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Nanobiotechnology-based strategies for enhanced crop stress resilience

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Nanobiotechnology approaches to engineering crops with enhanced stress tolerance may be a safe and sustainable strategy to increase crop yield. Under stress conditions, cellular redox homeostasis is disturbed, resulting in the over-accumulation of reactive oxygen species (ROS) that damage biomolecules (lipids, proteins and DNA) and inhibit crop growth and yield. Delivering ROS-scavenging nanomaterials to plants has been shown to alleviate abiotic stress. Here we review the current state of knowledge of using ROS-scavenging nanomaterials to enhance plant stress tolerance. When present below a threshold level, ROS can mediate redox signalling and defence pathways that foster plant acclimatization against stress. We find that ROS-triggering nanomaterials, such as nanoparticulate silver and copper oxide, have the potential to be judiciously applied to crop species to stimulate the defence system, prime stress responses and subsequently increase the stress resistance of crops.

Enhancing the intrinsic ability of crops to survive and thrive under stressed or marginal conditions is a key pathway to reduce agricultural inputs and sustain crop production in a changing climate[1,2]. When plants are under stress, the over-accumulation of reactive oxygen species (ROS) leads to the damage of important biomolecules such as nucleic acids and proteins, resulting in phytotoxicity and growth inhibition[3]. Therefore, modulating ROS homeostasis is a potential pathway to develop plants with an enhanced tolerance to stress[4].

Nanomaterials (NMs) have unique physicochemical properties such as small size and excellent catalytic activities that enable unique integration with cellular metabolic processes. NMs with enzyme-like catalytic activities are defined as nanozymes[5]. Until now, a number of NMs have been found to have ROS-scavenging capacities that functionally mimic the activity of antioxidant enzymes. For instance, cerium oxide nanoparticles (CeO_2 NPs) possess superoxide dismutase (SOD)-like activities, which can catalyse the decomposition of ROS[6]. A previous study[7] proposed to use ROS-scavenging CeO_2 NPs to augment plant photosynthesis. The authors reported that negatively charged poly(acrylic acid) CeO_2 NPs inserted into chloroplasts can efficiently increase photosynthetic activities by trapping and quenching free radicals prior to organelle damage. These findings demonstrate the promising potential of using ROS-scavenging nanozymes to augment inherent antioxidant functions and constitutively enhance the stress tolerance abilities of plants.

ROS is like a double-edged sword. On one hand, the overproduction of ROS damages cell membranes, DNA and protein. On the other hand, when below the threshold value, ROS act as signalling molecules that play key roles in response to abiotic and biotic stresses, such as stress sensing, the integration of different stress-response signalling networks and the activation of stress-response genes[8,9]. Given this, we hypothesize that below a certain dose, ROS-triggering NMs could be applied to enhance the stress tolerance of plants by stimulating a broad range of defensive pathways. Different from ROS-scavenging NMs, which serve as a 'recovery or curative' strategy (stress occurs » ROS-scavenger added » stress alleviated; Fig. 1), ROS-triggering NMs could be applied as a 'preventive' strategy to stimulate plant defence

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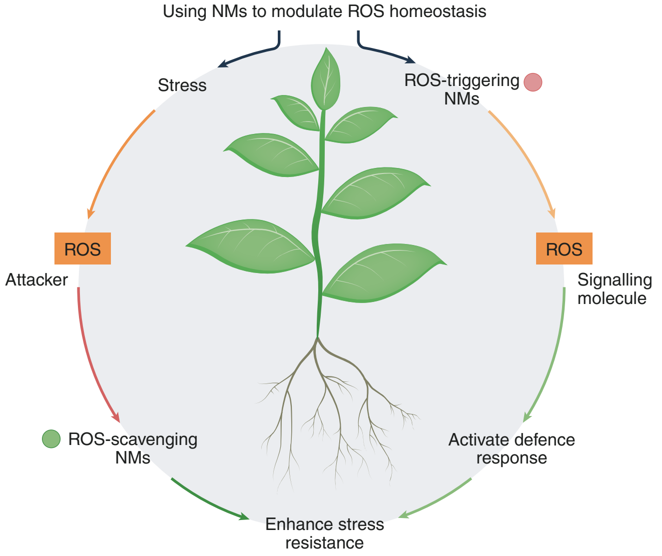

Fig. 1 | Schematic illustration of strategies of utilizing ROS-scavenging and ROS-triggering NMs to modulate ROS homeostasis for stress tolerance enhancement of plants. The left-side pathway is a 'recovery or curative' strategy, in which stress(es) occur first and ROS-scavenging NMs are subsequently used to eliminate excessive ROS, thereby alleviating the negative impacts of the stress. The right-side pathway is a 'preventive' strategy, in which ROS-triggering NMs stimulate stress responses in preparation for anticipated future stress(es).

systems through boosted signalling ROS and thereby metabolically prepare the plant for future stresses (prior to stress occurrence » ROS-generator triggers defence responses » enhancing resistance in preparation for future stresses; Fig. 1). To date, the use of ROS-triggering NMs to stimulate plant immunity and enhance stress resistance remains largely unexplored compared with ROS-scavenging nanozymes.

Here we provide a comprehensive review of the use of nanobiotechnology-based strategies for plant stress tolerance enhancement. We focus on recent discoveries of using ROS-modulating NMs to enhance stress resistance. We review the current research progress of utilizing ROS-scavenging nanozymes to enhance plant stress tolerance. We present directions of using ROS-triggering or defence-triggering NMs for disease or stress tolerance enhancement. Last, we discuss the current challenges and prospects of these applications as a sustainable tool to enhance agricultural productivity.

Dose-mediated toxicity and benefit of ROS in plants

ROS, such as superoxide anion ($O_2^{\bullet-}$), hydroxyl radical ($^{\bullet}OH$), hydrogen peroxide (H_2O_2) and singlet oxygen ($^1O_2$), consist of radical and non-radical oxygen species formed during the metabolism of oxygen[10]. ROS are continuously produced by a variety of metabolic pathways in plant cells[11]. The production of ROS in plant cells results in both detrimental and beneficial effects[12]. When ROS over-accumulate, these analytes can damage cell membranes and inhibit photosynthesis[3]. Plants have endogenous ROS elimination systems consisting of enzymatic (for example, SOD, catalase (CAT), ascorbate peroxidase (APX), glutathione reductase (GR), dehydroascorbate reductase (DHAR), glutathione peroxidase (GPX)) and non-enzymatic (for example, ascorbic acid, glutathione (GSH), phenolic acids, alkaloids, flavonoids, carotenoids, α-tocopherol, non-protein amino acids) antioxidants[13]. These antioxidant systems maintain the balance between ROS production and scavenging[3].

ROS have traditionally been considered as undesirable by-products of metabolic processes generated in different cellular compartments[14]. However, recently the roles of ROS in response to abiotic stress and immunity have been reported[9]. Separate from their damaging activities, ROS appear to play a central role in the acclimation process of plants to abiotic stress[15]. Plants possess ROS-producing enzymes (for example, nicotinamide adenine dinucleotide phosphate (NADPH) oxidases) in the plasma membrane[16], which are critical factors in the response to hormonal and environmental signals[17]. In addition, ROS can transport signals to the nucleus through the mitogen-activated protein kinase (MAPK) pathway to increase tolerance against diverse abiotic stresses[3]. Taken together, ROS-scavenging enzymes are crucial for stress alleviation, while ROS-producing enzymes are responsible for enhancing immunity to defend against pathogens or abiotic stresses (Fig. 2). Understanding the balance between ROS-producing and ROS-eliminating mechanisms in plants could better inform nanobionic approaches (that is, using NMs to modulate ROS homeostasis) to mitigate damage from external stressors.

Application of ROS-scavenging NMs

Given that excessive ROS can negatively impact photosynthesis, some recent studies show that delivering antioxidant NMs to chloroplasts can protect plants against ROS damage. For example, one study[18] reported that foliar injection of CeO_2 NPs (~11 nm, −16.9 mV) effectively protected the photosynthetic system of *Arabidopsis thaliana* from oxidative damage associated with excessive light, heat and chilling. Another study[19] further demonstrated that poly(acrylic acid)-coated CeO_2 NPs with catalytic scavenging $^{\bullet}OH$ capacity are effective in alleviating salinity stress in *A. thaliana*. The study reports that CeO_2 NPs applied to leaf mesophyll can significantly increase carbon assimilation rates (85%), quantum efficiency of photosystem II (9%) and chlorophyll content (14%) compared with controls after exposure to 100 mM NaCl for 3 days. The authors of another study[20] observed that CeO_2 NPs alleviated drought-induced oxidative stress in sorghum (*Sorghum bicolor* L. Moench) by eliminating free radicals. Foliar-applied CeO_2 NPs at 10 mg l^{-1} significantly increased leaf carbon assimilation rates by 38%, pollen germination by 31% and seed yield by 31% in drought-stressed plants relative to controls. A number of additional studies have investigated the use of CeO_2 NPs (10 to ~100 mg l^{-1}) to mitigate salinity stress in crop species such as maize (*Zea mays* L.)[21], cotton (*Gossypium hirsutum* L.)[22], grape (*Vitis vinifera* L.)[23] and Moldavian balm (*Dracocephalum moldavica* L.)[24]. The collective results highlight the strong potential of using ROS-scavenging CeO_2 NPs as antioxidants to alleviate a number of abiotic stresses in plants.

This demonstrated ability of CeO_2 NPs to scavenge ROS can enable plants to cope with extreme environmental conditions. CeO_2 NPs possess SOD-like (dismutation of $O_2^{\bullet-}$ into O_2 and H_2O_2) and/or CAT-like (breakdown of H_2O_2 into O_2 and H_2O) activities[25]. The multifunctional catalytic activities of CeO_2 NPs are largely due to the coexistence of two valence states (that is, oxidized Ce^{4+} and reduced Ce^{3+})[5]. The alternation between III/IV valence enables the reaction with oxygen radicals and hydrogen peroxide, catalysing a range of reversible redox reactions[5]. Compared with small molecular antioxidants or natural antioxidant enzymes that are consumed as they scavenge ROS, CeO_2 nanozymes are conserved as they catalyse the ROS-elimination reactions. Nanozymes are able to regenerate the catalytic sites of ROS scavenging, and this cycling/reusability property enables the action over days or weeks, providing plants with long-term protection under stress conditions. In addition, the high stability and durability of nanozymes enable them to cope with extreme environmental conditions, such as heat, cold and drought events.

Mn_3O_4 NPs also possess excellent ROS-scavenging capacities, exerting multiple enzyme mimicking activities, for example, SOD- and CAT-like, as well as hydroxyl radical scavenging activities[26]. A recent study[27] reported that foliar application of Mn_3O_4 NPs (~5 nm) at 1 mg per plant significantly alleviated salinity stress of cucumber (*Cucumis sativus*) plants. The authors found that Mn_3O_4 NPs increased endogenous low-molecular-weight antioxidants in the leaves, including

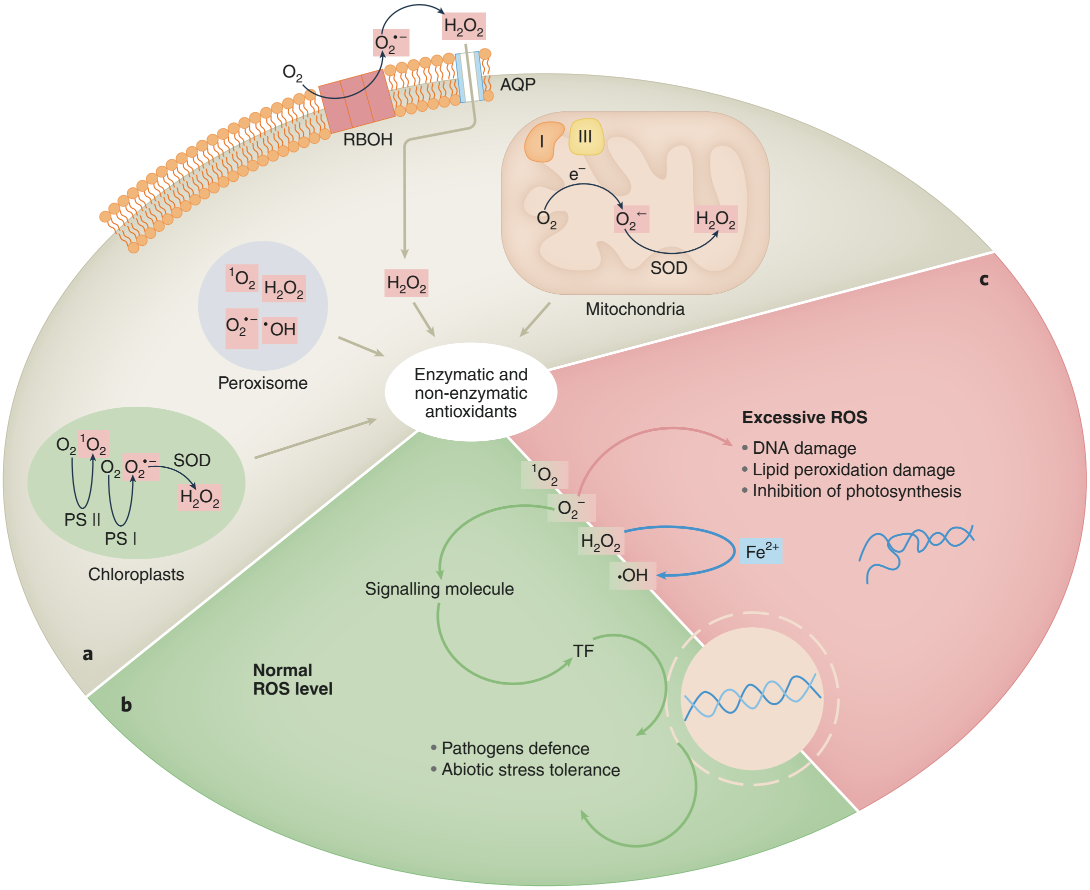

Fig. 2 | Schematic diagram explaining ROS generation and functions in plant cells. a, ROS generating and scavenging mechanisms in different organs (grey section). **b**, ROS function as signalling molecules and activating defence pathways when they are in appropriate doses in cells (green section). **c**, The potential damage of ROS when they are excessive in cells (red section). AQP, aquaporins; PS I, photosystem I; PS II, photosystem II; TF, transcription factors.

resveratrol, chlorogenic acid, dihydroxycinnamic acid, benzenetriol, hydroxybenzoic acid, trihydroxybenzene, quinic acid and catechin. The multifunctional catalytic behaviour of Mn_3O_4 NPs arise from the coexistence of Mn (II) and Mn (III) oxidation states, and the switch between the II and III valence resembles the mechanism of redox enzymes, which is very similar to CeO_2 NPs.

In addition to directly acting as ROS-scavenger, NMs can act as carriers to deliver ROS-eliminating compounds to enhance plant stress tolerance. The authors of a recent study[28] designed an ROS-responsive star polymer (RSP) that successfully alleviated plant stress by simultaneous ROS-quenching and nutrient release. Specifically, RSP was foliar-applied to stressed tomato (*Solanum lycopersicum*) leaves. The RSP penetrated the leaf epidermis and entered into the chloroplasts where it efficiently eliminated H_2O_2, which subsequently triggered the release of the nutrient (Mg^{2+}) from the polymer. This study highlights the potential of using RSP as an ROS-responsive NM to manage short-term plant stress.

Apart from foliar application, ROS-scavenging CeO_2 NPs have been applied to roots. It has been reported that CeO_2 NPs at 100 and 500 mg l^{-1} applied to hydroponic cultivated rice (*Oryza sativa*) can significantly increase the nitrogen levels in roots and shoots by 6–12% and 22–30%, respectively, compared with controls[29]. Similarly, ref. [30] added graphene (5 g kg^{-1}) to the growth media of alfalfa (*Medicago sativa* L.), and found that the amendment alleviated salinity and alkalinity stresses by modulating antioxidant defence systems and genes related to antioxidant defence and photosynthesis. The treatment of graphene significantly increased dry biomass of alfalfa by 29.4% and 24.3%, respectively, in salinity and alkalinity conditions. In another study, root delivery of ROS-eliminating CeO_2 NPs (98 µg l^{-1}) to hydroponically cultivated rice plants was shown to improve rice tolerance under salinity stress, increasing chlorophyll content (23.9%) and yield (47.1%)[31].

ROS-scavenging NMs have also been reported as a seed treatment agent to improve stress resistance. For example, ref. [32] found that cotton (*G. hirsutum* L.) seeds primed with poly(acrylic acid)-coated CeO_2 NPs at 500 mg l^{-1} for 24 h exhibited significantly increased root vitality by 114% under salt stress. Similarly, ref. [33] found that salt-sensitive rapeseeds (*Brassica napus*) seeds primed with poly(acrylic acid)-coated CeO_2 NPs (8.5 ± 0.2 nm, −43.3 ± 6.3 mV) exhibited enhanced salt tolerance by modulating ROS homeostasis. These studies suggest that using ROS-scavenging NMs to treat seeds can alleviate stress at germination stage (both studies were conducted within 7 days), although the duration of this protective benefit is currently unknown. Figure 3 summarizes the current known or hypothesized mechanisms by which ROS-scavenging NMs alleviate plant stress.

Application of ROS-triggering NMs

ROS are important signalling molecules that mediate redox signalling pathways and contribute to acclimatization against a range of stresses[12]. One study[34] demonstrated that an ROS wave is required to activate systemic acquired acclimation of plants to heat or high light stresses, highlighting the important biological function of this signalling molecule to the acclimation against abiotic stresses. In addition, an ROS-generating-associated gene respiratory burst oxidase homologue (RBOH) has been shown to be critical to plant stress responses[17]. Given the known response of plants to select lower-level

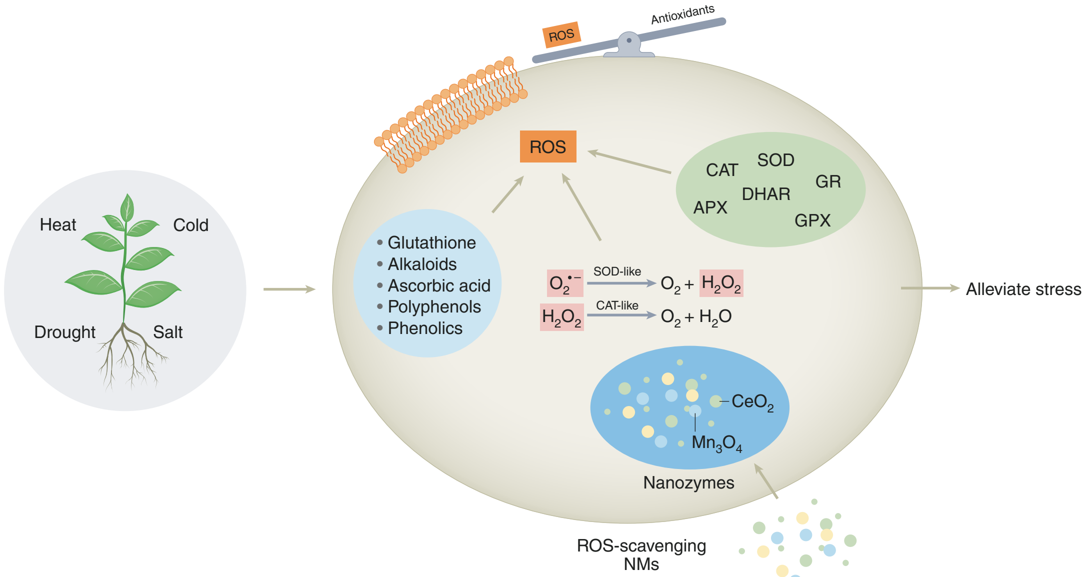

Fig. 3 | Scheme showing the mechanisms of using ROS-scavenging NMs to alleviate plant abiotic stress. In this case, plants that suffer from abiotic stress accumulate excessive ROS, and ROS-scavenging NMs are used to eliminate ROS and protect the plant from damage.

ROS that elicit redox signalling pathways, the concept of pretreating or priming plants with ROS-triggering NMs to stimulate defence systems and acquire systemic acquired acclimation may be an effective strategy to increase stress tolerance. In this strategy, plant stress resistance will be acquired via the initiated adaptive responses by ROS-triggering NMs. ROS-triggering NMs could be used to prime plants through a 'stress memory', which provides a mechanism for acclimation and adaptation, thereby improving the tolerance/avoidance abilities[35–37]. Whereas ROS-scavenging NMs serve as a 'curative' strategy, ROS-triggering NMs are more like a 'preventive' strategy. Currently, only a limited number of studies have employed ROS-triggering nanozymes to increase plant stress resilience, and the researchers are primarily focusing on silver nanoparticles (AgNPs).

AgNPs are known to catalyse ROS generation in cells[38,39]. A previous study[40] reported that seed priming with AgNPs (20 mg l^{-1}, 20 h) enhanced the tolerance of pearl millet (*Pennisetum glaucum* L.) to salinity stress by activating the antioxidant enzymes. AgNP seed priming significantly increased the fresh and dry weights of plants by 58% and 34%, respectively, compared with plants grown in 150 mM salt. The underlying mechanisms may be that AgNPs activated defence pathways during seed priming, forming the 'stress memory' and subsequently enhancing resilience to stress. The mechanisms for AgNPs generating ROS have been reported in recent studies. By using electron spin resonance, ref. [41] demonstrated that AgNPs can directly produce $^{\bullet}OH$ in the presence of H_2O_2, and Ag(I) is generated during this process; importantly, Ag ions did not catalyse the production of $^{\bullet}OH$. Similar results were obtained by another study[38]. A more recent study[42] demonstrated that AgNPs possess peroxidase-mimicking activities, which catalyse oxidation of substrate TMB (3,3′,5,5′-tetramethylbenzidine) in the presence of H_2O_2. The formation of $^{\bullet}OH$ by AgNPs is similar to a Fenton reaction in which AgNPs act as a Fenton-like reagent[41].

Under a changing climate, the frequency of seed exposure to abiotic stresses will increase, which could result in reduced germination and loss of vigour, threatening crop yield[43]. As such, accelerating the germination speed and enhancing the seed vigour are critical. One study[44] reported that AgNP seed priming (40 mg l^{-1}, 24 h) accelerated the germination speed and yield of Chinese cabbage (*B. campestris* L.). Another study[45] showed that AgNP priming (31.3 mg l^{-1}, 12 h) promoted the germination, growth and yield of watermelons (*Citrullus lanatus*). Nanoscale zero valent iron (nZVI), also known to be a Fenton-like reagent, can catalyse the generation of ROS. Another study[46] used nZVI (20 mg l^{-1}) as an ROS-modulator to pretreat rice seeds. This study found that priming generated an optimum level of endogenous ROS via Fenton's reaction, resulting in higher seed germination rate and greater seed vigour. Unfortunately, the study did not further evaluate whether nZVI priming can increase the stress tolerance of seeds or seedlings, but given the observed hormone biosynthesis upregulation and increased antioxidant enzyme activity, nZVI seed priming should be explored as a potential strategy to promote the stress tolerance of rice and other plant species. Collectively, ROS-modulating NM-based seed treatments may be a promising strategy to mitigate climate-change-associated stress.

Under stress conditions, although ROS over-accumulation is common, ROS can still act as signalling molecules, which interplay with other signalling molecules such salicylic acid to activate defence-related genes. These metabolic processes help plants to establish systemic acquired acclimation or systemic acquired resistance, enhancing the resistance to abiotic or biotic stresses[47]. Therefore, NMs that can trigger the upregulation of defence-related hormones/signalling molecules or genes may also enhance stress resistance. One study[48] reported that silica nanoparticles (SiO_2 NPs) at 100 and 1,000 mg l^{-1} enhanced disease resistance of *Arabidopsis* plants by up-regulating the production of salicylic acid, a defence hormone and an important signalling molecule. Similarly, another study[49] demonstrated that copper-based NMs (CuO nanosheets, 50 and 250 mg l^{-1}) successfully alleviated damage of soybeans to sudden death syndrome by triggering the upregulation of a broad array of defence-related genes (two- to sevenfold). One study[50] reported that foliar spray of commercial $Cu(OH)_2$ nanoparticles (Kocide 3000; 25 mg Cu per plant) significantly increased antioxidant defence-related genes, for example, SOD, GPX, MDAR (monodehydroascorbate reductase) and WRKY transcription factor, in cucumber plants, although the potential benefits to stress tolerance were not evaluated. Taken together, these studies demonstrate that NMs that can trigger ROS production or stimulate defence pathways can activate systemic acquired resistance of plants, enhancing the protection against disease or stresses through a classic adaptation response (Fig. 4).

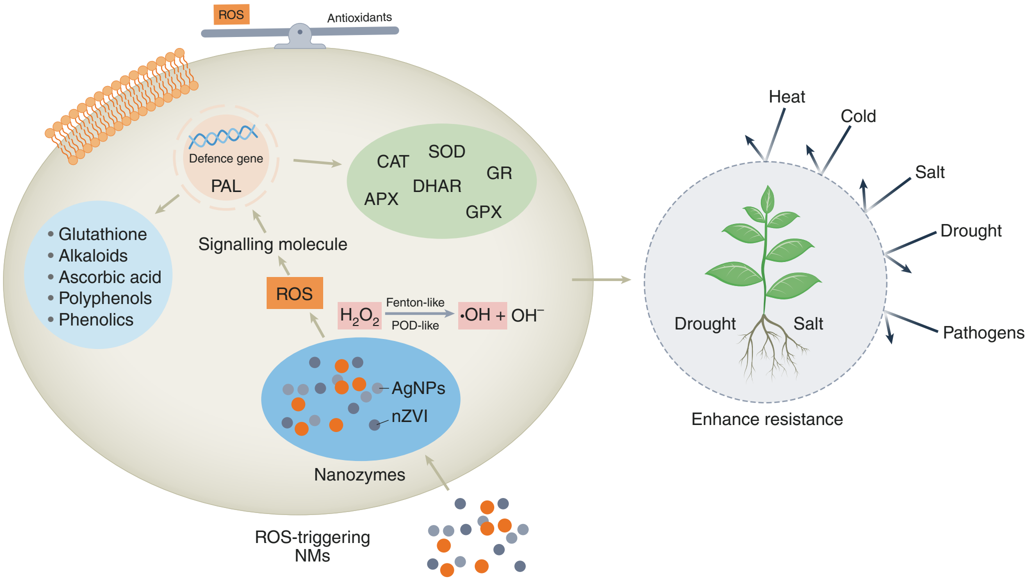

Fig. 4 | Scheme showing the mechanisms of using ROS-triggering NMs to enhance resistance of plants to abiotic stresses. In this case, ROS-triggering NMs pre-activate the defence response to enhance the tolerance of plants to abiotic stresses. PAL, phenylalanine ammonia-lyase; POD, peroxidase.

Delivery pathways of NMs to plants

For both ROS-scavenging NMs and ROS-triggering NMs, efficiently penetrating barriers and entering into plant cells is critical for modulating ROS levels and participating in metabolic activities. As such, an in-depth understanding of the uptake pathways of NMs is fundamental for the efficient application of nanobiotechnology in agriculture. Here, we briefly discuss the possible uptake pathways for NMs into plants, including foliar, root and seed application (Fig. 5).

Foliar application has been the most extensively used delivery pathway. There are several pathways for the entry of nanoscale particles into leaves, including the cuticle and stomata. One study[51] reported that foliar-applied gold nanoparticles (AuNPs; 3 to ~50 nm) in wheat can reach the mesophyll by either the cuticle or stomata, and move through the plant vasculature. Recent studies have noted that the stomatal uptake pathway is more efficient than the cuticle for Cu-based NPs[52]. In addition, nanoparticle properties (size and surface chemistry) and leaf biointerface (structure, hydrophobic) are important factors influencing the uptake and translocation of NPs[52]. More mechanisms for foliar-uptake pathways can be referenced to excellent reviews[53–55].

Compared with foliar application, delivering ROS-modulating NMs to plants via the roots has been less investigated. It has been reported that the application of ROS-modulating NMs to plant roots is more effective under hydroponic cultivation than under soil-grown conditions. In the soil system, NMs will undergo aggregation, adsorption and dissolution, confounding interaction with plant roots. A recent study[56] compared the leaf and root application of ROS-scavenging CeO_2 NPs on alleviating salt stress of cucumber, and found that foliar-sprayed CeO_2 NPs enabled better cucumber salt tolerance than root application. The pathways for NMs entering into the root include apoplastic and symplastic pathways[57].

Using ROS-modulating NMs to prime seeds could be a more cost-effective and environmentally friendly strategy than foliar and root application[58]. This type of approach would not only reduce the release of engineered NMs in the environment (less overall material used) but would also result in decreased worker exposure to these materials. Using ROS-modulating NMs to treat seeds might be a promising strategy to increase seed quality, promote growth and increase the yield. Additionally, nano-enabled seed treatment is an efficient way to load mineral nutrients into seeds[59]. By using transmission electron microscopy, one study[60] observed that FeNPs (19 to ~30 nm) were absorbed on the watermelon seed coat during the priming process and slowly translocated into the seed endosperm. By using transmission electron microscopy with energy-dispersive X-ray spectroscopy, another study[61] also demonstrated the presence of FeNPs (10–80 nm) inside the seeds after the priming. These results demonstrate that NPs can effectively penetrate the seed coat and enter into seeds, although the mechanisms of action remain unclear and must be evaluated.

Perspectives and future outlook

Using NMs to modulate ROS homeostasis is a promising strategy to enhance stress tolerance of crop species. It is a rapidly developing area of research, with the vast majority of publications dating from only 2017 to 2022. We propose that additional mechanistic studies are needed to explore the potential of this approach.

First, compared with the ROS-scavenging NMs strategy, the ROS-triggering NMs approach remains largely unexplored. Using ROS-triggering NMs to stimulate defence pathways at early growth stage, for example, seed or seedling, could enhance the immunity or resistance of plants to abiotic and biotic stresses. This 'preventive' strategy combined with an ROS-scavenging NM-based 'recovery' strategy may provide a versatile and effective solution for stress tolerance. Notably, ROS-scavenging nanozymes can sometimes also induce early ROS stimulation to enhance plant stress tolerance[56]. As such, ROS-scavenging nanozymes could be applied as a 'preventive' strategy as well.

In addition, ROS-triggering NMs may temporarily shift energy and resources to defence pathways, potentially impacting carbon and nitrogen metabolism in ways that could compromise biomass accumulation. As such, the regimen of application will be highly important. For example, one could apply ROS-triggering NMs simultaneously with nutrients (nanoscale or conventional) in order to more broadly support the plant's defence system. Abiotic stresses often occur in combination (for example, heat and drought) or in succession (for example, flooding followed by drought)[62], and as such, future studies need to evaluate the performance of ROS-modulating NMs under multiple stressor scenarios.

Furthermore, a comprehensive understanding of the mechanisms for modulating ROS via NMs to enhance plant stress tolerance is needed prior to deployment of these strategies in the field. The relevant mechanisms include the following: (1) the pathway for NM entry into leaves,

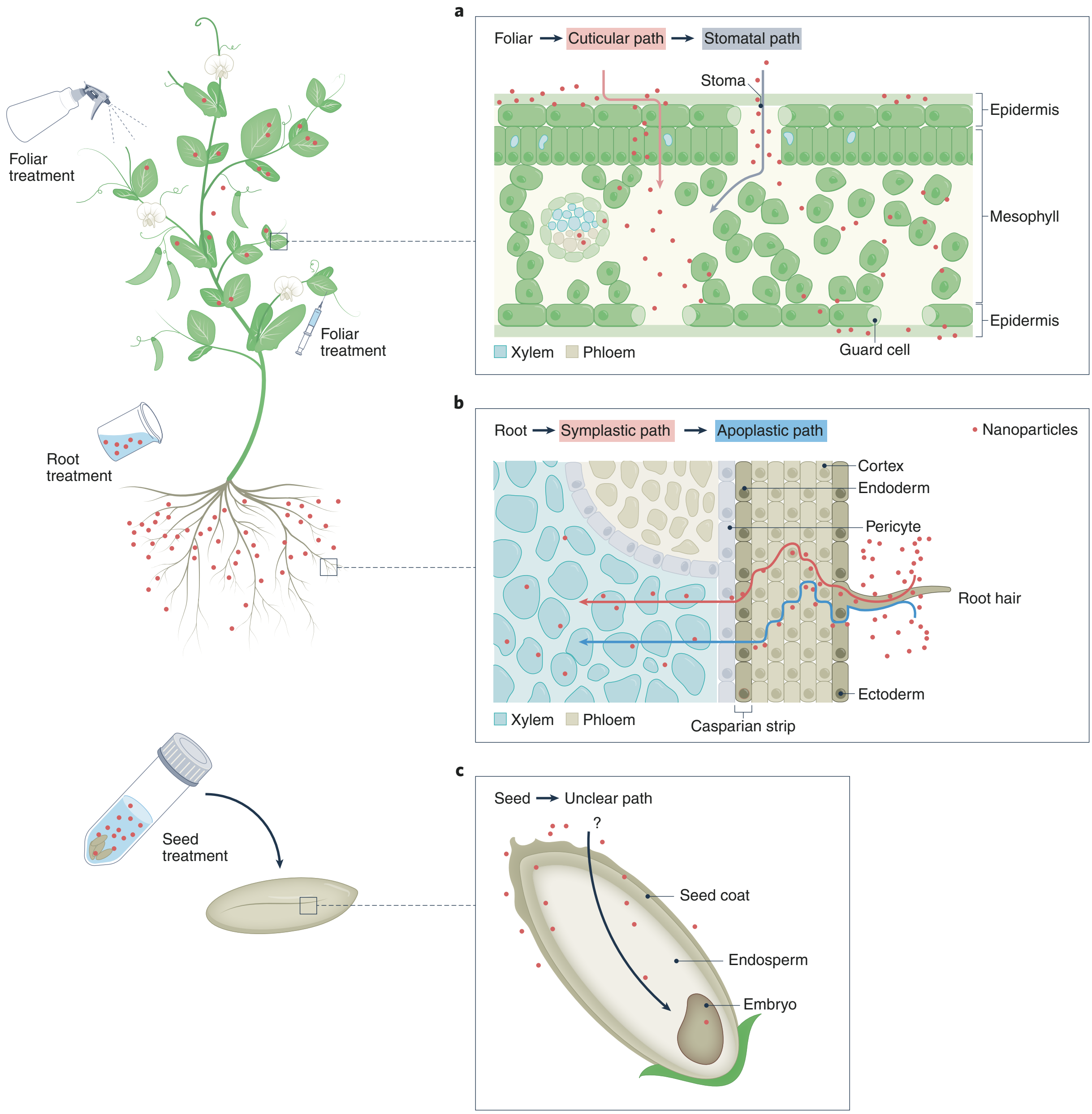

Fig. 5 | Schematic diagram of uptake pathways of ROS-modulating NMs in plants. a, Foliar application: uptake pathways include cuticular and stomatal. **b**, Root application: uptake pathways include apoplastic and symplastic pathways. **c**, Seed application: the entry pathways for NMs into seeds are not clear.

roots and especially seeds; (2) the catalytic mechanisms of nanozymes, and how the size, surface charge, pH and environmental conditions impact the catalytic activities of NMs; (3) the intracellular kinetics of ROS-scavenging or ROS-triggering mechanisms of NMs; (4) the precise metabolic pathways by which ROS-triggering NMs enhance plant stress resistance (for example, signalling molecules, transcription factors and stress resistance genes,); and (5) the cellular, biochemical and molecular level response of plants to NMs under different treatment regimens, especially transcriptome and metabolic reprogramming induced by ROS-triggering NMs. The orthogonal approach of transcriptomics, proteomics, metabolomics and epigenetics will be a powerful tool to address these questions.

Nano-enabled stress tolerance strategies represent a rapidly developing interdisciplinary field of research. We need to pay attention to new findings from both plant and NMs fields, for instance, new knowledge regarding the response mechanism of plants to abiotic and biotic stresses, and state-of-the-art ROS-regulating nanozymes, which will push forward the application of nanozymes in crop stress tolerance. For example, a study recently reported that Huanglongbing, a devastating disease of citrus, is an immune-mediated disease that stimulates the production of ROS as well as the upregulation of genes encoding ROS-producing NADPH oxidases[63]. Given that Huanglongbing is related to ROS-overproduction, ROS-modulating NMs may have significant impact on the disease course. In the nanozyme field, novel ROS-triggering nanozymes are constantly being synthesized. NADPH oxidase, also referred to as RBOH, is a transmembrane enzyme complex that controls the generation of superoxide, which plays an important role in immune signalling pathways[64]. A recent study[65] synthesized a Fe–N-doped graphene (FeNGR) nanomaterial that could mimic the activity of NADPH oxidase (NOX) by efficiently catalysing the conversion of NADPH into $NADP^+$, subsequently triggering the generation of oxygen radicals. Given these demonstrated

ROS-generating properties, FeNGR nanozymes may be applied to cultivate stress-resistant crops. To date, no studies have employed this nanozyme with NADPH oxidase-like activity for stress tolerance enhancement. Thus, the linkage between plant science and nanozyme fields of study could significantly move this field forward.

Last, applications of NMs in agriculture need to consider the potential environmental and human health risks. For example, the impacts of NMs on non-target biota needs to be evaluated. The impacts of NMs on soil microbial and fungal communities that are critical to nutrient uptake of plants, as well as carbon and nitrogen cycling, must be evaluated. In addition, the bioaccumulation of NMs, particularly in edible tissues, needs to be investigated to avoid potential transfer in food chains that could negatively impact human or ecosystem health. However, it is clear that sustainable nano-enabled strategies to promote crop species' tolerance to abiotic and biotic stresses has the potential to be a powerful tool to fight global food insecurity.

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Competing interests

The authors declare no competing interests.

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