SPECIAL TOPIC: Biomaterials and Bioinspired Materials

Microbial-driven fabrication of rare earth materials

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ABSTRACT   Rare earth elements (REEs) are essential raw materials vital for the advancement of modern high-tech industries. However, their extraction often leads to environmental concerns. The similar chemical properties of REEs contribute to high energy consumption and significant pollution emissions during the separation process. To address these challenges and promote sustainable development and efficient resource utilization, synthetic biology techniques have been leveraged to engineer microorganisms for rare earth fabrication. Establishing an engineered microorganism manufacture platform allows for the *in-situ* synthesis of high-value rare earth biomaterials. This innovation not only supports clinical translational research but also enhances applications in cutting-edge fields. This article offers a comprehensive review of the rational construction of rare earth cell factories, the synthesis of high-value rare earth biomaterials, and their diverse applications in high-tech industries. Moreover, it examines the perspectives and challenges within the domain of lanthanide materials fabrication using microbial systems.

Keywords: rare earth, biomanufacturing platform, engineered microorganisms, biomaterial, high-value application

INTRODUCTION

Rare earth elements (REEs), encompassing lanthanides, scandium, and yttrium, consist of a group of 17 elements extensively utilized in agriculture [1], industry [2], and military sectors [3]. They play a vital role as resources supporting the development of cutting-edge defense technologies and the production of innovative materials. The global demand for REEs is rapidly increasing, with estimates projecting it to reach 1.6 million tons by 2050 [4]. However, traditional extraction processes for rare earth minerals are energy-intensive and environmentally harmful. Mining rare earth minerals, known for their dispersed distribution in the Earth's crust, often leads to the generation of acidic wastewater and radioactive waste [5]. Additionally, the separation of similar REEs typically involves cascade extraction methods [6], resulting in significant emissions of waste acids and organic compounds. In recent years, bioadsorption techniques based on peptides or proteins have emerged as promising alternatives for REE recovery [7]. Various peptides and proteins with an affinity for REEs have been identified and designed.

Researchers are focusing on discovering and characterizing highly specific proteins and biomolecules binding to REEs, collectively termed the rare earth genome, aiming for selective extraction of REEs. Moreover, bioleaching conditions are relatively mild and environmentally friendly. For instance, copper bioleaching demonstrates success, with 20% of global copper obtained through bioleaching, effectively addressing pollution and energy consumption issues associated with chemical extraction [8]. Therefore, the development of engineered microorganisms suitable for rare earth separation and the creation of peptides and proteins with efficient affinity and selectivity for REEs using protein engineering techniques hold significant research value in the realm of chemical biology.

Guided by a modular strategy, synthetic biology constructs life systems with specific functions, providing solutions for large-scale green industrial production [9]. It plays a pivotal role, particularly in microbial engineering and the creation of high-value-added products. Synthetic biology enables microorganisms to modulate metabolites by introducing relevant genes and gene mutations, significantly enhancing affinity and selectivity for REEs. Researchers have showcased Lanmodulin (LanM), a novel REE-binding protein, displayed on the cell surface of the fungus *Yarrowia lipolytica*. Engineered *Y. lipolytica* featuring LanM demonstrates notably improved adsorption capacity for various REEs [10]. Recently, our team established a microbial synthetic system enabling the active biological manufacturing of high-purity rare earth products [11]. These methods prioritize environmental friendliness and sustainability, reducing reliance on traditional rare earth ore mining while decreasing environmental pollution and energy consumption. Moreover, synthetic biology can leverage gene editing and metabolic engineering to produce high-value-added products associated with rare earths [12–27]. By utilizing synthetic biology techniques, the interactions between microorganisms and biomolecules with rare earths can be controlled, allowing precise manipulation of material properties. For instance, research led by Lu and colleagues [28] demonstrated that silkworms fed on rare earth-enriched feed produced robust silk fibers with increased tensile strength and toughness. In another approach, Chen and colleagues [29] proposed a modular engineering strategy, focusing on proteins undergoing an α-helix conformational transition induced by rare earth ions. This enhances the stacking density and molecular interactions of adhesive proteins, resulting in a

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super adhesive heterologous protein. Customized rare earth biomaterials developed through these methods find extensive applications in catalysts, biomedicine, and other fields, showcasing significant economic and scientific value. These advancements unveil innovative pathways for sustainable rare earth resource utilization, driving the development of high-value products.

This article outlines the development of rare earth microorganisms and the creation of high-value rare earth biomaterials. It offers an in-depth exploration of screening and modifying rare earth microorganism systems for leaching and enrichment, along with the design and synthesis of rare earth biomaterials. These biomaterials find applications in rare earth separation, mechanical support, catalysis, and diagnostics. Additionally, it discusses future research directions and prospects for manufacturing rare earth biomaterials and their application in high-value materials (Fig. 1).

CONSTRUCTION OF A MICROBIAL SYSTEM FOR RARE EARTH ELEMENT LEACHING

The basis of the leaching of REEs lies in the dissolution of the ore. This process can be realized by utilizing microorganisms' oxidizing or reducing properties to dissolve the metals within the minerals. Alternatively, it can be achieved by utilizing microbial metabolites (such as citric acid, oxalic acid, and Fe^{3+}) or by employing metal complexes within the minerals for oxidizing and reducing the minerals, thereby facilitating their dissolution. The bioleaching process is usually carried out at relatively low temperatures and atmospheric pressures and does not depend on expensive and aggressive reagents and high-temperature conditions common in hydrometallurgical processing.

Wild-type rare earth leaching microorganisms

The leaching of rare earth ores primarily occurs due to the organic acids produced by the metabolism of heterotrophic microorganisms. These acids can lower the pH of the solution, providing the organic acid anions of the proton–rare earth complexes and facilitating the dissolution of REEs in the minerals through proton exchange. Organic acids are regular metabolites and metabolic intermediates in the metabolism of microorganisms. These organic acids produce low-pH environments, advancing acidolysis and mineral dissolution through complexation. Most rare earth leaching microorganisms identified in current studies are phosphate-solubilizing microorganisms, which convert insoluble phosphates into more soluble forms. Most studies on REE bioleaching have been conducted with phosphate-solubilizing microorganisms, which can promote the dissolution of elemental phosphorus and REEs by releasing organic acids and phosphatases. *Acidithiobacillus ferrooxidans*, a mining microorganism commonly used in acidolysis, which oxidizes sulfur elements in the environment into
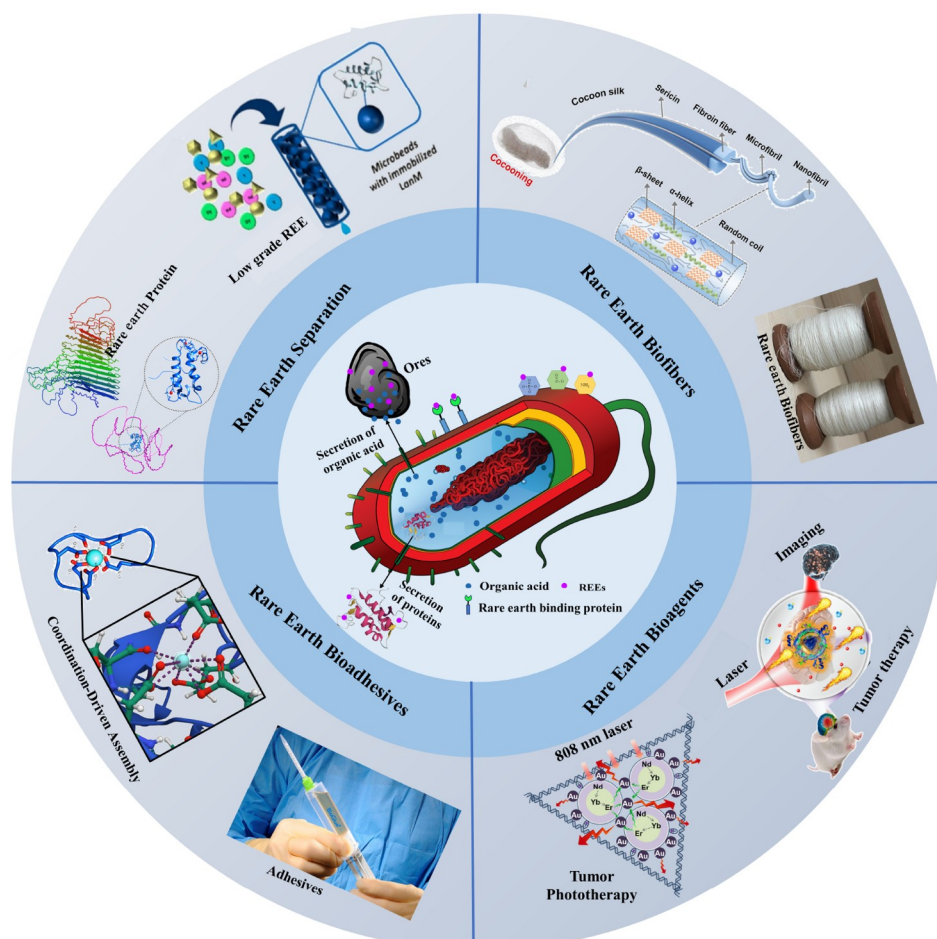

Figure 1 Overview of the topics covered in this review.

sulfates for chemoautotrophic purposes (Fig. 2a). It is commonly used in bioleaching processes of metallic elements, especially copper (Fig. 2b) [30]. Bioleaching of REEs from waste can be realized by producing sulfuric acid from the metabolism of *A. ferrooxidans*. This process makes less environmental waste and boasts substantial selectivity for REEs compared with traditional chemical processes [31]. A recent study showed that *Arthrobacter pascens* H19 and *Burkholderia anthina* G21 efficiently dissolve silica in bauxite by secreting citric, malic, and succinic acids and extracellular polymers (EPS) and aluminum, thereby allowing the release of REEs [32].

Engineered rare earth leaching microorganisms
The bioleaching performance of microorganisms for REEs can be improved by modulating their growth and metabolism *via* gene knockout and other methods. Wild-type *Gluconobacter oxidans* has been used to recover REEs from phosphorus powder (RPP, phosphor powder) and spent fluid catalytic cracking (FCC) in laboratory situations due to their ability to secrete gluconic acid. However, the leaching efficiency of unmodified *G. oxidans* for REEs in FCC was only 49%. In contrast, the genetically engineered microorganism *G. oxidans* increased the REE leaching efficiency to 67% (Fig. 2c) [33,34]. Meanwhile, disruption of the supply of membrane-bound glucose dehydrogenase by the absence of the pyrroloquinoline quino (PQQ) cofactor (due to disruption) reduced the rare earth leaching rate by 94%. This study proves the feasibility of improving the leaching efficiency of engineering microorganisms through gene editing. The microorganisms also released REEs from the ore by desilication.

The use of organic acids in bioleaching shows that increasing the concentration of organic acid can enhance the efficiency of leaching processes. It is noteworthy that cell-free culture supernatants of *G. oxidans*, containing 10–15 mM gluconic acid, exhibit superior leaching performance compared with solutions of organic acids with higher concentrations of gluconic acid. This indicates that other components secreted by microorganisms also play a significant role in the leaching of REEs [33].

CONSTRUCTION OF MICROBIAL SYSTEMS FOR ADSORPTION AND ACCUMULATION OF RARE EARTHS

The resource processing of low-grade raw rare-earth ores, rare-earth tailings, and rare-earth wastes, as well as the utilization of the rare-earth resources therein, have been a global challenge. The traditional methods of rare earth extraction and utilization could be less economically efficient and may cause environmental pollution. Bio-extraction of REEs is a new process involving adsorption and accumulation of REEs from raw rare earth ores, rare earth tailings, and rare earth wastes through specific microorganisms. This process enriches and concentrates these elements or transforms them into high-value-added products to realize the resource utilization of poor ores, tailings, and wastes. Microorganisms can adsorb rare earth ions dissolved in water through electrostatic interactions, ion exchange, surface complexation, precipitation, and other reactions with carboxyl and phosphate groups on the cell surface. Microorganisms boast the advantages of multiple surface active sites, high enrichment efficiency, and high specificity. Therefore, the adsorption of REEs by microorganisms is a relatively rapid process. Microbial accumulation describes the bacteria's reliance on the energy generated by cellular metabolism. This reliance involves using monovalent or divalent ions from the ion transfer system to transport metal ions into the cell. Such a mechanism enables the survival of cells in environments with heavy metals by facilitating the transfer of extracellular metal ions to the intracellular space through processes such as lipophilic transport, ion channel-mediated endocytosis, and other pathways.

Microbial enrichment of rare earth ions is usually divided into two phases. The initial phase involves rapid uptake, primarily attributed to the biosorption of rare earth ions on the cell wall (largely passive uptake). Differences in the cell wall composition among various microbial populations, such as algae, fungi, yeasts, and bacteria, result in substantial variations in the type and quantity of rare earth ions bound to them. The second phase is the microbial-mediated transfer of rare earth ions into the cytoplasm (active uptake), i.e., bioaccumulation, which refers to the uptake of metal ions from the environment by microorganisms relying on their metabolism and progressive accumulation in the body. Therefore, biological methods based on microbial bioaccumulation can be an alternative to metal recycling and remediation [11].
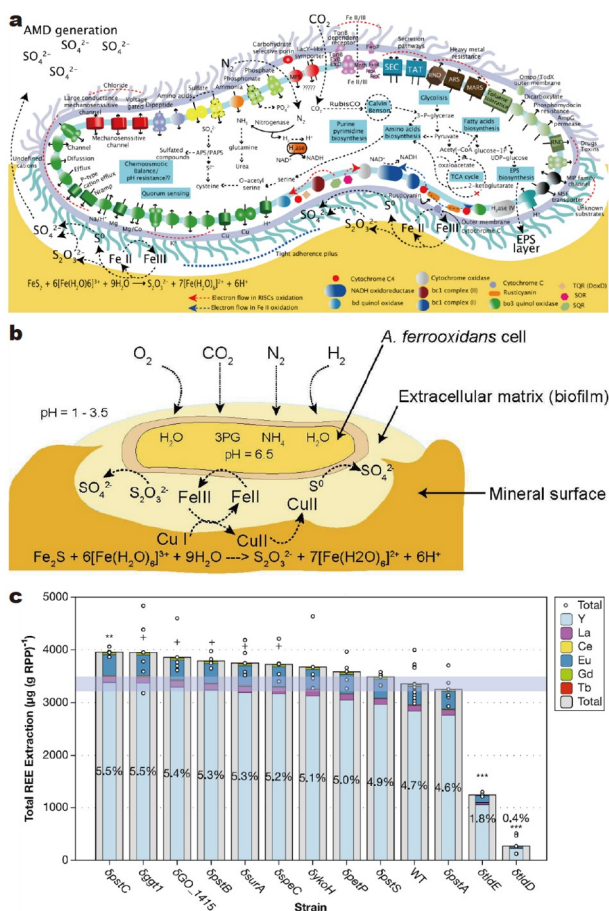

Figure 2 Schematic diagram of metabolic pathways and bioleaching/biomining of chemoenergetic autotrophic microorganisms. (a) Metabolism and transport modeling of *A. ferrooxidans* ATCC 23270 cells. Reprinted with permission from Ref. [30]. Copyright 2008, BioMed Central. (b) Schematic diagram of the bioleaching of elemental copper by *A. ferrooxidans*. Reprinted with permission from Ref. [30]. Copyright 2008, BioMed Central. (c) Acidified *G. oxydans* B58 increases rare earth leaching. Reprinted with permission from Ref. [34]. Copyright 2021, The Authors.

Wild-type rare earth adsorbing and accumulating microorganisms

There are negatively charged groups on the cell wall of microorganisms, which have a certain enrichment effect on REEs. Gram-positive bacteria, such as *Bacillus licheniformis*, *B. subtilis*, *B. shortis*, and *Rhodococcus reuteri*, have a high capacity to accumulate rare earths, and the microbial accumulation of REEs increases at higher pH and solution concentration. *B. licheniformis* can bioaccumulate Ce, and phosphate groups and carboxylic acidic groups on the surface of the cells may be the reason for the adsorption of Ce^{3+} (Fig. 3a). *B. licheniformis* can convert Ce^{3+} into nanoscale mineralization ($CePO_4/CeO_2$) (Fig. 3b) [35]. Hydrothermal treatment accelerates this process. In a 2023 study, *in situ* nanoscale phosphate synthesis of all REEs was possible based on the adsorptive capacity of wild-type *Pseudomonas kunmingensis* TR-21, which had been isolated from rare earth-rich environments, such as rare earth tailings, and on *in situ* synthesis techniques [11]. Biosynthesis by microorganisms is less polluting and less costly compared with chemical methods. Rare earth phosphates boast good chemical

Figure 3 (a) Scanning electron microscopy (SEM)/energy dispersive X-ray spectroscopy (EDS) image of microorganisms after interaction with Ce^{3+}. The interaction of Ce with the microbial surface was verified. Reprinted with permission from Ref. [35]. Copyright 2021, Elsevier. (b) Transmission electron microscopy (TEM) image of microorganisms after interaction with Ce^{3+}. Reprinted with permission from Ref. [35]. Copyright 2021, Elsevier. (c) Purification of XoxF-type MDH from *M. extorquens* after co-cultivation of rare earth tailings with *M. extorquens*. The obtained MDH not only contained La, Ce, Pr, and Nd elements, but also remained catalytically active. Reprinted with permission from Ref. [30]. Copyright 2023, Wiley-VCH.

and thermal stability and are commonly used to prepare luminescent materials.

Methylotrophic microorganisms can convert monocarbon into a carbon source for growth through self-synthesized methanol dehydrogenase (MDH), whose active site contains PQQ and metal ions [36,37]. The *Methylobacterium extorquens* AM1 strain features a genome in which *mxaF* and *mxaI* genes encode for the large and small subunits of MDH, respectively, with calcium ions as the core. Meanwhile, a conserved PQQ-binding domain gene, *xoxF*, similar to *mxaF*, was present in *M. extorquens* AM1. The expression of *xoxF* was demonstrated to be comparable to that of *mxaF* in the natural environment of *M. extorquens* AM1, and the methanol dehydrogenation activity of the product of this gene's expression confirmed that XoxF catalyzes the oxidation of methanol [38–40]. In 2011, Kawai and coworkers [41,42] described the role of La and Ce in the XoxF-MDH active site, confirming the vital of REEs in *Methylobacterium radiotolerans* NBRC15690 strain. In 2014, REEs were first found to be essential elements in the water of the Solfatara mudponds for *M. fumariolicum* SolV [43]. In 2023, our research group utilized *M. extorquens* AM1 to enrich REEs directly from tailings into cells and purify XoxF-MDH-containing REEs from the AM1 strain (Fig. 3c) [11]. The results demonstrated that microbial REEs in tailings utilization and biosynthesis can be utilized with specificity and selectivity, serving as selective adsorbents for rare earths to separate and purify REEs. The property of *M. extorquens* AM1 to utilize single-carbon compounds to grow with REEs has made it a vital chassis organism in the synthetic bio-economy, and a series of chemical products have already been achieved for bioproduction [44–47]. Additionally, inducible orthologous promoters with varying strengths were constructed in *M. extorquens* AM1 to regulate the expression of rare earth microbial chassis [45].

Overall, the existing research on the construction of rare earth microbial chassis based on natural rare earth microorganisms has a specific guiding significance for future chassis modification research, especially the screening and modification of natural microorganisms in rare earth-rich environments, which can solve to a greater extent the problems faced by the REEs in the mining, isolation, and application of REEs.

Engineered rare earth adsorption and accumulation of microorganisms

Based on elucidating the interaction mechanism between microorganisms and rare earths, microorganisms can be modified in three ways: genetic engineering, rare earth-bound labeled cell-surface display, and chemical modification.

In recent years, progress has also been made in the *in situ* synthesis of nanoparticles (NPs) based on engineered microorganisms. Through genetic engineering techniques, recombinant *Escherichia coli* DH5α carrying pYJ-MT-PCS synthesized NPs of 21 metals, including La, Ce, Fe, Ni, and Co [48]. Recombinant DH5α allowed *in situ* synthesis of 7 irregular rare-earth NPs (La to Gd, except Pm) (Fig. 4a).

As chassis microorganisms commonly employed in synthetic biology, *E. coli* and yeast have addressed numerous scientific and engineering problems [49–57]. However, due to the toxicity of free-state rare earth ions, *E. coli* and yeast cells cannot be effectively compatible with rare earth-containing biosynthetic systems. Therefore, it is essential to introduce peptides or proteins with rare-earth binding functions into these chassis
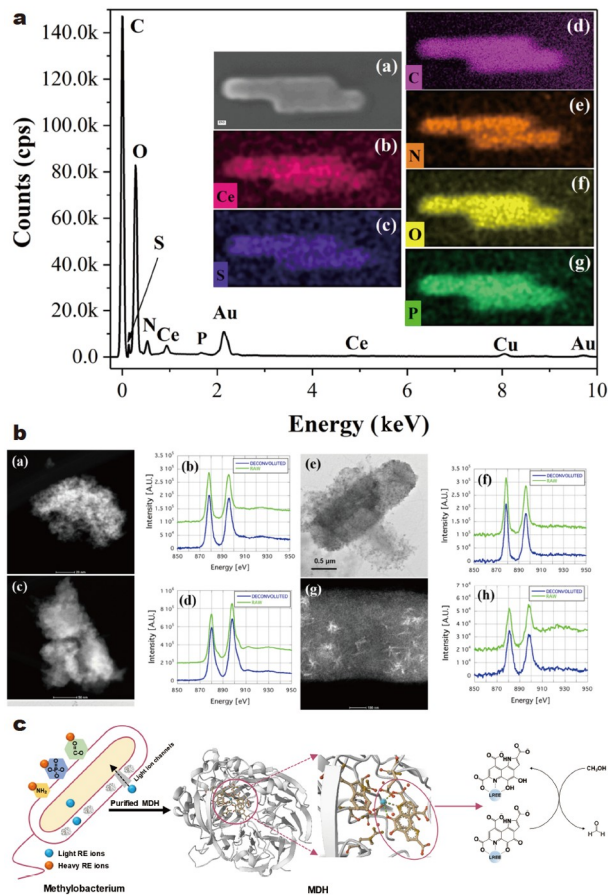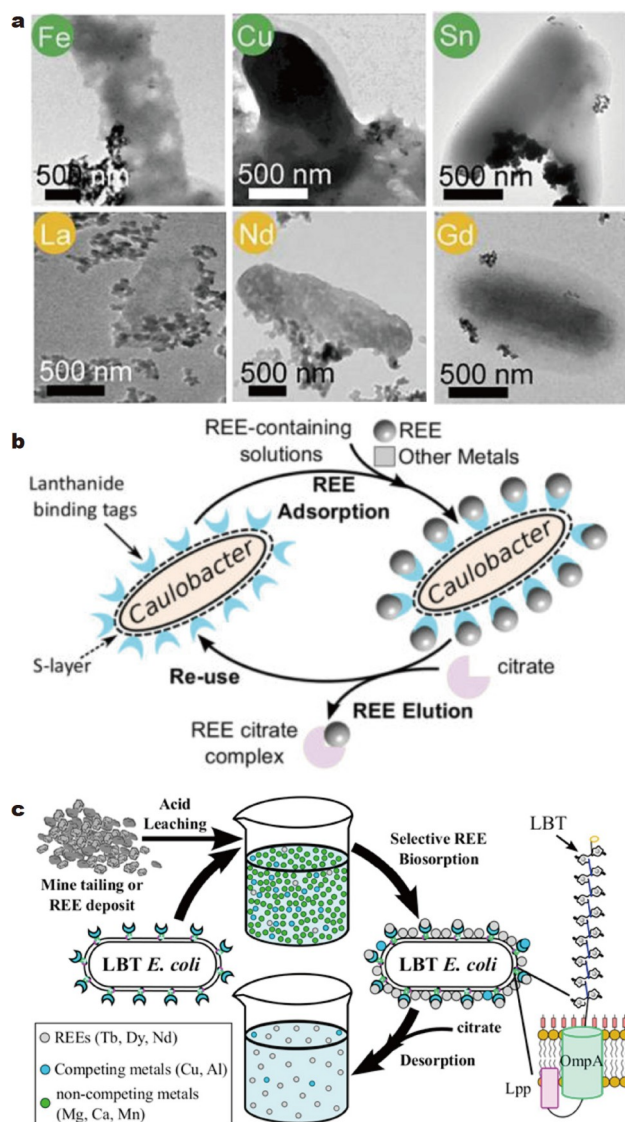
Figure 4 (a) Biosynthesis of single metal NPs. Reprinted with permission from Ref. [16]. Copyright 2018, National Academy of Sciences. (b) Adsorption of REE by displaying LBT on the surface of S-layer high-density cells of *Caulobacter crescentus*. Reprinted with permission from Ref. [58]. Copyright 2016, American Chemical Society. (c) *E. coli* expressed dLBT can be used to enrich for REEs. Reprinted with permission from Ref. [60]. Copyright 2017, American Chemical Society.

microorganisms. The first artificially designed rare-earth ion-binding peptide was named lanthanide binding tags (LBT) (Fig. 4b) [58]. The sequence design of LBT was based on a natural metal ion-binding fragment and was obtained by fluorescence screening. LBT can bind rare-earth ions without affecting the properties of the protein to which it is attached, making it a potential candidate for enhancing rare-earth ion biocompatibility [59]. Due to the high affinity and selectivity of LBT for rare-earth ions, it is believed that dimeric or even multimeric LBTs can directly participate in constructing rare-earth biosystems and facilitate the separation process of rare-earth elements. An engineered *E. coli* with rare-earth element adsorption function was successfully built by displaying dLBT, an octamer of LBT, on the surface of *E. coli* through Lpp-OmpA (Fig. 4c) [60]. The iron recognition peptide of *E. coli* PmrA/

PmrB system was replaced by LBT, which realized the recognition of extracellular rare earth ions by *E. coli* [61,62]. The system can realize extracellular expression of rare earth binding peptides [10]. *E. coli*, as an effective chassis microorganism, was also used to synthesize rare earth binding proteins such as lut gene clusters, LanM, and Lanpepsy (LanP) [63–69].

The results of metabolomics studies in yeast indicate that REEs can enter the yeast cell cytosol and induce a series of metabolic changes, laying the groundwork for the extracellular display of biological macromolecules [70]. Through molecular biology techniques, the rare earth ion-binding protein LanM was successfully immobilized on the protein anchor locus CWP110 on the surface of *Y. lipolytica*, confirming the feasibility of yeast as a eukaryotic rare earth microorganism. This achievement realized the efficient and economical broad-spectrum recovery of REEs from acidic wastewater (Fig. 5a) [71].

Furthermore, it has been shown that P-yeast, prepared by chemical modification of yeast cells using sodium tripolyphosphate, can be employed for the adsorption of REEs in the strong acidic water of the Tamagawa hot spring in Japan (Fig. 5b) [72]. P-yeast can realize selective adsorption and recovery of REEs even in the low concentration of REEs and the absence of multiple contaminants. The recovery concentration can reach tens of ppb.

RARE EARTH BIOMATERIALS

Rare earth biological separations

Structural proteins for rare earth separations
REEs, particularly lanthanides, play vital roles in various technologies such as permanent magnets [73], hybrid electric vehicle batteries [74], lasers [75], phosphors [76], and smartphones [77], resulting in a substantial commercial demand [78]. However, the extensive utilization of these elements [79] contrasts sharply with the scarcity of commercially exploitable reserves [80] and the complexities involved in their extraction from ores [81]. Additionally, the insolubility of rare earth salts [82] and the similarity of their chemical properties [83] necessitate environmentally damaging [84] and time-consuming mining and separation methods. The technological importance of rare earths and the challenges associated with their extraction have spurred the exploration of more convenient and eco-friendly biotechnological approaches for their separation.

Cotruvo Jr. and colleagues [63] have identified LanM, a highly selective lanthanide-binding protein, in a model methylotrophic bacterium. In contrast to other proteins with EF-hands [85], LanM undergoes a transition from a disordered to a compact ordered state in response to picomolar concentrations of all lanthanide elements, while it only responds to calcium ions at concentrations close to the millimolar range. Notably, the far ultraviolet (UV) circular dichroism (CD) spectrum of LanM exhibits a prominent peak at 203 nm, consistent with an irregular structure with little helical character. Importantly, all lanthanide ions (except Pm and Y) cause an approximately 200% increase in the molar ellipticity at 222 nm, reaching a ratio of about 4 equiv. This suggests an increase in α-helix content and a decrease in spectral features associated with random coil structures. The addition of up to 8 equiv. (160 μM) of calcium ions only leads to a slight increase in helical features (Fig. 6a). Thus, LanM selectively transitions from a predominantly disordered
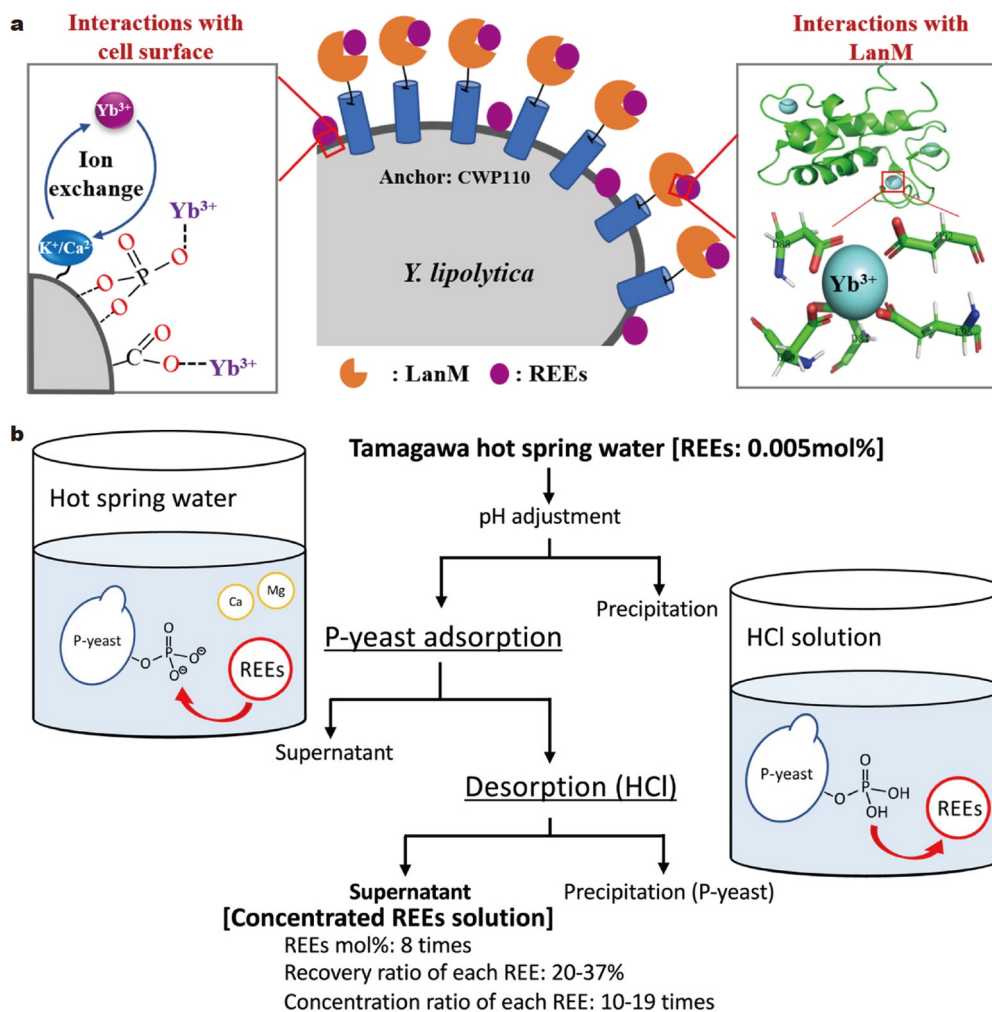
Figure 5 (a) Rare earth ion-binding protein LanM was immobilized to protein anchor localization sites on the surface of *Y. lipolytica*. Reprinted with permission from Ref. [71]. Copyright 2022, Elsevier. (b) Schematic diagram of P-yeast cells enriched for REEs. Reprinted with permission from Ref. [72]. Copyright 2022, Elsevier.

state to an ordered state. The discovery of LanM provides a new method for the exploration and separation of lanthanide elements.

In recent years, there has been growing interest in studying proteins involved in sensing [86], uptake [87], and utilization of lanthanide elements [88]. In a study by Hemmann *et al.* [65], proteomic methods were employed to analyze proteins regulated in the presence of lanthanides. This analysis led to the discovery of several novel proteins, including Mfla_0908, a periplasmic 19 kDa protein without functional annotation. Mfla_0908, also known as LanP, contains two characteristic PepSY domains. Through dye competition experiments, ICP-MS for quantitative lanthanide binding, and isothermal titration calorimetry, it was demonstrated that LanP possesses multiple lanthanide binding sites and exhibits selectivity for chemically similar calcium ions. When 4 µM LanP was incubated with 20 µM La^{3+}, 3.2 ± 0.3 equiv. of La^{3+} was recovered from the protein isolate. Furthermore, when the protein was incubated with a mixture of 100 µM La^{3+} and 100 µM Ca^{2+}, similar to the competition experiment, 3.8 ± 0.2 equivalents of La^{3+} were bound, even in the presence of Ca^{2+}. To determine if certain elements exhibited preferential binding to LanP, a mixture of five REEs (Ce^{3+}, La^{3+}, Nd^{3+}, Y^{3+},

and Pr^{3+}) was used. Each element was present at 20 µM, except Pr^{3+} at 10 µM. Equal binding was observed for Ce^{3+} (0.81 ± 0.09 equiv.), La^{3+} (0.8 ± 0.1 equiv.), and Nd^{3+} (0.77 ± 0.06 equiv.). Y^{3+} (0.53 ± 0.06 equiv.) and Pr^{3+} (0.47 ± 0.04 equiv.) showed lower binding in the protein isolate (Fig. 6b). Although LanP exhibits some variability in the separation of REEs, critical technical challenges remain due to the subtle differences in ionic radii and coordination numbers among these elements. Overall, these findings shed light on the lanthanide binding properties of LanP and highlight the challenges associated with studying these elements due to their subtle differences in physical properties.

Mattocks and colleagues [89] subsequently characterized a new LanM derived from *Hansschlegelia quercus* (named Hans-LanM). The oligomeric state of Hans-LanM was found to be sensitive to the ionic radius of lanthanide ions. Dimerization of Hans-LanM was induced by lanthanum ions (III), resulting in significantly higher compactness compared with dimerization induced by dysprosium ions(III), with over 100 times difference. Despite the low sequence similarity (only 33%) with Mex-LanM and structural differences in the EF-hand motif, particularly at positions one, two, and nine. Hans-LanM exhibited a minimal helical structure at 222 nm in the absence of metals. Remarkably,
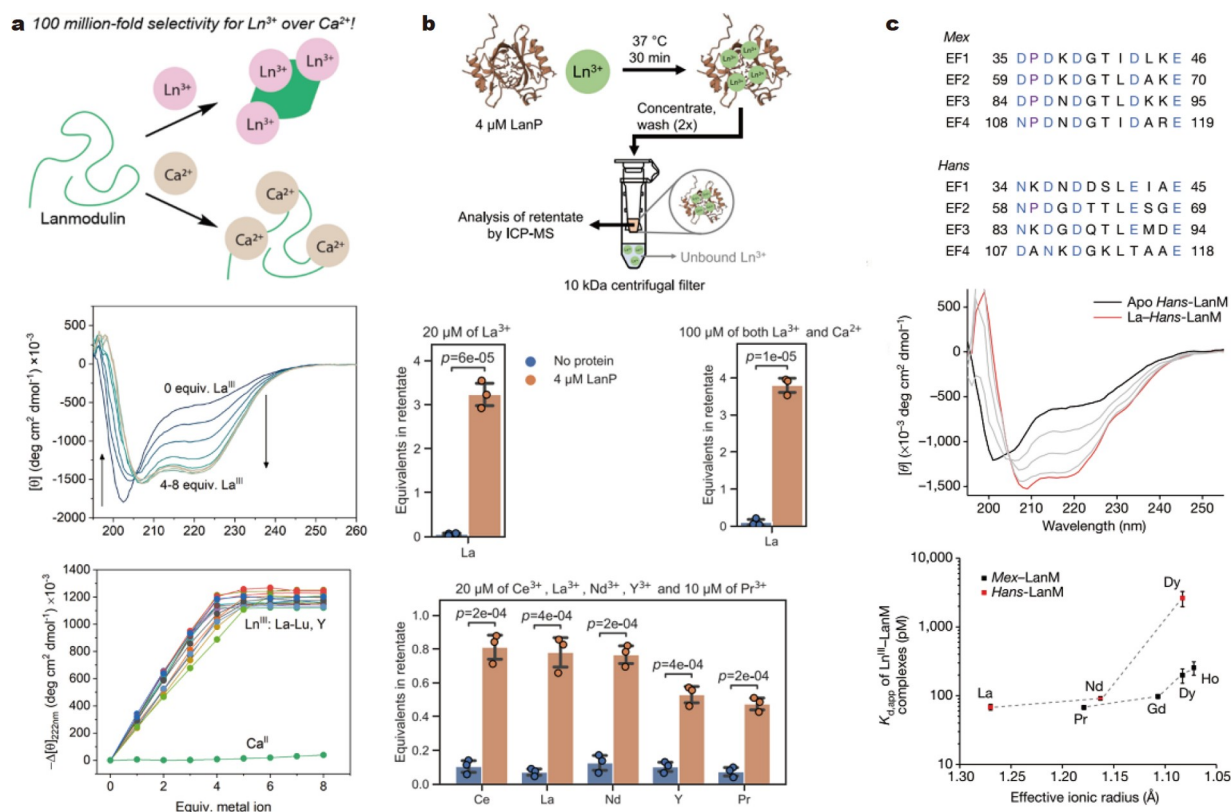
Figure 6 (a) LanM undergoes a conformational change selectively in the presence of Ln^{3+}. CD spectra of LanM (20 μM) in the presence of 0–8 equiv. of La^{3+}. Magnitude of molar ellipticity change for CD titrations of LanM (20 μM) with 0–8 equiv. of Ln^{3+}. Reprinted with permission from Ref. [63]. Copyright 2018, American Chemical Society. (b) Inductively coupled plasma mass (ICP-MS) analyses of retentates obtained by ultrafiltration of LanP incubated with different REEs. In the negative control, no protein was present (blue bars). For the assays with protein (orange bars), 4 μM LanP was incubated with 20 μM LaCl$_3$, 100 μM LaCl$_3$, and 100 μM CaCl$_2$, and 20 μM of each CeCl$_3$, LaCl$_3$, NdCl$_3$, YCl$_3$, and 10 μM PrCl$_3$. Each assay was repeated three times, and the error bars depict the standard deviation. Reprinted with permission from Ref. [65]. Copyright 2023, Elsevier. (c) Comparison of the sequences of the four EF hands of Mex- and Hans-LanMs. CD spectra from a representative titration of Hans-LanM with La^{3+}, apoprotein is bold black, La^{3+}-saturated protein is bold red. Comparison of $K_{d,app}$ values (pH 5.0) for Mex-LanM (black18) and Hans-LanM (red), plotted *versus* ionic radius. Mean ± s.e.m. from three independent experiment. Reprinted with permission from Ref. [89]. Copyright 2023, The Authors.

the conformational change in Hans-LanM was triggered by the binding of just 2 equiv. of La^{3+} or Dy^{3+}, leading to a complete alteration in its structure. Circular dichroism spectroscopy was used to determine the apparent dissociation constants ($K_{d,app}$) of Hans-LanM, reflecting its selectivity for lanthanide and non-lanthanide ions under competitive conditions for lanthanide recovery. Binding of La^{3+} and Nd^{3+} to Hans-LanM increased the molar ellipticity at 222 nm by 2.3-fold. In contrast, Mex-LanM exhibited only a modest preference for light rare earths [90]. Subsequently, a key residue at the dimer interface of Hans-LanM was modulated through structure-guided mutagenesis, regulating dimerization in solution and achieving single-stage column-based separation of a mixture of Pr^{3+} and Dy^{3+}, resulting in each ion with purity over 98% (Fig. 6c). This study demonstrates the natural diversity of selective lanthanide recognition motifs and unveils lanthanide-sensitive dimerization as a biological principle that can regulate the performance of biomolecular separation processes.

Certain plant species have the remarkable ability to hyper-accumulate REEs [91]. Unraveling the biological mechanisms behind this phenomenon is crucial for the advancement of environmentally friendly REE recovery technologies [92]. Zheng and colleagues [91] have identified an REE transporter called NRAMP REE transporter 1 (NREET1) from the REE hyper-

accumulator fern *Dicranopteris linearis*. When expressed in yeast, NREET1 exhibited REE transport activity but was unable to transport divalent metals, such as zinc, nickel, manganese or iron. NREET1 was predominantly expressed in the roots of *D. linearis* and was mainly localized to the plasma membrane. Expression studies in Arabidopsis revealed that NREET1 acts as a transporter to mediate REE uptake and translocation between the root cell wall and the cytoplasm. Furthermore, NREET1 displayed a higher affinity for light REEs than for heavy REEs. Notably, NREET1 displayed a higher affinity for light REEs compared with heavy REEs, suggesting its role in preferential uptake and accumulation of specific REEs. These findings lay the foundation for the development and construction of sustainable plant-based REE recovery systems using synthetic biology approaches.

Protein complexes for rare earth separation
The utilization of environmentally friendly and highly customizable biomaterial tools, including microorganisms and biomolecules, for REE separation, holds great promise, offering advantages such as high selectivity and precision. However, the industrial application of biomaterials still faces major challenges in efficiently extracting REEs from ores. Thus, developing a new generation of bioinspired materials for versatile biorefineries is

essential. One such bioinspired material is LanM, naturally found in *M. extorquens*, which exhibits the ability to selectively form complexes with trivalent REE ions, demonstrating high structural stability. However, the REE adsorption capacity of monomeric LanM is relatively weak. Therefore, the development of engineered LanM-derived REE units is necessary to achieve strong recovery performance.

Our team has successfully constructed a novel chimeric protein DLanM, which possesses eight EF-hands [11]. This distinctive design allows DLanM to bind up to six REE ions with an adsorption efficiency of 1:4 (protein:REE), offering superior stability and selectivity for REEs compared with the original LanM. The original LanM, with only two binding sites, had an adsorption efficiency of 1:2 (protein:REE) [67]. By bioconjugating the engineered protein DLanM, we achieved clear quantitative separation of REE, resulting in yields of 99.9% Eu, 97.1% La, and 92.7% Dy, respectively (Fig. 7a). Notably, to facilitate the conversion of DLanM into a flowable product for REE recovery, we employed click chemistry of the amino groups to conjugate DLanM onto the modified agarose gel beads. To evaluate the REE adsorption capacity of immobilized DLanM under flow conditions, we packed a fixed-bed column with the DLanM conjugates. Given the higher abundance of lanthanum in ore deposits, we selected lanthanum as the representative REE element. The bioconjugate column demonstrated excellent reusa-

bility, maintaining good REE recovery performance for dozens of cycles. Furthermore, we tested the selectivity of the DLanM column for REEs and other metal elements using a mixed solution. After elution with 10 column volumes, 77.1% of the Eu ions were still adsorbed in the feed solution. The adsorption of La and Dy was only 39.2% and 23.3%, respectively. These anomalous adsorption properties of DLanM are different from those of the LanM column and show potential for the separation applications of REEs.

To overcome the limited recyclability of bioadsorbents for REEs, Hussain *et al.* [93] proposed a strategy involving the fusion of a thermoresponsive protein and a selective REE-binding domain. This fusion protein, named RELP, combines the REE-selective binding capability of LanM with the convenient regeneration property of the elastin-like polypeptide (ELP) domain through thermal cycling. It can be easily recycled for at least six repeated cycles while maintaining efficiency. Specifically, ELP [94] and RELP were purified using inverse transition cycling (ITC) after expression in *E. coli* cells. The purified ELP and RELP had theoretical molecular weights of approximately 63 and 75 kDa, respectively. Protein bands corresponding to ELP and RELP were observed in the protein gels. The purity of the ELP species was more than 95%. The phase transition properties of ELP and RELP were determined by monitoring solution turbidity at 350 nm (A350 nm). Impor-
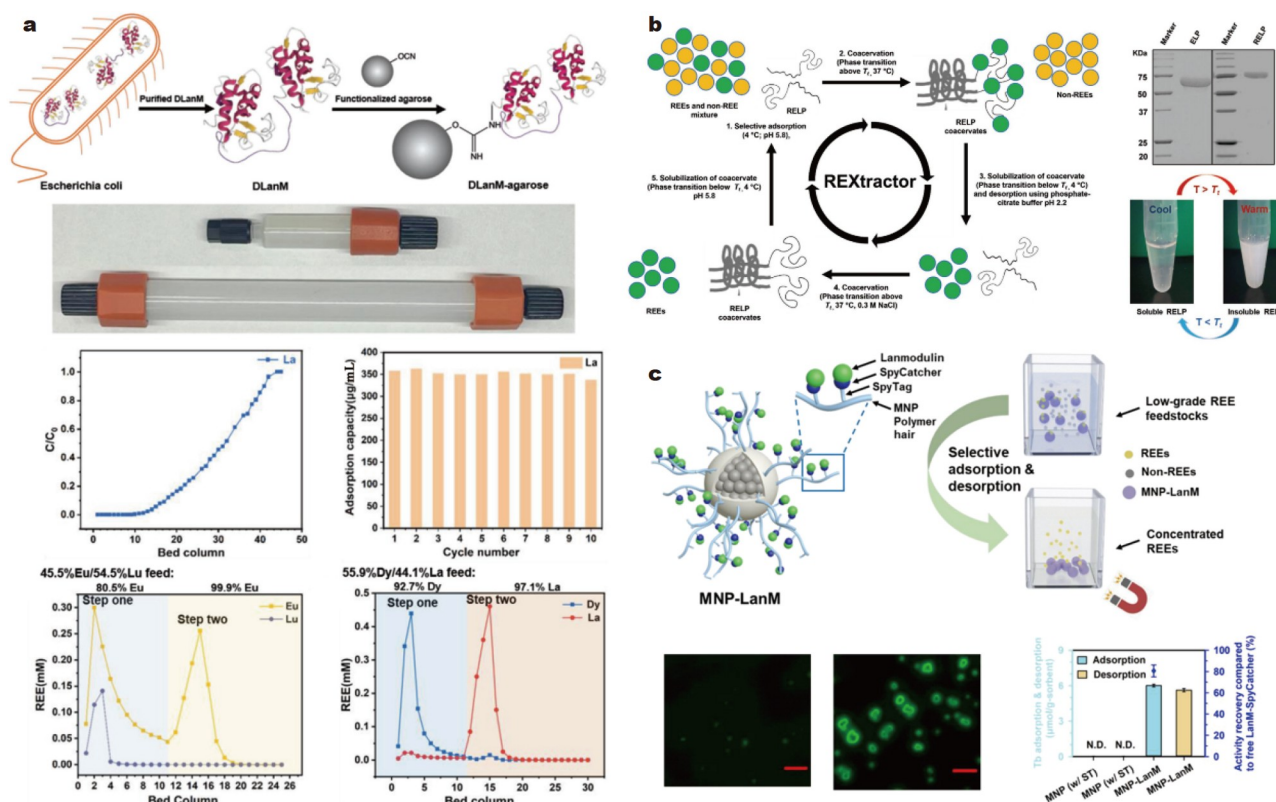

Figure 7 (a) Adsorption capacity and selectivity test of immobilized DLanM device. A new rare-earth functional protein DLanM was designed and biosynthesized. A series of rare-earth biosorbent columns were developed by coupling with adsorbent agarose microbeads. Reprinted with permission from Ref. [30]. Copyright 2023, Wiley-VCH. (b) Schematic of the proposed REXtractor technology for selective REE recovery using RELP. Depiction of inverse phase transition by RELP for cooling and heating. Reprinted with permission from Ref. [93]. Copyright 2021, Wiley-VCH. (c) Illustration of the structure and activity of the MNP-LanM biosorbent. Fluorescence microscopic observation of MNPs without SpyTag (ST) functionalization and ST-functionalized MNPs immobilized with fluorescein isothiocyanate-labeled LanM-SpyCatcher. The scale bar is 5 μm. Terbium (Tb) adsorption and desorption by ST-functionalized MNPs without LanM immobilization (the control) and the MNP-LanM. Reprinted with permission from Ref. [68]. Copyright 2023, American Chemical Society.

tantly, the fusion of LanM had no significant impact on the phase transition properties of RELP (Fig. 7b). The coacervation of RELP was reversible, as the precipitate completely redissolved when the solution temperature was reduced below the transition temperature (T_t). Furthermore, RELP demonstrated its potential as a selective and reusable platform for the recovery of REEs from steel slag leachate. However, the selective separation and enrichment of REEs from low-quality wastewater still pose significant challenges [95]. Immobilization of proteins on support materials is a viable strategy to improve their stability and reusability.

To address these issues, Ye et al. [68] developed a novel bioadsorbent for the selective separation and recovery of REEs from wastewater by anchoring Lanmodulin-SpyCatcher (LanM-SpyCatcher) on the surface of SpyTag-functionalized magnetic NPs (MNPs). The resulting bioadsorbent, named MNP-LanM, had an adsorption capacity of 6.01 ± 0.11 μmol terbium g^{-1} sorbent and possessed fast adsorption kinetics. The adsorbed REEs could be desorbed with an efficiency of >90%. MNP-LanM selectively adsorbed REEs in the presence of a wide range of non-REEs. Compared with the free LanM-SpyCatcher, MNP-LanM showed a two-fold increase in protein storage stability. MNP-LanM could be efficiently separated by a magnet and retained approximately 95% of its original activity after eight adsorption–desorption cycles, demonstrating extremely stable reusability (Fig. 7c). Moreover, MNP-LanM could selectively adsorb and enrich REEs from the leachates of coal combustion fly ash and geothermal brines, thereby increasing the REE purity by 967-fold.

Other biomaterials for rare earth separation
In addition to proteins, a wide range of biomolecules, including enzymes [96], antibiotics [97], and bioactive peptides [98] possess diverse functional groups such as ketones, carboxyl, hydroxyl, phosphate, and mercapto. These functional groups endow these biomolecules with potential advantages in ion exchange [99], complexation [100], precipitation [101], chelation [102], and physical adsorption [103]. Therefore, they have also been used for the separation and recovery of REEs. Yan et al. [104] prepared a functional bionanomaterial (FeNPs-EPS) through biofabrication using *Bacillus cereus* as a potential approach for recovering REEs. Upon exposure to high concentrations of Eu^{3+} and Tb^{3+} in mining wastewater, the synthesized FeNPs-EPS exhibited great potential to remove these two cations from wastewater, with the adsorption efficiency of Tb^{3+} reaching 94% and Eu^{3+} reaching 92% within 5 min. Although FeNPs have attracted considerable attention in REE extraction [105], pure FeNPs perform poorly in selective REE extraction due to the high agglomeration and relatively few active functional groups on the surface of chemically synthesized FeNPs. Yang et al. [106] successfully used FeNPs synthesized with euphorbia cochinchinensis extracts for the selective recovery of REEs from real mine wastewater, with a removal efficiency of 89.4% for Y^{3+}, 79.8% for Ce^{3+}, and only 6.15% for Zn^{2+}. Moreover, the cell wall [107], owing to its abundance of carboxyl and other chelating groups and its capacity to provide more adsorption sites for REEs, serves as the primary enrichment site in hyperaccumulator plants. Zhao et al. [108] fabricated a series of composite aerogels based on key active components in the cell wall, namely, pectin and cellulose, for the efficient adsorption of Ce^{3+} from leaching tailings. The adsorption fitted the Langmuir

model, and the maximum adsorption capacity of Ce^{3+} was 337.36 mg g^{-1}. Adsorption experiments in a leaching tailings sample showed that the composite aerogel achieved adsorption efficiencies of 68% and 81% for Ce^{3+} and Eu^{3+}, respectively. It displayed good selectivity and practicality.

Functional rare earth protein materials

Rare earth protein fibers with high strength and high toughness
Protein fiber materials have been extensively employed in the biomedical field due to their lightweight [109], high mechanical strength [110], and good biocompatibility [111]. In particular, the high coordination capability controlled by the 4f5d electronic features of REEs can significantly enhance the supramolecular interactions within fibers, thereby improving the mechanical properties of protein fibers. Sun et al. [112] developed a novel approach to produce high-quality rare earth protein fibers. The high-performance rare-earth protein fibers were achieved by constructing protein fibers via electrostatic interactions between dopamine-based surfactant (DSS) and positively charged ELPs. Upon metal ion treatment, the fibers exhibited a uniform cylindrical fiber structure and surface morphology. In addition, chelation of the Tb element effectively improved the toughness and stiffness of the fibers. The tensile strength and Young's modulus increased substantially to approximately 66 MPa and 7.8 GPa, respectively (Fig. 8a). Therefore, this study provides a new strategy for the mechanical regulation of engineered protein fibers.

To achieve mass production of robust silk fibers, researchers have explored various post-treatment methods, including wet spinning [113], dry spinning [114], and microfluidic spinning [115]. However, these methods involve tedious procedures [116], and their dissolution process [117] damages the hierarchical structure of silk, resulting in limited improvement in mechanical performance. Lu et al. [28] reported a simple approach to producing robust silk fibers by feeding silkworms with a diet modified by rare earth ions-reinforced silk fibers (RRSFs). The obtained silk fibers showed a magnificent appearance and significantly improved tensile strength and toughness with maximum values of 0.97 ± 0.04 GPa and 188 ± 19 MJ m^{-3}, respectively, approaching the performance of spider towline silk. Remarkably, 24 fibers were able to suspend a glass ball weighing 1.7×10^6 times the fiber weight. In addition to the structural changes, the introduction of RE^{3+} also led to intriguing variations in the optical properties of silk fibers. A new absorption peak appeared in the range of 380–470 nm under indoor light, which resulted in a pale-yellow hue (Fig. 8b). Furthermore, by comparing the tensile strength and toughness of different functional-material-enhanced silk fibers, it was obvious that rare-earth-ion-modified silk fibers possessed both high strength and high toughness, making them potential candidates for structural materials.

Strong rare earth protein adhesives
Protein adhesives [118] offer immense potential in biomedicine due to their exceptional underwater adhesion [119], excellent biocompatibility [120], and degradability [121]. The incorporation of REEs can significantly enhance the adhesion strength through multiple coordination, increasing cohesive forces, and altering the protein's secondary structure to enhance protein packing density. Chen et al. [29] proposed a modular engi-
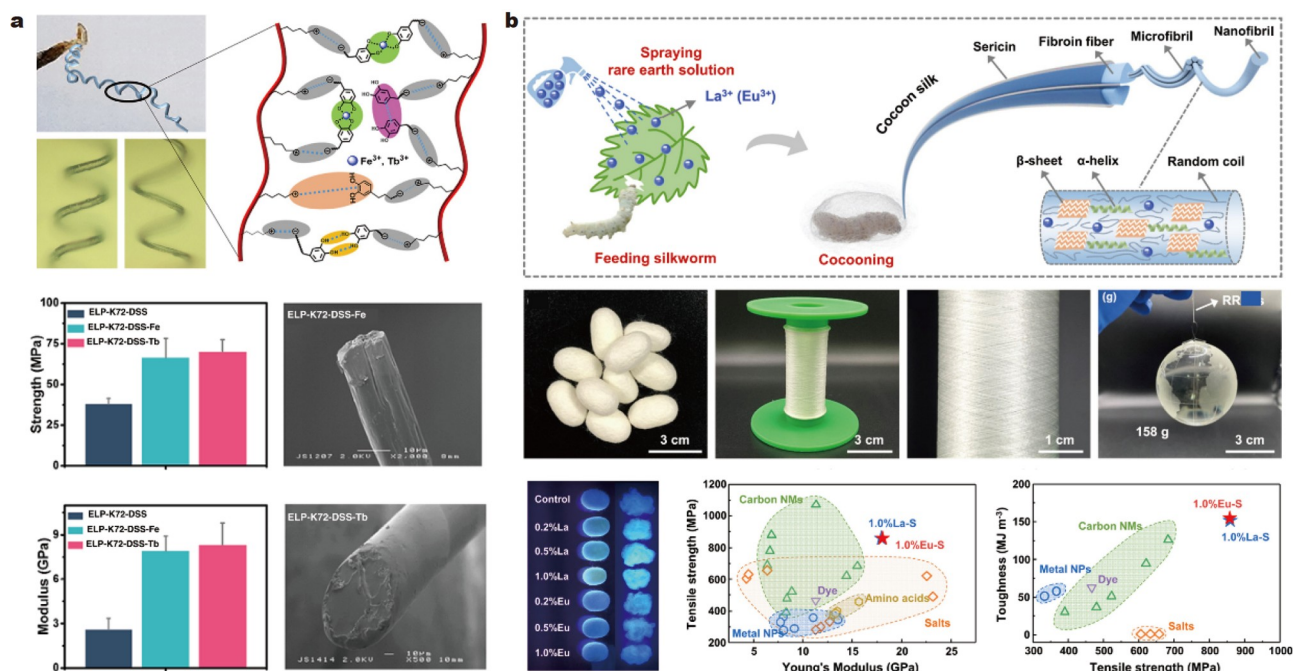
Figure 8 (a) Investigation of metal coordination effect on mechanical properties of the ELP-DSS fibers. All error bars represent standard deviation ($n = 3$). SEM was used to investigate the surface morphology and cross section of the broken ELP fibers. The scale bar is 10 μm. Reprinted with permission from Ref. [112]. Copyright 2020, Chinese Chemical Society. (b) Preparation process and structural illustration of RRSFs. An optical picture of the rare earth ion-modified cocoons. A roll of silk obtained by reeling of 6 cocoons. The enlarged view of the reeled silk. A bundle of RRSFs (24 fibers) hanging a glass earth weighing of 1.7×10^6 times its own weight (158 g), showing the high strength of RRSFs. Optical pictures of cocoons and silk under a 312 nm UV light irradiation. Comparison of Young's modulus and tensile strength, tensile strength and toughness of different silk fibers prepared by feeding various functional nanomaterials to silkworms. NMs: nanomaterials. Reprinted with permission from Ref. [28]. Copyright 2023, Science China Press.

neering strategy, selecting a lysine (K)-rich elastin-like polypeptide (KP) as an adhesive module. As another adhesive module, a tandem conformational change LanM was developed, which self-assembled with KPs to form a heterogeneous protein adhesive. This adhesive exhibited remarkable adhesive behavior by leveraging electrostatic complexation between the metallized protein and Food and Drug Administration (FDA)-approved sodium dodecyl benzene sulfonate (SDBS). It could glue two steel plates together and easily lift a dumbbell loaded with a weight of 11 kg. These results demonstrated the excellent adhesion and moisture-resistant properties of the modular protein-based adhesive. In the protein complex, the tandem conformational change LanM exhibited a lanthanide-induced α-helical conformational transition. This transition led to an increase in α-helicity, which was suggested to enhance the adhesive strength of the protein adhesive. The increased packing density and intermolecular interactions, including chelate interactions and hydrogen bonds, contributed to the adhesive system's remarkable adhesive behavior. The adhesive strength reached an impressive value of 31.7 MPa, surpassing many supramolecular and polymeric adhesives (Fig. 9a). *Ex vivo* and *in vivo* experiments also demonstrated its durable adhesive performance in surgical closure and healing applications.

Adhesive hydrogels commonly suffer from swelling [122] when applied to hydrated tissues, leading to a significant reduction in their mechanical strength. This drawback often results in adhesion failure during wound healing and can cause tissue compression and complications in the wound microenvironment. To address this issue, Sun *et al.* [123] developed a

novel, non-swelling protein adhesive for underwater and *in vivo* applications (Fig. 9b). In this soft material, electrostatic complexation between overcharged polypeptides and oppositely charged surfactants with 3,4-dihydroxyphenylalanine or azobenzene groups plays a dominant role in the formation of adhesive coacervates. Notably, its adhesive performance exceeds that of commercial cyanoacrylate when tested under ambient conditions. In addition, it has improved adhesion underwater. *Ex vivo* and *in vivo* experiments demonstrated its durable adhesive properties and excellent wound closure and healing effects.

Traditional supramolecular adhesives, which are severely limited due to their limited environmental compatibility [124], face major challenges in practical applications. The development of robust adhesives with extreme temperature tolerance has significant application value. Zhao *et al.* [125] developed a novel class of temperature-tolerant rare-earth crown ether protein adhesives by exploiting cooperative host-guest molecular interactions between engineered crown ethers and proteins. The composite hydrogel undergoes a reversible transparent-to-turbid phase transition upon temperature fluctuation. This phase transition significantly enhances the syneresis of adhesives, thereby promoting multiple supramolecular interactions (e.g., host–guest interaction, cation–π interaction, electrostatic interaction, hydrophobic interaction, and π–π interaction) within the micelles, which remarkably improves the adhesive property of adhesives at elevated temperatures (Fig. 9c). Furthermore, the tensile-shear strength of Eu^{3+}-complexed adhesives is higher than that of the original adhesive due to the coordination.
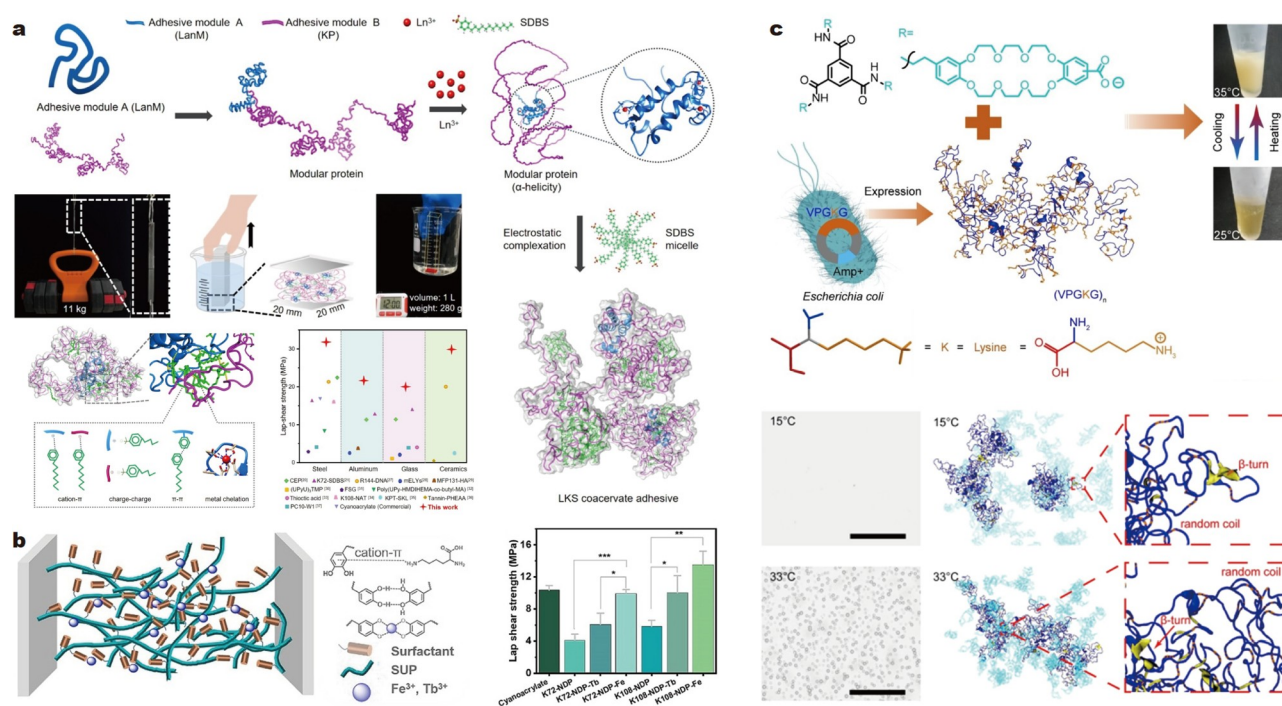
Figure 9 (a) Preparation and characterization of robust adhesives by engineering modular protein. Proposed molecular mechanism for the robust adhesive of modular-protein-based coacervates. A 30 ns molecular simulation presented the interactions between LK protein and SDBS during the complex-coacervation process. The comparison of the lap-shear adhesion strengths and adhesion energies between our LKS adhesive and the reported adhesives on steel, aluminum, glass, and ceramics substrates. Reprinted with permission from Ref. [29]. Copyright 2023, Wiley-VCH. (b) Schematic for the adhesion mechanism of adhesives. The effect of different metal ions on the bonding strength of adhesives on steel. Reprinted with permission from Ref. [123]. Copyright 2021, Wiley-VCH. (c) Fabrication of supramolecular crown-ether-protein adhesive and the characterization, computer simulations during the phase transition process. Scale bars are 100 μm. Reprinted with permission from Ref. [125]. Copyright 2022, Wiley-VCH.

Additionally, the adhesive exhibits an ultralow-to-high shear adhesion strength of 22 MPa over a wide temperature range of −196 to 200 °C, outperforming other established supramolecular or polymer adhesives. This work pioneers a molecular engineering approach to developing adhesives with tailored applications in extreme environments.

Rare earth protein catalysts
Until 2011, REEs were not recognized for their specific roles in biological processes. However, it has since been discovered that the growth of certain microorganisms is highly dependent on the availability of REEs, as they serve as cofactors for crucial enzymes [126]. Notably, REEs act as cofactors for ExaF-type ethanol dehydrogenases (EtDHs) and XoxF-type MDHs in methylotrophs. Recent research suggests that the function of REEs as cofactors extends beyond methylotrophs. For instance, PedH, an ExaF homolog from non-methylotrophic *Pseudomonas putida* KT2440, is subject to transcriptional regulation in response to the availability and presence of light REEs [127]. In addition, REEs also affect the metabolism of Bradyrhizobium, resulting in the production of a large amount of extracellular polysaccharides (EPS) in the presence of Ce^{3+}, which is probably because of the binding of light REEs to Ca sites on Ca-dependent proteins and enzymes. La and Ce stimulated the activities of MDH in *M. radiotolerans*, *M. zatmanii*, and *M. fujisawaense* by 4- to 6-fold, and may be involved in activating potential genes. The addition of La stimulated the growth of a mutant strain of *M. extorquens* on methanol, due to the increased activity of the La-dependent MDH. To date, a series of REE-dependent enzymes have been discovered in microorganisms [41,43,128–132]. Studies have shown that, especially for XoxF, its activity is higher with light REEs (e.g., La^{3+}, Ce^{3+}, Pr^{3+}, and Nd^{3+}) than heavy ones, and La^{3+} is preferred over Nd^{3+} as a cofactor. The properties of REEs, such as the smaller ionic radii of metal ions, coordination number, substrate preference and activation, ligand exchange rate, and hydrogen bond formation, collectively affect the specific activity of enzymes [133].

Other rare earth protein functional materials
Currently, REEs are widely used in fluorescence imaging [134], magnetic resonance imaging (MRI) [135], photodynamic therapy [136], and theranostics [137]. However, the instability of traditional rare earth ion complexes may result in the release of toxic rare earth ions upon environmental changes, and the potential health risks limit their wider applications. To address this challenge, Min *et al.* [138] reported a novel personalized near-infrared (NIR) light-activatable nanoplatform. This platform integrates a light-activatable platinum (IV) prodrug with a cysteine-aspartic protease-imaging peptide conjugated silica-coated upconversion luminescent NPs (UCNPs), allowing for remote control of anticancer platinum prodrug activation and real-time imaging of apoptosis induced by activated cytotoxicity. Hu *et al.* [139] reported a silk fibroin (SF)-based upconversion photon amplifier (SFUCPA) integrated into optoelectronic devices, providing a practical option for subcutaneous charging and communication *via* an NIR laser. Compared with the control, SFUCPA showed a 4-fold enhancement in fluorescence, resulting in a 47.3-fold increase in the subcutaneous NIR-to-

electricity power conversion efficiency of a single-fiber dye-sensitized solar cell. Due to the flexible, biocompatible, and cost-effective design of SFUCPA, as well as its NIR-driven opto-electronic properties, SFUCPA holds great promise in applications for recharging subcutaneous medical electronics, storing information, and controlling implantable devices.

Other rare earth biomaterials

Apart from proteins, other biomolecules including nucleic acids [140], polysaccharides [141], and liposomes [142] also have many advantages. Nucleic acids (such as DNA and RNA) have the functions of genetic information storage and transmission; polysaccharides have the functions of structural support and energy storage. In terms of self-assembly ability, lipids can also self-assemble to form cell membranes. The diversity, self-assembly and self-organization capability, and biocompatibility of biomolecules make them important tools and materials for the study of high value-added products of rare earth biomolecules.

In a recent study, Zhang et al. [15] developed a multiscale engineering approach to assembling highly ordered DNA bulk fibers. Rare-earth ions involvement enabled the programmable assembly and orientation of DNA-metal assemblies across multiple length scales, ranging from molecules and nanoribbons to macroscopic fibers. This strategy significantly enhanced the mechanical properties of DNA fibers. Among the stretched rare-earth DNA fibers, the La^{3+}-induced fibers exhibited the highest tensile strength of 408 ± 34 MPa, while Yb^{3+}-constructed fibers showed a tensile strength of only 296 ± 5 MPa. Furthermore, the lanthanide ions could induce the transformation of DNA conformation from the B form to the Z form (Fig. 10a). A robust fiber with a length of 1000 m and containing 50 mg of DNA was further fabricated by continuous spinning, demonstrating the

high scalability of this approach. This holds great potential in the applications of DNA-based materials in mechano-biology, bioelectronics, and other fields.

In the field of catalysis, Lelyveld et al. [143] proposed that the electrophilic substrate activation by monometallic ions is inferior to the native bimetallic mechanism. It was found that the insufficient catalytic activity of divalent activated DNA polymerases can be improved by trivalent rare-earth and transition-metal cations. In particular, Sc^{3+} imparts highly sequence-selective unnatural $N3' \rightarrow P5'$ phosphoramidate (NP) bond-forming activity with 2 orders of magnitude higher kinetic enhancement than calcium ions, generating NP-DNA chains up to 100 nucleotides in length (Fig. 10b). In the theranostics field, Liu et al. [144] developed a novel injectable DNA-mediated upconversion and gold NP (DNA-UCNP-Au) composite hydrogel with near-infrared light responsiveness. A super-strong photothermal effect was observed due to the confined and enriched microenvironment caused by the interactions between adjacent DNA strands and UCNP-Au NPs. A high photothermal efficiency of up to 42.7% was achieved in the hydrogel, surpassing that of pure inorganic counterparts. The hydrogel was intratumorally injected and upon 808 nm laser irradiation, the tumor was eradicated without recurrence (Fig. 10c). Meanwhile, owing to the localized treatment, no side effects were observed in normal tissues. The excellent photothermal therapeutic efficacy, biocompatibility, and flexible manipulation of the system demonstrated a new approach for malignant tumor treatment.

In another study, Kataria et al. [145] reported a novel lanthanide-dextran polymeric hydrogel with tunable emission properties. This hydrogel demonstrated a reversible "turn-on/off" fluorescent response to Fe^{2+}/ethylenediaminetetraacetic acid by suppressing the "antenna effect". This reversible response makes it suitable for biorelevant applications where reversible
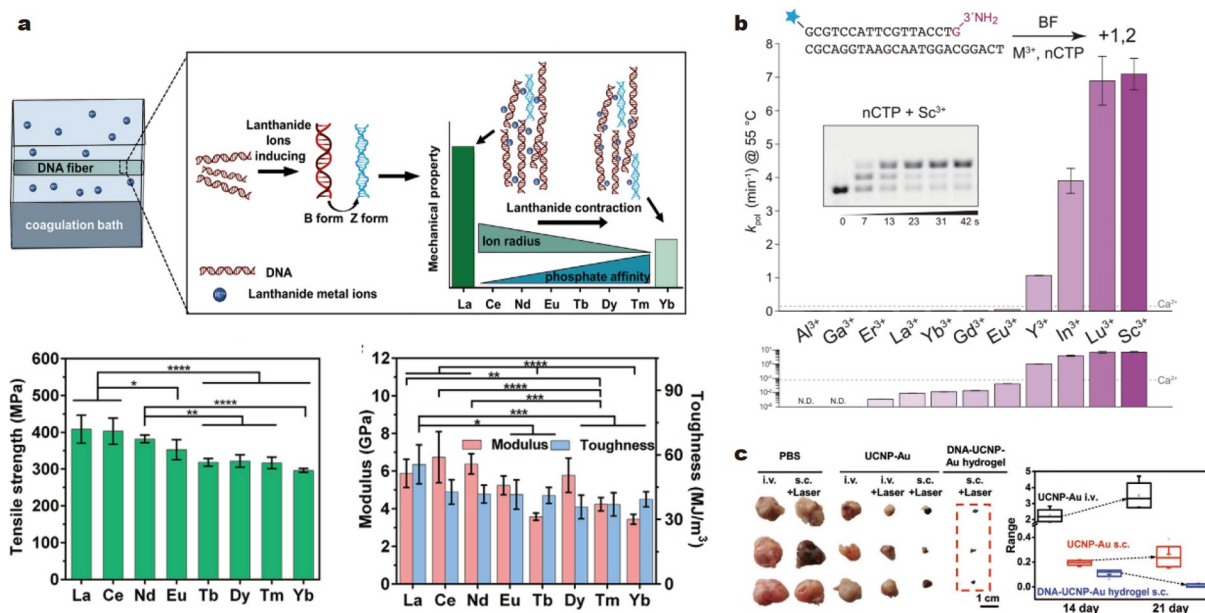

Figure 10 (a) Schematic of the lanthanide-induced DNA fiber assembly with the conformational transitions of DNA building blocks. The tensile strength, toughness, and Young's modulus analysis of the post-stretched Ln-DNA fibers. Reprinted with permission from Ref. [15]. Copyright 2023, Elsevier. (b) Pre-steady-state kpol estimates for extension of a 3'-aminoterminal DNA primer on a DNA template (inset cartoon) by BF F710Y/D598A at 55°C in the presence of various 1:1 ammonium citrate-buffered trivalent metal cations at 5 mM in 40 mM Tris-HCl, pH 8.8, 2 mM bME, in reactions initiated by the addition of 250 mM nCTP. Reprinted with permission from Ref. [144]. Copyright 2023, American Association for the Advancement of Science. (c) Results of the isolated tumors after different treatments. Reprinted with permission from Ref. [143]. Copyright 2020, Wiley-VCH.

behavior is desired. The findings offer promising prospects for utilizing this hydrogel in various biorelevant applications.

CONCLUSIONS

Rare earth bioseparation stands out as a rapidly evolving technology with promising engineering applications. Synthetic biology methodologies have been pivotal over the past decade in reshaping rare earth-responsive microbial systems. The introduction of lanthanide-binding proteins through genetic engineering and bioinformatics analyses has significantly propelled the advancement of rare earth bioseparation. Moreover, the distinctive coordination capabilities and versatile functionalities guided by the 4f5d orbitals of rare earths have unlocked the potential for high-value rare earth biomaterials across domains like mechanical support, catalysis, and diagnostics. This summary delves into the ongoing research on microbial separation, emphasizing the interplay between natural microorganisms and lanthanides, while also stressing the importance of tailored host cell designs to optimize the bioleaching and biosorption of rare earths. Notably, the development and deployment of lanthanide-binding proteins are highlighted as key components, enriching the toolkit available for protein-based lanthanide separation and enhancing protein materials. Furthermore, the rapid progress in creating high-value rare earth biomaterials for biomedicine, combined with efficient processes for manufacturing and utilizing premium products sourced from lanthanide elements, establishes a robust foundation for the next phase of rare earth utilization platforms.

Despite significant advancements in rare earth biomanufacturing and the utilization of high-value materials, persisting limitations demand attention. While lanthanide-binding proteins displayed on engineered microbial surfaces offer environmentally friendly rare earth extraction, their selectivity remains a concern, especially towards neighboring elements like Pr and Nd. Current microbial engineering predominantly targets engineered bacteria with specific promoters, neglecting the screening and modification of rare earth-associated microorganisms in mining locales. Addressing obstacles related to optimizing plasmids and promoters in non-model microorganisms can be tackled through novel recombinase systems facilitating Red/ET recombination engineering. These versatile systems not only streamline editing processes in native strains but also extend their efficacy across diverse non-model strains, significantly amplifying genomics-guided explorations of natural products from these microorganisms. While rare earths hold industrial importance, research gaps persist concerning their high-value applications in biomedicine. A deficiency in comprehensive studies exploring the synergy between rare earths' unique properties and biomolecule performance optimization exists. Therefore, the discovery of novel proteins exhibiting heightened rare earth binding affinity and selectivity rooted in rare earth-associated microorganisms, coupled with enhancing rare earth leaching and co-enrichment capacities *via* internal pathway engineering in microorganisms, is crucial for efficient rare earth material fabrication. In the realm of rare earth bioseparation, leveraging the metabolic byproducts of rare earth biomolecules for high-value applications can curtail rare earth loss and optimize REE utilization for increased value creation. Overall, rare earth biomanufacturing remains at an early research stage, necessitating intensified efforts to devise innovative strategies for large-scale rare earth biofabrication that not only align with practical requirements but also target high-value applications effectively.

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Author contributions Cui H focused on the microbial system for rare earth leaching and accumulation, while Wang F contributed to the section on rare-earth functional materials. The project idea was conceived by Liu K. All authors actively participated in the general discussion.

Conflict of interest The authors declare that they have no conflict of interest.

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基于微生物的稀土材料制备

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摘要 稀土元素(REEs)作为现代高科技产业发展的关键原材料, 在多个前沿领域具有广泛应用. 然而, 由于稀土元素分布相对分散, 其提取往往伴随着环境退化. 此外, 稀土元素的相似化学性质导致了分离过程中的高能耗和过度污染排放. 为了实现稀土的绿色发展和高效资源利用, 通过合成生物学技术构建了工程稀土微生物. 此外, 我们建立了工程稀土微生物合成平台, 实现了原位合成高附加值的稀土生物材料, 推动了临床转化研究和应用的进展. 本文综述了稀土微生物的合理设计、高价值稀土生物材料的合成及其应用. 最后, 简要讨论了该领域的未来研究和发展前景.