RESEARCH ARTICLE

Applications of Synthetic Biology in Materials Science

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Abstract: Materials are the basis for human being survival and social development. To keep abreast with the increasing needs from all aspects of human society, there are huge needs in the development of advanced materials as well as high-efficiency but low-cost manufacturing strategies that are both sustainable and tunable. Synthetic biology, a new engineering principle taking gene regulation and engineering design as the core, greatly promotes the development of life sciences. This discipline has also contributed to the development of material sciences and will continuously bring new ideas to future new material design. In this paper, we review recent advances in applications of synthetic biology in material sciences, with the focus on how synthetic biology could enable synthesis of new polymeric biomaterials and inorganic materials, phage display and directed evolution of proteins relevant to materials development, living functional materials, engineered bacteria-regulated artificial photosynthesis system as well as applications of gene circuits for material sciences.
Keywords: Synthetic biology; material sciences; genetic circuits; biomaterials

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1 Introduction

Materials are the material basis for human survival and development and the symbol of human progress. From the stone age to the bronze age, and then to the iron age, the quality of human clothing, food, housing and transportation has been greatly improved due to the development of materials. As early as 20 years ago, the traditional material science began to experience the process from macro research to micro exploration, and nano materials came into being. The systematic study of the properties of materials in micro and nano scales makes people understand all aspects of the properties of materials in nano and micron scales. Therefore, the design of materials can be said to transition from completely relying on experience to rational design. The most direct inspiration of rational design often comes from nature. A variety of multi-level self-assembled materials in nature show precise nanostructures and excellent material properties. Their structural stability and performance advantages are unmatched by current synthetic materials. People urgently need to make a more reasonable interpretation of "biological inspiration and biological bionic materials" and further optimize and upgrade the materials. Taking the underwater adhesive as an example, the traditional polymer adhesive has poor water resistance and low underwater bonding strength. It has inherent deficiencies in wound healing, tissue repair and fine repair of ship hull and dam. It is found that the organisms attached to the rocks in the coastal intertidal zone, such as mussels, barnacles, sand castle worms, are still firmly attached to the rock surface under the blow of sea wind and waves. Therefore, such adhesive organisms, such as mussels, provide new ideas for the development of adhesives. Through the analysis of mussels, it is found that the mussel foot silk protein Mfp3/5 is rich in a large amount of catechol (3,4-dihydroxyphenyl-L-alanine, DOPA) structure. On this basis, people embed the DOPA structure in Among polymer materials, a series of underwater adhesives have been developed, such as Poly[(3,4-dihydroxystyrene)-co-styrene], copolymers of PEO, PPO and DOPA, and multifunctional coating materials such as dopamine. However, design intelligence, dynamic controllability, bonding, and self-healing bonding are still important bottlenecks in the field of adhesive materials. The development of synthetic biology is expected to break through the above bottlenecks and bring new ideas to the design of adhesive materials.

2 Cell factory synthesizes high molecular biomaterials

Realizing the green sustainability of material production and the high efficiency and multi-functionality of materials is an important goal for the development of materials science. Synthetic biology has excellent characteristics such as modularization, standardized operation, intelligence, and fine control. The combination of these characteristics and materials science will greatly promote the development of materials science from two aspects: material production methods and material properties. Biological factories have the characteristics of green sustainability, low consumption and high output, and naturally become an important material preparation method. Well-known work includes the use of microorganisms, cells, etc. to produce medical pharmaceutical preparations, such as enzyme preparations, insulin, etc. Lee et al. used microorganisms to produce various plastic monomers. The laboratory of Professor Guoqiang Chen of Tsinghua University has successfully improved the production and performance of polyhydroxy fatty acid esters by modifying the bacterial β-oxidation pathway. As a kind of plastic with excellent properties, polyhydroxy fatty acid ester has the characteristics of biodegradability and biocompatibility. The above scheme is to use micro as a production factory to use the bacteria's own metabolic pathways to prepare corresponding material molecules; another strategy is to rationally design materials through genetic modular manipulation. The Tirrell research group of California Institute of Technology, with the help of genetic engineering strategy, has constructed protein molecules with good cell compatibility and at the same time forms a gel under physiological conditions. The Lu research group of MIT used synthetic biology technology to fuse CsgA (the main structural protein of E. coli biofilm, which can self-assemble to form a fibrous structure) and Mgfp3/5 (the two main binding proteins of mussels). Expressed, the fusion protein fully combines the inherent adhesive properties of CsgA and the interface adhesive properties of Mfp, and exerts powerful underwater adhesive properties [2].

3 Biological preparation of inorganic nanomaterials

Natural or engineered microbial organelle structures can be used as templates to prepare nano and micron materials of different dimensions. The diameter of microcells in the biological world varies from 9nm to 500nm. This structure can be used to synthesize nanomaterials of different scales. At the same time, different microstructures can be used as molds, such as virus particles, to synthesize nanomaterials with different arrangements. In the preparation process, the nanomaterials can be directly functionalized to meet the needs of people in many aspects. In addition to using various nanostructures as templates to synthesize nanomaterials, organisms themselves can also be used as factories for synthesizing inorganic nanomaterials. Some prokaryotes, such as MV-4, can produce iron oxide or iron sulfide magnetic nanoparticles through metabolism. Compared with artificial magnetic nanoparticles, bacterial magnetic nanoparticles have the characteristics of good dispersibility and uniform particle size, and the nanoparticles are synthesized in the organism, the reaction conditions are mild, no additional reducing additives are needed, energy is saved, and the environment is protected[3].

Park et al. introduced the use of E. coli to synthesize a variety of nanoparticles. Using Escherichia coli exogenous expression of plant complexin synthase (PCS) or metallothionein (MT), the size of synthesized nanoparticles can be adjusted by changing the initial amount of metal ions added. The synthesized nanoparticles were analyzed using transmission electron microscope (TEM) and confocal microscope (Confocal microscope) and other characterization methods, and it was found that the nanoparticles synthesized by E. coli reached good indicators in terms of physical, chemical and electrical properties. Stürzenbaum et al. used earthworms to synthesize luminescent quantum dots. In addition, scientists used Rhodospirillum rubrum to express foreign gene clusters related to the synthesis of magnetic nanomaterials, and successfully synthesized magnetic nanoparticles in the bacteria. These examples point out a new type of preparation path for inorganic nanomaterials. In the future, synthetic biology technology can be used to more rationally synthesize nanomaterials with controllable chemical composition, morphology, and even crystal orientation, including biocompatible nanomaterials used in bioimaging and metals that play a role in catalysis, energy and the environment And metal semiconductor nanomaterials [4].

4 Phage display and protein directed evolution strategy screening and optimization of molecular materials

There is a saying in the theory of evolution that "things compete with natural selection, and the fittest survive." Inspired by Darwin's theory of evolution, people imitated the process of natural selection and creatively invented the molecular biology technology-directed protein evolution. This technology simulates natural selection. Under given experimental screening conditions, protein molecules that can meet specific performance requirements can be quickly screened from a huge variant gene library. Due to the high efficiency of this technology, it is widely used in improving protease activity, protein stability, and enhancing specific protein interactions. Phage display technology is a technology in which a foreign short peptide or protein gene and a phage specific protein gene are fused and expressed on its surface. In a sense, this is a primary version of directed evolution of protein [5].

As a mature screening technology, phage display technology is widely used in the field of antibody screening and protein interaction research, and it also plays a wide role in materials science. The Sarikaya research group of the University of Washington in Seattle, USA used phage display technology to screen out various metal or semiconductor-bound short peptides. These short peptides can be used in the surface modification of inorganic materials and have important applications in biosensor detection. In addition, as early as 2000, the Belcher Laboratory in the United States used this technology to display peptides that recognize inorganic nanomaterials on the surface of bacteriophages, and used the bacteriophages as templates to synthesize magnetic nanowires and semiconductor nanowires as the electrodes of ion batteries.

In addition, Lee's team at Perkins University in the United States has developed a phage-based "self-templating assembly" technology (Self-templating assembly), which uses phage spiral nanofibers to form optical properties, biomaterial properties, and electrical properties. Regulated structures have important applications in the fields of tissue regeneration and energy-producing materials.

In 2014, Wilke et al. used phage display technology to display short peptide libraries with adhesive properties on the surface of phage, and screened them on aluminum. After 3 cycles of "display-screen-amplification", peptides with strong adhesion properties were obtained. The analysis of the short peptides selected from the DOPA content, the properties of DOPA surrounding amino acids and the hydrophilicity and hydrophobicity of the entire short peptide provides an idea for the next rational design of the adhesive based on mussel foot silk protein. It should be pointed out that the adhesive protein selected is actually a solid binding peptide. In addition, the Morse team at the University of California used protein evolution strategies to screen mineralized proteins. They used a cell-free system to build a "cell-like" platform, and screened mineralized proteins with the help of particle surface display technology and flow cytometry (FACS) and other screening methods. The screened proteins have the function of promoting the crystallization of inorganic materials[6] .

However, the application potential of protein directed evolution technology in materials science has not yet been tapped. The main challenge lies in how to establish an effective screening platform and method based on material properties. It is believed that with the invention of various high-throughput material characterization methods, this technology is expected to promote the implementation of the current material genome project.

5 Living functional materials

Using synthetic biology methods, scientists use non-standard amino acid injection methods to introduce functional modifications in the process of target protein synthesis. Such as direct introduction of methionine modified by heavy metal elements to promote protein crystallization; introduction of amino acids containing azide groups during protein translation for click chemistry reactions to study the interaction between proteins. In addition, the DOPA structure is directly introduced during the synthesis of the Mfp protein, so that it directly exerts its adhesive function, avoiding post-transcription (or post-purification) modification.

In recent years, some scientists have tried to use organisms (including extracellular matrix, etc.) as materials. Escherichia coli, Bacillus subtilis, etc. mostly live in groups under natural conditions, and the biofilm structure ensures the stable existence of the flora. There are many types of biofilms, rich in proteins, lipopolysaccharides, nucleic acids and other substrates. They have the characteristics of stable properties, acid and alkali resistance, and renewable properties, and can be used as a coating material. Joshi uses the E. coli biofilm CsgA system to express some functional proteins (such as mineralization protein, binding protein, and binding protein) with CsgA, and at the same time anchors CsgA with CsgB (another component of E. coli biofilm) As well as the stability of the overall structure of the biofilm, functional proteins are displayed on the surface of Escherichia coli and play corresponding functional roles [7].

The experimental results show that the functional display platform based on E. coli biofilm can fully realize the expected protein function display. Chen et al. Proposed dynamic and controllable multifunctional biological living materials based on CSGA system. The authors constructed the orthogonal induction system engineering bacteria of csgahis, ATC of CSGA and AHL respectively. In the process of co culture of the two engineering bacteria, a polymer structure similar to block copolymer was obtained by changing the proportion of the initial concentration of the two bacteria and the concentration of inducer. With the functionalization of gold nanoparticles, the block copolymer can be used as a conductive device coating.

Turing proposed a "reaction diffusion" model to explain the formation of embryonic hierarchy. In 2005, Basu observed pattern formation based on programmed regulation at the cell level by designing two open pathways with different starting efficiency. These studies provide a reference for the design of dynamically adjustable hierarchical multifunctional materials at the cell level.

Biosensor is a device that converts external input signals into signals that can be easily observed and recorded by means of biological platforms (such as enzymes, antibodies, microorganisms, etc.). With the help of synthetic biology technology, scientists have equipped E. coli with "eyes" and "watches". Levskaya et al designed light controlled engineering bacteria to regulate the expression of downstream genes by limiting the autophosphorylation of proteins by red light irradiation.

Scientists can use this technology to achieve spatial control of the expression of engineered bacterial communities, so that they can express target proteins in specific locations and ranges according to people's needs. In addition, Chen et al. grafted the kaiABC gene cluster of cyanobacteria into Escherichia coli, expressed green fluorescent protein in tandem downstream, and recorded phosphorylation and dephosphorylation. Experiments have found that the kaiABC gene cluster of cyanobacteria can still periodically undergo phosphorylation and dephosphorylation in Escherichia coli, and the intensity of the fluorescence signal changes periodically.

6 Application of gene circuits in materials science

Based on the versatility of the genetic code, scientists can not only directly overexpress the endogenous protein, such as the aforementioned Chen and Joshi respectively overexpress the CsgA fusion protein in E. coli; but also express the foreign protein in a certain organism, such as Giessen In E. coli, the EncTm derived from Thermotoga maritima was expressed. Gene circuit design, as the cornerstone of the entire synthetic biology, has done a great deal in editing and regulating cell behavior and function. For example, programming an organism at the genetic level can allow organisms to quickly indicate changes in the external environment, such as light and heat. In 2015, Huber and Schreiber et al. used E. coli exogenously to express amphiphilic proteins based on gene regulation, and relied on the hydrophilic and hydrophobic properties of the proteins to self-assemble into artificial "organelles" in the body. The organelle can be used not only as a reaction unit or drug storage carrier, but also as a building block. The article mentioned that the introduction of functionalized amino acids in the process of protein formation can give the entire organelle more diverse functions. At the same time, it is worth mentioning that by adjusting the ratio and arrangement of hydrophilic and hydrophobic regions, the morphology of the entire "organelle" can be adjusted [8].

In 2016, Din et al. designed a drug release model based on "quorum sensing" and "oscillation mode" regulation. Quorum sensing effect refers to the phenomenon that when the density of bacteria reaches a certain level, the bacteria spontaneously produce a signal molecule (such as AHL, etc.) to induce other bacteria to produce corresponding behaviors. The engineered bacteria constructed in the article have two parallel gene circuits, and the AHL signal molecule controls the expression of three downstream proteins (reporter protein, drug protein and suicide protein). As the bacteria grow and reproduce, quorum sensing triggers the massive expression of three downstream proteins, among which the reporter protein (sfGFP) is used as an indicator of the number of bacteria to survive. The large expression of suicide protein (φX174E) can lyse and kill cells. On the one hand, it avoids the adverse effects of excessive bacterial growth on the body's homeostasis. On the other hand, it releases the expressed drug protein (hlyE) to exert a therapeutic effect. As the number of bacteria decreases, the group effect disappears, and the expression of suicide protein and therapeutic protein ceases. After that, the bacteria continue to grow and reproduce, re-initiate the group effect, and enter the next cycle of treatment. The above two aspects are just the proof of basic concepts or the application of biomedicine. It is believed that over time, gene circuits will better promote the development of biological materials and living functional materials.

7 Conclusion

The intersection of synthetic biology technology and material science can meet people's requirements for high precision and multi-function of materials; on the other hand, it can also meet people's requirements for intelligent and controllable production processes. The early synthetic biology technology has allowed people to successfully improve the quality and properties of materials, and realize the regeneration and functionalization of materials; at the same time, the characteristics of biological metabolism can be adjusted and the reaction conditions are mild in the production process of materials. , Initially achieved the goal of green production. At this stage, the application of synthetic biology in materials science has been fully upgraded, including from the use of biology to the transformation of biology, from single-component to multi-component material design, from simple engineering materials to biological inspiration or biomimetic multi-function

Materials, from static materials to dynamic smart materials. Based on the characteristics of synthetic biology, such as green synthesis, gene programmable, fine regulation at the molecular level, and high efficiency and scalable production, synthetic biology is bound to continue to play an important role in material science in the future. How to combine existing synthetic biology technology and material science issues more scientifically and effectively will be the key link for us to successfully take the next step.

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