

REVIEW

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2020, 4, 1930**Biosafety materials: an emerging new research direction of materials science from the COVID-19 outbreak**Yingjie Yu,^{†abc} Fanqiang Bu,^{†d} Huiling Zhou,^{ab} Yongheng Wang,^a Jianxun Cui,^e Xing Wang,^{id d} Guohui Nie^c and Haihua Xiao^{id *ab}

The coronavirus disease 2019 (COVID-19) pandemic is a serious biosafety event that is causing a severe impact on the global society and economy. Thus, the importance of biosafety is once again being valued worldwide. Due to the outbreak of COVID-19, most national governments have been encouraged to speed up the development of biosafety, which places higher requirements on researchers in biosafety and relevant fields. Many problems have been exposed due to the outbreak of COVID-19, including unavailability of effective drugs and vaccines, difficulty in fast or real-time virus detection, insufficient protective equipment, and shortage of transportation equipment for infected patients. To a certain extent, these biosafety problems are partly due to the limited biosafety-related research in materials science. Currently, the tremendous research efforts in materials science around the world have provided a wide variety of materials with peculiar properties to solve biosafety problems. This review attempts to give a perspective on how the development of novel materials can help scientists tackle the challenges in biosafety. Considering the importance of materials science in the biosafety field, it is urgent for us to officially propose the brand new concept of “biosafety materials”, which can be a future scientific discipline that utilizes materials science and theory simultaneously to produce materials, related products, and equipment to solve biosafety problems. Herein, we have aimed to draw worldwide attention on the new discipline of biosafety materials and the active cooperation between materials scientists and biosafety-related scientists to propel its development.

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1. Biosafety: in the spotlight once again**1.1 The outbreak of COVID-19: a reconsideration of the importance of biosafety**

The rapid development of modern biotechnology and the process of economic globalization have resulted in a series of biosafety issues, such as the escape of genetically modified organisms, invasion of alien species, and the global outbreak of infectious diseases, which pose a huge threat to the diversity of species, ecological environment and human society.¹ To date, the continued deterioration of the COVID-19 pandemic has severely affected the society and economic development around

the world.^{2–4} In response to the unprecedented challenges from the COVID-19 pandemic, the Chinese government immediately decided to include biosafety in its national security system, which brings the concept of “biosafety” into the spotlight again.⁵

The anthrax envelope bioterrorism attack resulted in several people being infected after the event of September 11, 2001.^{6,7} In 2014, the occurrences of laboratory safety accidents such as the infection of *Bacillus anthracis* and H5N1 influenza virus were mainly due to poor awareness of biosafety.^{8–10} Furthermore, multiple consecutive reports of biosafety events have attracted international attention to biosafety issues. Currently, the outbreak of COVID-19 brings biosafety to the forefront of people’s consciousness, which fully strengthens the necessity for the related scientific research in the field of biosafety.^{11,12} After the outbreak of COVID-19, most national governments have been encouraged to speed up the development of biosafety, which puts forward higher requirements for researchers in biosafety and relevant fields.¹³ Therefore, it is necessary to enhance our awareness toward biosafety and implement dynamic real-time detection, identification and tracking of biosafety issues such as environmental disasters and biological threats and carry out surveillance and control measures immediately.

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1.2 The research areas of biosafety

The concept of biosafety has already been defined by the scientific community.^{14–16} It refers to the prevention and control of hazards caused by biological risk factors such as biotechnology and pathogens. However, there are two easily confused concepts: biosafety and biosecurity.¹⁷ Biosafety is the prevention of the large-scale loss of biological integrity, focusing both on ecology and human health. It emphasizes the passive prevention and control of unintentionally induced biotechnology and microbial biological hazards.¹⁸ In contrast, biosecurity refers to proactive measures to prevent intentional biological hazards and often refers to areas such as national security, biological weapon control, epidemic prevention management, food security, and species invasion.¹⁹ Although the two words biosafety and biosecurity have some subtle differences in meaning, without special emphasis, biosafety is generally used. Therefore, herein, the term “biosafety” is used in all subsequent sections.

The research purpose of biosafety is taking effective measures against biological threats. As summarized in Fig. 1, the research areas of biosafety cover a wide range of topics, including controlling infectious diseases, monitoring biotechnology risks, ensuring laboratory biological safety, protecting biological resources, preventing invasion of alien species, defending against biological warfare and biological terrorist attacks.

2. The proposal of biosafety materials science

2.1 Definition of biosafety materials science

Materials science has shaped the world around us ever since the dawn of civilization. A variety of game changing materials with peculiar properties have been developed to achieve

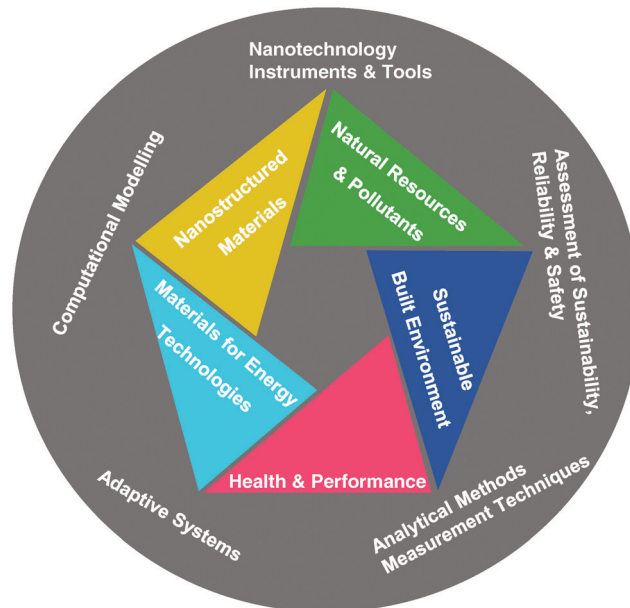


Fig. 2 Classification of materials.

unmet needs.^{20–24} The Swiss Federal Laboratories for Materials Testing and Research (EMPA) briefly categorizes materials as nanostructured materials, materials for energy technology, materials for natural resources and pollutants, materials for health and performance, and materials for a sustainable built environment (Fig. 2).²⁵ Over the past few decades, we have witnessed a revolution in materials science and how it has pushed forward the development of technology.

At this stage, the entire world is still experiencing a shortage of effective materials in response to biosafety threats. In the COVID-19 pandemic, the lack of biological safety personal protection equipment (PPE) such as masks, protective clothing, goggles, and negative pressure ambulance has resulted in a failure to protect numerous medical professionals.^{26–30} Moreover, insufficient sensitive and fast virus detection kits greatly impeded patients from being diagnosed, resulting in rapid spread of this pandemic.^{31,32} Hence, the marriage of biosafety with materials science will greatly help in resolving the existing challenges in biosafety fields, including the detection and disinfection of pathogens, viral vaccines, PPE and biological species preservation (Fig. 3).^{33–38} Therefore, here, we attempt to give a perspective on how the development of novel materials can help scientists tackle the challenges in biosafety. It is urgent and timely for us to officially propose the brand-new concept of “biosafety materials”, which can be a future scientific discipline that utilizes materials science and theory simultaneously to produce materials, related products, and equipment to solve biosafety problems. To the best of our knowledge, the concept of “biosafety materials” as well as “biosafety material science” has never been officially proposed; therefore, the development of biosafety materials may still lack basic guiding ideology. As a result, researchers in materials science may not realize the problems and understand the challenges in biosafety, while researchers in biosafety may have no idea how materials can be applied to solve the biosafety

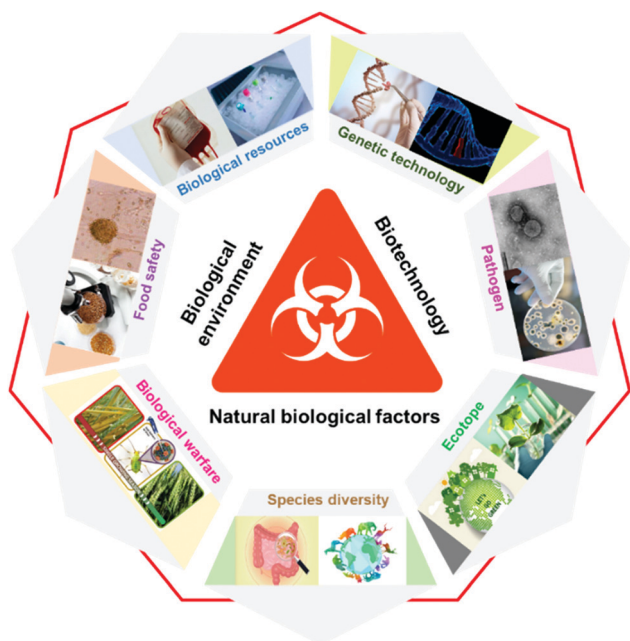


Fig. 1 Research areas of biosafety.



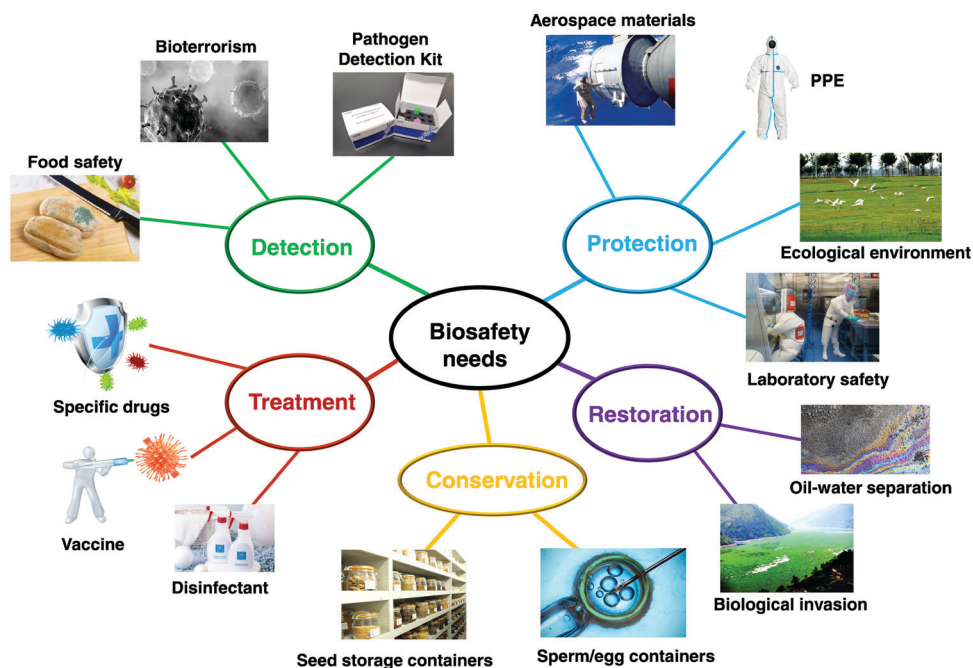


Fig. 3 Biosafety needs and their corresponding biosafety materials.

problems they face. Overall, it is of great significance and timely to put forward the brand-new concept of biosafety materials. By clarifying the concepts and role as well as the importance of biosafety materials, relevant researchers can work together to design advanced biosafety prevention and control materials, which will eventually improve our ability to tackle biosafety-related problems.

2.2 Current challenges in the field of biosafety

To address biosafety-related issues with materials, the current challenges in this field need to be specified.^{39–41} For example, the current mainstream pathogen detection method still largely relies on polymerase chain reaction (PCR), which is time-consuming and laborious. Point-of-care testing (POCT) devices are highly desired due to their convenience.^{42–45} Luminescent materials provided a powerful tool to achieve sensitive and timely detection.^{46–48} Table 1 briefly summarizes the major challenges in biosafety from the perspective of materials science.

2.3 “Biomaterials” and “biomedical materials”

The term “biosafety materials” is also different from “biomaterials” and “biomedical materials”. A biomaterial is any substance that has been engineered to interact with biological systems for a medical purpose, either a therapeutic (treat, augment, repair or replace a tissue function of the body) or diagnostic one.^{49–52} As a science, biomaterials is about fifty years old. The study of biomaterials is called biomaterials science or biomaterials engineering. It has experienced steady and strong growth over its history, with many companies investing large amounts of money into the development of new products. Biomaterials science encompasses elements of medicine, biology, chemistry, tissue engineering and materials science.^{53–55} Biomedical materials are biomaterials that are

manufactured or processed to be suitable for use as medical devices (or components thereof), which are usually intended to be in long-term contact with biological materials.^{54,56} However, biosafety materials emphasize the use of materials for the prevention and control of biological safety issues. Taken together, biosafety materials are different from both “biomaterials” and “biomedical materials”.

2.4 “Biosafety materials” and “biosafety of materials”

The biological safety of materials is mentioned frequently when people study biomaterials.^{57–59} Herein, considering that the concepts of “biosafety materials” and “biosafety of materials” are confusing, a comprehensive comparison between them is provided here. “Biosafety materials” in essence can be “materials for biosafety”, which denote the application of materials and related theory to tackle biological safety issues. However, the latter “biosafety of materials” denotes whether materials are safe to biological systems, how toxicity occurs and to which extent there is toxicity. In general, the “biosafety” in the term “biosafety materials” refers to biological safety, namely, the biological parameters, such as virus and bacteria may cause safety issues to the environment and human body; however, the “biosafety” in the term “biosafety of materials” refers to the safety of certain materials to bio-organisms. The two biosafety terms are the same in written word, but they are terms used in different research fields from different backgrounds, and thus their meanings and connotations vary greatly.

Taking nanomaterials as an example, when the concept of nanomaterials was first proposed, most scientists were attracted by the fascinating properties nanomaterials brought with them, but few realized and considered their safety issues. In 2001, Prof. Yuliang Zhao from The National Center for Nanoscience



Table 1 Current challenges in biosafety

Biosafety field	Category	Challenges
Pathogen detection	Cultivation and identification Pathology instrumentation Immunological detection Molecular biological detection	Detection process is time consuming Low sensitivity, specificity False negative results
Pathogen disinfection	Physical disinfection (ultraviolet rays, high temperature, ionizing radiation, <i>etc.</i>) Chemical disinfection (alcohols, chlorine-containing disinfectants, phenols, quaternary ammonium salts, and iodine-containing disinfectants)	Low efficiency Scented Hazardous chemical residues Drug resistance Corrosive Personnel must leave the field during disinfection
Treatment drugs	Anti-bacterial drugs Anti-viral drugs	Drug resistance The virus has no cell structure, few targets, and drug development is difficult
Vaccines	Inactivated vaccine Live attenuated vaccine Subunit vaccine Genetic engineering vaccine	Slow R & D Invalid after virus mutation Safety issues Lack of good adjuvant
Protective equipment	Protective suit Mask Gloves	Poor anti-toxicity, breathability, and heat dissipation Low protection against aerosols Unable to be reused
Protection of biological resources	Protect plant resources Protect blood resources Protection of human genetic resources	Extraction is easily contaminated Plant seeds are vulnerable to environmental restrictions
Detection of biological invasion	Natural intrusion protection Unintentional introduction of protection Intentional introduction of protection	Difficult to detect at the initial introduction stage Gene drift is prone to occur after invasion
Protection of ecosystem	Control of environmental pollution Improving climate warming Protecting biodiversity	Low oil-water classification efficiency Difficulty in detecting radiation species Low harmful gas adsorption rate Low removal rate of heavy metal pollution
Biochemical weapon	Biological weapon protection Biological warfare agent protection Chemical weapon protection Bioterrorism protection	Investigation difficulties Large-scale popular Easily misdiagnosed Ineffective vaccine
Genetic technology	Optimizing GMOs Suppression of gene mutations Reduce or increase resistance Pharmaceutical biotechnology	Gene drift Negative changes in resistance Genetic mutation Genes affecting non-target organisms
Food biosafety	Detection of carcinogens Screening for contaminants Food preservation Pesticide drug testing	Food shelf-life is too short Easy to be contaminated by microorganisms Hard to detect carcinogens
Aerospace biosafety	Control of body environment Personal protection Aerospace lifesaving	Cosmic radiation Physical and chemical corrosion Mechanical wear

and Technology in China firstly proposed the concept “biosafety of nanomaterials”, which is also termed nanotoxicity (nanosafety).⁶⁰ Since then, the importance of the negative side (such as toxicity) of nanomaterials has been realized by scientists around the world. They further established the CAS (Chinese

Academy of Sciences) Key Laboratory for Biological Effects of Nanomaterials and Nanosafety in China. However, biosafety nanomaterials refer to the use of nanotechnology and nanomaterials to address biosafety issues, which is significantly different from the concept of nanotoxicity and biosafety of nanomaterials. To better



Table 2 Biosafety materials and biosafety of materials

Item	Biosafety materials	Biosafety of materials
Definition	Develop materials for prevention and control biological safety issues.	Evaluate the side effects and toxicity of materials.
Research content	Design and develop new materials for biosafety issues; evaluate their abilities for prevention and control of the biological threat.	Study the toxicity and toxicology of materials to biological species.
Research aim	Protect human health and other species. Conserve the biodiversity. Protect the ecological environment. Prevention and control other biological issues.	Determine whether there is any toxicity of materials. Understand to what extent the toxicity of materials is and how the toxicity occurs. Determine the possible acceptable dosage of materials
Research direction	Find the most efficient, cheapest and best materials to solve biosafety issues.	Reduce the toxicity of materials to the human body.

understand this, these two terms, “biosafety of materials” and “biosafety materials”, are compared in detail in Table 2.

3. State-of-the-art of biosafety materials

Although the concept of “biosafety material science” has not been officially proposed to date, we can still find a number of studies related to the biosafety materials, including pathogen detection,^{61–63} virus detection,^{64–68} prevention and control of infectious diseases,^{69–71} PPE,^{72–75} preservation of biological and human resources,^{76–79} biological invasion monitoring,^{80–82} biological weapons and biological terrorist defense.^{83–87} Herein, the state-of-the-art biosafety materials are discussed in depth, which provides a comprehensive understanding for researchers in the related field and can help propel this concept in the newly emerging field.

3.1 Biosafety materials for viral vaccines

The long battle history between viruses and humans has proven that vaccination is the best solution to completely contain the spread of viruses.^{88–90} It effectively prevents disease through boosting the immune system against a pathogen. Since there are safety concerns on viral delivery systems, several biosafety materials have been extensively investigated for the *in vivo* delivery and controlled release of viral vaccines, including liposomes, polymers, cationic proteins and biological membranes.^{91,92} Viral vaccines can be delivered in the form of DNA, mRNA or protein,⁹³ all of which can be easily enzymatically degraded upon entering the blood circulation.^{94,95} Taking SARS-CoV-2 for example, it contains 1273 amino acids with a molecular weight of about 140 kDa. The DNA encoding SARS-CoV-2 is more than 3800 bp.⁹⁶ Thus, to protect the vaccine in circulation and help it be endocytosed into the cells, delivery vehicles are required. Moderna utilizes ionizable liposomes to carry negatively charged mRNA for the SARS-CoV-2 spike protein.^{97,98} A phase I clinical trial is underway in Seattle, (NCT04283461, USA). Moreover, research has shown that polymers such as low-molecular-weight polyethyleneimine (PEI) modified with fatty chains and poly(β -amino) esters (PABEs) can be designed to deliver DNA

and mRNA.^{92,99} In addition, protamine, as a natural cationic protein, can form complexes with negatively charged nucleic acids, and thereby be utilized to deliver mRNA-based therapeutics and stimulate an immune response.⁹² Furthermore, biological membranes such as red blood cell membranes and extracellular vesicles including exosomes, apoptotic bodies and microvesicles can be isolated and utilized for the delivery of biomolecule-based vaccines.^{100,101} Recently, the microneedle patch, as a novel drug delivery system, has attracted extensive scientific interest due to its excellent properties such as painless penetration and excellent therapeutic efficacy. It provides a highly efficient transdermal delivery system to create sophisticated devices with superior features for biomedical applications. Gambotto's group in the University of Pittsburgh developed the SARS-CoV-2 vaccine based on microneedle arrays (Fig. 4).¹⁰² Compared to the traditional subcutaneous needle injection, MNA SARS-CoV-2 subunit vaccines elicited strong and long-lasting antigen-specific antibody responses. In summary, biosafety materials are of great importance in the development of biomolecule-based therapeutics and are already used to combat viral infections.

3.2 Biosafety materials for pathogen detection

3.2.1 Biosafety materials for viral detection. The development of vaccines and drugs usually takes as long as several years, which means there is possibly no effective way to protect against infectious pathogenic microorganisms in the early stage of infectious disease outbreaks.¹⁰³ Hence, the early detection of viruses is the key to combating the spread of infectious diseases. This is because the information from tests can help governments make public health decisions about measures for the control and prevention of an outbreak. Reverse transcriptase polymerase chain reaction (RT-PCR) has been widely used as a gold standard for virus detection. Although it can provide a reliable result, the process for detection is laborious and time-consuming. Normally, it can take several days or up to even one week to obtain results on an exceptional circumstance, which can cause the best timing to control the disease outbreak to be missed. Thus, rapid virus detection systems such as POCT, with high sensitivity and selectivity are highly desired in the clinic. Accordingly, emerging materials with peculiar properties provide new options to meet this unmet demand.



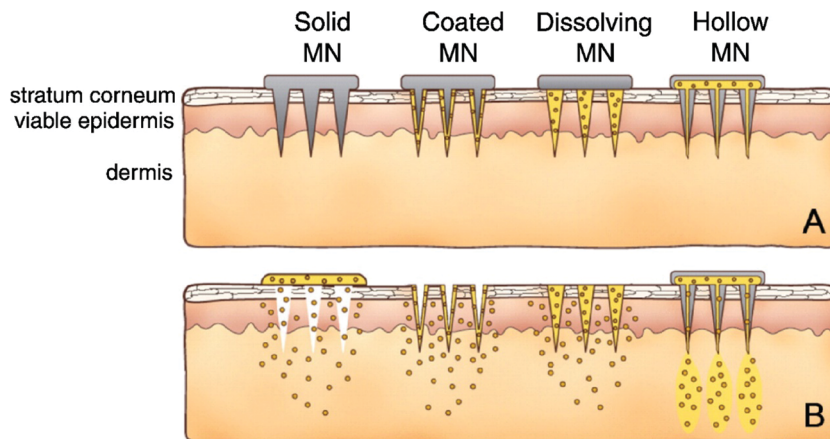


Fig. 4 Biosafety materials based on the microneedle patch for SARS-CoV-2 vaccine delivery. (A) Solid MNs pierce through the outer layers of the skin, leaving open space. (B) Vaccine diffuses into the skin through the open pores. Reproduced with permission from ref. 102. Copyright 2012, Elsevier.

Microfluidics is a revolutionary technology that manipulates small amounts of fluids (10^{-9} – 10^{-18} L), thereby becoming powerful for viral detection (Fig. 5B). Yeh *et al.* reported a portable and high-throughput microfluidic VIRRION platform

containing carbon nanotube arrays (Fig. 5A).¹⁰⁴ VIRRION not only effectively captures different viruses by size, but also performs real-time nondestructive identification of virus using surface-enhanced Raman spectroscopy (SERS) coupled to a

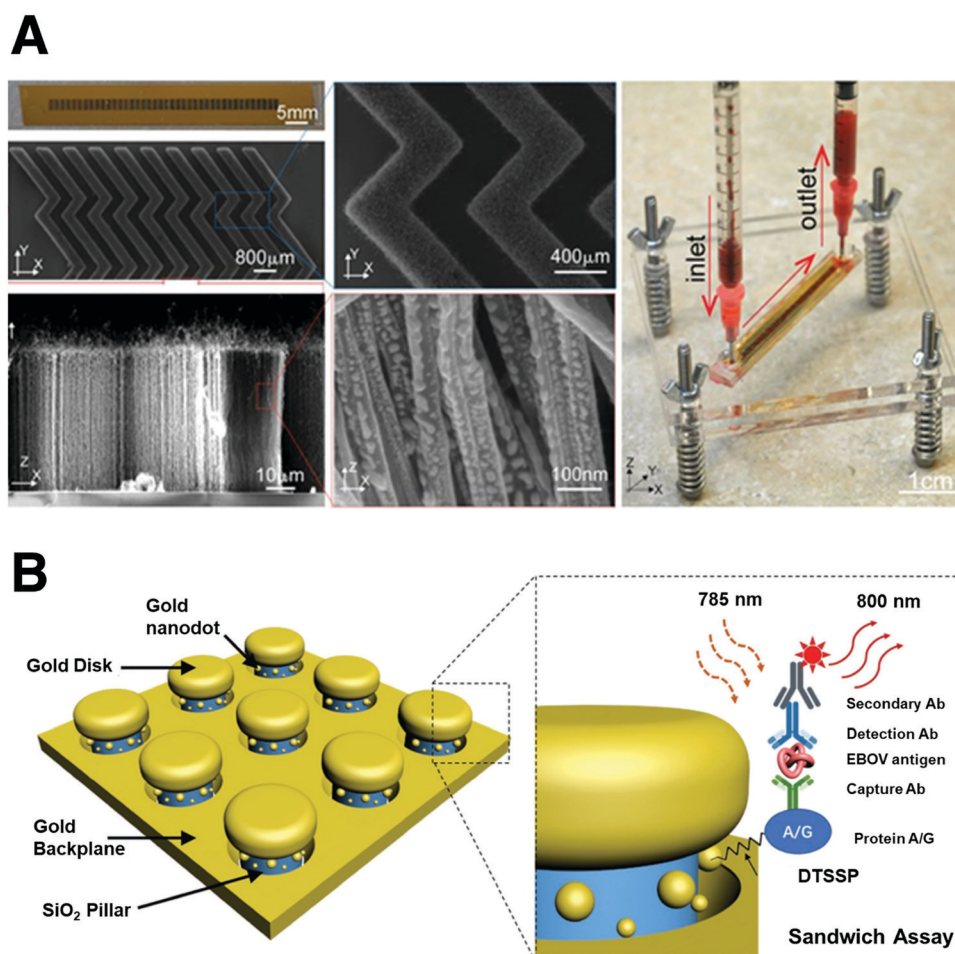


Fig. 5 Biosafety materials for virus capture and detection. (A) High-throughput microfluidic VIRRION platform containing carbon nanotube arrays for influenza virus capture and identification. Reproduced with permission from ref. 104. Copyright 2020, National Academy of Sciences. (B) Schematic illustration of 3D plasmonic nanoantenna array for EBOV sensor. Reproduced with permission from ref. 106. Copyright 2019, Wiley-VCH.



machine learning and database. The research team validated this device using different subtypes of avian influenza A viruses and human samples with respiratory infections, reporting the successful enrichment of rhinovirus, influenza virus and parainfluenza viruses. This device is also reported to maintain stoichiometric viral proportions when samples contain more than one type of virus, suggesting it can also be functional in cases where coinfection has occurred. The processing time (including viral enrichment as well as detection) takes only a few minutes with a 70-fold enrichment enhancement. The sensitivity of this system can reach as little as 10^2 EID₅₀ per mL, with a virus specificity of 90%, indicating its potential to realize POCT. Furthermore, Sun *et al.* designed a point-of-care micro-fluid system integrated with a smartphone for live virus detection. The detection limit is comparable to the traditional RT-PCR, with the result achieved within 30 minutes.¹⁰⁵ Hence, microfluid technology endows detection systems with appealing versatility and reliability, exhibiting distinct advantages over traditional RT-PCR.

The outbreak of the Ebola virus (EBOV) in West Africa underscored the need to develop highly sensitive tests for diagnosis as early as possible. Chou *et al.* developed a 3D plasma nano-antenna measurement sensor as an on-chip immunoassay platform for the ultra-sensitive detection of the EBOV antigen (Fig. 5B).¹⁰⁶ Compared with the flat gold substrate, the EBOV sensor exhibited a significant increase in fluorescence intensity. The nano-antenna-based biosensor could detect EBOV soluble glycoprotein at a concentration as low as 220 fg mL^{-1} . The sensitivity of this biosensor is 240 000 times higher than the existing FDA (Food and Drug Administration)-recommended immunoassay-based tests. This sensor can be further adapted to a universal biosensing platform for other viruses. Zheng *et al.* utilized carbon nanotubes to develop a portable device that can selectively capture viruses based on their size.¹⁰⁷ This carbon nanotube assay can selectively capture and aggregate viruses in diluted samples based on the size of the virus, thus increasing

the detection threshold of the virus by a factor of 100. During the whole isolation process, no antibody is required for detection, which simplifies the operation for viral detection.

Nanoenzymes, as functional nanomaterials with enzyme-like characteristics, have gained tremendous attention in viral detection.^{108,109} For example, nanoenzymes demonstrated remarkable sensitivity and specificity in detecting the avian influenza A (H5N1) virus. Ahmed *et al.* utilized Au NP as peroxidase to amplify the signal for avian influenza A virus detection (Fig. 6A).¹¹⁰ This dual enhanced colorimetric immunosensor enabled the detection of H5N1 with a limit of detection (LOD) as low as 1.11 pg mL^{-1} , suggesting that it was more sensitive than ELISA or bioassays based on plasmonics. It has been further applied to detect other avian influenza A viruses such as H4N6 and H9N2. In addition, Yan's group developed an Fe₃O₄ magnetic nanoparticle (MNP)-based nanoenzyme-strip for the detection of EBOV, which is 100-fold more sensitive than the standard strip method, thereby providing a valuable simple screening tool for the diagnosis of various pathogens (Fig. 6B).¹¹¹

3.2.2 Biosafety materials for bacteria detection. Most bacteria are harmless and even beneficial, but some bacteria are pathogens that can cause many infectious diseases such as tuberculosis, which result in about two million deaths each year.^{112,113} Moreover, the worldwide trend of the increasing prevalence of antimicrobial resistance resulting from the outright abuse of antibiotics has become a major public health problem. Thus, the development of POCT can significantly help identify an effective antibiotic for the infection of a patient. Xiao *et al.* developed a novel biosensor for the high-throughput detection of bacteria based on the DNA molecular machine.¹¹⁴ The platform successfully realized single-step, fast and multi-channel high-throughput bacterial detection, as shown in Fig. 7A. The SDwalker drop biosensor platform adopts the trigger spontaneous motion mechanism of a walking molecular machine, which has the characteristics of rapid analysis and single bacterial analysis. The signal amplification strategy based on SDwalker drop operation can

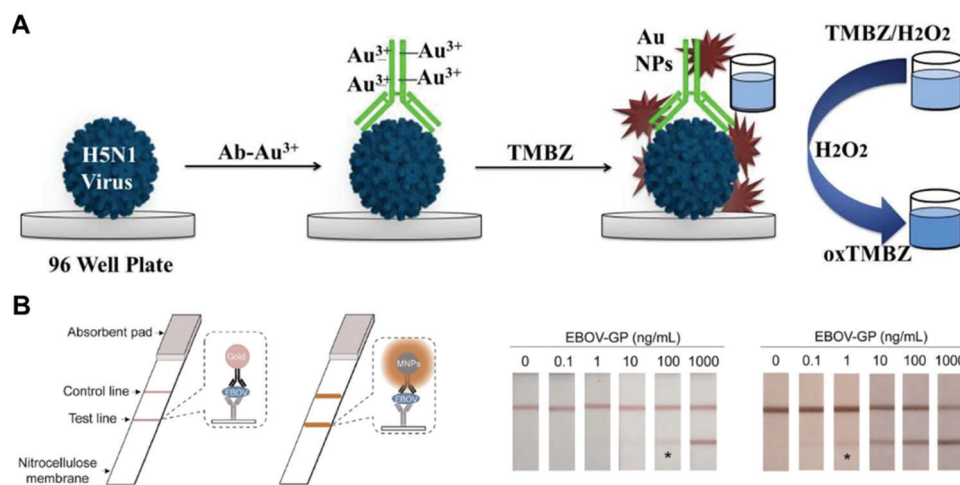


Fig. 6 Nanoenzyme-based biosafety materials applied in virus detection. (A) Mechanism of immunosensor with Au NPs for the detection of the avian influenza virus. Reproduced with permission from ref. 110. Copyright 2017, Ivspring International Publisher. (B) Nanozyme strip based on MNP for the detection of EBOV. Reproduced with permission from ref. 111. Copyright 2015. Elsevier.



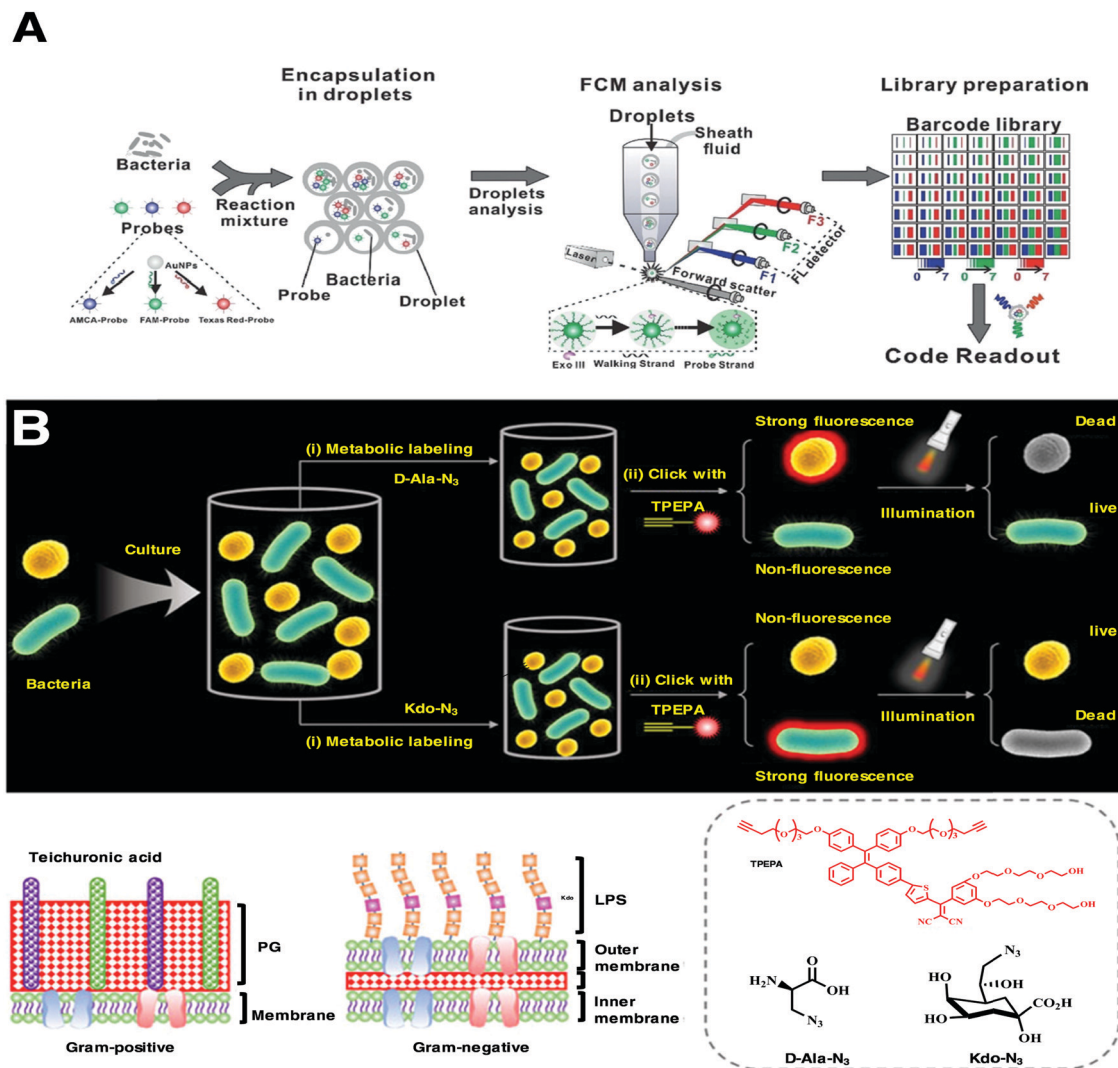


Fig. 7 Biosafety materials for the detection of bacteria. (A) Schematic of the SDwalker-Drop platform for super-multiplex bacterial phenotype analysis. Reproduced with permission from ref. 114. Copyright 2019, Wiley-VCH. (B) Schematic illustration of the use of an AIE material for the discrimination and precise ablation of bacterial pathogens. Reproduced with permission from ref. 122. Copyright 2019, American Chemical Society.

be used for the highly sensitive detection of bacteria (1 CFU mL^{-1}), exhibiting a promising platform for the detection of bacteria.

Traditional fluorescent probes have the effect of aggregation-induced quenching (ACQ), but the complex physiological environment can reduce the selectivity and sensitivity of fluorescent probes.^{115,116} In contrast, molecules with the aggregation-induced emission (AIE) effect can overcome the shortcomings of traditional fluorescent molecules, and no complicated washing steps are required due to their property of low fluorescent background.^{117,118} These advantages of AIE molecules endow sensitivity and reliability to detection systems.^{119–121} Liu *et al.* designed a bioorthogonal fluorescence turn-on probe, TPEPA, for the discrimination and precise ablation of bacterial pathogens.¹²² TPEPA (tetraphenylene polyethylene glycol AIEgen) is a type of AIE photosensitizer with good water solubility, and its alkynyl group can be linked to an azide group *via* click reaction (Fig. 7B). Taking advantage of the difference in bacterial structures, TPEPA can discriminate pathogens *via* selective imaging of metabolically

decorated Gram-negative bacteria with Kdo-N₃ and Gram-positive bacteria with D-Ala-N₃, respectively, thus achieving the selective detection and killing of bacteria *in situ*. The use of the fluorescent properties of organic materials solves the problems of difficulty in accurately identifying pathogens in a short time.^{123–126}

3.3 Biosafety materials for disinfection

The wide use of disinfection is beneficial in preventing infectious diseases, and thus is beneficial for the public health. It relies on physical or chemical methods to eliminate pathogens that stay on different transmission vehicles, thereby cutting off the transmission route to prevent and control the spreading of infections. Various chemical compounds such as alcohol, iodine-containing disinfectants, chlorine-containing disinfectants, peroxides, phenols, and quaternary ammonium salts have been widely used as disinfectant. However, these compounds suffer from multiple drawbacks such as harmfulness and corrosive nature.



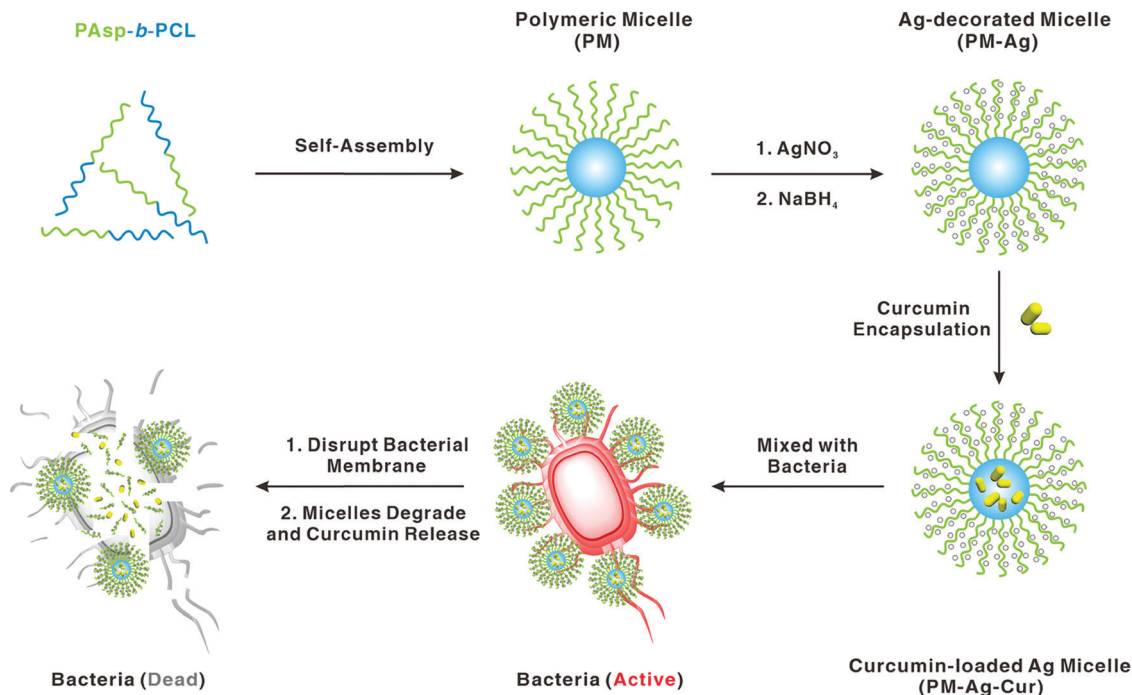


Fig. 8 Biosafety materials based on Ag NPs for disinfection. Schematic illustration of the formation of silver-decorated polymeric micelles encapsulating curcumin simultaneously for enhanced antibacterial activity. Reproduced with permission from ref. 128. Copyright 2017, American Chemical Society.

Nanomaterials exhibit antimicrobial effects owing to their high surface-area-to-volume ratio and unique physical and chemical properties. Particularly, tremendous attention has been paid to Ag NPs due to their practical applications in our daily life. They have been widely used in different sectors such as silver-based air/water filters, textiles, animal husbandry, biomedical industry and food packaging.¹²⁷ Huang *et al.* designed a novel polymeric micelle for simultaneously decorating Ag NPs and encapsulating curcumin as a combination strategy to improve the antibacterial efficiency (Fig. 8).¹²⁸ Through rational design, the aggregation of Ag NPs could be avoided, and the solubility of curcumin was improved simultaneously. Excellent antibacterial activity toward the Gram negative *P. aeruginosa* and Gram positive *S. aureus* has been well demonstrated, thereby proving its potential in disinfection.

3.4 Biosafety materials for drug treatment

The discovery of anti-microbial agents has revolutionized our strategy to treat bacterial diseases in the twentieth century.^{129,130} However, the misuse and outright abuse of antibiotics have resulted in multidrug-resistant (MDR) pathogenic bacteria. Nanotechnology-based antibacterial strategies significantly enrich the tools to fight against MDR bacteria. As shown in Fig. 9A, Liang's group designed near infrared (NIR)-activated TRIDENT (Thermo-Responsive-Inspired Drug-Delivery Nano-Transporter) for effectively eradicating clinical methicillin-resistant *Staphylococcus aureus*.¹³¹ Imipenem (IMP, a broad-spectrum antibiotic) and IR 780 (a photosensitizer molecule) were encapsulated to fabricate smart triple-functional thermo-responsive nanoparticles. The temperature increase generated by NIR not only melted the

nanotransporter *via* a phase change mechanism, but also damaged the bacterial membranes to facilitate imipenem permeation, thereby achieving robust bactericidal capabilities *via* chemo-photothermal therapy. The unique properties of carbon-based materials significantly aid in dealing with antimicrobial resistance. As shown in Fig. 9B, Zheng *et al.* designed an La@GO nanocomposite library for killing antibiotic-resistant bacteria.¹³² Unlike conventional antibiotics or Ag, long-term exposure to La@GO at sub-MIC for 30 days did not induce detectable secondary resistance in *E. coli*. A novel extracellular multitarget invasion (EMTI) mechanism was also proposed to explain the result, which can help scientists develop more specific systems based on this system. The first antibiotic penicillin was discovered in 1928. Subsequently, numerous lives have been saved, and a variety of antibiotics have contributed to the control of infectious diseases. However, currently, there are very few antibiotics under development, and the number of effective antibiotics is declining. Thus, novel materials with versatile properties provide new strategies to treat MDR bacteria and viruses, providing a different route to overcome drug resistance.

3.5 Biosafety materials for PPE

Serving as the first line of defense in the fight against viruses, high-performance PPE is crucial for protecting frontline medical professionals and the general public.^{133,134} Current PPE suffers from poor light resistance, and no antimicrobial effect is provided. Furthermore, it is difficult for PPE materials to be effectively disinfected under the premise of good preservation.^{135,136} Hence, stable and protective materials with broad antimicrobial activity are in high demand.



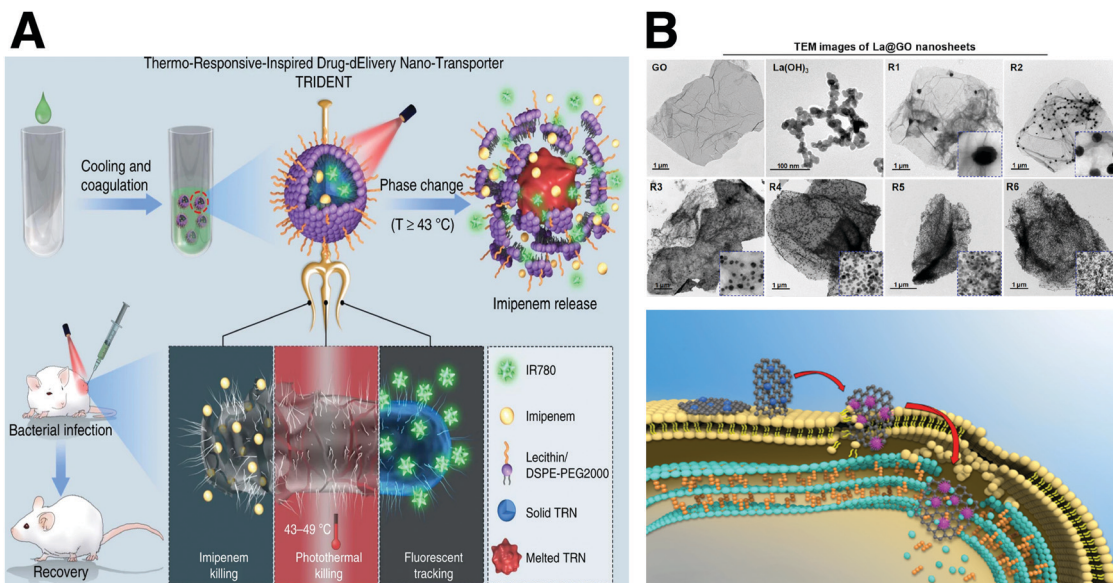


Fig. 9 Biosafety materials for combatting MDR bacteria. (A) Schematic illustration of near infrared (NIR)-activated TRIDENT for killing antibiotic-resistant bacteria. Reproduced with permission from ref. 131. Copyright 2019, Nature. (B) Graphene oxide nanocomposite for preventing the evolution of antimicrobial resistance. Reproduced with permission from ref. 132. Copyright 2019, American Chemical Society.

For stopping the spread of highly infectious diseases, air filtration has become an efficient passive pollution control strategy. Nevertheless, most of the commercial air purifiers solely rely on dense fibrous filters, which can effectively remove particulate matter but lack antibacterial activity. Li *et al.* designed a series of metal-organic frameworks (MOFs) with photocatalytic bactericidal properties to fabricate a nano-fiber membrane.¹³⁷ It can effectively produce biocidal reactive oxygen species (ROS), which is driven by sunlight (Fig. 10A). Specifically, a zinc-imidazole MOF (ZIF-8) exhibits almost complete inactivation of *Escherichia coli* (*E. coli*) (> 99.9999% inactivation efficiency) in saline within 2 h of simulated solar irradiation. This MOF filter provides new insights into the sustainable, self-charging, and adaptive development of protective materials, which represents the next generation of PPE. Moreover, a polymer material was developed to make face mask protection equipment (Fig. 10B). Liu *et al.* designed a novel self-powered electrostatic adsorption face mask (SEA-FM) based on a poly(vinylidene fluoride) electrospun nanofiber film (PVDF-ESNF) and a triboelectric nanogenerator (TENG).¹³⁸ Up to 99.2% particulate removal efficiency could be achieved, which is much higher than that of the commercial mask. After the outbreak of COVID-19, the demand for masks has exploded worldwide. However, the disposal of the massive number of single-use masks poses a significant environmental threat to society. Thus, to ease this problem, reusable and recyclable graphene masks with outstanding superhydrophobic and photothermal performances were developed by Li *et al.* The high surface temperature of the masks under solar illumination can effectively sterilize the surface viruses. It is believed that more advance materials can be properly applied by scientists to produce multi-functional masks.¹³⁵

Surgical suits are special clothing required by doctors to perform surgical operations. The materials used need to possess protective properties to block viruses and bacteria from invading

medical personnel, which should not only be sterile, dust-free and disinfection resistance, but also isolate bacteria, antibacterial and comfortable. Accordingly, a three-layer antiviral surgical suit with non-woven spunbond polypropylene, polyester and microporous PTFE film was developed.¹³⁹ Plasma technology was used to treat the outer layer of the spunbond polypropylene. The results showed that the plasma-treated surgical gown had a 99.04% reduction in microbes compared to the non-plasma-treated surgical gown, providing a microbial barrier for medical staff.^{140–143}

Respirators are a type of sanitary product, generally referring to that worn in the nose and mouth to filter the air entering the nose and mouth to block harmful gases, odors, droplets, viruses and other substances. Masks have a certain filtering effect on the air entering the lungs. When respiratory infectious diseases are prevalent and when working in a polluted environment such as a dusty area, wearing a mask is necessary to keep workers safe.^{144,145} Novel material fabrication technology such as 3D printing has been applied to manufacture masks.¹⁴⁶ The N95 filtering facepiece respirator was custom designed for medical staff. Comfort and fit are essential while wearing an FFR, especially for medical professionals who need to work for a long period to treat patients. The face seal prototypes of masks were prepared with acrylonitrile butadiene styrene (ABS) plastic using 3D printing, which provide improved contact pressure for users.

3.6 Biosafety materials for protection and preservation of biological resources

With economic globalization, environmental pollution and global warming, biodiversity has faced unprecedented challenges. The preservation of biological resources provides a guarantee for the biodiversity of the ecological system. Generally, biological genetic resources mainly include the extraction and protection of



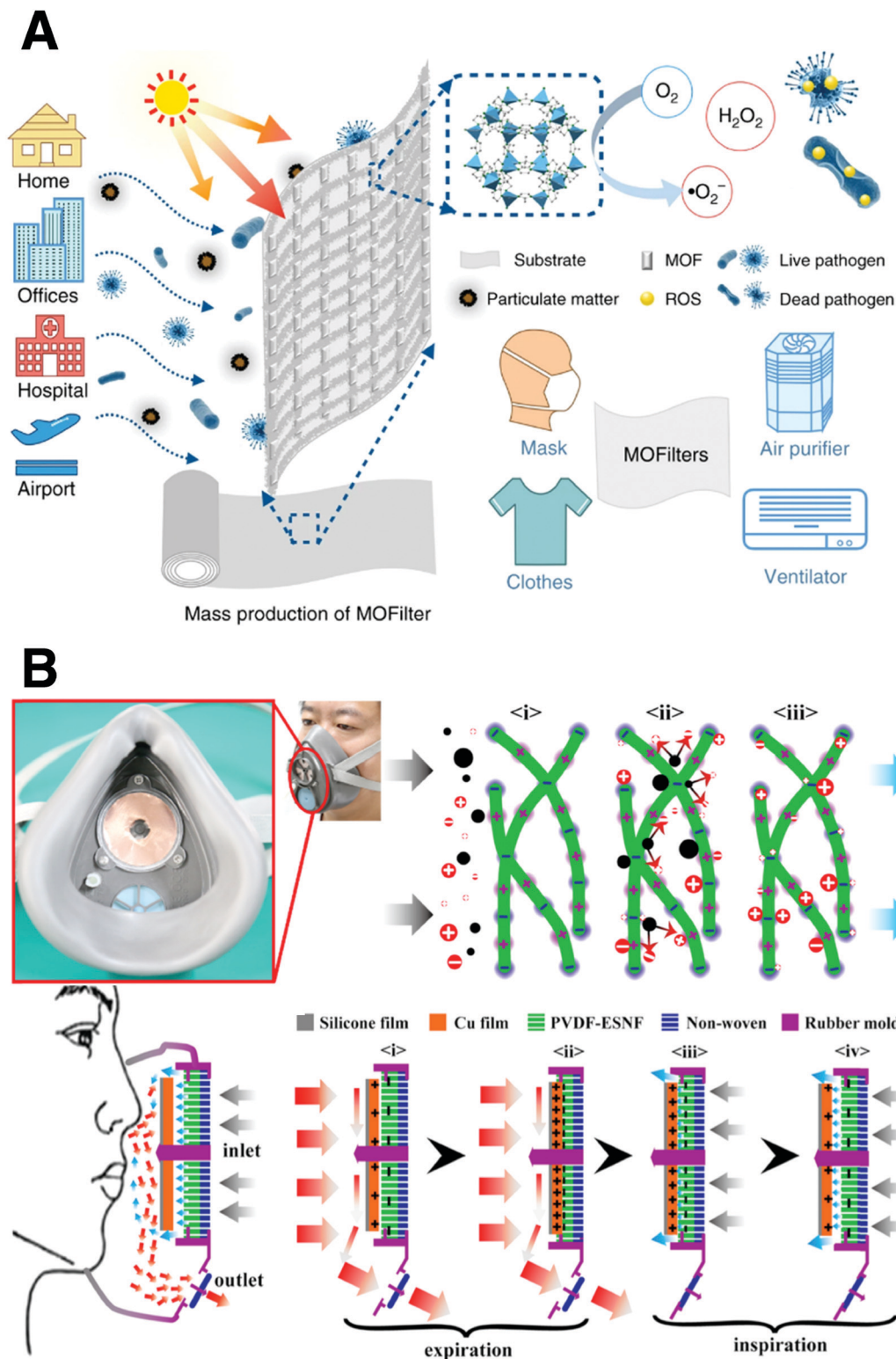


Fig. 10 Biosafety materials for PPE with antimicrobial capacity. (A) Schematic illustration of metal–organic framework (MOF)-based filter. Reproduced with permission from ref. 137. Copyright 2019, Nature. (B) Schematic illustration of the filtration mechanism of the polymeric material mask. Reproduced with permission from ref. 138. Copyright 2018, American Chemical Society.

animal and plant genetic materials such as biological genes, sperm and eggs.^{147–150} The major shortcomings for the current protection methods are the low survival rate of seeds and possibility of

uncontrollable mutation. Cheng *et al.* discovered that PVP (polyvinylpyrrolidone) and PVPP (polyvinylpolypyrrolidone) could effectively remove multiple phenolic compounds and terpenoids



during the process of extracting DNA.¹⁵¹ Therefore, the addition of an appropriate amount of PVP or PVPP to the DNA extraction solution can improve DNA purity, remove polysaccharides, and reduce polyphenol contamination. This is a good example that biosafety materials display protective significance on genetic resources. The PVP method has now been accepted as one of the most used DNA extraction techniques, thereby indicating that the development of materials actually changes the technic in protecting biological resources.^{152–155}

The protection of plant seeds is also a crucial biosafety issue.^{156,157} Seed enhancement technologies play a pivotal role in supporting food security by enabling the germination of seeds in degraded environments. Marelli *et al.* combined silkworm cocoon S molecules and trehalose to design a new seed coating method.¹⁵⁸ As shown in Fig. 11A, this formulation is capable of precisely coating seeds with biofertilizers and releasing them in

the soil to boost seed germination and mitigate soil salinity. The coated seeds yielded plants that grew faster and stronger in the presence of saline soil. Hence, this study opens the door to the application of advanced biosafety materials in precision agriculture, introducing the drug delivery concept to seed protection. Furthermore, polymeric materials have been proven to reduce environmental side effects and improve seed survival, suggesting the importance of composite materials in the protection of biological resources.^{159–162}

Cryopreservation is the classical way to preserve human genetic resources.¹⁶³ However, the mechanical damage effect of ice crystals is the major problem in cryopreservation. Inspired by the regenerable solid epicuticular wax on the surface of land plant leaves, Wang *et al.* developed solid organogel materials with a regenerable sacrificial alkane surface (Fig. 11B).¹⁶⁴ This type of surface material was demonstrated to be of great

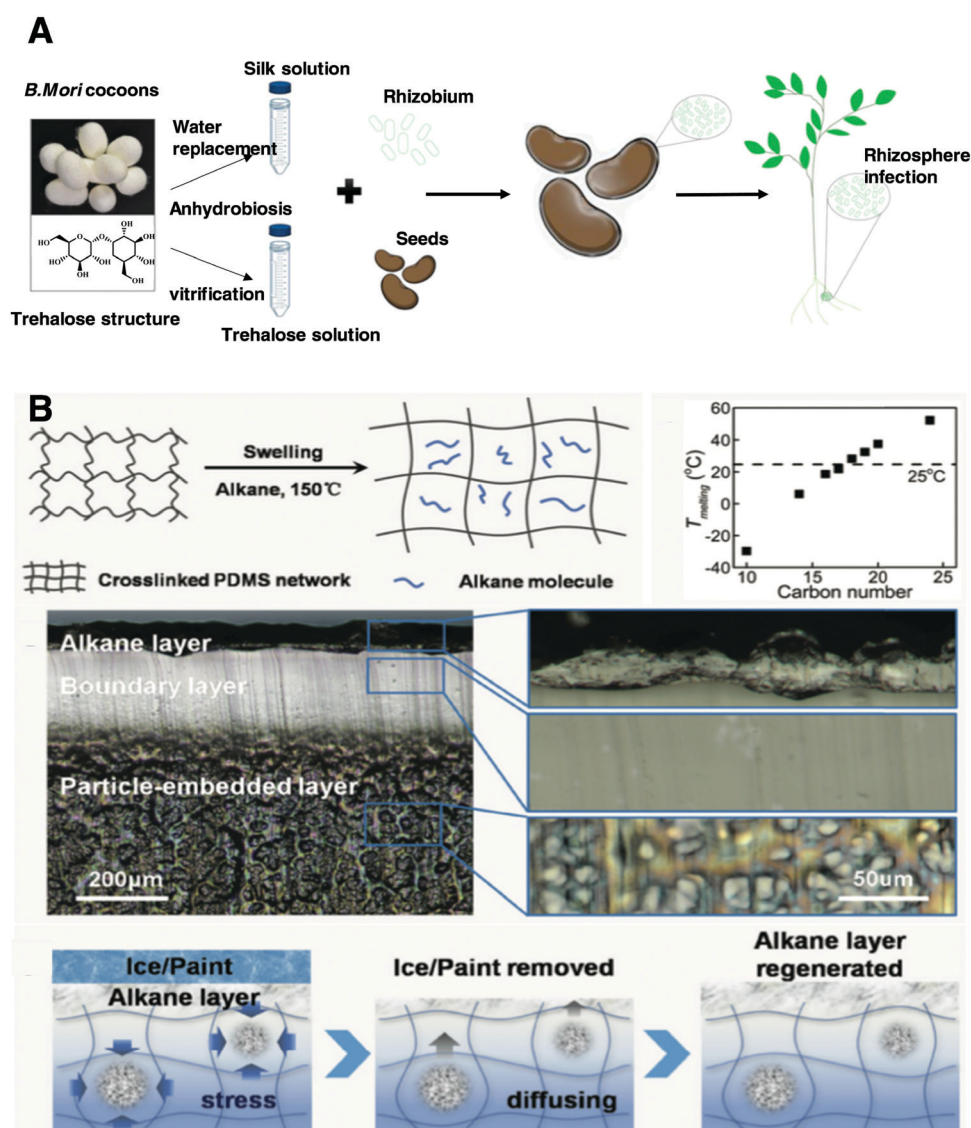


Fig. 11 Biosafety materials for the protection and preservation of biological resources. (A) Biosafety materials based on silk fibroin and trehalose for seed coating, which can boost germination and mitigate abiotic stress. Reproduced with permission from ref. 158. Copyright 2019, National Academy of Sciences. (B) Principle of the solid organogel material to cryopreserve biological resources. Reproduced with permission from ref. 164. Copyright 2017, Wiley-VCH.



practical importance for tackling solid deposition, such as anti-icing, anti-graffiti, and antifouling. Compared with the ice adhesion strength of aluminum ($372.2 + 47.4$ kPa) and PDMS ($146.3 + 9.5$ kPa), the ice adhesion strength of the solid organic gel was reduced to $68.8 + 10.4$ kPa. The adhesion value remained almost unchanged when the temperature decreased from -20 °C to -70 °C, indicating its potential for the cryopreservation of natural biological resources.

3.7 Biosafety materials for the prevention of biological invasion

Biological species invasion has been considered as one of the most critical ecological disturbances that threatens the native biodiversity.^{165–167} In 1996, the Global Invasive Species Program was launched. Since then, biological invasion has been a focus and heavily studied.^{168,169} Biological invasions can be divided into several stages, including introduction, escape, population establishment and harm. Except for purposeful introduction, the early detection of other invasion ways is challenging. If the invasion reaches a detectable range, it is hard to be removed. Hence, early detection is crucial to prevent biological invasion. The development of genetic detection technology has facilitated the detection of biological invasions. Wang *et al.*¹⁷⁰ developed a sensitive nucleic-acid sensing platform based on superhydrophilic microwells spotted on a superhydrophobic substrate (Fig. 12). The difference in wettability facilitated the conversion of trace analyte between the micropores and surrounding substrate into superhydrophilic microporous materials. Due to the condensation enrichment effect, ultratrace DNA detection was realized, and the detection limit reached 2.3×10^{-16} M. The genome of certain species can be rapidly determined using a gene library, enabling the fast identification of invading species.

Since invasive alien species have no natural enemy, they can rapidly settle in a new environment and quickly grow into an overlord community, eventually destroying the local ecosystem and inhibiting the growth of other local species. The loss of biodiversity in ecosystems further leads to irreversible consequences, such as the disappearance of forests, pastures degradation, and

water pollution. Hence, in addition to the early detection of biological invasion, it is of great significance to effectively eliminate invaded alien species. Fortunately, the biosynthesis of metal nanoparticles provides an environmentally friendly approach to fight against invading alien species. *Oscillatoria*, as one of the most common cyanobacterial genera known to produce neurotoxins, has negative impacts on aquatic organisms. To stop the growth of *Oscillatoria*, the Ag-NPs biosynthesized by specific alga exert outstanding negative impacts on it, which significantly alleviates the environment burden through green synthesis.¹⁷¹ A similar biosynthesis strategy has also been found for controlling vector mosquitoes. The plant-synthesized AgNPs developed by Rajakumar *et al.* can effectively eliminate mosquitoes, providing an effective way to control mosquito-borne diseases.¹⁷² Hence, the development of materials science provides bio-friendly alternatives for the prevention of biological invasion, enriching the methods to deal with difficult environmental-related issues.

3.8 Biosafety materials for protection of ecological environment

The ecological environment is a prerequisite for ensuring species diversity. The 2010 Deepwater Horizon oil spill in the Gulf of Mexico has been regarded as the worst environmental disaster in the United States, which released about 4.9 million barrels of crude oil, and had a huge impact on the ecological system. Thus, efficient and cost-effective separation strategies for spilled oil are greatly needed. Janus particles are colloidal particles with more than one type of surface chemistry or composition, which provide a suitable system for oil separation. Song *et al.* developed magnetic Janus particles with a convex hydrophilic surface/concave oleophilic surface, realizing the rapid and efficient separation of microscale tiny oil droplets from water (Fig. 13).¹⁷³ Ren *et al.*¹⁷⁴ developed a phase-selective organic gelling agent, which not only showed the ability to selectively condense oil from oily water, but also could easily separate colloidal oil and water from the human body. This powder gelator exhibited remarkable ability to achieve rapid gelation of crude oils of widely ranging viscosities within minutes at room temperature.

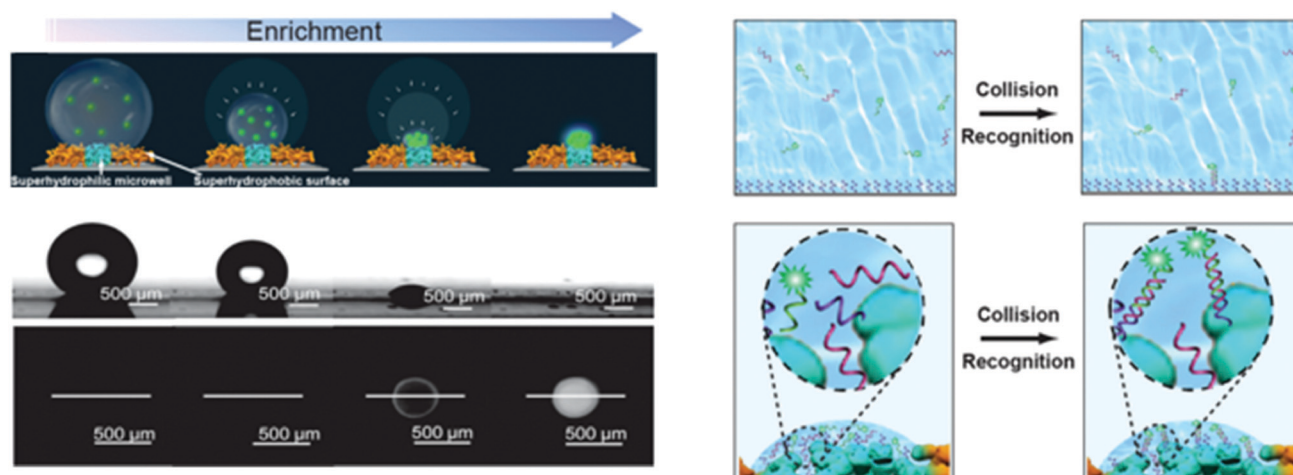


Fig. 12 Biosafety materials for the early detection of biological invasion. Ultratrace DNA detection based on superhydrophilic microwells spotted on a superhydrophobic substrate. Reproduced with permission from ref. 170. Copyright 2015, Wiley-VCH.



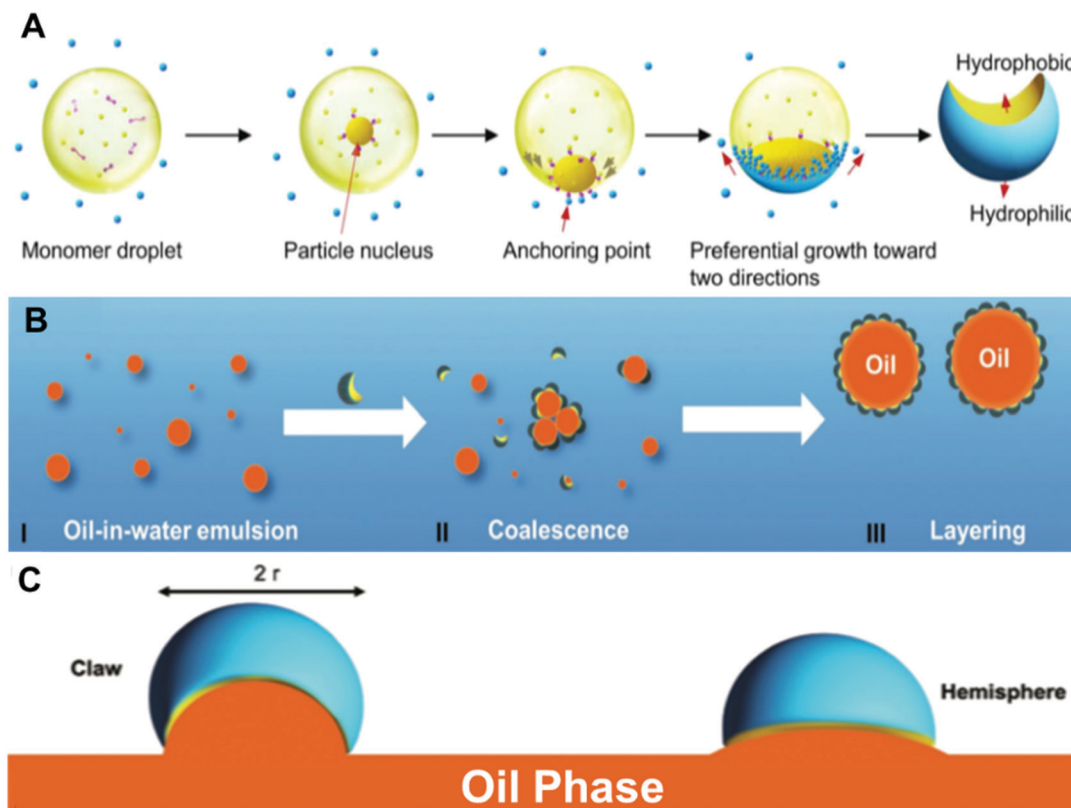


Fig. 13 Biosafety materials for separating spilled oil from water. (A) Schematic illustration of the principle of hydrophilic/oleophilic magnetic Janus particles. (B) Schematic of the separation of tiny oil droplets by Janus particles. (C) Schematic of two different types of Janus particles. Reproduced with permission from ref. 173. Copyright 2018, Wiley-VCH.

Heavy metals are harmful and toxic pollutants that are difficult to degrade. They not only cause a degradation in soil quality, but also enter the human body through direct contact or the food chain. In recent years, scientists have gradually realized that heavy metals have a massive impact on the microbes in soil, which eventually influence the soil microbial activity, microbial community, and soil enzyme activity. Thus, to ameliorate this condition, scientists have developed novel materials to remove heavy metal pollution in the soil ecosystem.¹⁷⁵ Lian *et al.* developed a simple and economical path to prepare mercapto-functionalized nanosilica.¹⁷⁶ Nanosilica, which has excellent compatibility with soils, was chosen as the matrix. This biosafety material efficiently remediated Pb/Cd-contaminated soils, exhibiting a high immobilization efficiency of 99.12% and 98.23% towards Pb and Cd, respectively.¹⁷⁶ In addition to silica, carbon-based materials have also been selected to deal with this problem due to their excellent absorption capacity, providing versatile methods to protect the ecological environment.^{177,178}

3.9 Biosafety materials for protection against bioterrorism

Bioterrorist attacks have been regarded as the most important biosecurity threat in modern society. Monitoring and medical and health response are the two critical measures for preventing bioterrorism. The biological warfare agents that terrorists can use for attack include *Bacillus anthracis*, *Brucella*, *Rickettsia prowalskii*, and *Yersinia pestis*. These agents are mainly spread

through aerosols, food and water sources. Bioterrorism possesses the characteristics of strong infectivity, strong concealment, simple production process, and wide impact. Anthrax spores are an ideal biological weapon since they are highly lethal to human beings and animals.^{179–181} Thus, rapid detection methods for anthrax spores are in great demand. As shown in Fig. 14, Tang *et al.* designed a rare earth-functionalized micelle nanoprobe for the ratiometric fluorescence detection of an anthrax spore biomarker, pyridine dicarboxylic acid (DPA).¹⁸² The detection strategy was ascribed to the Tb³⁺ ions in the lanthanide-functionalized micelle, which can be sensitized to emit intrinsic luminescence upon the addition of DPA due to the occurrence of energy transfer when the DPA chromophore coordinates with the Tb³⁺ ion. This nanoprobe can detect DPA within a linear range of 0–7 μM within a few seconds, and the detection limit is up to 54 nM. It is believed that the defense against biological weapons can be strengthened by incorporating novel materials with peculiar properties into the detection system.

Because of the acute neurotoxicity caused by biological weapons, saving victims after exposure remains challenging. Neurodrugs are organophosphorus compounds (OPS) that block the communication between the nerves and organs, which have been used as biological weapons.^{183–185} Jiang *et al.* developed a nanoscavenger, which exhibited a long-term protective effect on OPS poisoning in rodents (Fig. 15).¹⁸⁶ It could catalyze the decomposition of toxic OPS, and exhibited excellent pharmacokinetic



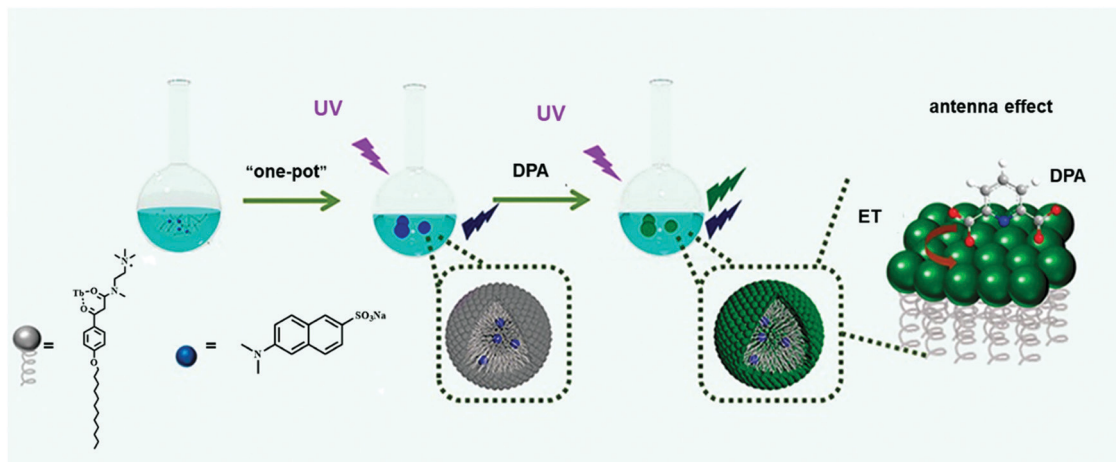


Fig. 14 Biosafety materials based on a ratiometric fluorescence lanthanide-functionalized micelle for the detection of an anthrax spore biomarker. Schematic illustration of the "one-pot" self-assembly of terbium-functionalized micelle in H₂O and its response property for DPA. Reproduced with permission from ref. 182. Copyright 2018, American Chemical Society.

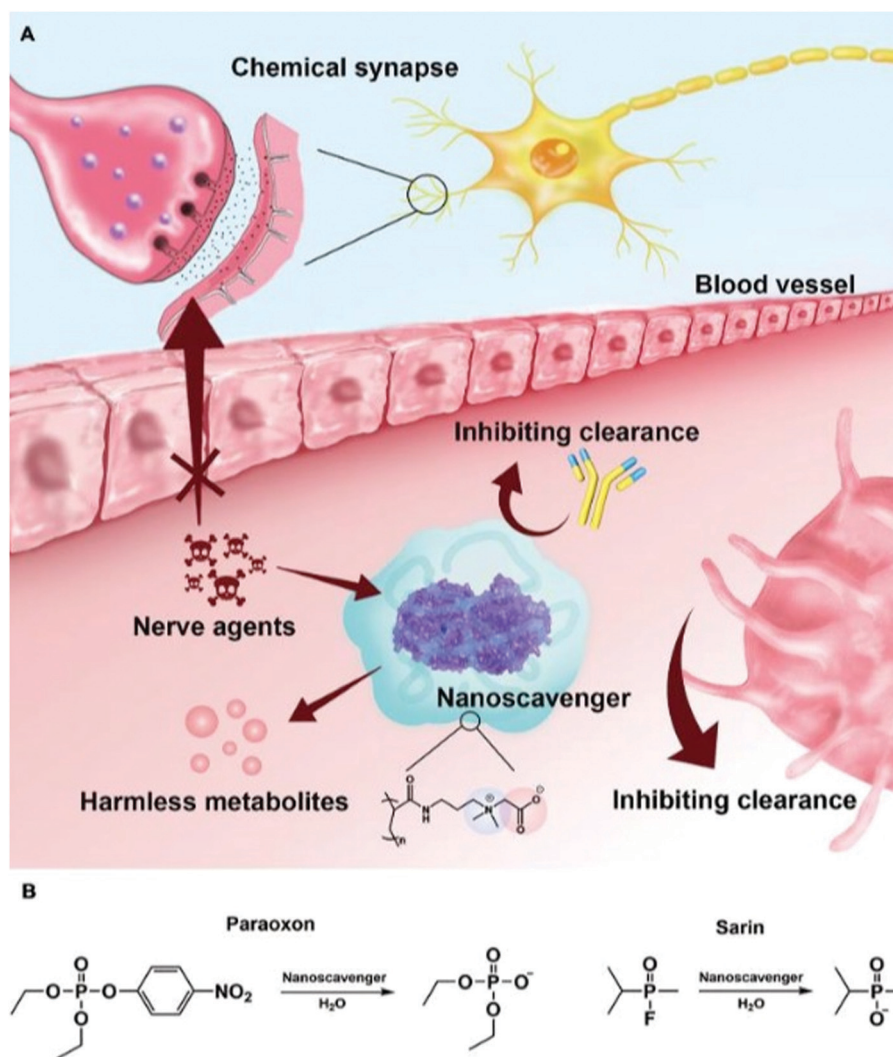


Fig. 15 Biosafety materials as nanoscavengers to remove neuro-drugs. (A) Schematic illustration of the protection mechanism of nanoscavengers. (B) Hydrolysis of paraoxon and sarin mediated by nanoscavengers. Reproduced with permission from ref. 186. Copyright 2019, American Association for the Advancement of Science.



characteristics and negligible immune response in OP-poisoned rats. In a guinea pig model, the single prophylactic administration of nanoscaevengers effectively prevented death after repeated exposure to sarin within one week, demonstrating the translational significance of nanoscaevengers in clinical and military settings.

3.10 Biosafety materials for genetic technology

The emergence of genetic technology directly broke the original pattern of science and promoted the development of medical, agricultural and other fields. However, it also brought problems such as gene mutation and hybridization, indicating the double-sidedness of gene technology. The conventional genetic engineering technique targets the nuclear genome, resulting in problems in the proliferation of foreign genes to weedy relatives. Target delivery to specific organelles is highly desirable for plant genetic engineering, which can be achieved *via* nanoparticle-mediated transformation. Wong *et al.* designed a gene carrier based on chitosan-complexed single-walled carbon nanotubes (SWNTs) for chloroplast transformation.¹⁸⁷ The nanotube carrier could deliver plasmid DNA to the chloroplast of different plant species without external biolistic or chemical aid, thereby rendering a chloroplast transgene delivery platform for mature plants across different species. In Fig. 16, Wang *et al.* summarized a series of functionalized nanomaterials that provide diverse platforms capable of traversing barriers (*e.g.*, multilayered cell walls) to deliver exogenous plasmid pDNA and siRNA in to intact plant cells.¹⁸⁸

3.11 Biosafety materials for food safety

Food safety, as a global public health issue, has been regarded as a biosafety problem.^{189–191} The major issues in food safety are summarized as follows. (1) The presence of microorganisms directly causes mold, which can easily spread during the process of production, distribution and packaging.^{192–195} (2) The emergence of additives greatly helps in the manufacture of food that meets certain requirements, but if the amount of food additives used exceeds the standard level, it poses a serious threat to human health.^{196,197} (3) The overuse of chemical fertilizers and pesticides leads to severe pollution and food safety problems, which places a vast burden on human health.^{198,199} Thus, to tackle these challenges, materials scientists have proposed various solutions for food safety problems in testing, packaging, and storage.^{200–203}

Hydrogen sulfide (H₂S) with rotten egg odor is produced in rotten food. Thus, the rapid and sensitive detection of H₂S is important to forewarn of food spoilage or pollution incidents with respect to this gas. Tang *et al.* prepared an Ag@Au core-shell nanoprobe combined with headspace single-drop micro-extraction (HS-SDME).²⁰⁴ Smartphone nanocolorimetry with the aid of a smartphone camera and color picker software was applied to detect and quantify H₂S (Fig. 17). The limit of detection for this nanocolorimetric approach was as low as 65 nM, which represents an ideal *in situ* analytical approach for the determination of H₂S. Hence, the development of biosafety materials provides technical support for food safety.

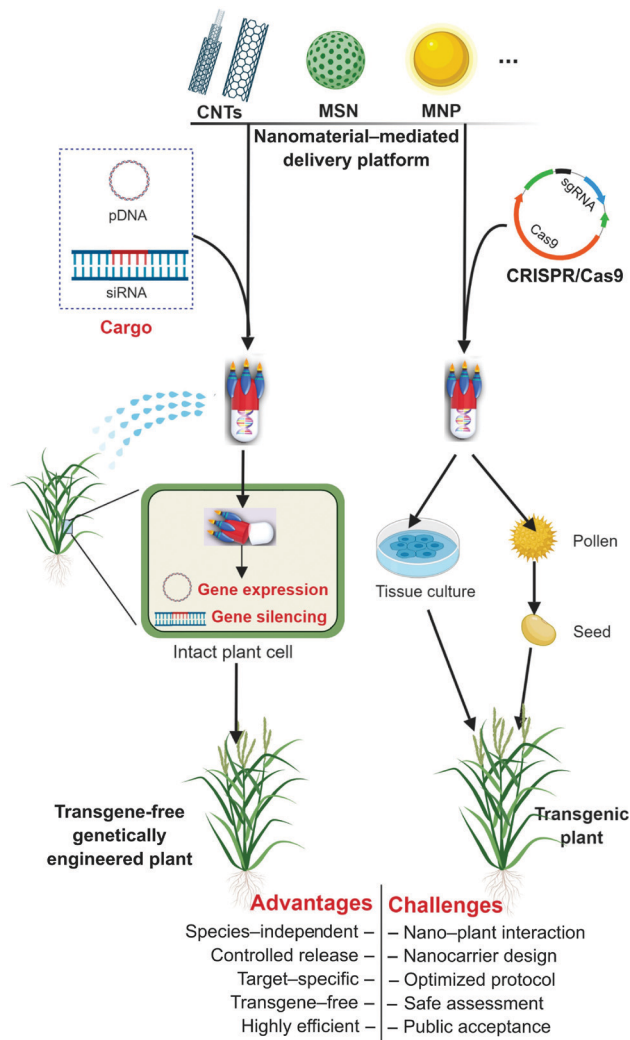


Fig. 16 Biosafety materials for plant genetic engineering. Multiple nanotechnology-based materials and cargos for gene delivery have been developed, improving our ability to specifically deliver gene-editing agents. Reproduced with permission from ref. 188. Copyright 2019, Elsevier.

3.12 Biosafety materials for aerospace safety

The space radiation environment is mainly composed of Milky Way cosmic rays, solar high-energy particles, and particles in the radiation zone of the near-Earth anomaly zone. After long-term analysis of the space radiation environment, NASA officially listed astronauts as radioactive workers in the 1980s, which indicates that aerospace safety is a biosafety problem. Doherty *et al.* reported a high-absorptivity/high-emissivity bone char-based thermal control surface known as SolarBlack for use on rigid and flexible metallic substrates, including titanium, aluminium, copper alloys (Fig. 18).²⁰⁵ This technology has been qualified for use on the front surface of the Solar Orbiter heat shield, thereby providing astronauts with biological safety protection.²⁰⁶

The harm caused by an impact accident in a space environment can directly lead to a devastating consequence. Thus, a polymer material that can self-heal within one second after impact has been developed to solve this problem.²⁰⁷ The rapid



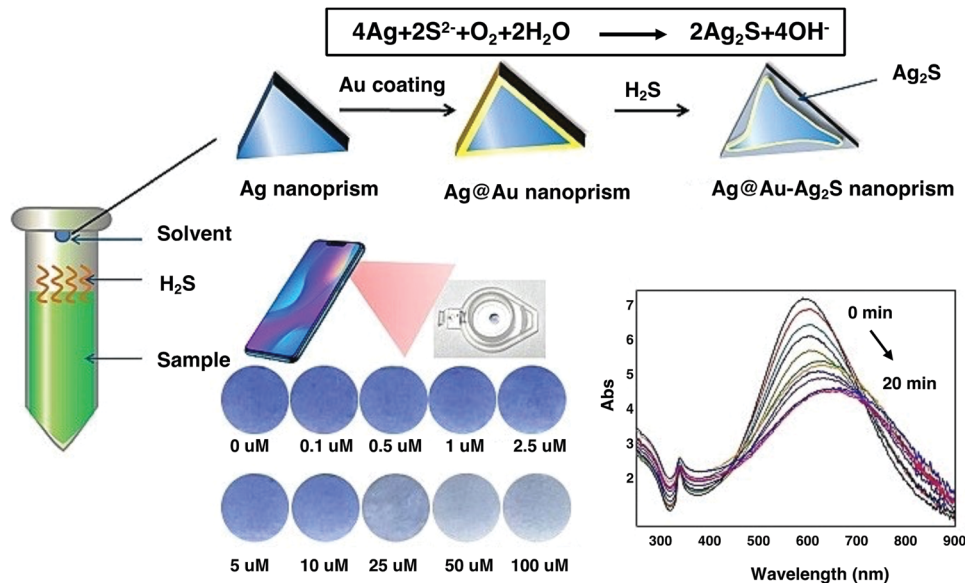


Fig. 17 Biosafety materials for food safety. Schematic illustration of the H_2S sensing mechanism based on the Ag@Au core-shell nanoprobe. Reproduced with permission from ref. 204. Copyright 2019, American Chemical Society.

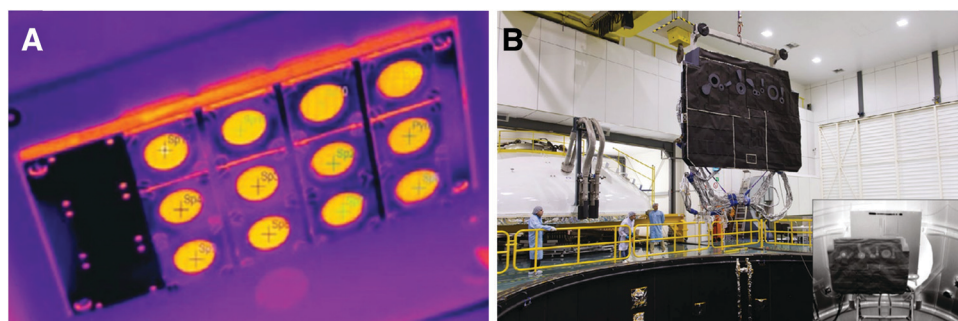


Fig. 18 Biosafety materials for aerospace safety. (A) SolarBlack material samples during testing in the Synergist Temperature Accelerated Testing (STAR) facility in the ESA/ESTEC center. (B) Solar orbiter heatshield based on SolarBlack technology. Reproduced with permission from ref. 205. Copyright 2015, Elsevier.

reaction rates was achieved by thiol-ene-alkylborane formulations, providing astronauts with biological safety protection at the physical level, which ensures the safety of human life and improves the efficiency of related work in the process of exploring space.

4. Outlook and prospects

In summary, a variety of materials, such as polymers, MOFs, graphene, and carbon nanotubes, have dramatically changed our strategy in facing grand challenges for biosafety, but no clear definition and detailed plan on the development of biosafety materials have been given to date. Numerous reports on the progress of materials science prove its capacity to solve the difficult biosafety problems. To the best of our knowledge, we are the first to officially propose the brand-new concept of “biosafety materials” to specify the role of materials science in biosafety, aiming at raising the awareness of the scientific community to actively integrate the two different subjects and

advocate the marriage of both concepts. This brand-new concept of “biosafety materials” can help solve problems related to biosafety. Since biosafety covers a wide range of topics including pathogen detection, biological invasion prevention, protection and prevention of biological resources, and genetic technology, solely relying on a single discipline to address these issues in biosafety is impossible. Thus, the integration of biosafety and materials science can significantly facilitate the development of effective biosafety materials, thus providing a powerful toolbox for professionals to solve biosafety-related problems.

Overall, despite the significant progress in recent years, the development of biosafety materials is still in the early stage, and great efforts should be made to improve the current technologies and facilitate the development of biosafety materials. Thus, the following measures are suggested.

Firstly, biosafety materials science majors should be opened in universities and research institutes to strengthen biosafety materials science disciplines, train professional teams, and direct biosafety materials professionals in basic research in the field of



infectious diseases. The development of biosafety materials can support future work on the traceability and transmission of pathogens of high incidence, sudden infectious diseases, understanding infection and pathogenic mechanisms, and determining anti-infection means. Secondly, scientific research laboratories and research centers related to biosafety materials science and research platforms should be built to strengthen the integration of relevant scientific research, which can finally improve the biosafety research system. Thirdly, professional associations related to biosafety materials science should be established, and developing professional journals and magazines to expand the influence of biosafety materials science is necessary. Finally, well-known enterprises specialized in biosafety materials to develop related products and equipment for biosafety issues should be formed. Biosafety materials research and development centers could be further built in these enterprises to support human health, social stability, and national security.

Taken together, globalization makes the current biosafety threat not only a problem for a single country. No country can protect itself from biological risks without cooperation with other countries. Hence, we hope scientists worldwide will share data and information to use biosafety materials collaboratively to tackle biosafety risks. Finally, we sincerely hope that biosafety materials science will become an independent discipline in the near future, and can flourish worldwide. The government will soon pay more attention to the development of biosafety materials science. An increasing number of researchers can realize its importance and join the research community to explore more and more biosafety materials as well as related products and equipment. Ultimately, the development of biosafety materials science will provide a solid guarantee for the health and well-being of society, economic prosperity, and national security worldwide.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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