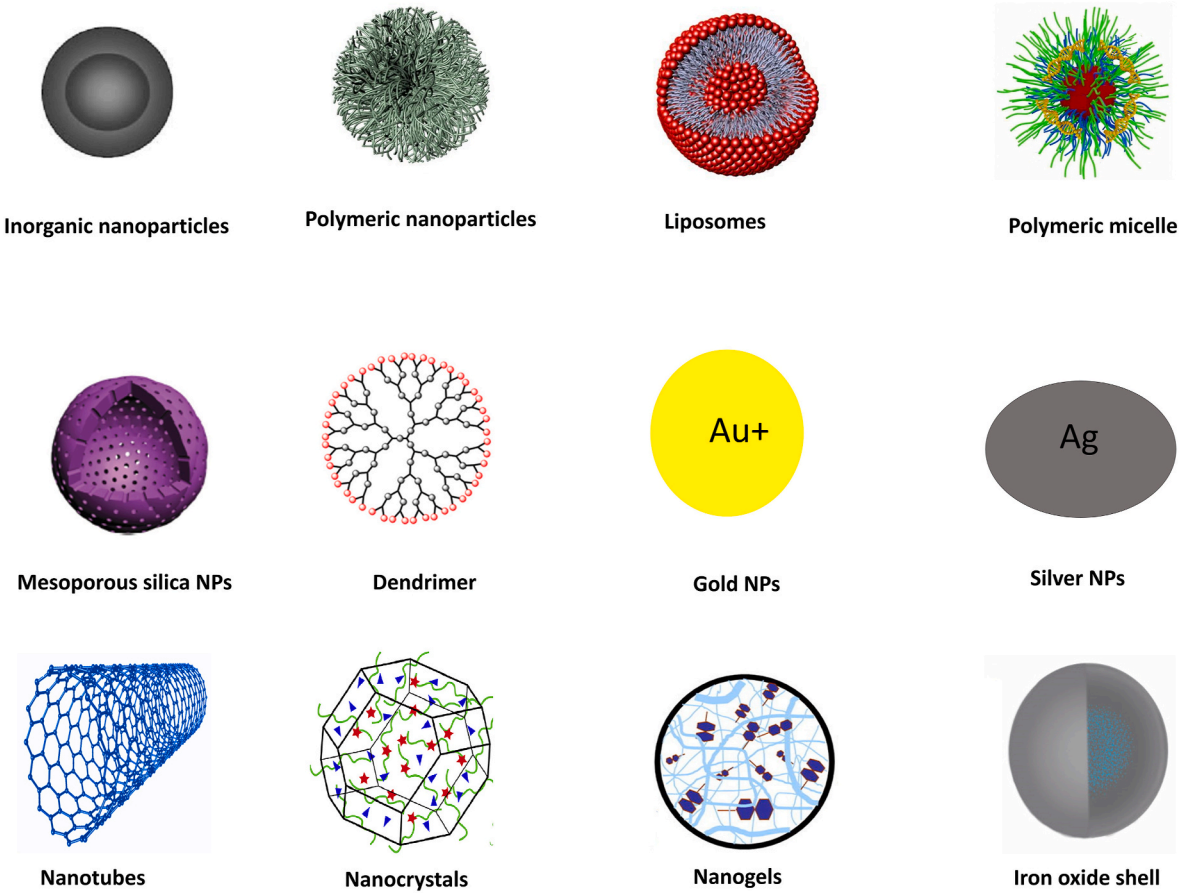

Fig. 3. Nanocarrier platforms utilized for combination drug therapeutics.

Table 4
Coronavirus diagnostics based on nanoparticles.

NP-based detection	Target	virus	Notes	size	Ref.
AuNP-based colorimetric assay	Upstream of E pro gene and ORF 1a	MERS-CoV	Visual detection Inexpensive, fast (10 min) LOD: 1 pmol/μl	-	[185]
SFNPs	Target cDNA	SARS-CoV-2	Quick technique, High specificity and sensitivity	-	[186]
AuNPs	viral RNA	SARS	association of AuNPs via the formation of dsDNA,	13 nm	[185,187, 188,190]
	viral cDNA Upstream of envelope protein gene and ORF-1A	MERS, MTB MERS-CoV	cDNAs inhibiting aggregation of AgNPs prompted via acpcPNA, high quality detection, cost-effective, fast (10 min), LOD: 1 pmol/μl	19 nm	
	N/A	SARS-CoV-2	Detection kit; COVID-19 point-of-need diagnostic test (Mologic Ltd)		
	N/A	SARS-CoV-2	Detection kit; COVID-19 Rapid Test Cassette (SureScreen Diagnostics Ltd)		
	N/A	SARS-CoV-2	Detection kit; COVID-19 Rapid POC high sensitivity and reliability of visual detection, applied in point-of-care tests (NanoComposix)	–	
AuNRs	N/A	SARS-CoV-2	Detection kit; Lateral flow (Sona Nanotech, Inc.)		[190]
MNPs	Viral RNA	SARS-CoV-2	One-step, easy, sensitive, great paramagnetic characteristic, numerous purity, and fecundity, no toxic reagents	-	[189]

acpcPNA: Anthraquinone-labeled pyrrolidinyl peptide nucleic acid, AgNPs, Silver nanoparticles, AuNPs: gold nanoparticles, AuNRs: Au NanoRods, Cdna: Complementary DNA, dsDNA: double strand DNA, E pro: Envelope protein, LOD: Limit of Detection, MNPs: Magnetic Nanoparticles, N/A: not applicable, MERS-CoV: Middle East Respiratory Syndrome Coronavirus, NPs: nanoparticles, ORF: Open Reading Frame, POC: Point-of-care, SARS-CoV: Severe acute respiratory syndrome coronavirus, SFNPs: Silk fibroin nanoparticles.

with various moieties, for instance, antigens and antibodies [193,194]. AuNPs have been extensively used in colorimetric hybridization assays, the disulfide bond-based colorimetric assay designed by Kim et al. is a good example of which [185]. The specific thiolated probes form the complementary single-stranded deoxyribonucleic acid (ssDNA) with the target sites of MERS-CoV and, through continuous disulfide bond formation, make a disulfide-induced long self-assembled hybrid complex [195]. This structure protects citrate ion-headed AuNPs from the salt-persuaded assembly. Nonetheless, in the absence of a target gene, this protection will no longer exist, resulting in the accumulation of AuNPs. The same dependable colorimetric hybridization method of SARS-CoV was planed via particular hybridization of ssDNA-AuNPs and target DNA sequence, leading to Accumulation and color alteration (Fig. 4A) [187]. AuNPs based elementary electrochemical hybridization methods have been described with a gene-sensor, which includes thiolated-DNA comb immobilized on AuNPs carbon terminal to hybridize biotinylated target DNA of SARS-CoV (Fig. 4B) [196]. Star-shaped chiroplasmonic AuNPs (CAuNPs) based on chiral gold nanohybrids conjugated with quantum dots (QDs) were recently used for detection of specific viral strains, including CoVs [196,197]. In this

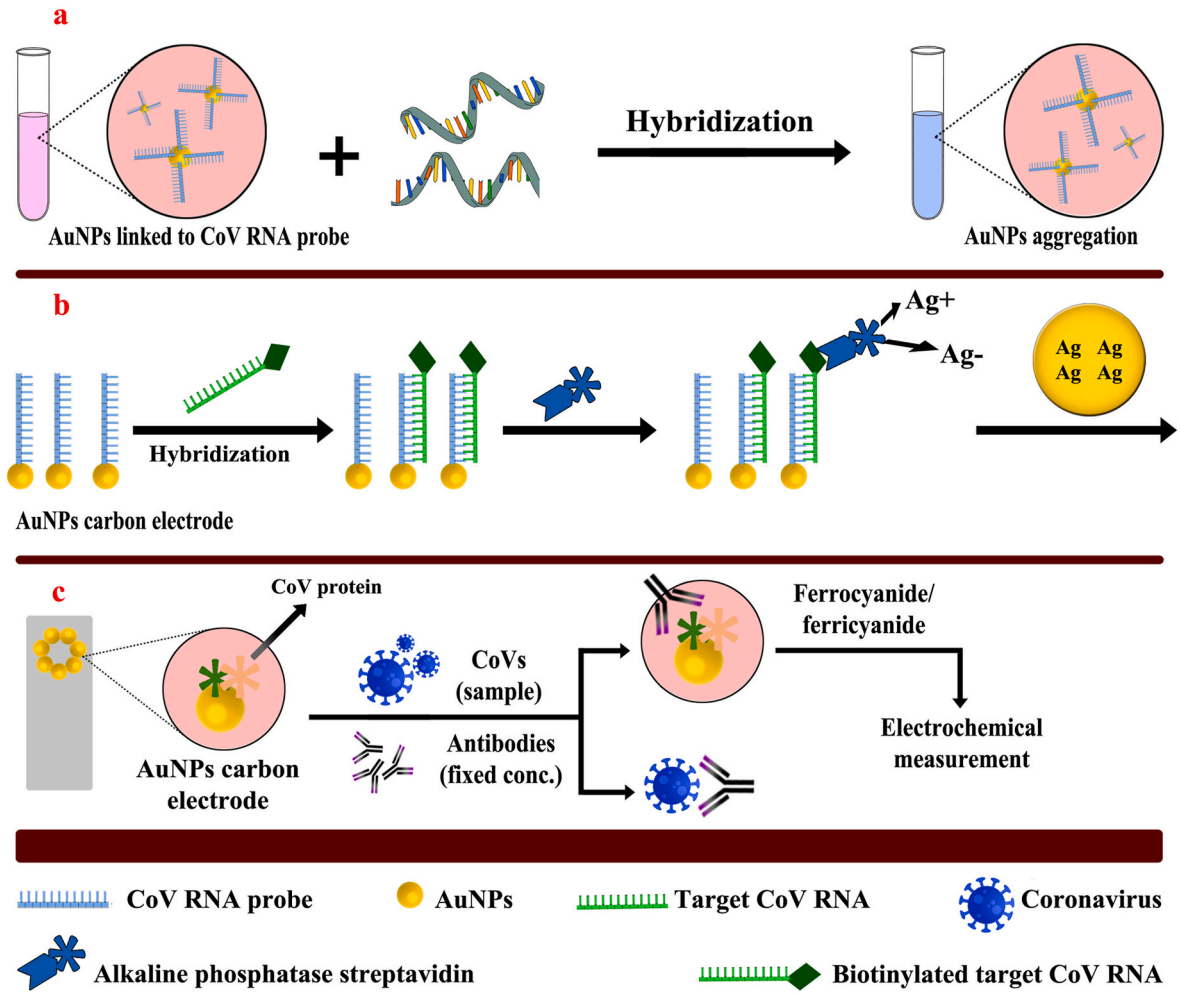

Fig. 4. Nanoparticle-based assays for CoVs. a) Colorimetric hybridization assays, b) Electrochemical hybridization assays, c) electrochemical immunosensor assay (modified from Refs. [20,191]).

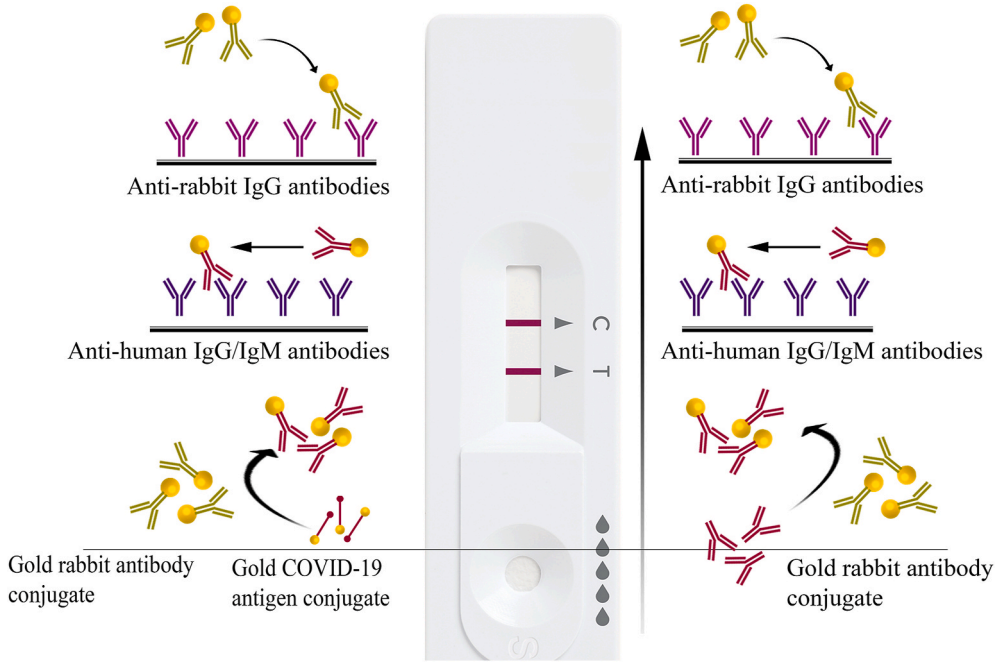

Fig. 5. Emerging tests for SARS-CoV-2 detection. C: Control well; G: Conjugate pad; S: Sample well; T: Testing well (modified from Ref. [20]).

procedure, any of CAuNPs and QDs were electrostatically conjugated to two various target virus targeted antibodies. In the attendance of the target virus, a nano-sandwich configuration is generated, bringing about superior plasmonicresonance coupling with QD beta particles [197]. AuNPs can also be used for identification of CoVs-specific antibodies [198] through an electromagnetic immunosensor assay containing a chip and a C-terminal that include a variety of AuNPs to recognize CoV-special antibodies [199]. This particular approach was taken for detection of antibody-immobilized MERS-CoV proteins across AuNPs anodes, leading to emulation of free viruses in the prototype with immobilized MERS-CoV protein [200]. A ferrocyanide probe was used for electrochemical measurement. This chip was used for multiplexed identification together through velocity terminals on the same chip, with every electrode attached to distinct viral antigens [201]. According to recent investigations, NP-based flow detection strips are perhaps are sufficiently augmented to speed up detection and lift the time-consuming prerequisite to send samples to labs (Fig. 4C). NP-based flow detection strips have been confirmed to speed up SARS-CoV-2 detection (Fig. 5. Modified from Ref. [20]). Vertical stream (VF) recognition was formerly performed to visually detect the N protein gene of MERS-CoV by means of reverse transcription loop-mediated isothermal amplification procedure (RT-LAMP-VF) [202]. MERS-CoV RNA was amplified by RT-LAMP and bound to streptavidin-AuNP conjugates via fluorescein isothiocyanate (FITC) and biotin. This FITC-labeled complex was procured via an anti-FITC antibody immobilized a strip, producing a well-known color line [202]. This FITC-labeled complex is prepared via immobilized anti-FITC antitoxin on a strip and delivering a color line in 10 min [203].

6. Challenges & limitations

Nanomedicine propose in the field of vaccination, innovative steps to detects, molecular diagnosis, and Countless opportunities against coronaviral infections. However, notwithstanding of interferences, it this yet very Controversial to securely translate NPs from lab novation to the infirmary. The main challenge and obstacles in various levels, from beginning to realize the viruses genomic and proteomic compound to clinical translation. Whereas SARS-CoV-2 genomic and proteomic studies were rapidly recognition to help scheme and expand NP-based Performance against the virus, the number of multiple mutations and genetic diversity more still remains an obstacle for successful treatment. In the case of NP-based RBD vaccines, RBD is a changed segment in the CoV genome [204]. In addition, it is not yet known which amino acids in the S protein of SARS-CoV-2 might induce hepatotoxicity [46,175]. So, full-length S protein may encounter immune problems when used as an antigen [46]. Viruses are simply targeted without influence host cells and Viruses do not have their own metabolism and need host cells to produce new products. Therefore, we can study the weaknesses of the virus and the vulnerability of infected cells to allow us to scheme solutions for particular ligands that can utilize the functional NPs of the virus surface and life cycle. SARS-CoV-2 is emerging as a coronavirus, which first appeared in China in late 2019 and causes a respiratory disease called “Coronavirus 2019 (COVID-19)". The virus does not have enough animal models. Which is needed for clinical trials. While the behavior of each virus is different, they all have the same goal, and the host response to SARS-CoV-2 is needed to better understand the illness pathogenesis. In this regard, it is necessary to produce new nano-drugs with higher quality and safety because this virus has a great spread due to the disappointing slow production of drugs across the globe. In this regard, it is necessary to produce new nano-drugs with higher quality and safety because this virus has more and more spread due to the disappointing slow production of drugs around the world.

7. Conclusion & future perspective

Coronavirus the COVID-19 virus is a major global crisis and the greatest challenge we have faced since World War II [205]. The Corona virus epidemic (COVID-19) 2019 is a major disaster that has also disrupted health, human casualties and many more. Despite many efforts by all countries of the world with many studies and also with the beginning of many clinical experiments, but no treatment has yet been proven to control the coronavirus. As well as an important role of Nano medicine to the novel SARS-CoV-2, this study highlights various customary treatment methods. Replacement of drugs, for example remdesivir and chloroquine, is a quick method to Achieving secure treatments and the relevant experimental studies have unfolded the Successful evidence against COVID-19. Furthermore, one of the scientific solutions used to decrease viral load is nano-metal vaccines, which are mostly basis on the antigenic attributes of protein S. However, a large number of studies provide evidence to support NP-based diagnostic and therapeutic tools, which have been reported for SARS-CoV-2. Therefore, it is necessary for all researchers from all over the world to expand their research in the arena of NP-based therapy. The important thing is that in order to prevent and treat the correct COVID-19 or any viral pandemic, we must have enough information about the virus’s virulence and transmission. This will enable us to identify various encoded unstructured proteins, enzymes, and functional mechanisms, and most importantly, to understand the transmission of the virus between species. Therefore, we can identify and targeted therapeutic goals using functional level NPs. Therefore, if we have sufficient and appropriate information about the virus life cycle and host answer, it will allow us to start a clinical trial to create an efficient Nano-vaccine. According to studies by researchers conducted by scientists around the world, we expect to be able to develop a universal NP-based vaccine that has effective immunogenicity in the near future. Microfluidics has the advantages of fast detection and portability Therefore, our prediction is that they can perform a significant part in the diagnosis of CoV [206].

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] Y.-Z. Zhang, E.C. Holmes, A genomic perspective on the origin and emergence of SARS-CoV-2, Cell 181 (2020) 223–227.
[2] J.R. Koo, A.R. Cook, M. Park, Y. Sun, H. Sun, J.T. Lim, C. Tam, B.L. Dickens, Interventions to mitigate early spread of SARS-CoV-2 in Singapore: a modelling study, Lancet Infect. Dis. 20 (2020) 678–688.
[3] T.G. Ksiazek, D. Erdman, C.S. Goldsmith, S.R. Zaki, T. Peret, S. Emery, S. Tong, C. Urbani, J.A. Comer, W. Lim, A novel coronavirus associated with severe acute respiratory syndrome, N. Engl. J. Med. 348 (2003) 1953–1966.
[4] E. Mahase, Coronavirus: Covid-19 Has Killed More People than SARS and MERS Combined, Despite Lower Case Fatality Rate, British Medical Journal Publishing Group, 2020.
[5] A. Taghizadieh, H. Mikaeili, M. Ahmadi, H. Valizadeh, Acute kidney injury in pregnant women following SARS-CoV-2 infection: a case report from Iran, Respiratory medicine case reports 30 (2020) 101090.
[6] R. Sheervalilou, M. Shirvaliloo, N. Dadashzadeh, S. Shirvalilou, O. Shahraki, Y. Pilehvar-Soltanahmadi, H. Ghaznavi, S. Khoei, Z. Nazarlou, COVID-19 under spotlight: a close look at the origin, transmission, diagnosis, and treatment of the 2019-nCoV disease, J. Cell. Physiol. 235 (2020) 8873–8924.
[7] M. Ghaebi, A. Osali, H. Valizadeh, L. Roshangar, M. Ahmadi, Vaccine development and therapeutic design for 2019-nCoV/SARS-CoV-2: challenges and chances, J. Cell. Physiol. 235 (2020) 9098–9109.
[8] R. Sheervalilou, M. Shirvaliloo, S. Sargazi, S. Shirvalilou, O. Shahraki, Y. Pilehvar-Soltanahmadi, A. Sarhadi, Z. Nazarlou, H. Ghaznavi, S. Khoei, Application of nanobiotechnology for early diagnosis of SARS-CoV-2 infection in the COVID-19 pandemic, Appl. Microbiol. Biotechnol. (2021) 1–10.

[9] R. Sheervalilou, M. Shirvaliloo, S. Sargazi, H. Ghaznavi, Recent advances in iron oxide nanoparticles for brain cancer theranostics: from in vitro to clinical applications, Expet Opin. Drug Deliv. (2021) 1–29.
[10] S. Shirvalilou, S. Khoei, S. Khoee, S. Emamgholizadeh Minaei, Magnetic Graphene Oxide Nanocarrier as a drug delivery vehicle for MRI monitored magnetic targeting of rat brain tumors, Iranian Journal of Medical Physics 15 (2018), 134-134.
[11] K. Nejati, M. Dadashpour, T. Gharibi, H. Mellatyar, A. Akbarzadeh, Biomedical applications of functionalized gold nanoparticles: a review, J. Cluster Sci. (2021) 1–16.
[12] A. Sadeghi, S. Tahmasebi, A. Mahmood, M. Kuznetsova, H. Valizadeh, A. Taghizadieh, M. Nazemiyeh, L. Aghebati-Maleki, F. Jadidi-Niaragh, S. Abbaspour-Aghdam, Th17 and Treg cells function in SARS-CoV2 patients compared with healthy controls, J. Cell. Physiol. 236 (2021) 2829–2839.
[13] Y. Saylan, A. Denizli, Virus Detection Using Nanosensors, Nanosensors for Smart Cities, Elsevier, 2020, pp. 501–511.
[14] M. Soler, C.S. Huertas, L.M. Lechuga, Label-free plasmonic biosensors for point-of-care diagnostics: a review, Expert Rev. Mol. Diagn. 19 (2019) 71–81.
[15] H. Valizadeh, S. Abdolmohammadi-Vahid, S. Danshina, M.Z. Gencer, A. Ammari, A. Sadeghi, L. Roshangar, S. Aslani, A. Esmaeilzadeh, M. Ghaebi, Nano-curcumin therapy, a promising method in modulating inflammatory cytokines in COVID-19 patients, Int. Immunopharm. 89 (2020) 107088.
[16] B.S. Chhikara, B. Rathi, J. Singh, F. Poonam, Corona virus SARS-CoV-2 disease COVID-19: infection, prevention and clinical advances of the prospective chemical drug therapeutics, Chem. Biol. Lett. 7 (2020) 63–72.
[17] G. Widjaja, A.T. Jalil, H.S. Rahman, W.K. Abdelbasset, D.O. Bokov, W. Suksatan, M. Ghaebi, F. Marofi, J.G. Navashenaq, F. Jadidi-Niaragh, Humoral Immune Mechanisms Involved in Protective and Pathological Immunity during COVID-19, Human Immunology, 2021.
[18] A. Esmaeilzadeh, S. Rostami, P.M. Yeganeh, S. Tahmasebi, M. Ahmadi, Recent advances in antibody-based immunotherapy strategies for COVID-19, J. Cell. Biochem. 122 (2021) 1389–1412.
[19] L.-J. Xiong, M.-Y. Zhou, X.-Q. He, Y. Wu, X.-L. Xie, The role of human coronavirus infection in pediatric acute gastroenteritis, Pediatr. Infect. Dis. J. 39 (2020) 645–649.
[20] N.H. Abd Ellah, S.F. Gad, K. Muhammad, G.E. Batiha, H.F. Hetta, Nanomedicine as a promising approach for diagnosis, treatment and prophylaxis against COVID-19, Nanomedicine 15 (2020) 2085–2102.
[21] J.K. Malik, A. Kumar, H. Soni, Epidemiology of novel corona virus (Covid-19): a review, J. Clin. Pharmaco Epidemiol. Res. (2020) 5–13.
[22] S. Chauhan, Comprehensive review of coronavirus disease 2019 (COVID-19), Biomed. J. 43 (4) (2020) 334–340.
[23] A. Zeidler, T.M. Karpinski, SARS-CoV, MERS-CoV, SARS-CoV-2 comparison of three emerging Coronaviruses, Jundishapur J. Microbiol. 13 (2020).
[24] S. Tahmasebi, B.Q. Saeed, E. Temirgalieva, A.V. Yumashev, M.A. El-Esawi, J. G. Navashenaq, H. Valizadeh, A. Sadeghi, S. Aslani, M. Yousefi, Nanocurcumin improves Treg cell responses in patients with mild and severe SARS-CoV2, Life Sci. 276 (2021) 119437.
[25] S. Tahmasebi, M.A. El-Esawi, Z.H. Mahmoud, A. Timoshin, H. Valizadeh, L. Roshangar, M. Varshoch, A. Vaez, S. Aslani, J.G. Navashenaq, Immunomodulatory effects of nanocurcumin on Th17 cell responses in mild and severe COVID-19 patients, J. Cell. Physiol. 236 (2021) 5325–5338.
[26] M. Hassanpour, J. Rezaie, M. Nouri, Y. Panahi, The role of extracellular vesicles in COVID-19 virus infection, Infect. Genet. Evol. (2020) 104422.
[27] P. Gentile, A. Sterodimas, J. Pizzicannella, C. Calabrese, S. Garcovich, Research progress on mesenchymal stem cells (MSCs), adipose-derived mesenchymal stem cells (AD-MSCs), drugs, and vaccines in inhibiting COVID-19 disease, Aging and disease 11 (2020) 1191.
[28] M. McCallum, A.C. Walls, J.E. Bowen, D. Corti, D. Veesler, Structure-guided covalent stabilization of coronavirus spike glycoprotein trimers in the closed conformation, Nat. Struct. Mol. Biol. 27 (2020) 942–949.
[29] C.-H. Kim, SARS-CoV-2 evolutionary adaptation toward host entry and recognition of receptor O-Acetyl sialylation in virus–host interaction, Int. J. Mol. Sci. 21 (2020) 4549.
[30] L. Shu, C. Niu, R. Li, T. Huang, Y. Wang, M. Huang, N. Ji, Y. Zheng, X. Chen, L. Shi, Treatment of severe COVID-19 with human umbilical cord mesenchymal stem cells, Stem Cell Res. Ther. 11 (2020) 1–11.
[31] K. Dhama, K. Sharun, R. Tiwari, M. Dadar, Y.S. Malik, K.P. Singh, W. Chaicumpa, COVID-19, an emerging coronavirus infection: advances and prospects in designing and developing vaccines, immunotherapeutics, and therapeutics, Hum. Vaccines Immunother. 16 (2020) 1232–1238.
[32] D. Roy, S. Tripathy, S.K. Kar, N. Sharma, S.K. Verma, V. Kaushal, Study of knowledge, attitude, anxiety & perceived mental healthcare need in Indian population during COVID-19 pandemic, Asian journal of psychiatry 51 (2020) 102083.
[33] S. Chen, H. Li, G. Yuan, R. Guan, T. Li, Complete genome sequence of a novel rhabdo-like virus from the Chinese black cutworm Agrotis ipsilon (Lepidoptera: noctuidae), Arch. Virol. 165 (2020) 989–991.
[34] S.A. Azizi, S.-A. Azizi, Neurological injuries in COVID-19 patients: direct viral invasion or a bystander injury after infection of epithelial/endothelial cells, J. Neurovirol. (2020) 1–11.
[35] M. Aruru, H.-A. Truong, S. Clark, Pharmacy Emergency Preparedness and Response (PEPR): a proposed framework for expanding pharmacy professionals' roles and contributions to emergency preparedness and response during the COVID-19 pandemic and beyond, Res. Soc. Adm. Pharm. 17 (2020) 1967–1977.
[36] S.E. Oliver, J.W. Gargano, M. Marin, M. Wallace, K.G. Curran, M. Chamberland, N. McClung, D. Campos-Outcalt, R.L. Morgan, S. Mbaeyi, The advisory committee on immunization practices' interim recommendation for use of pfizer-BioNTech COVID-19 vaccine—United States, December 2020, MMWR (Morb. Mortal. Wkly. Rep.) 69 (2020) 1922.
[37] R.L. Graham, D.J. Deming, M.E. Deming, B.L. Yount, R.S. Baric, Evaluation of a recombination-resistant coronavirus as a broadly applicable, rapidly implementable vaccine platform, Commun. Biol. 1 (2018) 1–10.
[38] V.D. Menachery, L.E. Gralinski, H.D. Mitchell, K.H. Dinnon III, S.R. Leist, B. L. Yount Jr., E.T. McAnarney, R.L. Graham, K.M. Waters, R.S. Baric, Combination attenuation offers strategy for live attenuated coronavirus vaccines, J. Virol. 92 (2018) e00710-00718.
[39] J.M. Jimenez-Guardeño, J.A. Regla-Nava, J.L. Nieto-Torres, M.L. DeDiego, C. Castaño-Rodriguez, R. Fernandez-Delgado, S. Perlman, L. Enjuanes, Identification of the mechanisms causing reversion to virulence in an attenuated SARS-CoV for the design of a genetically stable vaccine, PLoS Pathog. 11 (2015), e1005215.
[40] M. Spruth, O. Kistner, H. Savidis-Dacho, E. Hitter, B. Crowe, M. Gerencer, P. Brühl, L. Grillberger, M. Reiter, C. Tauer, A double-inactivated whole virus candidate SARS coronavirus vaccine stimulates neutralising and protective antibody responses, Vaccine 24 (2006) 652–661.
[41] E.J. Anderson, N.G. Rouphael, A.T. Widge, L.A. Jackson, P.C. Roberts, M. Makhene, J.D. Chappell, M.R. Denison, L.J. Stevens, A.J. Pruijssers, Safety and immunogenicity of SARS-CoV-2 mRNA-1273 vaccine in older adults, N. Engl. J. Med. 383 (2020) 2427–2438.
[42] H.-W. Chen, C.-Y. Huang, S.-Y. Lin, Z.-S. Fang, C.-H. Hsu, J.-C. Lin, Y.-I. Chen, B.-Y. Yao, C.-M.J. Hu, Synthetic virus-like particles prepared via protein corona formation enable effective vaccination in an avian model of coronavirus infection, Biomaterials 106 (2016) 111–118.
[43] J. Lu, G. Lu, S. Tan, J. Xia, H. Xiong, X. Yu, Q. Qi, X. Yu, L. Li, H. Yu, A COVID-19 mRNA vaccine encoding SARS-CoV-2 virus-like particles induces a strong antiviral-like immune response in mice, Cell Res. 30 (2020) 936–939.
[44] T.W. Kim, J.H. Lee, C.-F. Hung, S. Peng, R. Roden, M.-C. Wang, R. Viscidi, Y.-C. Tsai, L. He, P.-J. Chen, Generation and characterization of DNA vaccines targeting the nucleocapsid protein of severe acute respiratory syndrome coronavirus, J. Virol. 78 (2004) 4638–4645.
[45] S.-F. Wang, S.-P. Tseng, C.-H. Yen, J.-Y. Yang, C.-H. Tsao, C.-W. Shen, K.-H. Chen, F.-T. Liu, W.-T. Liu, Y.-M.A. Chen, Antibody-dependent SARS coronavirus infection is mediated by antibodies against spike proteins, Biochem. Biophys. Res. Commun. 451 (2014) 208–214.
[46] J. Zhang, H. Zeng, J. Gu, H. Li, L. Zheng, Q. Zou, Progress and prospects on vaccine development against SARS-CoV-2, Vaccines 8 (2020) 153.
[47] A.N. Zakhartchouk, C. Sharon, M. Satkunarajah, T. Auperin, S. Viswanathan, G. Mutwiri, M. Petric, R.H. See, R.C. Brunham, B.B. Finlay, Immunogenicity of a receptor-binding domain of SARS coronavirus spike protein in mice: implications for a subunit vaccine, Vaccine 25 (2007) 136–143.
[48] P. Kalita, A.K. Padhi, K.Y. Zhang, T. Tripathi, Design of a peptide-based subunit vaccine against novel coronavirus SARS-CoV-2, Microb. Pathog. 145 (2020) 104236.
[49] U.J. Buchholz, A. Bukreyev, L. Yang, E.W. Lamirande, B.R. Murphy, K. Subbarao, P.L. Collins, Contributions of the structural proteins of severe acute respiratory syndrome coronavirus to protective immunity, Proc. Natl. Acad. Sci. Unit. States Am. 101 (2004) 9804–9809.
[50] Y. Takashima, M. Osaki, Y. Ishimaru, H. Yamaguchi, A. Harada, Artificial molecular clamp: a novel device for synthetic polymerases, Angew. Chem. Int. Ed. 50 (2011) 7524–7528.
[51] D. Dynavax, in: D.T. Corporation (Ed.), Clover Biopharmaceuticals Announce Research Collaboration to Evaluate Coronavirus (COVID-19) Vaccine Candidate with CpG 1018 Adjuvant, 2020.
[52] E. Kim, G. Erdos, S. Huang, T.W. Kenniston, S.C. Balmert, C.D. Carey, V.S. Raj, M. W. Epperly, W.B. Klimstra, B.L. Haagmans, Microneedle array delivered recombinant coronavirus vaccines: immunogenicity and rapid translational development, EBioMedicine 55 (2020) 102743.
[53] S.A. Azam, L. Myers, B.K. Fields, N.L. Demirjian, D. Patel, E. Roberge, A. Gholamrezanezhad, S. Reddy, Coronavirus Disease 2019 (COVID-19) Pandemic: Review of Guidelines for Resuming Non-urgent Imaging and Procedures in Radiology during Phase II, Clinical imaging, 2020.
[54] F. Ghasemi, T.M. Tessier, S.F. Gameiro, A.H. Maciver, M.J. Cecchini, J. S. Mymryk, High MHC-II expression in Epstein–Barr virus-associated gastric cancers suggests that tumor cells serve an important role in antigen presentation, Sci. Rep. 10 (2020) 1–16.
[55] Q. Fang, C. Zhou, K.S. Nandakumar, Molecular and cellular pathways contributing to joint damage in rheumatoid arthritis, Mediat. Inflamm. (2020) 2020.
[56] G. Forlani, M. Shallak, F. Celesti, R.S. Accolla, Unveiling the hidden treasury: CIITA-driven MHC class II expression in tumor cells to dig up the relevant repertoire of tumor antigens for optimal stimulation of tumor specific CD4+ T helper cells, Cancers 12 (2020) 3181.
[57] G. Criner, M. Mobasher, C. Hill, S. Hu, S. Mahabhashyam, J. Brody, T. Marron, S. Willingham, R. Miller, 325 Immunotherapy with B Cell Activating Antibody CPI-006 in Patients (Pts) with Mild to Moderate COVID-19 Stimulates Anti-SARS-CoV-2 Antibody Response, Memory B Cells and Memory T Effector Cells, BMJ Specialist Journals, 2020.
[58] S. Eissa, M. Zourob, Development of a low-cost cotton-tipped electrochemical immunosensor for the detection of SARS-CoV-2, Anal. Chem. (2020).

[59] J.S. Bhatti, G.K. Bhatti, N. Khullar, A.P. Reddy, P.H. Reddy, Therapeutic strategies in the development of anti-viral drugs and vaccines against SARS-CoV-2 infection, Mol. Neurobiol. 57 (2020) 4856–4877.
[60] W.S. Lee, A.K. Wheatley, S.J. Kent, B.J. DeKosky, Antibody-dependent enhancement and SARS-CoV-2 vaccines and therapies, Nat. Microbiol. 5 (2020) 1185–1191.
[61] Y. Sefidi-Heris, A. Jahangiri, A. Mokhtarzadeh, M.-A. Shahbazi, S. Khalili, B. Baradaran, J. Mosafer, A. Baghbanzadeh, M. Hejazi, M. Hashemzaei, Recent Progress in the Design of DNA Vaccines against Tuberculosis, Drug Discovery Today, 2020.
[62] Z.A. Wainberg, H.S. Hochster, E.J. Kim, B. George, A. Kaylan, E.G. Chiorean, D. M. Waterhouse, M. Guiterrez, A. Parikh, R. Jain, Open-label, phase I study of nivolumab combined with nab-paclitaxel plus gemcitabine in advanced pancreatic cancer, Clin. Cancer Res. 26 (2020) 4814–4822.
[63] R. Shetty, A. Ghosh, S.G. Honavar, P. Khamar, S. Sethu, Therapeutic opportunities to manage COVID-19/SARS-CoV-2 infection: present and future, Indian J. Ophthalmol. 68 (2020) 693.
[64] P. Pandey, J.S. Rane, A. Chatterjee, A. Kumar, R. Khan, A. Prakash, S. Ray, Targeting SARS-CoV-2 spike protein of COVID-19 with naturally occurring phytochemicals: an in silico study for drug development, J. Biomol. Struct. Dyn. (2020) 1–11.
[65] T.R. Smith, A. Patel, S. Ramos, D. Elwood, X. Zhu, J. Yan, E.N. Gary, S.N. Walker, K. Schultheis, M. Purwar, Immunogenicity of a DNA vaccine candidate for COVID-19, Nat. Commun. 11 (2020) 1–13.
[66] F.-C. Zhu, Y.-H. Li, X.-H. Guan, L.-H. Hou, W.-J. Wang, J.-X. Li, S.-P. Wu, B.-S. Wang, Z. Wang, L. Wang, Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial, Lancet 395 (2020) 1845–1854.
[67] S. Shatzmiller, R. Krieger, mRNA Technologies for the Combat with COVID-19.
[68] T.J. Ripperger, J.L. Uhrlaub, M. Watanabe, R. Wong, Y. Castaneda, H.A. Pizzato, M.R. Thompson, C. Bradshaw, C.C. Weinkauf, C. Bime, Orthogonal SARS-CoV-2 serological assays enable surveillance of low-prevalence communities and reveal durable humoral immunity, Immunity 53 (2020) 925–933, e924.
[69] K.L. Flanagan, E. Best, N.W. Crawford, M. Giles, A. Koirala, K. Macartney, F. Russell, B.W. Teh, S.C. Wen, Progress and pitfalls in the quest for effective SARS-CoV-2 (COVID-19) vaccines, Front. Immunol. 11 (2020) 2410.
[70] F. Wang, R.M. Kream, G.B. Stefano, An evidence based perspective on mRNA-SARS-CoV-2 vaccine development, Med. Sci. Mon. Int. Med. J. Exp. Clin. Res.: Int. Med. J. Exp. Clin. Res. 26 (2020) e924700–924701.
[71] F. Oroojalian, A. Haghbin, B. Baradaran, N. Hemat, M.-A. Shahbazi, H.B. Baghi, A. Mokhtarzadeh, M.R. Hamblin, Novel insights into the treatment of SARS-CoV-2 infection: an overview of current clinical trials, Int. J. Biol. Macromol. (2020).
[72] R.L. Graham, E.F. Donaldson, R.S. Baric, A decade after SARS: strategies for controlling emerging coronaviruses, Nat. Rev. Microbiol. 11 (2013) 836–848.
[73] N.M. Okba, V.S. Raj, B.L. Haagmans, Middle East respiratory syndrome coronavirus vaccines: current status and novel approaches, Current opinion in virology 23 (2017) 49–58.
[74] S. Fukushi, A. Fukuma, T. Kurosu, S. Watanabe, M. Shimojima, K. Shirato, N. Iwata-Yoshikawa, N. Nagata, K. Ohnishi, M. Ato, Characterization of novel monoclonal antibodies against the MERS-coronavirus spike protein and their application in species-independent antibody detection by competitive ELISA, J. Virol Methods 251 (2018) 22–29.
[75] A. Fukuma, H. Tani, S. Taniguchi, M. Shimojima, M. Saijo, S. Fukushi, Inability of rat DPP4 to allow MERS-CoV infection revealed by using a VSV pseudotype bearing truncated MERS-CoV spike protein, Arch. Virol. 160 (2015) 2293–2300.
[76] Y. Chen, S. Lu, H. Jia, Y. Deng, J. Zhou, B. Huang, Y. Yu, J. Lan, W. Wang, Y. Lou, A novel neutralizing monoclonal antibody targeting the N-terminal domain of the MERS-CoV spike protein, Emerg. Microb. Infect. 6 (2017) 1–7.
[77] L. Jiaming, Y. Yanfeng, D. Yao, H. Yawei, B. Linlin, H. Baoying, Y. Jinghua, G. F. Gao, Q. Chuan, T. Wenjie, The recombinant N-terminal domain of spike proteins is a potential vaccine against Middle East respiratory syndrome coronavirus (MERS-CoV) infection, Vaccine 35 (2017) 10–18.
[78] J. Sui, W. Li, A. Murakami, A. Tamin, L.J. Matthews, S.K. Wong, M.J. Moore, A.S. C. Tallarico, M. Olurinde, H. Choe, Potent neutralization of severe acute respiratory syndrome (SARS) coronavirus by a human mAb to S1 protein that blocks receptor association, Proc. Natl. Acad. Sci. Unit. States Am. 101 (2004) 2536–2541.
[79] L. Du, Y. He, Y. Zhou, S. Liu, B.-J. Zheng, S. Jiang, The spike protein of SARS-CoV—a target for vaccine and therapeutic development, Nat. Rev. Microbiol. 7 (2009) 226–236.
[80] H.O. Besedovsky, A. del Rey, Immune-neuro-endocrine interactions: facts and hypotheses, Endocr. Rev. 17 (1996) 64–102.
[81] S.S. Bappy, S. Sultana, J. Adhikari, S. Mahmud, M.A. Khan, K.K. Kibria, M. M. Rahman, A.Z. Shibly, Extensive Immunoinformatics study for the prediction of novel peptide-based epitope vaccine with docking confirmation against Envelope protein of Chikungunya virus: a Computational Biology Approach, J. Biomol. Struct. Dyn. (2020) 1–16.
[82] B.E. Gilbert, N. Patel, H. Lu, Y. Liu, M. Guebre-Xabier, P.A. Piedra, G. Glenn, L. Ellingsworth, G. Smith, Respiratory syncytial virus fusion nanoparticle vaccine immune responses target multiple neutralizing epitopes that contribute to protection against wild-type and palivizumab-resistant mutant virus challenge, Vaccine 36 (2018) 8069–8078.
[83] S.F. Ahmed, A.A. Quadeer, M.R. McKay, Preliminary identification of potential vaccine targets for the COVID-19 coronavirus (SARS-CoV-2) based on SARS-CoV immunological studies, Viruses 12 (2020) 254.
[84] B.W. Neuman, G. Kiss, A.H. Kunding, D. Bhella, M.F. Baksh, S. Connelly, B. Droese, J.P. Klaus, S. Makino, S.G. Sawicki, A structural analysis of M protein in coronavirus assembly and morphology, J. Struct. Biol. 174 (2011) 11–22.
[85] J. Liu, Y. Sun, J. Qi, F. Chu, H. Wu, F. Gao, T. Li, J. Yan, G.F. Gao, The membrane protein of severe acute respiratory syndrome coronavirus acts as a dominant immunogen revealed by a clustering region of novel functionally and structurally defined cytotoxic T-lymphocyte epitopes, J. Infect. Dis. 202 (2010) 1171–1180.
[86] M.V. Khodoun, R. Strait, L. Armstrong, N. Yanase, F.D. Finkelman, Identification of markers that distinguish IgE-from IgG-mediated anaphylaxis, Proc. Natl. Acad. Sci. Unit. States Am. 108 (2011) 12413–12418.
[87] H. Sekimukai, N. Iwata-Yoshikawa, S. Fukushi, H. Tani, M. Kataoka, T. Suzuki, H. Hasegawa, K. Niikura, K. Arai, N. Nagata, Gold nanoparticle-adjuvanted S protein induces a strong antigen-specific IgG response against severe acute respiratory syndrome-related coronavirus infection, but fails to induce protective antibodies and limit eosinophilic infiltration in lungs, Microbiol. Immunol. 64 (2020) 33–51.
[88] H. Hofmann, K. Hattermann, A. Marzi, T. Gramberg, M. Geier, M. Krumbiegel, S. Kuate, K. Überla, M. Niedrig, S. Pöhlmann, S protein of severe acute respiratory syndrome-associated coronavirus mediates entry into hepatoma cell lines and is targeted by neutralizing antibodies in infected patients, J. Virol. 78 (2004) 6134–6142.
[89] R.L. Kruse, Therapeutic strategies in an outbreak scenario to treat the novel coronavirus originating in Wuhan, China, F1000Research 9 (2020).
[90] D. Ndwandwe, C.S. Wiysonge, COVID-19 vaccines, Curr. Opin. Immunol. (2021).
[91] W.C.-V.T.a.L. https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines.
[92] W.S.o.C.-V.w.W. EUL/PQ, E.P. https://extranet.who.int/pqweb/sites/, default/files/documents/Status_COVID_VAX_29June2021.pdf.
[93] A. Nagy, B. Alhatlani, An overview of current COVID-19 vaccine platforms, Comput. Struct. Biotechnol. J. (2021).
[94] M. Wang, R. Cao, L. Zhang, X. Yang, J. Liu, M. Xu, Z. Shi, Z. Hu, W. Zhong, G. Xiao, Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro, Cell Res. 30 (2020) 269–271.
[95] M.L. Holshue, C. DeBolt, S. Lindquist, K.H. Lofy, J. Wiesman, H. Bruce, C. Spitters, K. Ericson, S. Wilkerson, A. Tural, First Case of 2019 Novel Coronavirus in the United States, New England Journal of Medicine, 2020.
[96] A. Zumla, J.F. Chan, E.I. Azhar, D.S. Hui, K.-Y. Yuen, Coronaviruses—drug discovery and therapeutic options, Nat. Rev. Drug Discov. 15 (2016) 327–347.
[97] J.A. Al-Tawfiq, H. Momattin, J. Dib, Z.A. Memish, Ribavirin and interferon therapy in patients infected with the Middle East respiratory syndrome coronavirus: an observational study, Int. J. Infect. Dis. 20 (2014) 42–46.
[98] C.-Y. Wu, J.-T. Jan, S.-H. Ma, C.-J. Kuo, H.-F. Juan, Y.-S.E. Cheng, H.-H. Hsu, H.-C. Huang, D. Wu, A. Brik, Small molecules targeting severe acute respiratory syndrome human coronavirus, Proc. Natl. Acad. Sci. Unit. States Am. 101 (2004) 10012–10017.
[99] C. Chu, V. Cheng, I. Hung, M. Wong, K. Chan, K. Chan, R. Kao, L. Poon, C. Wong, Y. Guan, Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings, Thorax 59 (2004) 252–256.
[100] B. Cao, Y. Wang, D. Wen, W. Liu, J. Wang, G. Fan, L. Ruan, B. Song, Y. Cai, M. Wei, A trial of lopinavir–ritonavir in adults hospitalized with severe Covid-19, N. Engl. J. Med. (2020).
[101] J.-M. Rolain, P. Colson, D. Raoult, Recycling of chloroquine and its hydroxyl analogue to face bacterial, fungal and viral infections in the 21st century, Int. J. Antimicrob. Agents 30 (2007) 297–308.
[102] M.J. Vincent, E. Bergeron, S. Benjannet, B.R. Erickson, P.E. Rollin, T.G. Ksiazek, N.G. Seidah, S.T. Nichol, Chloroquine is a potent inhibitor of SARS coronavirus infection and spread, Virol. J. 2 (2005) 1–10.
[103] Y. Yan, Z. Zou, Y. Sun, X. Li, K.-F. Xu, Y. Wei, N. Jin, C. Jiang, Anti-malaria drug chloroquine is highly effective in treating avian influenza A H5N1 virus infection in an animal model, Cell Res. 23 (2013) 300–302.
[104] A. Savarino, L. Di Trani, I. Donatelli, R. Cauda, A. Cassone, New insights into the antiviral effects of chloroquine, Lancet Infect. Dis. 6 (2006) 67–69.
[105] W. Li, M.J. Moore, N. Vasilieva, J. Sui, S.K. Wong, M.A. Berne, M. Somasundaran, J.L. Sullivan, K. Luzuriaga, T.C. Greenough, Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus, Nature 426 (2003) 450–454.
[106] P. Zhou, X.-L. Yang, X.-G. Wang, B. Hu, L. Zhang, W. Zhang, H.-R. Si, Y. Zhu, B. Li, C.-L. Huang, A pneumonia outbreak associated with a new coronavirus of probable bat origin, Nature 579 (2020) 270–273.
[107] R. Lu, X. Zhao, J. Li, P. Niu, B. Yang, H. Wu, W. Wang, H. Song, B. Huang, N. Zhu, Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding, Lancet 395 (2020) 565–574.
[108] U. Karakus, M.O. Pohl, S. Stertz, Breaking the convention: sialoglycan variants, coreceptors, and alternative receptors for influenza A virus entry, J. Virol. 94 (2020).
[109] X. Xu, P. Chen, J. Wang, J. Feng, H. Zhou, X. Li, W. Zhong, P. Hao, Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission, Sci. China Life Sci. 63 (2020) 457–460.
[110] L. Orleans, H. is Vice, L. Manchikanti, Expanded umbilical cord mesenchymal stem cells (UC-MSCs) as a therapeutic strategy in managing critically ill COVID-19 patients: the case for compassionate use, Pain Physician 23 (2020) E71–E83.
[111] D.J. Weiss, I. Bertoncello, Z. Borok, C. Kim, A. Panoskaltsis-Mortari, S. Reynolds, M. Rojas, B. Stripp, D. Warburton, D.J. Prockop, Stem cells and cell therapies in lung biology and lung diseases, Proc. Am. Thorac. Soc. 8 (2011) 223–272.
[112] J. Alijotas-Reig, E. Esteve-Valverde, C. Belizna, A. Selva-O'Callaghan, J. Pardos-Gea, A. Quintana, A. Mekinian, A. Anunciacion-Lunell, F. Miró-Mur,

Immunomodulatory therapy for the management of severe COVID-19. Beyond the anti-viral therapy: a comprehensive review, Autoimmun. Rev. (2020) 102569.
[113] T. Janowitz, E. Gablenz, D. Pattinson, T.C. Wang, J. Conigliaro, K. Tracey, D. Tuveson, Famotidine use and quantitative symptom tracking for COVID-19 in non-hospitalised patients: a case series, Gut 69 (2020) 1592–1597.
[114] D.E. Freedberg, J. Conigliaro, T.C. Wang, K.J. Tracey, M.V. Callahan, J. A. Abrams, M.E. Sobieszczyk, D.D. Markowitz, A. Gupta, M.R. O'Donnell, Famotidine use is associated with improved clinical outcomes in hospitalized COVID-19 patients: a propensity score matched retrospective cohort study, Gastroenterology 159 (2020) 1129–1131, e1123.
[115] R. Arshad, M. Barani, A. Rahdar, S. Sargazi, M. Cucchiarini, S. Pandey, M. Kang, Multi-functionalized nanomaterials and nanoparticles for diagnosis and treatment of retinoblastoma, Biosensors 11 (2021) 97.
[116] S. Sargazi, M.R. Hajinezhad, A. Rahdar, M. Mukhtar, M. Karamzadeh-Jahromi, M. Almasi-Kashi, S. Alikhanzadeh-Arani, M. Barani, F. Baino, CoNi alloy nanoparticles for cancer theranostics: synthesis, physical characterization, in vitro and in vivo studies, Appl. Phys. A 127 (2021) 1–12.
[117] M. Barani, M. Mukhtar, A. Rahdar, S. Sargazi, S. Pandey, M. Kang, Recent advances in nanotechnology-based diagnosis and treatments of human osteosarcoma, Biosensors 11 (2021) 55.
[118] M. Barani, A. Rahdar, S. Sargazi, M.S. Amiri, P.K. Sharma, N. Bhalla, Nanotechnology for Inflammatory Bowel Disease Management: Detection, Imaging and Treatment, Sensing Bio-Sensing Research, 2021, p. 100417.
[119] C.I. Colino, J.M. Lanao, C. Gutiérrez-Millán, Recent advances in functionalized nanomaterials for the diagnosis and treatment of bacterial infections, Mater. Sci. Eng. C (2021) 111843.
[120] M. Rai, S. Bonde, A. Yadav, Y. Plekhanova, A. Reshetilov, I. Gupta, P. Golińska, R. Pandit, A.P. Ingle, Nanotechnology-based promising strategies for the management of COVID-19: current development and constraints, Expert Rev. Anti-infect. Ther. (2020) 1–10.
[121] K.S. Park, J.D. Bazzill, S. Son, J. Nam, S.W. Shin, L.J. Ochyl, J.A. Stuckey, J. L. Meagher, L. Chang, J. Song, Lipid-based vaccine nanoparticles for induction of humoral immune responses against HIV-1 and SARS-CoV-2, J. Contr. Release 330 (2021) 529–539.
[122] R. Saravani, S. Sargazi, R. Saravani, M. Rabbani, A. Rahdar, P. Taboada, Newly crocin-coated magnetite nanoparticles induce apoptosis and decrease VEGF expression in breast carcinoma cells, J. Drug Deliv. Sci. Technol. 60 (2020) 101987.
[123] S. Sargazi, M.R. Hajinezhad, M. Barani, A. Rahdar, S. Shahraki, P. Karimi, M. Cucchiarini, M. Khatami, S. Pandey, Synthesis, characterization, toxicity and morphology assessments of newly prepared microemulsion systems for delivery of valproic acid, J. Mol. Liq. 338 (2021) 116625.
[124] S. Sargazi, M. Mukhtar, A. Rahdar, M. Barani, S. Pandey, A.M. Díez-Pascual, Active targeted nanoparticles for delivery of poly (ADP-ribose) polymerase (PARP) inhibitors: a preliminary review, Int. J. Mol. Sci. 22 (2021) 10319.
[125] A. Rahdar, M.R. Hajinezhad, S. Sargazi, M. Bilal, M. Barani, P. Karimi, G.Z. Kyzas, Biochemical effects of deferasirox and deferasirox-loaded nanomicellesin iron-intoxicated rats, Life Sci. 270 (2021) 119146.
[126] S. Sargazi, M.R. Hajinezhad, M. Barani, M. Mukhtar, A. Rahdar, F. Baino, P. Karimi, S. Pandey, F127/Cisplatin microemulsions: in vitro, In Vivo Comput. Stud. Appl. Sci. 11 (2021) 3006.
[127] Z. Gounani, M.A. Asadollahi, J.N. Pedersen, J. Lyngsø, J.S. Pedersen, A. Arpanaei, R.L. Meyer, Mesoporous silica nanoparticles carrying multiple antibiotics provide enhanced synergistic effect and improved biocompatibility, Colloids Surf. B Biointerfaces 175 (2019) 498–508.
[128] L. Singh, H.G. Kruger, G.E. Maguire, T. Govender, R. Parboosing, The role of nanotechnology in the treatment of viral infections, Therapeutic advances in infectious disease 4 (2017) 105–131.
[129] A. Rahdar, M.R. Hajinezhad, M. Barani, S. Sargazi, M. Zaboli, E. Ghazy, F. Baino, M. Cucchiarini, M. Bilal, S. Pandey, Pluronic F127/Doxorubicin microemulsions: preparation, characterization, and toxicity evaluations, J. Mol. Liq. (2021) 117028.
[130] M. Barani, M. Reza Hajinezhad, S. Sargazi, M. Zeeshan, A. Rahdar, S. Pandey, M. Khatami, F. Zargari, Simulation, in vitro, and in vivo cytotoxicity assessments of methotrexate-loaded pH-responsive nanocarriers, Polymers 13 (2021) 3153.
[131] A. Rahdar, M.R. Hajinezhad, S. Sargazi, M. Zaboli, M. Barani, F. Baino, M. Bilal, E. Sanchooli, Biochemical, ameliorative and cytotoxic effects of newly synthesized curcumin microemulsions: evidence from in vitro and in vivo studies, Nanomaterials 11 (2021) 817.
[132] S. Shirvalilou, S. Khoei, S. Khoee, S.R. Mahdavi, N.J. Raoufi, M. Motevalian, M. Y. Karimi, Enhancement radiation-induced apoptosis in C6 glioma tumor-bearing rats via pH-responsive magnetic graphene oxide nanocarrier, J. Photochem. Photobiol. B Biol. 205 (2020) 111827.
[133] R. Afzalipour, S. Khoei, S. Khoee, S. Shirvalilou, N.J. Raoufi, M. Motevalian, M. Y. Karimi, Thermosensitive magnetic nanoparticles exposed to alternating magnetic field and heat mediated chemotherapy for an effective dual therapy in rat glioma model, Nanomed. Nanotechnol. Biol. Med. 31 (2021) 102319.
[134] F.R. Formiga, R. Leblanc, J. de Souza Rebouças, L.P. Farias, R.N. de Oliveira, L. Pena, Ivermectin: an award-winning drug with expected antiviral activity against COVID-19, J. Contr. Release 329 (2021) 758–761.
[135] S. Kamat, M. Kumari, C. Jayabaskaran, Nano-engineered tools in the diagnosis, therapeutics, prevention, and mitigation of SARS-CoV-2, J. Contr. Release (2021).
[136] O. Changizi, S. Khoei, A. Mahdavian, S. Shirvalilou, S.R. Mahdavi, J.K. Rad, Enhanced radiosensitivity of LNCaP prostate cancer cell line by gold-photoactive nanoparticles modified with folic acid, Photodiagnosis Photodyn. Ther. 29 (2020) 101602.
[137] Z. Rajaee, S. Khoei, A. Mahdavian, S. Shirvalilou, S.R. Mahdavi, M. Ebrahimi, Radio-thermo-sensitivity induced by gold magnetic nanoparticles in the monolayer culture of human prostate carcinoma cell line DU145, Anti Cancer Agents Med. Chem. 20 (2020) 315–324.
[138] L. Kiamohammadi, L. Asadi, S. Shirvalilou, S. Khoei, S. Khoee, M. Soleymani, S. E. Minaei, Physical and biological properties of 5-fluorouracil polymer-coated magnetite nanographene oxide as a new thermosensitizer for alternative magnetic hyperthermia and a magnetic resonance imaging contrast agent: in vitro and in vivo study, ACS Omega 6 (2021) 20192–20204.
[139] N.H. Abd Ellah, H.M. Tawfeek, J. John, H.F. Hetta, Nanomedicine as a future therapeutic approach for Hepatitis C virus, Nanomedicine 14 (2019) 1471–1491.
[140] L. Lu, R. Sun, R. Chen, C.-K. Hui, C.-M. Ho, J.M. Luk, G. Lau, C.-M. Che, Silver nanoparticles inhibit hepatitis B virus replication, Antivir. Ther. 13 (2008) 253.
[141] R.W.-Y. Sun, R. Chen, N.P.-Y. Chung, C.-M. Ho, C.-L.S. Lin, C.-M. Che, Silver nanoparticles fabricated in Hepes buffer exhibit cytoprotective activities toward HIV-1 infected cells, Chem. Commun. (2005) 5059–5061.
[142] H.H. Lara, L. Ixtepan-Turrent, E.N. Garza-Treviño, C. Rodriguez-Padilla, PVP-coated silver nanoparticles block the transmission of cell-free and cell-associated HIV-1 in human cervical culture, J. Nanobiotechnol. 8 (2010) 1–11.
[143] L. Sun, A.K. Singh, K. Vig, S.R. Pillai, S.R. Singh, Silver nanoparticles inhibit replication of respiratory syncytial virus, J. Biomed. Nanotechnol. 4 (2008) 149–158.
[144] I. Papp, C. Sieben, K. Ludwig, M. Roskamp, C. Böttcher, S. Schlecht, A. Herrmann, R. Haag, Inhibition of influenza virus infection by multivalent sialic-acid-functionalized gold nanoparticles, Small 6 (2010) 2900–2906.
[145] E. Ruiz-Hitzky, M. Darder, B. Wicklein, C. Ruiz-Garcia, R. Martín-Sampedro, G. Del Real, P. Aranda, Nanotechnology responses to COVID-19, Adv. Healthcare Mater. 9 (2020) 2000979.
[146] V.S. Sivasankarapillai, A.M. Pillai, A. Rahdar, A.P. Sobha, S.S. Das, A. C. Mitropoulos, M.H. Mokarrar, G.Z. Kyzas, On facing the SARS-CoV-2 (COVID-19) with combination of nanomaterials and medicine: possible strategies and first challenges, Nanomaterials 10 (2020) 852.
[147] N.H. Abd Ellah, S.A. Abouelmagd, Surface functionalization of polymeric nanoparticles for tumor drug delivery: approaches and challenges, Expet Opin. Drug Deliv. 14 (2017) 201–214.
[148] R. Zamani, S.F. Aval, Y. Pilehvar-Soltanahmadi, K. Nejati-Koshki, N. Zarghami, Recent advances in cell electrospining of natural and synthetic nanofibers for regenerative medicine, Drug Res. 68 (2018) 425–435.
[149] H. Serati-Nouri, A. Jafari, L. Roshangar, M. Dadashpour, Y. Pilehvar-Soltanahmadi, N. Zarghami, Biomedical applications of zeolite-based materials: a review, Mater. Sci. Eng. C 116 (2020) 111225.
[150] H. Mousazadeh, Y. Pilehvar-Soltanahmadi, M. Dadashpour, N. Zarghami, Cyclodextrin based natural nanostructured carbohydrate polymers as effective non-viral siRNA delivery systems for cancer gene therapy, J. Contr. Release (2020).
[151] N. Javan, M.H. Khadem Ansari, M. Dadashpour, M. Khojastehfard, M. Bastami, M. Rahmati-Yamchi, N. Zarghami, Synergistic antiproliferative effects of co-nanoencapsulated curcumin and chrysin on mda-mb-231 breast cancer cells through upregulating mir-132 and mir-502c, Nutr. Cancer 71 (2019) 1201–1213.
[152] S. Ahmad, A.A. Zamry, H.-T.T. Tan, K.K. Wong, J. Lim, R. Mohamud, Targeting dendritic cells through gold nanoparticles: a review on the cellular uptake and subsequent immunological properties, Mol. Immunol. 91 (2017) 123–133.
[153] L. Zhao, A. Seth, N. Wibowo, C.-X. Zhao, N. Mitter, C. Yu, A.P. Middelberg, Nanoparticle vaccines, Vaccine 32 (2014) 327–337.
[154] R. Pati, M. Shevtsov, A. Sonawane, Nanoparticle vaccines against infectious diseases, Front. Immunol. 9 (2018) 2224.
[155] Y.-S. Kim, A. Son, J. Kim, S.B. Kwon, M.H. Kim, P. Kim, J. Kim, Y.H. Byun, J. Sung, J. Lee, Chaperna-mediated assembly of ferritin-based Middle East respiratory syndrome-coronavirus nanoparticles, Front. Immunol. 9 (2018) 1093.
[156] R. Medhi, P. Srinoi, N. Ngo, H.-V. Tran, T.R. Lee, Nanoparticle-based strategies to combat COVID-19, ACS Appl. Nano Mater. 3 (2020) 8557–8580.
[157] C.M. Coleman, Y.V. Liu, H. Mu, J.K. Taylor, M. Massare, D.C. Flyer, G.M. Glenn, G.E. Smith, M.B. Frieman, Purified coronavirus spike protein nanoparticles induce coronavirus neutralizing antibodies in mice, Vaccine 32 (2014) 3169–3174.
[158] C. Wang, X. Zheng, W. Gai, G. Wong, H. Wang, H. Jin, N. Feng, Y. Zhao, W. Zhang, N. Li, Novel chimeric virus-like particles vaccine displaying MERS-CoV receptor-binding domain induce specific humoral and cellular immune response in mice, Antivir. Res. 140 (2017) 55–61.
[159] S.-Y. Lin, B.-Y. Yao, C.-M.J. Hu, H.-W. Chen, Induction of robust immune responses by CpG-ODN-loaded hollow polymeric nanoparticles for antiviral and vaccine applications in chickens, Int. J. Nanomed. 15 (2020) 3303.
[160] J.A. Wiley, L.E. Richert, S.D. Swain, A. Harmsen, D.L. Barnard, T.D. Randall, M. Jutila, T. Douglas, C. Broomell, M. Young, Inducible bronchus-associated lymphoid tissue elicited by a protein cage nanoparticle enhances protection in mice against diverse respiratory viruses, PLoS One 4 (2009), e7142.
[161] C.g.S.a.i.s.o.-n.v.m.-f.p.o.S.-C.-. infection, C.-I.N. https://clinicaltrials.gov/ct2/show/NCT04283461.
[162] C.g.A.t.i.t.s.a.e.o.o.B.v.a.C.-i.h.a. Identifier:, N. https://clinicaltrials.gov/ct2/show/NCT04537949.
[163] N. Pardi, S. Tuyishime, H. Muramatsu, Expression kinetics of nucleoside-modified mRNA delivered in lipid nanoparticles to mice by various routes, e. al. J. Contr. Release 217 (2015) 345–351.
[164] M. Mulligan, K. Lyke, n.N. Kitchi, Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults, e. al. Nature 586 (2020) 589–593.
[165] C.g.A.t.e.t.s.a.e.o.a.R.v.A.-i.h.a.I. NCT04668339., https://clinicaltrials.gov/ct2/show/NCT04668339.

[166] M.D. Buschmann, M.J. Carrasco, S. Alishetty, M. Paige, M.G. Alameh, D. Weissman, Nanomaterial delivery systems for mRNA vaccines, Vaccines 9 (2021) 65.
[167] C.g.A.s.t.e.t.s.a.i.o.v.C.i.h.a.i.G.f. COVID-19., I.N. https://clinicaltrials.gov/ct2/show/NCT04674189.
[168] I.U., Acuitas Therapeutics, 2020.
[169] C.g.C.m.v.i.h.a.I. NCT04566276., https://clinicaltrials.gov/ct2/show/NCT04566276.
[170] G.S.G. WO2020219941, 2020.
[171] C.g.E.o.t.s.a.i.o.a.S.-C.-r.n.v.w.w. Matrix-M, a.I.N. http://www.clinicaltrials.gov/ct2/show/NCT04368988.
[172] L. Milane, M. Amiji, Clinical approval of nanotechnology-based SARS-CoV-2 mRNA vaccines: impact on translational nanomedicine, Drug Deliv. Transl. Res. (2021) (Epub ahead of print).).
[173] Y. Panahi, M. Mohammadhosseini, K. Nejati-Koshki, A.J.N. Abadi, H.F. Moafi, A. Akbarzadeh, M. Farshbaf, Preparation, surface properties, and therapeutic applications of gold nanoparticles in biomedicine, Drug Res. 11 (2017) 77–87.
[174] M. Pourhassan-Moghaddam, N. Zarghami, A. Mohsenifar, M. Rahmati-Yamchi, D. Gholizadeh, A. Akbarzadeh, M. De La Guardia, K. Nejati-Koshki, Watercress-based gold nanoparticles: biosynthesis, mechanism of formation and study of their biocompatibility in vitro, Micro & Nano Lett. 9 (2014) 345–350.
[175] A. Mubarak, W. Alturaiki, M.G. Hemida, Middle East respiratory syndrome coronavirus (MERS-CoV): infection, immunological response, and vaccine development, J. Immunol. Res. (2019) 2019.
[176] H.K. Charlton Hume, J. Vidigal, M.J. Carrondo, A.P. Middelberg, A. Roldão, L. H. Lua, Synthetic biology for bioengineering virus-like particle vaccines, Biotechnol. Bioeng. 116 (2019) 919–935.
[177] M.J. Rohovie, M. Nagasawa, J.R. Swartz, Virus-like particles: next-generation nanoparticles for targeted therapeutic delivery, Bioeng. Transl. Med. 2 (2017) 43–57.
[178] T. Kato, Y. Takami, V.K. Deo, E.Y. Park, Preparation of virus-like particle mimetic nanovesicles displaying the S protein of Middle East respiratory syndrome coronavirus using insect cells, J. Biotechnol. 306 (2019) 177–184.
[179] T.A. Pimentel, Z. Yan, S.A. Jeffers, K.V. Holmes, R.S. Hodges, P. Burkhard, Peptide nanoparticles as novel immunogens: design and analysis of a prototypic severe acute respiratory syndrome vaccine, Chem. Biol. Drug Des. 73 (2009) 53–61.
[180] X. Huang, M. Li, Y. Xu, J. Zhang, X. Meng, X. An, L. Sun, L. Guo, X. Shan, J. Ge, Novel gold nanorod-based HR1 peptide inhibitor for Middle East respiratory syndrome coronavirus, ACS Appl. Mater. Interfaces 11 (2019) 19799–19807.
[181] Y. Han, P. Král, Computational design of ACE2-based peptide inhibitors of SARS-CoV-2, ACS Nano 14 (2020) 5143–5147.
[182] A. Łoczechin, K. Séron, A. Barras, E. Giovanelli, S. Belouzard, Y.-T. Chen, N. Metzler-Nolte, R. Boukherroub, J. Dubuisson, S. Szunerits, Functional carbon quantum dots as medical countermeasures to human coronavirus, ACS Appl. Mater. Interfaces 11 (2019) 42964–42974.
[183] B. Udugama, P. Kadhiresan, H.N. Kozlowski, A. Malekjahani, M. Osborne, V.Y. Li, H. Chen, S. Mubareka, J.B. Gubbay, W.C. Chan, Diagnosing COVID-19: the disease and tools for detection, ACS Nano 14 (2020) 3822–3835.
[184] C. Wang, P.W. Horby, F.G. Hayden, G.F. Gao, A novel coronavirus outbreak of global health concern, Lancet 395 (2020) 470–473.
[185] H. Kim, M. Park, J. Hwang, J.H. Kim, D.-R. Chung, K.-s. Lee, M. Kang, Development of label-free colorimetric assay for MERS-CoV using gold nanoparticles, ACS Sens. 4 (2019) 1306–1312.
[186] P. Gong, X. He, K. Wang, W. Tan, W. Xie, P. Wu, H. Li, Combination of functionalized nanoparticles and polymerase chain reaction-based method for SARS-CoV gene detection, J. Nanosci. Nanotechnol. 8 (2008) 293–300.
[187] H. Li, L. Rothberg, Colorimetric detection of DNA sequences based on electrostatic interactions with unmodified gold nanoparticles, Proc. Natl. Acad. Sci. Unit. States Am. 101 (2004) 14036–14039.
[188] P. Teengam, W. Siangproh, A. Tuantranont, T. Vilaivan, O. Chailapakul, C. S. Henry, Multiplex paper-based colorimetric DNA sensor using pyrrolidinyl peptide nucleic acid-induced AgNPs aggregation for detecting MERS-CoV, MTB, and HPV oligonucleotides, Anal. Chem. 89 (2017) 5428–5435.
[189] Z. Zhao, H. Cui, W. Song, X. Ru, W. Zhou, X. Yu, A Simple Magnetic Nanoparticles-Based Viral RNA Extraction Method for Efficient Detection of SARS-CoV-2, 2020. BioRxiv.
[190] P. Singh, D. Singh, P. Sa, P. Mohapatra, A. Khuntia, S.K. Sahoo, Insights from nanotechnology in COVID-19: prevention, detection, therapy and immunomodulation, Nanomedicine 16 (2021) 1219–1235.
[191] S.K. Upadhyay, S. Dan, M. Girdhar, K. Rastogi, Recent advancement in SARS-CoV-2 diagnosis, treatment, and vaccine formulation: a new paradigm of nanotechnology in strategic combating of COVID-19 pandemic, Curr. Pharmacol. Rep. (2021) 1–14.
[192] P. Gong, X. He, K. Wang, W. Tan, W. Xie, P. Wu, H. Li, Combination of functionalized nanoparticles and polymerase chain reaction-based method for SARS-CoV gene detection, J. Nanosci. Nanotechnol. 8 (2008) 293–300.
[193] S.H. Radwan, H.M. Azzazy, Gold nanoparticles for molecular diagnostics, Expert Rev. Mol. Diagn. 9 (2009) 511–524.
[194] A. Laromaine, L. Koh, M. Murugesan, R.V. Ulijn, M.M. Stevens, Protease-triggered dispersion of nanoparticle assemblies, J. Am. Chem. Soc. 129 (2007) 4156–4157.
[195] S.A. Lim, T.H. Lim, A.N. Ahmad, The Applications of Biosensing and Artificial Intelligence Technologies for Rapid Detection and Diagnosis of COVID-19 in Remote Setting, Diagnostic Strategies for COVID-19 and Other Coronaviruses, Springer, 2020, pp. 109–134.
[196] G. Martínez-Paredes, M.B. González-García, A. Costa-García, Genosensor for SARS virus detection based on gold nanostructured screen-printed carbon electrodes, Electroanalysis: An International Journal Devoted to Fundamental and Practical Aspects of Electroanalysis 21 (2009) 379–385.
[197] S.R. Ahmed, É. Nagy, S. Neethirajan, Self-assembled star-shaped chiroplasmonic gold nanoparticles for an ultrasensitive chiro-immunosensor for viruses, RSC Adv. 7 (2017) 40849–40857.
[198] L.A. Layqah, S. Eissa, An electrochemical immunosensor for the corona virus associated with the Middle East respiratory syndrome using an array of gold nanoparticle-modified carbon electrodes, Microchimica Acta 186 (2019) 1–10.
[199] Y. Wang, Z. Fan, L. Shao, X. Kong, X. Hou, D. Tian, Y. Sun, Y. Xiao, L. Yu, Nanobody-derived nanobiotechnology tool kits for diverse biomedical and biotechnology applications, Int. J. Nanomed. 11 (2016) 3287.
[200] K.E. Pascal, C.M. Coleman, A.O. Mujica, V. Kamat, A. Badithe, J. Fairhurst, C. Hunt, J. Strein, A. Berrebi, J.M. Sisk, Pre-and postexposure efficacy of fully human antibodies against Spike protein in a novel humanized mouse model of MERS-CoV infection, Proc. Natl. Acad. Sci. Unit. States Am. 112 (2015) 8738–8743.
[201] Y. Orooji, H. Sohrabi, N. Hemmat, F. Oroojalian, B. Baradaran, A. Mokhtarzadeh, M. Mohaghegh, H. Karimi-Maleh, An overview on SARS-CoV-2 (COVID-19) and other human coronaviruses and their detection capability via amplification assay, chemical sensing, biosensing, immunosensing, and clinical assays, Nano-Micro Lett. 13 (2021) 1–30.
[202] P. Huang, H. Wang, Z. Cao, H. Jin, H. Chi, J. Zhao, B. Yu, F. Yan, X. Hu, F. Wu, A rapid and specific assay for the detection of MERS-CoV, Front. Microbiol. 9 (2018) 1101.
[203] Z.Z. Rashid, S.N. Othman, M.N.A. Samat, U.K. Ali, K.K. Wong, Diagnostic performance of COVID-19 serology assays, Malays. J. Pathol. 42 (2020) 13–21.
[204] S. Duffy, Why are RNA virus mutation rates so damn high? PLoS Biol. 16 (2018), e3000003.
[205] A.R. Fehr, S. Perlman, Coronaviruses: an overview of their replication and pathogenesis, Coronaviruses (2015) 1–23.
[206] A.M. Foudeh, T.F. Didar, T. Veres, M. Tabrizian, Microfluidic designs and techniques using lab-on-a-chip devices for pathogen detection for point-of-care diagnostics, Lab Chip 12 (2012) 3249–3266.