Microchimica Acta (2019) 186:782
https://doi.org/10.1007/s00604-019-3922-7

REVIEW ARTICLE

Advances in chiral nanozymes: a review

Ruofei Zhang[1] · Yunlong Zhou[2] · Xiyun Yan[1,3] · Kelong Fan[1,3]

Received: 6 June 2019 / Accepted: 12 October 2019

Abstract

Nanomaterials with intrinsic enzymatic activity are often referred to as nanozymes. They exhibit many advantages over natural enzymes such as temporal and thermal stability, recyclability, controllable activity, and ease of large-scale preparation. Many efforts have been made in the past 5 years in order to improve their specificity for chiral substrates. This review (with 74 refs.) summarizes the state of the art in the design of nanozymes with chiral selectivity. Following an introduction into nanozymes and chiral selectivity in general, a first large section covers nanozymes based on the use of chiral chemicals. The next two sections describe nanozymes using amino acids and DNA as chiral ligands. A table summarizes the kinetic and selectivity parameters of the currently known chiral enzyme mimics. A concluding section addresses current challenges, and gives perspectives and an outlook on trends.

Keywords Nanozyme · Chirality · Enantioselectivity · Enzyme-like activity · Asymmetric catalysis · Enantiomer · Amino acids · Chiral chemicals · Nanoceria · Nanogold

Introduction

Endowing nanomaterials with the catalytic capacity of natural enzymes is an attractive idea. Compared with natural enzymes that are easily denaturized and inactivated, nanomaterials are stable, cost-effective, versatile, easy to prepare and preserve, and can be used under harsh conditions. In recent years, types of nanomaterials defined as nanozymes are found to possess intrinsic enzyme-like activity [1–5]. For instance, in the presence of H_2O_2, Fe_3O_4 nanoparticles efficiently catalyze the oxidation of typical peroxidase substrates, and exhibit a similar catalytic mechanism (ping-pong reaction) as natural horseradish peroxidase (HRP). [6] Nanozymes possess the characteristics of both inorganic catalysts and natural enzymes. Most of them belong to heterogeneous catalysts, such as metallic, metal oxides or carbon-based nanozymes. Different from homogeneous catalysts, nanozymes can be easily separated from the catalytic system and recycled. [1] In addition, unlike common heterogeneous catalysts requiring high temperature conditions (400-1000 K) to effectively catalyze [7, 8], nanozymes exhibit high catalytic activity under physiological conditions. Because of its great academic and practical value, the research on nanozymes has been extremely hot in recent years. Many efforts have been put on the discovery of new nanozymes, the optimization of catalytic activity and the explanation of catalytic mechanism of nanozymes. However, up to now, although there are a lot of literatures on improving the catalytic activity of nanozymes, little research has been done on improving their substrate selectivity [3, 9, 10].

Accurate substrate specificity is one of the most important characteristics of enzymes and also the main gap between nanozymes and natural enzymes. [9] Many enzymes are stereospecific, that is, when the substrates possess stereoisomers, the enzyme can only act on one of them. In addition, chiral discrimination on substrates' enantiomers is an important aspect of enzymes' stereospecificity. For example, L-amino acid oxidase can only catalyze the oxidation of L-amino acid, but has no effect on D-amino acid. [11] Enantioselective catalysis plays an important role in biomedical applications. Some

✉ Xiyun Yan
yanxy@ibp.ac.cn

✉ Kelong Fan
fankelong@ibp.ac.cn

[1] CAS Engineering Laboratory for Nanozyme, Key Laboratory of Protein and Peptide Pharmaceutical, Institute of Biophysics, Chinese Academy of Sciences, 15 Datun Road, Beijing 100101, China

[2] Wenzhou Institute of Biomaterials and Engineering, University of Chinese Academy of Sciences, Wenzhou 325000, China

[3] Joint Laboratory of Nanozymes in Zhengzhou University, Academy of Medical Sciences, Zhengzhou University, 40 Daxue Road, Zhengzhou 450052, China

Published online: 15 November 2019

drugs exhibit therapeutic effects only in one configuration, while other enantiomers may not work or even be toxic. For instance, the dextral-enantiomer of thalidomide, a drug used to alleviate pregnancy response, has sedative effect, while the levo-enantiomer may cause teratogenicity. [12, 13] However, chemical synthesis obtains racemic products in most conditions, requiring chiral catalysts to separate enantiomers. Many chemical synthetic molecules or natural enzymes have been used in chiral catalysis. [14–16] Although these chiral catalysts exhibit good enantioselectivity, they lack either recyclability or stability. Considering the unique advantages of nanozymes, the development of efficient enantioselective nanozymes for asymmetric catalysis of racemic products is very important. Additionally, life activities are closely related to chirality. Most of the biomolecules in life exhibit homochirality. For example, most of the amino acids composing proteins are left-handed and the riboses composing DNA are right-handed. Therefore, enantioselective nanozymes may exhibit better performance in vivo applications. Moreover, although it is still an unsolved mystery, most theories hold that the generation of homochirality is an important process in the origin of life, and it may also be an important factor in the initial generation of substrate specificity of natural enzymes. [17–19] Thus, in conclusion, enabling nanozymes to be enantioselective may not only broaden their industrial and biomedical applications, but also lay a good foundation for further improvement of the enzyme-like activity and selectivity of nanozymes.

Indeed, we note that substantial progress has been made in recent attempts to improve enantioselectivity of nanozymes. Nanozymes themselves are mostly fabricated from achiral molecules, so it is difficult for them to show enantioselectivity. Recent studies on chiral nanozymes mostly focus on the coupling of chiral ligands on the surface of nanozymes, such as amino acids, nucleic acids, and some chiral chemical compounds. To capture this development, we herein introduce some typical chiral nanozymes proved to be effective on enantioselective and asymmetric catalysis. Because the studies in this field are still in its infancy, most of which are proofs of concept. So, the main purpose of this review is not to systematically summarize, but to highlight current strategies and advances to attract more attention and attempts from researchers on chiral nanozymes.

Nanozymes using chemical compounds as chiral ligands

In one of the earliest studies, Qu's group prepared a nanozyme by conjugating chiral zinc finger protein-like alpha-helical supramolecular complexes ($[Fe_2L_3]^{4+}$) onto the surface of graphene oxide (GO-COOH). [20] This nanozyme exhibited enantioselective peroxidase-like activity. Previous studies have found that GO-COOH possess intrinsic peroxidase-like activity. In the presence of H_2O_2, GO-COOH catalyzed the oxidation reaction of 3,3′,5,5′-tetramethylbenzidine (TMB, a chromogenic substrate of HRP). [21] $[Fe_2L_3]^{4+}$ has two enantiomers, M-$[Fe_2L_3]^{4+}$ (Fe-M) and P-$[Fe_2L_3]^{4+}$ (Fe-P). The two enantiomers each contain two ferrous centers and three ligands coiled in a helical shape (Fig. 1a). Unexpectedly, both Fe-M and Fe-P showed slight peroxidase-like activity in this study. Fe-P possessed higher catalytic activity than Fe-M because of its higher affinity for aromatic substrates. Atomic force microscopy (AFM) confirmed that the two enantiomers of $[Fe_2L_3]^{4+}$ were bound to both sides of GO-COOH flakes by simple mixing. Two kind of chiral $[Fe_2L_3]^{4+}$-GO-COOH conjugates (Fe-M-GO-COOH and Fe-P-GO-COOH) were formed (Fig. 1b). Moreover, the peroxidase-like activity of $[Fe_2L_3]^{4+}$-GO-COOH was determined to be higher than the sum of the activities of $[Fe_2L_3]^{4+}$ and GO-COOH, indicating a synergistic effect between them. Despite the similar structures, Fe-M-GO-COOH and Fe-P-GO-COOH had slightly different enzymatic characteristics. Although they had the same optimum reaction pH (4.0) and temperature (45 °C), the optimum concentration of H_2O_2 for Fe-M-GO-COOH was 120 mM, while that for Fe-P-GO-COOH was 115 mM. Moreover, similar to Fe-M and Fe-P, Fe-P-GO-COOH exhibited better catalytic activity than Fe-M-GO-COOH under the same conditions.

In order to verify their enantioselectivity, these two chiral nanozymes were used to the discrimination of the enantiomers of dopa. L-dopa is an effective component in the treatment of Parkinson's disease, but the other enantiomer D-dopa may cause a series of side effects. [22, 23] Therefore, it has great medical value to effectively distinguish the two enantiomers of dopa (Fig. 1c). The results manifest that dopa was oxidized to dopachrome (DC) by $[Fe_2L_3]^{4+}$-GO-COOH in the presence of H_2O_2. The concentration of DC was determined by measuring the change of absorbance at 475 nm (Fig. 1d). Intriguingly, Fe-M-GO-COOH exhibited higher catalytic activity for the oxidation of D-dopa than that for L-dopa (Fig. 1e). In contrast, Fe-P-GO-COOH was more efficient in catalyzing L-dopa (Fig. 1f). Besides, Fe-M-GO-COOH exhibited a stronger enantioselectivity than Fe-P-GO-COOH. Therefore, Fe-M-GO-COOH is more valuable in enantiomer discrimination of dopa. In order to further amplify the asymmetric catalysis of Fe-M-GO-COOH to the dopa enantiomers, β-cyclodextrin (β-CD) was introduced into the catalytic system. The β-CD added specifically formed complex with L-dopa rather than with D-dopa, thus protecting L-dopa from oxidation. As expected, the asymmetric catalytic ability of Fe-M-GO-COOH increased significantly after adding β-CD (Fig. 1g). The oxidation degree of D-dopa catalyzed by Fe-M-GO-COOH increased to 1.63 times that of L-dopa.

Thiol with metal complexes as the terminal bound to gold nanoparticles (AuNPs) are reported to form nuclease-like

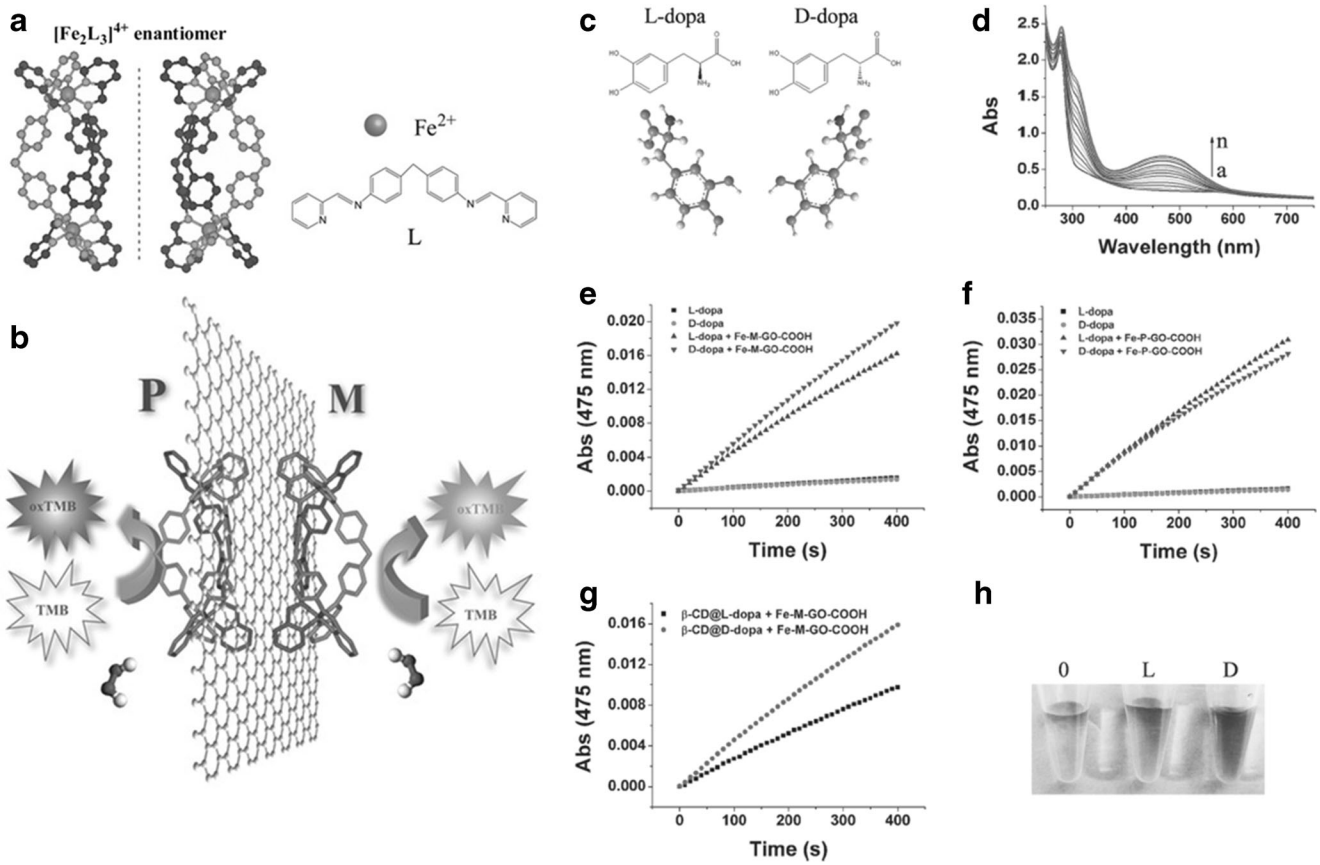

Fig. 1 **a** Structures of two enantiomers of $[Fe_2L_3]^{4+}$ complexes: Fe-M (left) and Fe-P (right). **b** Schematic illustration of chiral $[Fe_2L_3]^{4+}$-GO-COOH nanozymes. **c** Chemical structures of L- and D-dopa. **d** UV/Vis spectra of the oxidation of dopa in the presence of H_2O_2 and Fe-P-GO-COOH. The spectrum (a-n) was monitored at 2-min intervals from 2 min. The time-dependent absorbance changes of dopa at 475 nm in the presence of **e** H_2O_2 and Fe-M-GO-COOH; **f** H_2O_2 and Fe-P-GO-COOH and **g** β-CD, H_2O_2 and Fe-M-GO-COOH; **h** (0): without dopa, (L): L-dopa, (D): D-dopa. Reproduced with permission from ref. [20]. Copyright 2014 from John Wiley & Sons

nanozymes. [24–26] These nanozyme catalyzed the cleavage of phosphodiester bond and promoted the transphosphorylation reaction. Aiming at enantioselective discrimination, Prins et al. synthesized two chiral nanozymes (named as (+)-1 and (−)-1) by combining thiols with triazacyclononane (TACN) Zn^{2+}-binding head groups on the surface of AuNPs (Fig. 2). [27] The chirality of these nanozymes mainly comes from the serine of its head group. The chiral precursors self-assembled on the surface of AuNPs and formed actively catalytic pockets. The prepared chiral nanozymes showed good transphosphorylation catalytic activity. Two enantiomers of CF_3HPNP, a trifluoromethyl-substituted analogue of 2-hydroxypropylp-4-nitrophenyl phosphate (HPNP), were then used as substrates to analyze the catalytic performance of the chiral nanozymes. The results of catalytic kinetics suggest that, when (+)-CF_3HPNP was used as the substrate at pH 6.5, the catalytic efficiency of the (+)-1 nanozyme ($k_{cat} = 3.5 \times 10^{-3}$ s^{-1}) was 38% higher than that of the (−)-1 nanozyme ($k_{cat} = 2.5 \times 10^{-3}$ s^{-1}). In contrast, the catalytic efficiency of the (−)-1 nanozyme was higher than that of the (+)-1 nanozyme when catalyzing (−)-CF_3HPNP. Remarkably, the two nanozymes had same affinity toward (+)-CF_3HPNP by showing a similar K_M value to (+)-CF_3HPNP (0.24 ± 0.02 mM vs. 0.27 ± 0.02 mM). Therefore, their asymmetric catalytic ability was not resulted from the difference of affinity to substrates. Researchers speculated that the difference in catalytic activity may be ascribed to the difference in the transition states of the (+)-1 and (−)-1 nanozymes in contact with substrates. In addition, using dinucleotides (UpU, CpC, GpG and ApA) as substrates, the catalytic activity of the chiral nanozymes for natural components was verified. The (−)-1 nanozyme exhibited the highest cleavage efficiency for UpU, and its catalytic rate was 3.6 times that for GpG and 10 times that for ApA and GpG. Also, there was no difference between the catalytic efficiency of the (−)-1 and the (+)-1 for UpU. However, when the Zn^{2+} in active center was replaced by Cu^{2+}, the catalytic efficiency of the (−)-1 for UpU became 4 times that of the (+)-1 for catalyzing UpU. In brief, the gold-based nanozyme coupled with chiral metal-binding thiols displayed good enantioselectivity when catalyzing transphosphorylation.

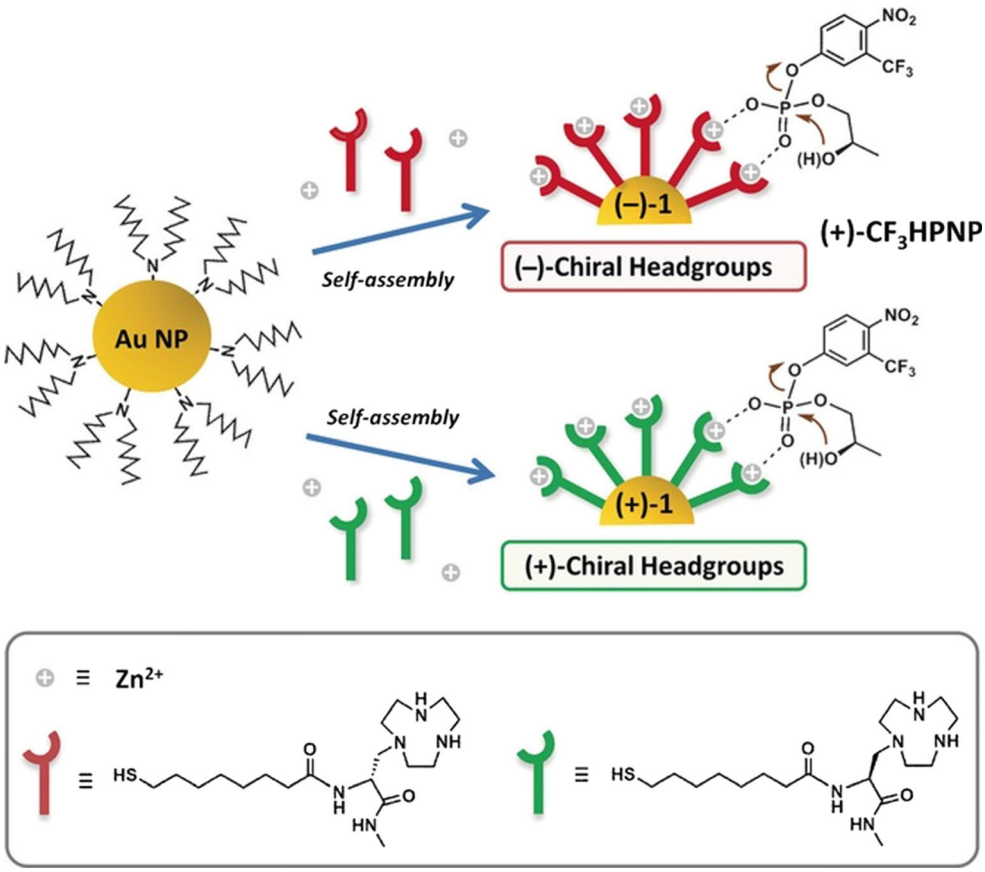

Fig. 2 Schematic illustration of the self-assembly of chiral [TACN·metal]-AuNPs nanozymes (shown as (−)-1 and (+)-1) and the chiral selective catalysis of CF3HPNP. Reproduced with permission from ref. [27]. Copyright 2016 from John Wiley & Sons

A worth-mentioning study recently found that an achiral liquid-crystalline trimer in the optically isotropic dark chiral conglomerate (DC) phase acting as a nanozyme catalyzed the direct aldol reaction of acetone with benzaldehyde. [28] However, although supramolecular chirality was generated in each chiral domain of DC phase by self-organization of achiral trimer molecules, the reaction did not show enantioselectivity. The chiral domains with opposite chirality in DC phase were almost equal in proportion. Even so, further studies using chiral liquid-crystalline trimer as ligands is still expected in catalyzing enantioselective aldol reaction.

Nanozymes using amino acids as chiral ligands

Most amino acids in nature are chiral, whose chirality and interaction with substrates are the basis of enantiomeric recognition of natural enzymes. [29–32] Therefore, the use of chiral amino acids as ligands may open a new portal for the construction of chiral nanozymes.

Cerium oxide nanoparticles (CeNPs) are the most widely studied and applied nanozymes. At present, CeNPs have been reported to exhibit catalase-like, superoxide dismutase-like and oxidase-like activities. [33–35] In order to endow CeNPs nanozymes with enantioselectivity, Qu et al. linked various amino acids (e.g., phenylalanine (Phe), alanine (Ala), tryptophan (Trp), histidine (His), glutamic acid (Glu), arginine (Arg), lysine (Lys), and tyrosine (Tyr)) to the surface of CeNPs and analyzed their catalytic ability for the oxidation of dopa enantiomers. [36] Among these amino acid-coated CeNPs, Phe-modified-CeNPs (CeNPs@Phe) exhibited the most excellent catalytic and enantioselective abilities. Enzymatic kinetics experiments demonstrated that CeNPs@L-Phe had higher catalytic capacity for D-dopa ($k_{cat} = 4.63 \times 10^{-3}$ s^{-1}) than that for L-dopa ($k_{cat} = 4.16 \times 10^{-3}$ s^{-1}), while CeNPs@D-Phe preferred to catalyze L-dopa ($k_{cat} = 3.12 \times 10^{-3}$ s^{-1}) rather than D-dopa ($k_{cat} = 1.94 \times 10^{-3}$ s^{-1}). The selectivity factors of CeNPs@L-Phe and CeNPs@D-Phe were 1.13 and 1.87 respectively, suggesting that CeNPs@D-Phe had stronger enantioselective ability (Fig. 3). Molecular docking analysis revealed that there are more hydrogen bonds or π-π stacking interactions between D-Phe and L-dopa, and between L-Phe and D-dopa. Therefore, the different affinity towards dopa enantiomers resulted from Phe modification may be the reason of the CeNPs@Phe's asymmetric catalytic activity.

In addition to using Phe as a chiral ligand, a recent study reported that chiral Phe can also be used as a structure-directing agent to mediate the synthesis of porous Cu_xO

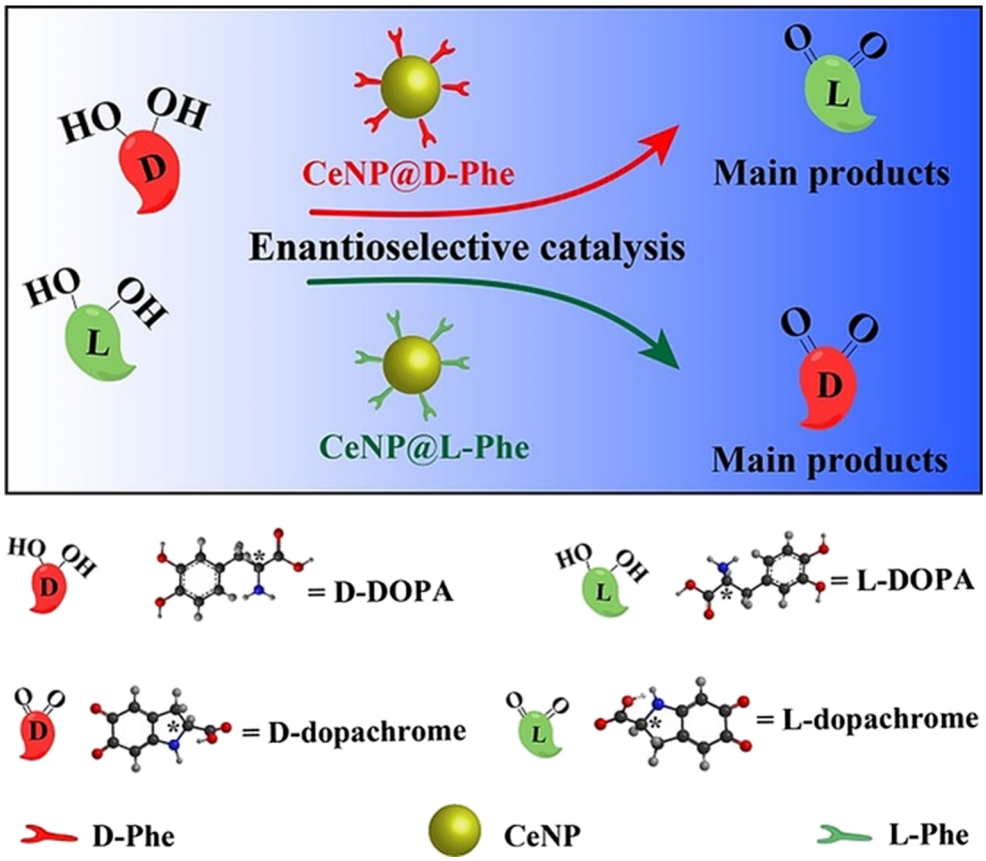

Fig. 3 Schematic illustration of the catalytic enantioselectivity of chiral Phe-modified-CeNPs nanozymes towards the dopa enantiomers. Reproduced with permission from ref. [36]. Copyright 2017 from John Wiley & Sons

nanozymes. [37] The prepared Cu_xO-Phe nanozyme mimicked the activities of peroxidase, superoxide dismutase, catalase, and glutathione peroxidase. However, the chiral selectivity of the Cu_xO-Phe nanozyme was not analyzed in that study.

In another study did by Qu et al., cysteine (Cys) as a chiral ligand was modified on the surface of AuNPs. The Cys-coated AuNPs were loaded into an expanded mesoporous silica (EMSN) carrier to form a chiral nanozyme (Cys@AuNPs-EMSN) with peroxidase-like activity (Fig. 4). [38] Previous studies have found that Cys is at the active site of natural enzymes that can specifically recognize L-dopa. [39] Inspired by this, these researchers attempted to use the chiral gold nanozymes for asymmetric catalysis of dopa. The results suggest that D-Cys@AuNPs-EMSN was more likely to catalyze the oxidation of L-dopa (selectivity factor = 1.47), while L-Cys@AuNPs-EMSN was more efficient for the oxidation of D-dopa (selectivity factor = 1.69). However, unlike previous studies, enzyme kinetic saturation curves revealed that the affinity between D-Cys@AuNPs-EMSN and D-dopa (K_M = 38.0 μM) was stronger than that between D-Cys@AuNPs-EMSN and L-dopa (K_M = 52.1 μM). Similarly, the affinity between L-Cys@AuNPs-EMSN and L-dopa (K_M = 39.4 μM) was stronger than that between L-Cys@AuNPs-EMSN and D-dopa (K_M = 50.8 μM). The researchers believed that the hydrogen bonds between L-Cys and L-dopa (or between D-cysteine and D-dopa) enhanced the binding force between them, but hindered the annealing reaction between amino acids and benzene rings on dopa. The differences in affinity thus reduced the catalytic efficiency, and eventually made L/D-Cys@AuNPs-EMSN enantioselective.

Molybdenum disulfide (MoS_2) nanoflowers and nanosheets have been reported to exhibit peroxidase-like activities. [40, 41] Based on previous studies, Wei et al. covalently modified the surface of MoS_2 quantum dots (MoS_2-QDs) with chiral Cys and synthesized a enantioselective nanozyme in a recent study. [42] It was found that neither unmodified MoS_2-QDs nor Cys-modified MoS_2-QDs displayed significant peroxidase-like catalytic activity. However, interestingly, when copper ions (Cu^{2+}) were present in the environment, MoS_2-QDs exhibited remarkable peroxidase-like activity. Because Cu^{2+} ions are in the active center of many natural enzymes [43, 44], it is possible that copper ions might form conjugates with Cys-MoS_2-QDs and played the role of active center. Then, using D-tyrosinol (Tyr) and L-Tyr as substrates, whose oxidation products can be detected by monitoring the absorbance change at 210 nm, L/D-Cys-MoS_2-QDs/Cu^{2+} conjugates were found to have enantioselectivity. The experimental results illustrate that L-Cys-MoS_2-QDs/Cu^{2+} was more likely to catalyze the oxidation of L-Tyr, while D-Cys-MoS_2-QDs/Cu^{2+} was more likely to catalyze D-Tyr. The K_M value of enantioselective steady-state kinetics presented that

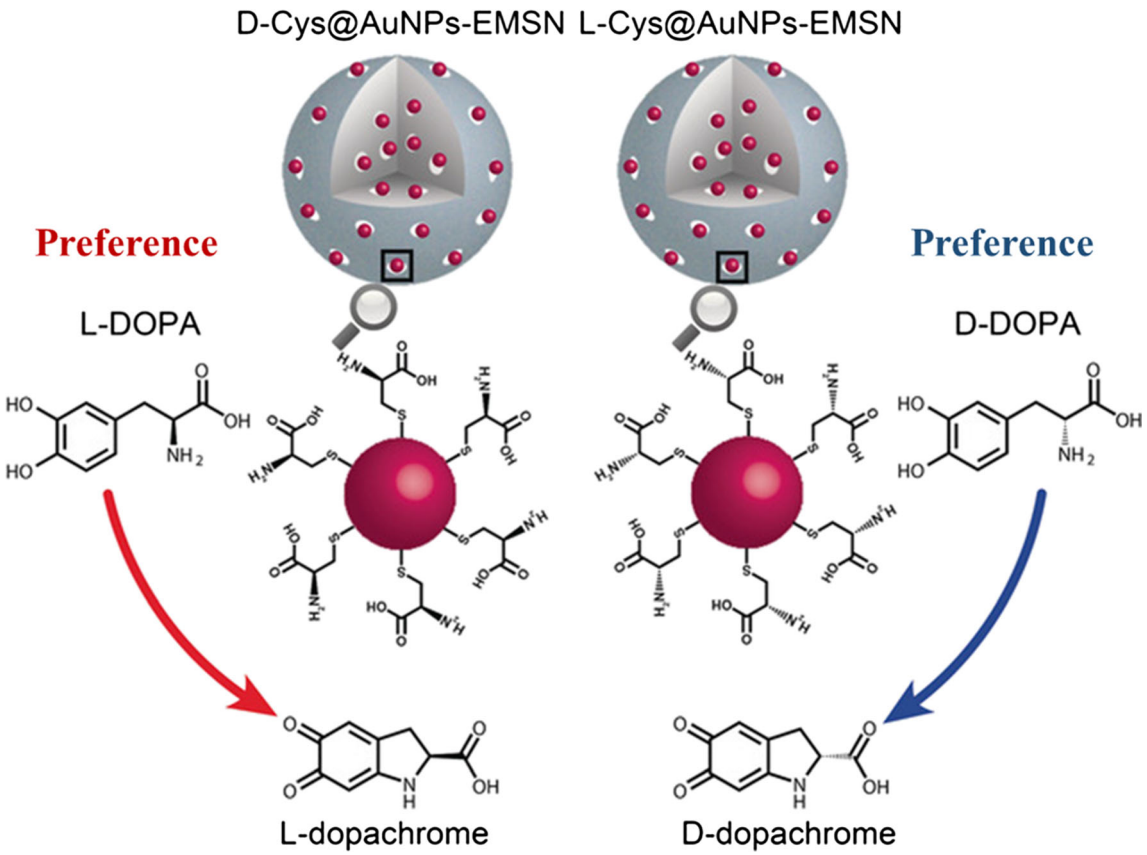

Fig. 4 Schematic illustration of the catalytic enantioselectivity of chiral Cys@AuNPs-EMSN nanozymes towards the dopa enantiomers. Reproduced with permission from ref. [38]. Copyright 2018 from John Wiley & Sons

the affinity of D-Cys-MoS_2-QDs/Cu^{2+} to D-Tyr was higher than to L-Tyr, while L-Cys-MoS_2-QDs/Cu^{2+} was the opposite. The k_{cat} value of these chiral nanozymes was not given in this study.

Nanozymes using DNA as chiral ligands

DNA is a kind of chiral biological molecule that can be transformed between random and multistrand states under different environmental conditions. [45–47] Using DNA as chiral ligand, Ding et al. synthesized a series of gold-based nanozymes that can recognize glucose enantiomers. [48] Uncoated AuNPs have been reported to possess a glucose oxidase-like activity that catalyzes the aerobic oxidation of glucose. Its activity is negatively correlated with the particle diameter, but it has no enantioselectivity. [49] In the study did by Ding et al., DNA with random-coiled or multi-stranded structures (e.g., duplex, i-motif, or G-quadruplex) were modified on the surface of AuNPs through multi-point Au-N coordination. These gold-based nanozymes modified with different DNA exhibited different enantioselectivity in catalyzing the oxidation of glucose enantiomers.

More specifically, the conformation and concentration of DNA played an important role in the chiral selectivity of nanozymes. Single strand DNA (ssDNA)-capped-AuNPs were more likely to catalyze L-glucose, and had an optimal chiral selectivity at ssDNA concentration of about 0.75 μM, with a selectivity factor of 1.333 ($k_{\text{L-glucose}}/k_{\text{D-glucose}}$). Double strand DNA (dsDNA)-capped-AuNPs were more likely to catalyze D-glucose, and showed an optimal chiral selectivity when DNA concentration was about 1.5 μM, with a selectivity factor of 1.367 ($k_{\text{D-glucose}}/k_{\text{L-glucose}}$). Furthermore, the sequence and length of DNA also affected the chiral selectivity of nanozymes. The optimal chiral selectivity of ssDNA rich in thymine and cytosine was higher than that of ssDNA rich in guanine and adenine bases. And the chiral selectivity of AuNPs treated with poly(A·T) dsDNA was lower than that of AuNPs treated with poly(G·C) dsDNA. The catalytic activity of nanozymes increased as the length of DNA decreased, but their chiral selectivity decreased. This may be due to the decrease of base stacking that reduced the chirality of DNA.

In addition to the factors of DNA ligands, the catalytic environment also affects the chiral selectivity of DNA-AuNPs nanozymes. Environmental temperature can affect the chiral selectivity of nanozymes by influencing intramolecular hydrogen bonds. High temperature may

promote the binding of DNA to AuNPs, but destroy intramolecular hydrogen bonds. Nevertheless, the chiral selectivity of the nanozyme was not significantly affected by temperature in the range of 5–35 °C. Interestingly, pH affected the chiral selectivity of nanozymes by influencing the structure of DNA. At pH 7.2, the 3-ssDNA (5′-CCCT AACCCTAACCCTAACCC-3′) was in an unfolded structure, and the AuNPs coated by them were more likely to catalyze the oxidation of L-glucose, with an optimal selection factor of 1.398 ($k_{\text{L-glucose}}/k_{\text{D-glucose}}$). When the pH was reduced to 5.2, this 3-ssDNA folded into i-motif conformation, making the nanozyme more efficient in catalyzing D-glucose with an optimal selection factor of 1.393 ($k_{\text{D-glucose}}/k_{\text{L-glucose}}$).

Along with the various DNA configurations mentioned above, G-quadruplex DNA has also been found to give AuNPs a catalytic propensity to D-glucose. In general, AuNPs coated with random-coiled DNA (ssDNA or DNA with irregular folding) preferred to catalyze the oxidation of L-glucose, and AuNPs modified with structured DNA (duplex, i-motif, G-quadruplex) were more likely to catalyze the oxidation of D-glucose (Fig. 5). As a control, uncoated AuNPs had no ability to asymmetry catalyze the enantiomers of glucose. The difference in chiral selectivity caused by DNA conformation might be attributable to the difference in chirality of DNA with different structures. The chirality of random-coiled DNA derived from the stacking and alignment of its bases, while the chirality of structured DNA derived mainly from its helical minor grooves between the bases. This difference leaded to diverse affinity towards different glucose enantiomers, which eventually affected the chiral selectivity of DNA-AuNPs nanozymes.

Perspectives

This review presents the latest advances in chiral nanozymes. Information on chiral nanozymes introduced in this review is summarized in Table 1. Enantioselectivity is a unique property of natural enzymes and plays an important role in the spatial recognition of substrates. [50, 51] In addition, asymmetric catalysis and enantioselective separation are crucial for drug preparation and industrial production. [52] Therefore, it is essential to improve the enantioselectivity of nanozymes for wider applications. Since nanozymes are mostly non-chiral inorganic nanomaterials, enantioselective ability of nanozymes depends on the conversion of them into chiral materials. At present, the mostly used strategy of synthesizing chiral nanozymes is to modify some chiral ligands (e.g., chiral chemical compounds, amino acids or DNA) on their surface. As shown in the Table 1, based on the diverse affinity of chiral ligands to enantiomers of substrates (the smaller the K_M value, the higher the affinity), these chiral nanozymes exhibit asymmetric catalytic activity for chiral substrates such as dopamine. Therefore, the coupling of chiral ligands is a feasible strategy to create enantioselective nanozymes. These preliminary studies opened a new portal for the development of chiral nanozymes. However, the enantioselectivity of chiral nanozymes still has much room for improvement. The enantioselectivity ratio of most of the chiral nanozymes toward paired enantiomers is only slightly larger than 1, which is far from meeting the industrial requirements. To enhance the enantioselectivity of chiral nanozymes, both experimental and theoretical aspects need to be developed simultaneously. As it is in the initial stage, there are still many problems in the study of chiral nanozymes that need to be remedied by follow-up research. Here, some suggestions on the problems of chiral nanozymes are put forward.

Firstly, the methods of synthesizing chiral nanozymes need further upgrading. Direct coupling of chiral ligands onto the surface of nanozymes is indeed a quite simple strategy for the synthesis of chiral nanozymes. However, this method may also cause some new problems, such as increasing the complexity of the synthesis process, compromising the catalytic activity and stability of nanozymes, and so on. Therefore, this strategy needs to take into account the binding ratio of chiral ligands to nanozymes and all other parameters that may hamper the useful properties of nanozymes. In addition to surface-coupled chiral ligands, some other strategies for synthesizing chiral nanozymes may be tried in future studies. For example, like natural enzymes consisting of chiral amino acids, chiral nanozymes may be constructed directly using chiral molecules as building materials. Alternatively, chiral molecules or chiral templates can be used to induce assembly of non-chiral molecules to form chiral nanozymes. For instance, it is reported recently that gold nanomaterials with three-dimensional chiral nanostructures can be synthesized under the induction and control of chiral amino acids and peptides. [53] Besides, although there are few studies on chiral nanozymes, the researches on chiral nanomaterials have been vast that may be used as references for the study of chiral nanozymes. [54–56] In addition, because a lot of nanomaterials have unique physical and chemical properties,

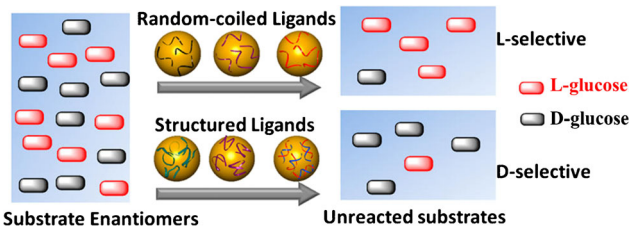

Fig. 5 Schematic illustration of the catalytic enantioselectivity of chiral DNA-capped-AuNPs nanozymes towards the glucose enantiomers. Reproduced with permission from ref. [48]. Copyright 2015 from American Chemical Society

Table 1 Kinetic parameters for catalyzing substrate enantiomers by chiral nanozymes

Chiral nanozymes	Chiral ligands	Enzyme-like activity	Substrates	K_M [M]	*V*max [M. s^{-1}]	k_{cat} [s^{-1}]	Ref.
$[Fe_2L_3]^{4+}$-GO-COOH	M-$[Fe_2L_3]^{4+}$	peroxidase	TMB[a]	2.02×10^{-4}	4.162	NA[b]	[20]
			L-dopa	NA	NA	NA	
			D-dopa	NA	NA	NA	
	P-$[Fe_2L_3]^{4+}$		TMB	1.09×10^{-4}	5.113	NA	
			L-dopa	NA	NA	NA	
			D-dopa	NA	NA	NA	
[TACN·metal]-AuNPs	(+)-[TACN·Zn^{2+}]	nuclease	(+)-CF_3HPNP	2.70×10^{-4}	NA	3.50×10^{-3}	[27]
			UpU[c]	NA	NA	2.31×10^{-2}	
	(−)-[TACN·Zn^{2+}]		(+)-CF_3HPNP	2.40×10^{-4}	NA	2.50×10^{-3}	
			UpU	NA	NA	2.50×10^{-2}	
	(+)-[TACN·Cu^{2+}]		UpU	NA	NA	4.30×10^{-4}	
	(−)-[TACN·Cu^{2+}]		UpU	NA	NA	1.74×10^{-3}	
CeNPs@Phe	L-Phe	oxidase	L-dopa	4.31×10^{-7}	NA	4.16×10^{-3}	[36]
			D-dopa	4.24×10^{-7}	NA	4.63×10^{-3}	
	D-Phe		L-dopa	1.68×10^{-7}	NA	3.12×10^{-3}	
			D-dopa	1.95×10^{-7}	NA	1.94×10^{-3}	
Cys@AuNPs-EMSN	L-Cys	peroxidase	L-dopa	3.94×10^{-5}	NA	5.79×10^{-2}	[38]
			D-dopa	5.08×10^{-5}	NA	1.17×10^{-1}	
	D-Cys		L-dopa	5.21×10^{-5}	NA	1.26×10^{-1}	
			D-dopa	3.80×10^{-5}	NA	5.81×10^{-2}	
Cys-MoS_2-QDs/Cu^{2+}	L-Cys	peroxidase	L-Tyr	9.96×10^{-3}	5.08×10^{-7}	NA	[42]
			D-Tyr	6.61×10^{-3}	1.97×10^{-7}	NA	
	D-Cys		L-Tyr	5.46×10^{-3}	1.83×10^{-7}	NA	
			D-Tyr	8.06×10^{-3}	4.95×10^{-7}	NA	
DNA-AuNPs	ssDNA	glucose oxidase	L-glucose	6.98×10^{-5}	NA	NA	[48]
			D-glucose	9.46×10^{-5}	NA	NA	
	dsDNA		L-glucose	8.90×10^{-5}	NA	NA	
			D-glucose	6.10×10^{-5}	NA	NA	

[a] TMB = 3,3′,5,5′-tetramethylbenzidine

[b] NA = not available

[c] UpU = uracil dinucleotides

the development of synthesis and assembly of chiral nanomaterials (e.g., chiral supramolecular [57–59], chiral noble metals [60–62], chiral metal-organic frameworks (MOFs) [63–65] and chiral quantum dots [66, 67], etc.) may also provide valuable experience for the discovery of chiral nanozymes with unique properties such as light response or high temperature resistance.

Secondly, there is no standardized characterization and stoichiometric method for the catalytic activity and enantioselectivity of chiral nanozymes. Because of this problem, the quantitative comparison of catalytic kinetics between the chiral nanozymes listed in the Table 1 is difficult. On the one hand, huge differences in size and structure between these nanozymes exists. So, it is difficult to define catalytic activity of nanozymes in a uniform standard. To solve this problem, Jiang et al. reported a method using the weight of nanomaterials as an important parameter to quantify the catalytic activity of peroxidase-like nanozymes. [68] However, this method is limited to the quantification of peroxidase-like nanozymes, and cannot be applied to other kinds of nanozymes. Besides, because the catalytic reactions catalyzed by nanozymes are basically carried out on their surfaces, it is controversial to calculate the activity of nanozymes only by considering their mass. Compared with mass, the specific surface area of nanomaterials that takes into account both the weight and surface area may be a more valuable quantitative unit for comparing the activity of different nanozymes. On the other hand, there is no clear stoichiometric definition of enantioselectivity of nanozymes. Although the parameters of steady-state kinetics are used to characterize the catalytic behavior of chiral nanozymes, different parameters are selected to calculate the enantioselectivity, such as k_{cat}, k_{cat}/K_M, or even K_M value. In enzymatic kinetics, K_M value characterizes the affinity between the enzyme and the substrate, while k_{cat} value characterizes the catalytic efficiency of the enzyme to the substrate, also known as turnover number. [69] When catalyzing a single chiral enantiomer, either K_M or k_{cat} may be used as an indicator to describe the chiral selectivity of nanozymes. However, in asymmetric catalytic reaction systems, chiral substrates often exist in the form of racemization, that is, there are two or more substrates at the same time. To characterize the enantioselectivity of nanozymes in such conditions, the affinity and the catalytic efficiency between nanozymes and substrate enantiomers need to be considered simultaneously. Therefore, the value of k_{cat}/K_M may be more suitable to characterize the enantioselectivity of nanozymes.

Thirdly, lack of appropriate theoretical models for enantioselectivity of chiral nanozymes may be one of the reasons for delaying their development. Presently, most of the enantioselective modification of nanozymes are based on the lock-and-key hypothesis. This hypothesis holds that the active center of the enzyme has a specific rigid structure that coincides very well with the structure of the substrate, just like a lock with a key. [70] This hypothesis seems pure and may be helpful to improve the spatial selectivity of nanozymes to some extent. However, the chiral nanozymes that synthesized based on the lock-and-key hypothesis may lack flexibility. A rigid ligand would be difficult to match the chiral substrates perfectly. In fact, the active center of the enzyme is soft rather than rigid. The structure of enzyme does not inherently complementary to the structure of substrates. Instead, its conformation changes correspondingly under the inducement of substrates. [70, 71] Inspired by this induce-fit theory of enzyme, the nanozymes that using flexible chiral ligands may exhibit improved enantioselectivity. In addition, some other theories may also help to improve the enantioselectivity of chiral nanozymes. For example, in 1948, A. G. Ogston put forward the "three-point attachment" hypothesis for the stereoisomeric specificity of enzymes. [72] The hypothesis believes that the binding of enzymes to substrates depends on at least three binding sites between them. Only when these three binding sites match each other can the enzyme bind to substrates and catalyze the reaction. [73, 74] These substrate selectivity theories of natural enzyme have important guiding significance for the development of chiral nanozymes.

Based on a suitable theoretical algorithm, the rational design of chiral nanozymes can be conducted with the help of computer simulation. Considering the feasibility, we believe that the first step of the rational design should still be based on finding suitable chiral ligands for now. Screening synthetic chemicals that bind specifically to substrate enantiomers may be an efficient way to make nanozymes chiral. However, the complexity of synthesizing chemical chiral ligands may be no less than using them in asymmetric catalysis. It should be more feasible to prepare biomolecules as chiral ligands, because they are mostly homochiral in organism. And because amino acids are the building blocks of natural enzymes, they have more advantages than other chiral biomolecules in computer-aided rational design. The key amino acids determining enantioselectivity can be found by analyzing the active centers of natural enzymes using computer simulation. Moreover, rational design of chiral nanozymes should also take into account the composition and sequence of amino acids. Like natural enzymes, using a series of amino acids to construct multiple coordination sites for substrate enantiomers would aid the enantioselectivity of nanozymes. After finding the suitable chiral ligand, the next step is to determine the assembly form of the nanozyme and ligand. A variety of assembly models can be proposed based on the unique characteristics of amino acids and nanozymes. In addition to be modified on the surface, chiral amino acids may also be used as structure-directing agents to mediate the construction of nanozymes' architecture. Algorithms can then be introduced to predict the enantioselectivity of the hypothetical models. Finally, the optimal strategy of rational design can be selected to the synthesize process.

In a word, choosing suitable synthesis methods, adopting appropriate substrate selectivity theory, combining chemical characterization and computer simulation is helpful to design next-generation chiral nanozymes. Currently, modifying chiral ligands are the most effective way to synthesize chiral nanozymes. But the selection of suitable chiral ligands and the balance between the activity and selectivity of nanozymes are still important issues to be faced. Although the research of chiral nanozymes is in the ascendant, as a new kind of enzyme-mimic nanomaterials with great potential, it is believed that enantioselective nanozymes will attract more and more researchers' interest and attention.

Acknowledgements This work was financially supported by the National Natural Science Foundation of China (No. 31871005, 31530026, 31900981), Chinese Academy of Sciences under Grant No. YJKYYQ20180048, the Strategic Priority Research Program (No. XDB29040101), the Key Research Program of Frontier Sciences (No. QYZDY-SSW-SMC013), Chinese Academy of Sciences and National Key Research and Development Program of China (No. 2017YFA0205501), and Youth Innovation Promotion Association CAS (2019093).

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

References

1. Wei H, Wang E (2013) Nanomaterials with enzyme-like characteristics (nanozymes): next-generation artificial enzymes. Chem Soc Rev 42(14):6060–6093. https://doi.org/10.1039/c3cs35486e
2. Lin Y, Ren J, Qu X (2014) Catalytically active nanomaterials: a promising candidate for artificial enzymes. Acc Chem Res 47(4): 1097–1105. https://doi.org/10.1021/ar400250z
3. Guan Y, Li M, Dong K, Gao N, Ren J, Zheng Y, Qu X (2016) Ceria/POMs hybrid nanoparticles as a mimicking metallopeptidase for treatment of neurotoxicity of amyloid-beta peptide. Biomaterials 98:92–102. https://doi.org/10.1016/j.biomaterials.2016.05.005
4. Ragg R, Tahir MN, Tremel W (2016) Solids go bio: inorganic nanoparticles as enzyme mimics. Eur J Inorg Chem 2016(13–14): 1906–1915. https://doi.org/10.1002/ejic.201501237
5. Gao N, Dong K, Zhao A, Sun H, Wang Y, Ren J, Qu X (2016) Polyoxometalate-based nanozyme: design of a multifunctional enzyme for multi-faceted treatment of Alzheimer's disease. Nano Res 9(4):1079–1090. https://doi.org/10.1007/s12274-016-1000-6
6. Gao L, Zhuang J, Nie L, Zhang J, Zhang Y, Gu N, Wang T, Feng J, Yang D, Perrett S (2007) Intrinsic peroxidase-like activity of ferromagnetic nanoparticles. Nat Nanotechnol 2(9):577–583
7. Grunes J, Zhu J, Somorjai GA (2003) Catalysis and nanoscience. Chem Commun 18:2257. https://doi.org/10.1039/b305719b
8. Bell AT (2003) The impact of nanoscience on heterogeneous catalysis. Science 299(5613):1688–1691
9. Zhou Y, Liu B, Yang R, Liu J (2017) Filling in the gaps between Nanozymes and enzymes: challenges and opportunities. Bioconjug Chem 28(12):2903–2909. https://doi.org/10.1021/acs.bioconjchem.7b00673
10. Wu J, Li S, Wei H (2018) Integrated nanozymes: facile preparation and biomedical applications. Chem Commun 54(50):6520–6530. https://doi.org/10.1039/c8cc01202d
11. Pawelek PD, Cheah J, Coulombe R, Macheroux P, Ghisla S, Vrielink A (2000) The structure of l-amino acid oxidase reveals the substrate trajectory into an enantiomerically conserved active site. EMBO J 19(16):4204–4215
12. Eriksson T, Björkman S, Höglund P (2001) Clinical pharmacology of thalidomide. Eur J Clin Pharmacol 57(5):365–376
13. Fabro S, Smith RL, Williams R (1967) Toxicity and teratogenicity of optical isomers of thalidomide. Nature 215(5098):296
14. Brown CJ, Bergman RG, Raymond KN (2009) Enantioselective catalysis of the Aza-cope rearrangement by a chiral Supramolecular assembly. J Am Chem Soc 131(48):17530–17531. https://doi.org/10.1021/ja906386w
15. Soares LC, Alberto EE, Schwab RS, Taube PS, Vanessa N, Rodrigues OED, Braga AL (2012) Ephedrine-based diselenide: a promiscuous catalyst suitable to mimic the enzyme glutathione peroxidase (GPx) and to promote enantioselective C-C coupling reactions. Org Biomol Chem 10(32):6595–6599
16. Chen X, Xu L, Wang A, Li H, Wang C, Pei X, Zhang P, Wu SG (2019) Efficient synthesis of the key chiral alcohol intermediate of Crizotinib using dual-enzyme@CaHPO4 hybrid nanoflowers assembled by mimetic biomineralization. J Chem Technol Biotechnol 94(1):236–243. https://doi.org/10.1002/jctb.5769
17. Cline DB (2005) On the physical origin of the homochirality of life. Eur Rev 13(S2):49–59
18. Blackmond DG (2004) Asymmetric autocatalysis and its implications for the origin of homochirality. Proc Natl Acad Sci 101(16): 5732–5736
19. Cech T. Evolution of biological catalysis: ribozyme to RNP enzyme. In: Cold Spring Harbor symposia on quantitative biology, 2009. Cold Spring Harbor Laboratory Press, pp 11–16
20. Xu C, Zhao C, Li M, Wu L, Ren J, Qu X (2014) Artificial evolution of Graphene oxide Chemzyme with Enantioselectivity and near-infrared Photothermal effect for Cascade biocatalysis reactions. Small 10(9):1841–1847. https://doi.org/10.1002/smll.201302750
21. Song Y, Qu K, Zhao C, Ren J, Qu X (2010) Graphene oxide: intrinsic peroxidase catalytic activity and its application to glucose detection. Adv Mater 22(19):2206–2210. https://doi.org/10.1002/adma.200903783
22. Fahn S (2008) The history of dopamine and levodopa in the treatment of Parkinson's disease. Mov Disord 23(S3):S497–S508
23. Schapira A, Emre M, Jenner P, Poewe W (2009) Levodopa in the treatment of Parkinson's disease. Eur J Neurol 16(9):982–989
24. Manea F, Houillon FB, Pasquato L, Scrimin P (2004) Nanozymes: gold-nanoparticle-based transphosphorylation catalysts. Angew Chem 116(45):6291–6295
25. Zaupa G, Mora C, Bonomi R, Prins LJ, Scrimin P (2011) Catalytic self-assembled monolayers on au nanoparticles: the source of catalysis of a transphosphorylation reaction. Chem Eur J 17(17):4879–4889
26. Diez-Castellnou M, Mancin F, Scrimin P (2014) Efficient phosphodiester cleaving nanozymes resulting from multivalency and local medium polarity control. J Am Chem Soc 136(4):1158–1161
27. Chen JLY, Pezzato C, Scrimin P, Prins LJ (2016) Chiral Nanozymes-gold nanoparticle-based Transphosphorylation catalysts capable of Enantiomeric discrimination. Chem Eur J 22(21): 7028–7032. https://doi.org/10.1002/chem.201600853
28. Yoshizawa A, Kurata M (2019) Porous surface of an achiral trimer in the chiral conglomerate phase catalyzes a direct aldol reaction. New J Chem 43(23):8865–8868. https://doi.org/10.1039/c9nj01913h
29. Roth A, Breaker RR (1998) An amino acid as a cofactor for a catalytic polynucleotide. Proc Natl Acad Sci 95(11):6027–6031

30. Szathmáry E (1999) The origin of the genetic code: amino acids as cofactors in an RNA world. Trends Genet 15(6):223–229
31. Wang SX, Mure M, Medzihradszky KF, Burlingame AL, Brown DE, Dooley DM, Smith AJ, Kagan HM, Klinman JP (1996) A crosslinked cofactor in lysyl oxidase: redox function for amino acid side chains. Science 273(5278):1078–1084
32. Fan K, Wang H, Xi J, Liu Q, Meng X, Duan D, Gao L, Yan X (2017) Optimization of Fe 3 O 4 nanozyme activity via single amino acid modification mimicking an enzyme active site. Chem Commun 53(2):424–427
33. Heckert EG, Karakoti AS, Seal S, Self WT (2008) The role of cerium redox state in the SOD mimetic activity of nanoceria. Biomaterials 29(18):2705–2709. https://doi.org/10.1016/j.biomaterials.2008.03.014
34. Pirmohamed T, Dowding JM, Singh S, Wasserman B, Heckert E, Karakoti AS, King JE, Seal S, Self WT (2010) Nanoceria exhibit redox state-dependent catalase mimetic activity. Chem Commun (Camb) 46(16):2736–2738. https://doi.org/10.1039/b922024k
35. Asati A, Santra S, Kaittanis C, Nath S, Perez JM (2009) Oxidase-like activity of polymer-coated cerium oxide nanoparticles. Angew Chem Int Ed Eng 48(13):2308–2312. https://doi.org/10.1002/anie.200805279
36. Sun Y, Zhao C, Gao N, Ren J, Qu X (2017) Stereoselective Nanozyme based on ceria nanoparticles engineered with amino acids. Chem Eur J 23(72):18146–18150. https://doi.org/10.1002/chem.201704579
37. Hao C, Qu A, Xu L, Sun M, Zhang H, Xu C, Kuang H (2019) Chiral molecule-mediated porous CuxO nanoparticle clusters with Antioxidation activity for ameliorating Parkinson's disease. J Am Chem Soc 141(2):1091–1099. https://doi.org/10.1021/jacs.8b11856
38. Qu X, Zhou Y, Sun H, Xu H, Matysiak S, Ren J (2018) Mesoporous-encapsulated chiral nanogold used for enantioselective reaction. Angew Chem Int Ed Eng. https://doi.org/10.1002/anie.201811118
39. Klabunde T, Eicken C, Sacchettini JC, Krebs B (1998) Crystal structure of a plant catechol oxidase containing a dicopper center. Nat Struct Mol Biol 5(12):1084
40. Yin W, Yu J, Lv F, Yan L, Zheng LR, Gu Z, Zhao Y (2016) Functionalized nano-MoS2 with peroxidase catalytic and near-infrared photothermal activities for safe and synergetic wound antibacterial applications. ACS Nano 10(12):11000–11011
41. Lin T, Zhong L, Guo L, Fu F, Chen G (2014) Seeing diabetes: visual detection of glucose based on the intrinsic peroxidase-like activity of MoS 2 nanosheets. Nanoscale 6(20):11856–11862
42. Zhang H, He H, Jiang X, Xia Z, Wei W (2018) Preparation and characterization of chiral transition-metal Dichalcogenide quantum dots and their Enantioselective catalysis. ACS Appl Mater Interfaces 10(36):30680–30688. https://doi.org/10.1021/acsami.8b10594
43. Bhagi-Damodaran A, Michael MA, Zhu Q, Reed J, Sandoval BA, Mirts EN, Chakraborty S, Moënne-Loccoz P, Zhang Y, Lu Y (2017) Why copper is preferred over iron for oxygen activation and reduction in haem-copper oxidases. Nat Chem 9(3):257–263
44. Silva CS, Durão P, Fillat A, Lindley PF, Martins LO, Bento I (2012) Crystal structure of the multicopper oxidase from the pathogenic bacterium campylobacter jejuni CGUG11284: characterization of a metallo-oxidase. Metallomics 4(1):37–47
45. Clever GH, Kaul C, Carell T (2007) DNA–metal base pairs. Angew Chem Int Ed 46(33):6226–6236
46. Ghosh S, Defrancq E (2010) Metal-complex/DNA conjugates: a versatile building block for DNA Nanoarrays. Chem Eur J 16(43):12780–12787
47. Kolpashchikov DM (2010) Binary probes for nucleic acid analysis. Chem Rev 110(8):4709–4723
48. Zhan P, Wang Z-G, Li N, Ding B (2015) Engineering gold nanoparticles with DNA ligands for selective catalytic oxidation of chiral substrates. ACS Catal 5(3):1489–1498. https://doi.org/10.1021/cs5015805
49. Comotti M, Della Pina C, Matarrese R, Rossi M (2004) The catalytic activity of "naked" gold particles. Angew Chem Int Ed 43(43):5812–5815
50. Koeller KM, Wong C-H (2001) Enzymes for chemical synthesis. Nature 409(6817):232–240
51. Jaeger K-E, Eggert T (2004) Enantioselective biocatalysis optimized by directed evolution. Curr Opin Biotechnol 15(4):305–313
52. Izake EL (2007) Chiral discrimination and enantioselective analysis of drugs: an overview. J Pharm Sci 96(7):1659–1676
53. Lee H-E, Ahn H-Y, Mun J, Lee YY, Kim M, Cho NH, Chang K, Kim WS, Rho J, Nam KT (2018) Amino-acid-and peptide-directed synthesis of chiral plasmonic gold nanoparticles. Nature 556(7701):360–365
54. Zhang J, Albelda MT, Liu Y, Canary JW (2005) Chiral nanotechnology. Chirality 17(7):404–418. https://doi.org/10.1002/chir.20178
55. Bag DS, Shami TC, Rao KUB (2008) Chiral nanoscience and nanotechnology. Def Sci J 58(5):626–635. https://doi.org/10.14429/dsj.58.1685
56. Xia YH, Zhou YL, Tang ZY (2011) Chiral inorganic nanoparticles: origin, optical properties and bioapplications. Nanoscale 3(4):1374–1382. https://doi.org/10.1039/c0nr00903b
57. Lorenzo MO, Baddeley CJ, Muryn C, Raval R (2000) Extended surface chirality from supramolecular assemblies of adsorbed chiral molecules. Nature 404(6776):376–379
58. Hirst AR, Smith DK, Feiters MC, Geurts HP (2010) Two-component dendritic gel: effect of stereochemistry on the supramolecular chiral assembly. Chem Eur J 10(23):5901–5910
59. Fouquey C, Lehn JM, Levelut AM (1990) Molecular recognition directed self-assembly of supramolecular liquid crystalline polymers from complementary chiral components. Adv Mater 2(5):254–257
60. Gautier C, Bürgi T (2009) Chiral gold nanoparticles. ChemPhysChem 10(3):483–492. https://doi.org/10.1002/cphc.200800709
61. Gabriel S, Olga K, Gil M, Tatiana M, Irit L, Kotlyar AB (2006) Chirality of silver nanoparticles synthesized on DNA. J Am Chem Soc 128(34):11006–11007
62. Kang YJ, Oh JW, Kim YR, Kim JS, Kim H (2010) Chiral gold nanoparticle-based electrochemical sensor for enantioselective recognition of 3,4-dihydroxyphenylalanine. Chem Commun 46(31):5665–5667
63. Song F, Wang C, Falkowski JM, Ma L, Lin W (2010) Isoreticular chiral metal-organic frameworks for asymmetric alkene epoxidation: tuning catalytic activity by controlling framework catenation and varying open channel sizes. J Am Chem Soc 132(43):15390–15398
64. Zang S, Su Y, Li Y, Zhu H, Meng Q (2006) One dense and two open chiral metal-organic frameworks: crystal structures and physical properties. Inorg Chem 45(7):2972–2978
65. Ma L, Abney C, Lin W (2009) Enantioselective catalysis with homochiral metal-organic frameworks. Chem Soc Rev 38(5):1248–1256
66. Moloney MP, Gun'Ko YK, Kelly JM (2007) Chiral highly luminescent CdS quantum dots. Chem Commun 38(38):3900–3902
67. Han C, Li H (2010) Chiral recognition of amino acids based on cyclodextrin-capped quantum dots. Small 4(9):1344–1350
68. Jiang B, Duan D, Gao L, Zhou M, Fan K, Tang Y, Xi J, Bi Y, Tong Z, Gao GF (2018) Standardized assays for determining the catalytic activity and kinetics of peroxidase-like nanozymes. Nat Protoc 13:1506–1520

69. Bisswanger H (2017) Enzyme kinetics: principles and methods. Wiley - VCH Publ, Weinheim
70. Koshland DE Jr (1995) The key–lock theory and the induced fit theory. Angew Chem Int Ed Eng 33(23–24):2375–2378
71. Koshland DE (1958) Application of a theory of enzyme specificity to protein synthesis. Proc Natl Acad Sci 44(2):98–104
72. Ogston A (1948) Interpretation of experiments on metabolic processes, using isotopic tracer elements. Nature 162(4129):963
73. Davankov VA (1997) The nature of chiral recognition: is it a three-point interaction? Chirality 9(2):99–102
74. Mesecar AD, Koshland DE Jr (2000) Structural biology: a new model for protein stereospecificity. Nature 403(6770):614–615