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Biosafety chemistry and biosafety materials: A new perspective to solve biosafety problems

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ABSTRACT

Coronavirus disease 2019 (COVID-19) has rapidly swept around the globe since its emergence near 2020. However, people have failed to fully understand its origin or mutation. Defined as an international biosafety incident, COVID-19 has again encouraged worldwide attention to reconsider the importance of biosafety due to the adverse impact on personal well-being and social stability. Most countries have already taken measures to advocate progress in biosafety-relevant research, aiming to prevent and solve biosafety problems with more advanced techniques and products. Herein, we propose a new concept of biosafety chemistry and reiterate the notion of biosafety materials, which refer to the interdisciplinary integration of biosafety and chemistry or materials. We attempt to illustrate the exquisite association that chemistry and materials science possess with biosafety -science, and we hope to provide a pragmatic perspective on approaches to utilize the knowledge of these two subjects to handle specific biosafety issues, such as detection and disinfection of pathogenic microorganisms, personal protective equipment, vaccine adjuvants and specific drugs, *etc.*. In addition, we hope to promote multidisciplinary cooperation to strengthen biosafety research and facilitate the development of biosafety products to defend national security in the future.

1. Introduction

Coronavirus disease 2019 (COVID-19) has rapidly spread across the globe since 2020 [1,2], bringing a heavy blow to countries worldwide by causing large numbers of casualties, interrupting people's lives and social orders as well as inciting international conflicts and compromising economic growth [3,4]. In April 2020, the World Health Organization (WHO) defined the COVID-19 epidemic as a "pandemic of acute respiratory infectious disease" [5,6], which drawed people's attention worldwide to biosafety-relevant fields.

Biosafety aims to ameliorate the potential negative impact on humankind or the environment brought by organisms and development of biotechnology. In other words, biosafety-relevant research focuses on preventing and solving problems induced by development and application of modern biotechnology that may jeopardize the ecosystem and human health [7,8]. Those harmful impact mainly includes the emergence of major infectious diseases, animal and plant epidemics, invasion of alien species, loss and preservation of biological and human genetic resources, and laboratory biosecurity, *etc.*.

The past few years have witnessed the rapid development of science and other subjects, which have eased human beings with fruitful results, but inevitably posed significant threats on the ecosystem and human health, leading to an increasingly serious situation for global biosafety [9,10]. As a result, conventional biosafety threats gradually exacerbate the problems, such as major infectious diseases and animal epidemics, including the Ebola virus, African swine fever, Spodoptera frugiperda, and more recently, COVID-19. The abuse of drugs further results in resistant pathogens [11–13]. Meanwhile, nonconventional biosafety threats, like cyberbiosecurity and hazardous biotechnology, are emerging for terrorists due to the spread of Internet. In short, current biosafety threat is intensifying and diverse, making it harder and harder to prevent.

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Among the new variables affecting international strategic patterns, the biosafety problem brings catastrophic consequences upon humans [14]. Therefore, preventing and solving biosafety threats is an urgent issue facing world today. Many countries have already enrolled biosafety in the national development strategies, advocating multidisciplinary cooperation to rapidly develop the biosafety research [15]. Notably, with the steady development of chemistry and materials science, numerous novel chemicals and multi-functional materials have already been created, which can help solve biosafety-related problems [7,8,14].

2. Chemistry can help solve biosafety problems

Chemistry is a subject that studies the composition, properties, structure, and change law of substances at molecular and atomic levels [16]. For instance, there are various chemically synthesized fibers in clothes [17]; the successful digestion of protein and fat in food within human bodies is achieved by chemical reactions; vehicles need fuel to run which heavily depends on chemical reactions and processing [18]. Taken together, chemistry is closely related to people's daily life. According to the research directions, chemistry can be further classified into inorganic chemistry, analytical chemistry, organic chemistry, physical chemistry, and polymer chemistry [19]. With the progress of science and technology and the development of inter-disciplines in recent years, new research areas could be gradually derived from chemistry, which plays an increasingly essential role in human life.

Chemical science may play a vital role in solving biosafety problems, including inspection, detection [20,21], disinfection, prevention, and treatment [22]. For example, chemical drugs and reagents, which can inhibit and kill microbes, have been widely applied in disinfection, antisepsis, and treatment as disinfectants, preservatives, therapeutic agents, *etc.* [22–25]. In addition, chemically designed sustained-release formulation of insecticide can be used to kill invading alien species. As chemistry plays such an important role in biosafety risk prevention, we hence propose a new concept of "biosafety chemistry" as an integrated discipline. Biosafety chemistry focuses on exploring novel chemical principles as well as technologies together with computer science, biology, and mathematics, *etc.*, to develop new substances and chemical structures to prevent and solve biosafety problems.

3. Materials science can help solve biosafety problems

Materials are substances human can utilize, while materials science mainly studies the interplay between material preparation or processing, structure, and properties. At present, materials are generally divided into polymer materials [26–28], inorganic nonmetallic materials (including ceramic materials, semiconductor materials, *etc.*.) [29,30], metals [31,32], composite materials [33–35], *etc.*

The progress of human civilization is accompanied by the discovery and utilization of "new materials", which profoundly affects humankind's production mode and lifestyle. The use of new materials significantly promotes human society's progress through productive force liberation, and serves as milestones that differentiate the stages of human civilization. It is notable that the continuous innovation and development of three primary synthetic materials known as rubber, plastic, and fiber significantly reduced human's dependence on natural materials like leather, wool, cotton, and silk. Moreover, these three synthetic materials partially or mostly replace metal, wood, and stone in specific fields. For example, the use of aluminum and its alloy helps the aerospace industry develop unprecedentedly, stimulating further development of materials science. Semiconductor materials, such as silicon, provide a solid support for informatization, resulting in everlastingly new approaches to transmit and store information. Scientists are turning the "invisibility cloak" into reality *via* metamaterials [36], which can also expedite information transmission, reduce energy consumption, significantly elevate the utilization efficiency of solar energy, and so on. The development of nanotechnology and nanodevices may fundamentally change human social life and production mode. Taken together, chemistry and materials are closely related to the daily life of human beings, including clothing, housing, transportation, energy, and death (Fig. 1).

The concept of biosafety materials has already been proposed to advocate developing and applying new materials to prevent and solve biosafety problems *via* the integration of biosafety and materials science. Biosafety materials can be used in the following aspects: 1) rapid detection and dis-infection of pathogenic microorganisms; 2) prevention and treatment for major infectious diseases, animal and plant epidemics; 3) preservation of human, animal, and plant genetic resources; 4) development of personal protection equipment; 5) design and preparation of vaccine adjuvants and specific drugs for major infectious diseases; 6) laboratory biosafety; 7) prevention of invasion of alien species; 8) counter-measures of biological warfare and bioterrorism attacks (Fig. 2). Meanwhile, we should point out that "biosafety materials" are different from "biosafety of materials". Biosafety of materials refers to whether materials are safe for the ecological environment and lives, whether and how the materials produce toxic and side effects as well as the underlying mechanisms, which is actually the toxicology of materials. Biosafety materials, instead, favor the research and design of new materials to prevent and solve biosafety problems [7,8,14].

4. Possible application of biosafety chemistry and biosafety materials

4.1. Pathogenic microbes' detection and disinfection

Pathogenic microbes' detection at an early stage is usually the essential step for biosafety risk prevention. In contrast, new chemicals and materials can wonderfully assist the rapid detection and preliminary screening of such pathogens. For example, we can develop new chemical reagents, novel materials, and clinical diagnostic kits for infectious diseases such as COVID-19, viral hepatitis, tuberculosis, AIDS, hemorrhagic fever, dengue fever, influenza, and diarrhea; we could also design high-throughput diagnostic chemical reagents or materials and supporting equipment accordingly that can simultaneously detect multiple pathogens and discrepancy in drug resistance [20,37]; chemically modified environmental-friendly metals like copper or silver nanoparticles, and even polymer-metal nanocomposites could be prepared for antibacterial or antiviral applications in sterilization [26,38–40]; novel chemical formulations, materials, sprays, gels, and other relevant products with photo [41–43], sound, magnetic [44,45] and thermal responsiveness might be developed; specifically designed disinfectants and biosafety cleaning systems could be applied for the open environment as well as confined space, especially with personnel on-site.

Standing as the golden standard to differentiate patients suffering from COVID-19, current nucleic acid detection methods are still quite limited, as the long duration process (>1 h) might induce more infected individuals even with relevant medical personnel involved [46]. Notably, the virus transmission rate far exceeds that of detecting infected people. Therefore, it is visionary and pragmatic to prepare rapid detection kits for pathogenic microorganisms through chemical synthesis and nanoscale preparation during sudden outbreaks of novel epidemics and pathogen-related major biosafety threats, which can achieve valid results within minutes. As shown in Fig. 3, Chen et al. developed a test kit for SARS-CoV-2 based on aggregation induced emission (AIE) materials [47]. The AIE dye and virus antigen on the surface of the nanoparticle were fabricated for early detection of the virus. The detection sensitivity of this method for IgM and IgG is

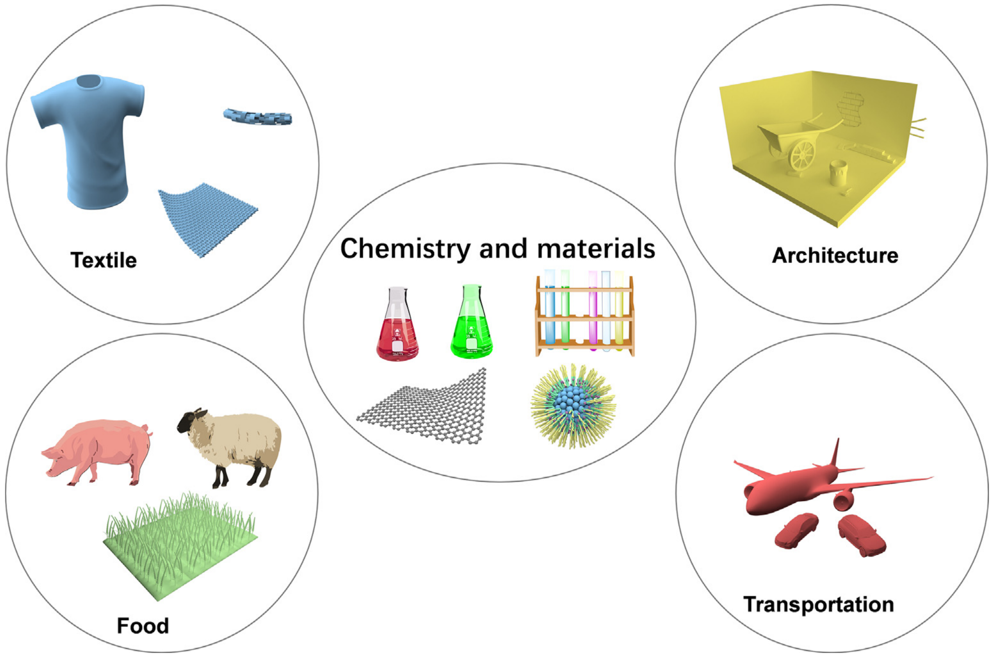

Fig. 1. Chemistry and materials are closely related to the daily life of human beings, including clothing, housing, transportation, energy, and death.

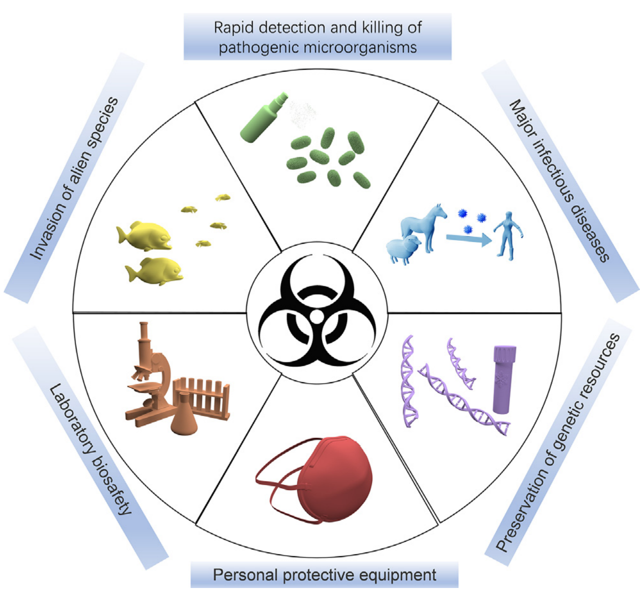

Fig. 2. Chemistry and materials can help the development of biosafety fields.

78% and 95%, respectively, which exemplifies the development of biosafety materials for pathogen detection.

After detecting pathogenic microorganisms, safe and efficient disinfectants usually become necessities which heavily depends on the development of chemistry and materials science. Except for disinfection in an open environment, more attention should be placed on sterilization in application scenarios like confined space, highly populated and personnel-detained areas, which in turn posed stricter requirements on the properties of disinfectants such as increased safety and higher efficiency with minimal toxicity and influence towards people, environment, apparatus, and equipment. For instance, SARS-CoV-2 virus is sensitive to ultraviolet radiation and heat, which can be inactivated after 30 min at 56 °C, or with chemical solvents, including ether, peracetic acid, 75% alcohol, chlorine-containing disinfectant, and chloroform [48]. However, given that the sterilization in confined space such as in ambulance, bus, subway, cruise, aircraft, and other facilities, disinfectants mentioned above have the following disadvantages: 1) peracetic acid is highly corrosive to kill viruses and intoxicates facilities at the same time; 2) alcohol and other flammable agents are highly explosive, leading to an inclination of accidents for equipments with complicated circuits and internal structures; 3) heat at 56 °C may induce body lesions, while ultraviolet light can hardly eradicate viruses concealed in blind sites inside air conditioning systems, seats, luggage racks, toilets, cargo cabinets, *etc.* [49]. Overall, it is imperative to apply new chemical subtances and materials to develop light, electric, sound, magnetic, and thermo-responsive disinfectants that are colorless, odorless, non-toxic, non-corrosive, environment-friendly, and degradable with no heavy metal residuals [41–43].

4.2. Personal protective equipment

Personal protective equipment refers to the safekeeping system to shield the respiratory tract and skin against toxic chemicals as well biological threats or injuries. In addition, such a firewall between people and pathogenic microorganisms provides a solid guarantee preventing pathogens from invading the human body [50–53]. Personal protective equipment is mainly categorized into respiratory and skin protective equipment. Respiratory protective equipment explicitly includes a gas mask, air respirator, and protective masks, *etc.* [54–56]. In contrast, skin protective equipment usually contains isolated protective clothing, totally enclosed protective clothing, ventilated protective clothing, and protective gloves, *etc.* [57]. Collective protective equipment, on the other hand, including protective tents and isolation compartments, *etc.*, refers to the safeguarding system required to form an enclosure for adequate protection against chemicals and other threats or injuries to ensure that personnel is exempted from nuclear, biological, and chemical hazards when implementing various rescue operations without wearing personal protective equipment. Therefore, novel chemical substances and materials are adopted to develop functional polymers such as rubbers and fibers for personal protective equipment, aiming to enhance its durability, achieve better wearer compliance, and reduce respiratory resistance [58]. For exam-

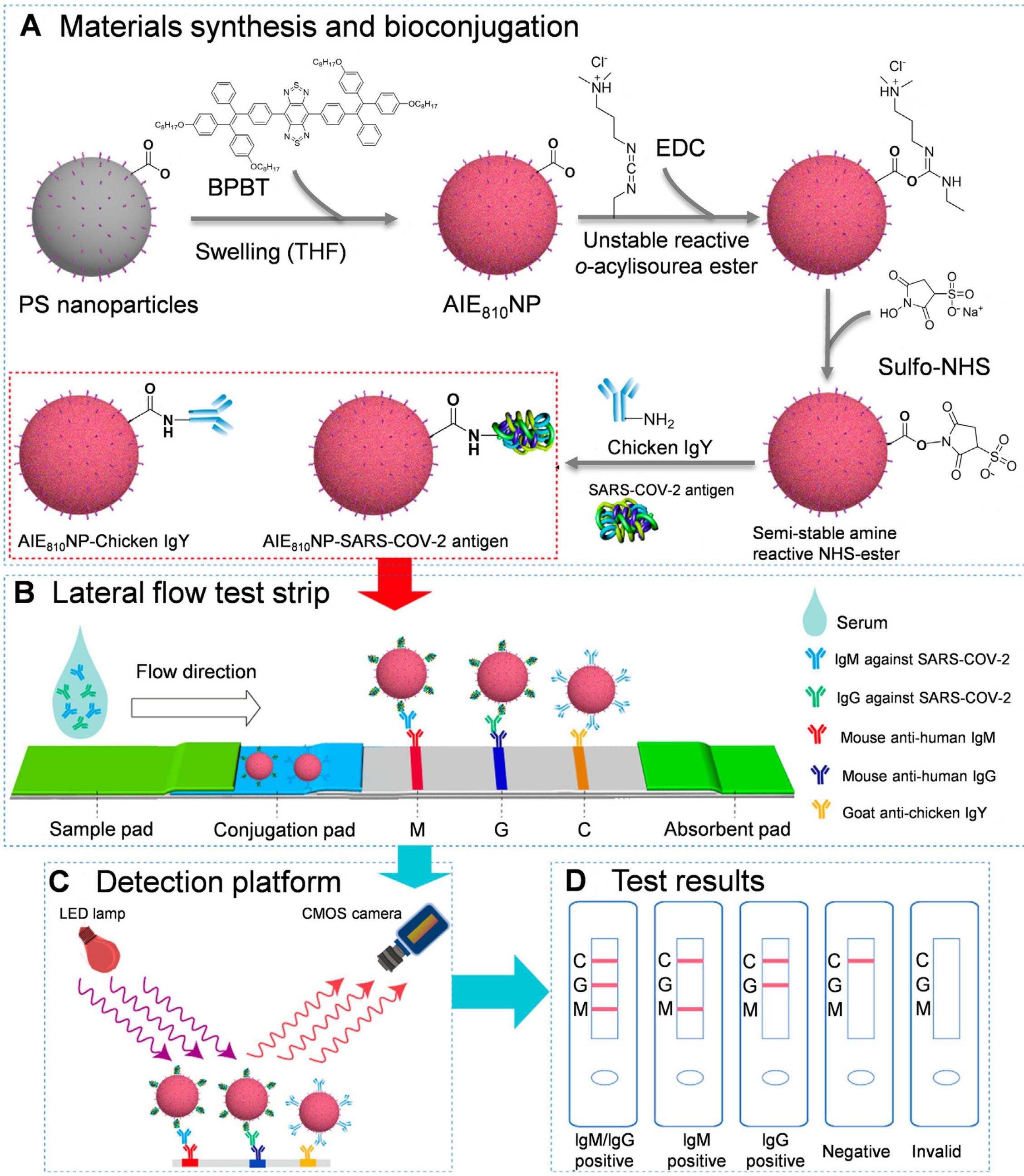

Fig. 3. Application of chemistry and materials to design test kits for SARS-CoV-2. A) Synthesis of detection material; B) Schematic of the developed test strip for coronavirus detection; C) Schematic of the portable reader; D) Interpretation of different test results. Reprinted with permission from Ref. [47], Copyright 2021 American Chemical Society.

ple, masks with better disinfection ability could be produced by introducing TiO_2 NWs filter via a photocatalytic process for reactive oxygen species (ROS) generation at the humid surface of TiO_2 NWs (Fig. 4). Notably, disposal of personal protective equipment could bring great pressure to global environment as the non-degradability of current personal protective equipment. Therefore, developing new generation of disposable personal protective equipment is urgent, and should be taken into account by the scientists in the field of chemistry and materials.

At last, biological and chemical protection can be well integrated into a comprehensive protection system to provide environmental and laser protection, fire prevention, self-decontaminating properties, and lower physiological burden, which significantly enhance the applicability of personel protective equipment. Meanwhile, the portability and efficacy of collective protective equipment should be improved. Therefore, all of these call for the progress of biosafety chemistry and biosafety materials.

4.3. Vaccines and adjuvants

A vaccine is an important "weapon" against infectious diseases and some non-communicable diseases [59–61]. As an effective means of control, it has almost eliminated smallpox, poliomyelitis, and many other diseases in human history. Yet, people have failed to effectively tackle with infections such as the human immunodeficiency virus (HIV). Additionally, some newly arised diseases, including SARS,

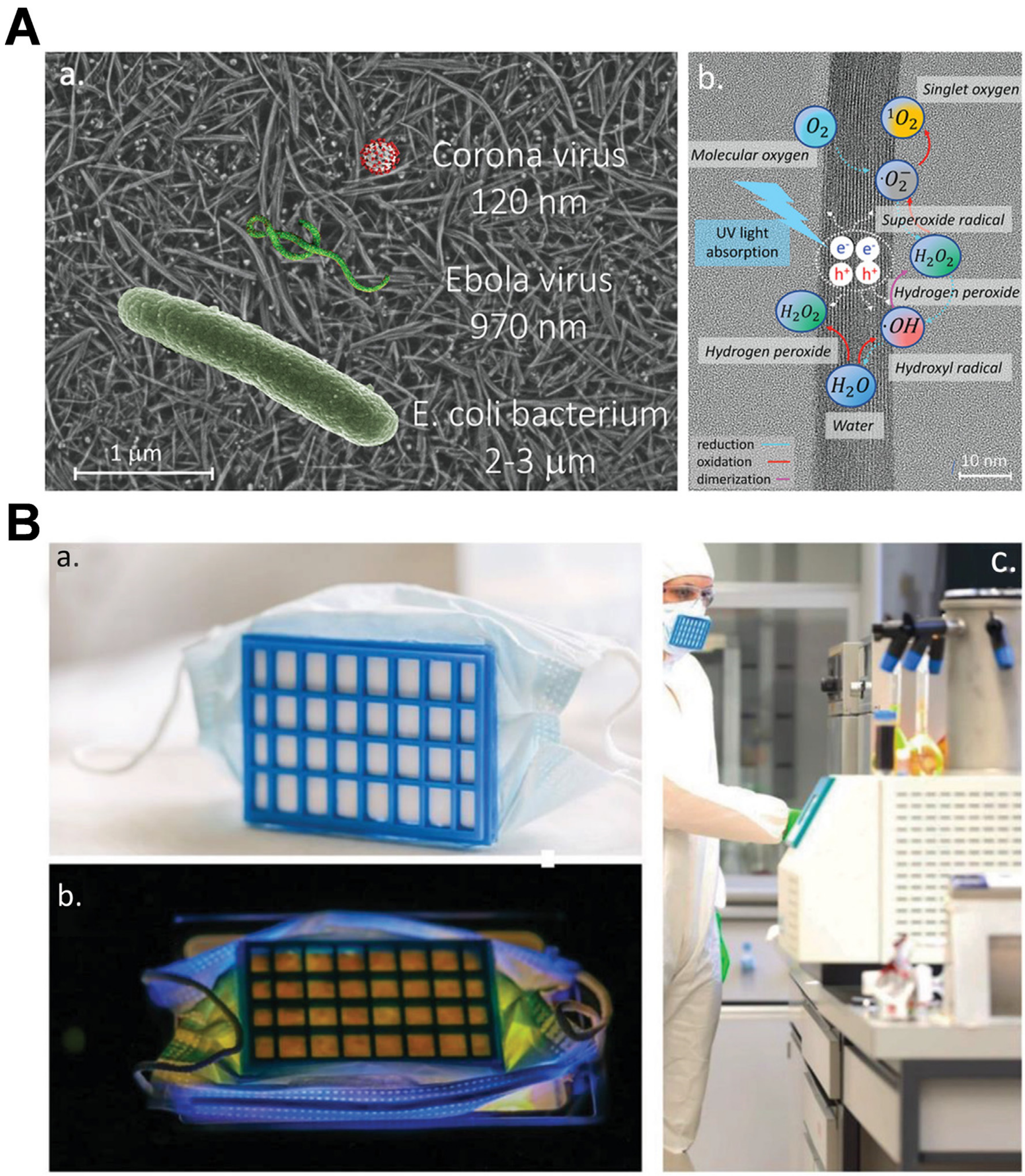

Fig. 4. Application of chemistry and materials to design PPE. A) The SEM image of the surface of the TiO_2 NWs filter (a) and the schematic illustration of photocatalytic processes leading to ROS generation at the humid surface of TiO_2 NWs (b); B) Photo of the mask prototype in which the TiO_2 NWs filter paper (a), photo of the mask prototype during its disinfection under 365 nm UV illumination (b) and photo of the reusable protective mask prototype in natural conditions (c). Reprinted with permission from Ref. [58], Copyright 2020 John Wiley and Sons.

highly pathogenic avian influenza, new influenza A virus, Ebola virus, and Zika virus, spread rapidly with a higher mortality rate, pushing people's well-being further at stake. Therefore, vaccines and specific drugs for infectious diseases prevention and control possess significant research value.

Vaccine adjuvants are substances that stimulate and enhance immune response of vaccine. Adjuvants can induce long-term and efficient immune response, improve the self-protective ability while concomitantly decreasing the dosage of immune substances and production cost of the vaccine. Generally, adjuvants can be classified into aluminum salt adjuvants, protein adjuvants, nucleic acid adjuvants, lipid adjuvants, and mixed adjuvants, *etc.* [62–64].

The adjuvant study has always been an essential link in the vaccine research process. An ideal adjuvant should be broad-spectrum with no pronounced side effects but a valid immune system activation effect and convenience for production and use. Nevertheless, almost no adjuvant has yet completely fulfilled these requirements. Therefore, comprehensively applying chemical and materials science to develop new adjuvant chemical reagents and materials with biodegradability, low toxicity, and even therapeutic ability with limited side effects indicates the future direction for adjuvant research. The emergence of such adjuvant materials would enable us to develop more advanced vaccines. Wang et al. fabricated nanoparticles made of viral protein S1 and Toll-like receptor agonist R848 on the red blood cell membrane to enhance the antiviral immune response, providing new method for the development of antiviral vaccines (Fig. 5) [65].

Pathogenic microorganisms leading to infections are susceptible to mutations, while the increasing numbers of mutated strains might attenuate or even neutralize the effects of the previous vaccines. As a result, preparing specific drugs also represents a significant concern. For example, it is possible to develop bio-responsive and bioactive polyesters, poly (amino acids), peptides, and their related formulations that could block coronavirus invasion into organisms or host cells and efficiently activate antiviral immune response or repair organ lesions in the early stage of infection using chemical and materials science. In these attempts, the specific chemical structures, chirality, and assembly morphology of those bio-responsive materials are utilized to block virus during different mutation stages, improving the overall performance of active prevention and control of coronavirus. In addition, people can also develop nanoscale antibiotics, specific or broad-spectrum anti-infection drugs, green pesticides, and veterinary drugs. Moreover, specific drugs with new adjuvants, dosage forms, delivery systems, and higher efficacy and safety could be designed to reduce inflammatory storm factors.

4.4. Preservation and loss of animal, plant, and human genetic material

Biogenetic resources are indispensable materials for human survival and essential strategic resources for sustainable development, which are of great importance in protecting biosafety and biodiversity [66,67]. Therefore, how to preserve biological, genetic resources safely for a prolonged timespan becomes a new research direction in the field of biosafety materials. Accordingly, new chemicals and materials are applied to study the long-term preservation and recovery efficiency of tissues and cells at room temperature or lower [68]. The ultimate goal is to build a new generation of biosafety materials with high efficacy for preserving biological resources and enhancing the survival rate, safety, recovery rate, and curtailing storage expenses.

5. Perspectives

A world with accelerated development, more thorough globalization, and a more prosperous economy awaits us in the future, whereas biosafety issues will become increasingly severe. Biosafety problem is like a “sword of Damocles” hanging over the world, prepared to cast catastrophe upon humankind at any moment. Hence, we must not be careless in handling biosafety risks.

At present, interdisciplinary integration can serve as necessary means to prevent and solve biosafety problems, which naturally gives rise to biosafety chemistry and biosafety materials as the crystal of biosafety and chemistry or materials science, respectively. However, to improve the overall capability of biosafety governance, we still need to establish the discipline directions for biosafety chemistry and biosafety materials, propose the detailed development plans and critical research focuses. Moreover, majors specifically tailored for biosafety chemistry and biosafety materials study with well-established curriculum schedules shall be set up, which could pave the way towards the construction of a talented team in biosafety chemistry and biosafety materials for defending national security as an indestructible wall.

We shall advocate the development of biosafety chemistry and biosafety materials as a novel research field. From the perspective of our people, biosafety is under their health, well-being, and social stability and harmony. The essential technologies and achievements of biosafety chemistry and biosafety materials can effectively help people prevent and treat infectious diseases to ensure their health and life safety. At the national level, biosafety chemistry and biosafety materials can help countries tackle extreme biosafety threats and promote the development of critical technologies and biosafety-related products, which can provide an indispensable guarantee for national security in the long run.

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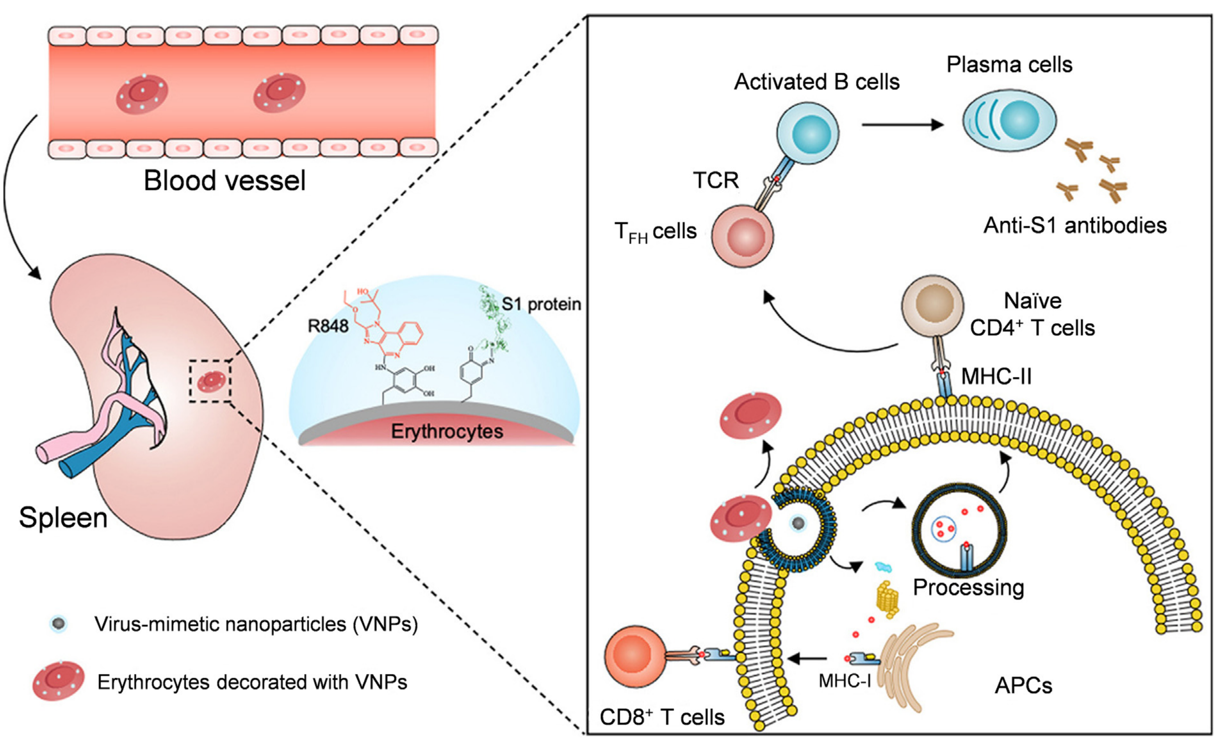

Fig. 5. Application of chemistry and materials for the development of vaccines. Development of virus-mimicking nanoparticles-decorated erythrocytes for inducing robust humoral and cellular immune responses. Reprinted with permission from Ref. [65], Copyright 2021 Elsevier.

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Conflict of interest statement

The authors declare that there are no conflicts of interest.

Author contributions

Yingjie Yu: Writing – Original Draft. **Jianxun Ding:** Writing – Review & Editing. **Yunhao Zhou:** Writing – Review & Editing, Visualization. **Haihua Xiao:** Conceptualization, Supervision. **Guizhen Wu:** Supervision.

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