5th IBDRC

INTERNATIONAL BIODESIGN RESEARCH CONFERENCE

BioDesign Research CBIITA

SPEAKERS

OCTOBER 18-21, 2024
NANJING, CHINA

Biomanufacturing Promoted by Synthetic Biology with High-Quality Productivity Forces

He Huang (黄和)
Nanjing Normal University

Abstract

Synthetic biology is a transformative field that unites biology, engineering, chemistry, and information technology to design and construct novel biological systems optimized for industrial applications. By integrating advancements in gene sequencing, biological engineering, and computer modeling, synthetic biology surpasses the limitations of natural biological systems, generating new frameworks that enhance efficiency, scalability, and sustainability. This multidisciplinary approach is being applied across sectors, including medicine, energy, chemical production, agriculture, and environmental management with offering solutions that are low-carbon, sustainable, and cost-effective. Currently, synthetic biology-based biomanufacturing is emerging as a primary driver of innovation and economic growth, positioning itself as a cornerstone of the future bioeconomy. Here, we highlight advancements in the production of next-generation functional sugars and acids et al., showcasing synthetic biology's role in transforming traditional manufacturing and setting new standards for efficiency and environmental stewardship.

Brief Biography

He Huang, an academician of the Chinese Academy of Engineering, Vice President of Nanjing Normal University, Professor, doctoral supervisor, has been awarded the National Distinguished Young Scholars Fund Project and other multiple national talent projects. Engage in research on metabolic engineering of industrial microorganisms and synthetic biology for a long time. The research achievements include two second prizes of the National Technology Invention Award and two first prizes of the Ministry of Education Technology Invention Award as the first completer. He has also received the Ho Leung Ho Lee Foundation Science and Technology Award-Young Innovation Award, the Min Enze Energy and Chemical Award- Outstanding Contribution Award, the Highest Scientific and Technological Award in Business in China and the Bill & Melinda Gates Foundation Young Scientist Award. He has been continuously selected as one of the most highly cited Chinese researchers in the field of chemical engineering by Elsevier from 2014 to 2022.

Next-Generation Precise Genome Editing Technologies and Their Applications in Crop Improvement

Caixia Gao (高彩霞)
Institute of Genetics and Developmental Biology, Chinese Academy of Sciences

Abstract

The development of targeted genome modification in plants has gone through an evolution from generating random mutations, to creating precise base substitutions, followed by producing insertions, substitutions, and deletions of small DNA segments, and finally achieving precision manipulation of large DNA segments. These four developments have laid a solid technological foundation for carrying out plant basic research and precise molecular breeding. In this presentation, I will describe these four stages of genome editing and systematically outline the technological principles underlying each developmental stage. I will also provide some examples demonstrating their application in the creation of new agricultural crops for the future.

Brief Biography

Caixia Gao is a principal investigator at the Institute of Genetics and Developmental Biology of the Chinese Academy of Sciences. Prior to joining the IGDB, she served as a research scientist at DLF's biotechnology group in Denmark. Her research group develops precise and specific genome editing technologies and applies modern biotechnologies to study plant genetic traits and develop high-quality traits including disease resistance and stress tolerance in a variety of crop plants. Her team has published more than 100 papers on plant genome editing, which have cumulatively been cited nearly 30,000 times.

Enzyme promiscuity, underground metabolism or hidden pathways in microbial metabolism: the good and the bad in Synthetic Biology applied to White Biotechnology

Jean Marie FRANCOIS
Toulouse Biotechnology Institute

Abstract

White biotechnology also termed industrial biotechnology aims at producing valuable goods by microbial fermentation from renewable -preferentially- non-edible biomass. Those valuable goods can be naturally produced compounds such as ethanol, lactic acid, succinic acid by the microorganism, but more often nowadays it is a non-natural substance that is wishing to be produced such as isobutyric acid, vanillin, 2, 4-dihydroxybutyric acid or even more complex molecules like amorphodiene and flavonoids. For these latter, synthetic biology tools are well appealing to generate metabolic pathways that do not exist in Nature. Beside all technical difficulties to design, implement, optimise the pathway reactions through the so-called DBLT cycle, the myriad of potential interactions between the components of the new metabolic pathway and the existing natural metabolic network unveils an underground metabolism or hidden metabolic pathway caused by the promiscuity of numerous metabolic enzymes, or triggers inhibitory crosstalk leading to a detour of metabolites from the new pathway by the promiscuity of enzyme activities in the existing metabolic network, making metabolic prediction models largely inaccurate. Through examples, I will expose that harnessing the power of underground metabolism can confer fitness advantage and adaptation under specific environments and thus can be exploited to enhance the physiological performance of a microbial factory1. On the other hand, the activation of an underground metabolism can be highly detrimental, thwarting the microorganisms' production capacity for its added-value compound[2].

Brief Biography

Jean Marie FRANCOIS is Exceptional class professor of at Federal University of Toulouse, National Institute of Applied Sciences, department of Bioengineering. His research activity concerns integrated physiology and functional genomics in microbial systems, with a specific focus on genetic and metabolic regulation and refactoring carbon and energy metabolism towards production of bio-based chemicals for renewable carbon sources. He is author of more than 230 papers in international journals, with a H-index of 70 (Scopus) and holds 27 patents. He is Editor-in-Chief of BMC Biotechnology for Biofuels and Bioproducts and Editor in Chief of Frontiers in Bioengineering and Biotechnology, section Synthetic Biology. He is member of the European Federation of Biotechnology.

Artificial Intelligence Systems for Enhancing Biomanufacturing

Baishan Fang (方柏山)
Xiamen University

Abstract

The biomanufacturing concept holds the promise of green industrial production of biofuel or chemicals, in which fossil resources are substituted by renewable biomass, securing sustainable socioeconomic development. In addition to an optimal microbial cell factory, the fermentation mode is also a key factor of biomanufacturing. Although fed-batch fermentation is generally an advantageous mode of submerged fermentation, it requires more sophisticated equipment for online measurement, control techniques for process management, and intelligent decisions during the entire operational process, which are great challenges for robust and green industrial production of Green Biosynthesis. Here, we developed an extraordinary artificial intelligence system for entirely automatic fed-batch fermentation of 1,3-propanediol, including a Sensor, Predictor, Controller, and automation system. Compared with the constant-speed fed-batch fermentation strategy, the artificial intelligence system could not only automatically regulate the feeding rate and maintain a low concentration of glycerol, but also increase the 1,3-PDO concentration and yield. Combined with dynamic metabolic flux analysis, we demonstrate that a low concentration of glycerol controlled by an artificial intelligence system contributes to the balance of the redox pool. The artificial intelligence system for automatic, robust, and enhanced 1,3-propanediol concentration and yield has been successfully developed which not only increases glycerol utilization efficiency but also decreases the medium cost. It also eliminates the dependency on expensive online instruments and staffing, which not only beneficial for the sustainable biosynthesis of 1,3-propanediol but also adapted to similar production processes.

Brief Biography

Prof. Baishan Fang is a Distinguished Professor at Xiamen University, China. He received B.S. degree in Chemical Engineering from Zhejiang University in 1982, and Ph.D. degree in Chemical Engineering from Tianjin University in 2000. He joined Institute of Biochemical Engineering, University of Stuttgart, Germany as a Visiting Scholar from 1991 to 1993, German Biotechnology Research Center as Visiting Scholar from 2000 to 2001, and then visited the University of Washington as a Senior Researcher in Dec. 2018. His research interest focuses on Synthetic biology and bioinformatics, directed enzyme evolution and biocatalysis, biorefining and bioprocess optimization, microecology and culturomics. He has published more than 100 papers in Nat Catal, AIChE *et al*.

Intelligent Drug Discovery in Practice on Challenging Targets

Shuangjia Zheng (郑双佳)
Shanghai Jiao Tong University

Abstract

The typical drug discovery paradigm is a tedious process, requiring extensive manual effort and relying heavily on expert intuition. Artificial intelligence (AI) has already started to transform this process and promises to transition drug discovery from intuition-driven to information-driven.

In this talk, I will discuss our efforts to broaden the application of deep representation learning in real-world drug discovery. I will begin by outlining our approaches to molecular representation learning, where we have developed several algorithmic tools to effectively capture protein-ligand interactions and perform data-driven virtual screening. Following this, I will delve into our recent advancements in dynamic complex structure modeling using physics-aware diffusion networks, demonstrating how these models facilitate real-world drug development and lead to the discovery of numerous potent molecular candidates targeting challenging proteins. Finally, I will share our latest work in rational PROTAC and antibody design using deep generative models, highlighting the identification of lead candidates with high potency and favorable developability

Brief Biography

Shuangjia Zheng is an Assistant Professor at the Global Institute of Future Technology (GIFT), Shanghai Jiao Tong University. His research interests focused on applying machine learning for the discovery and design of novel therapeutic biomolecules. He earned his Ph.D. in Computer Science at Sun Yat-sen University and served as a visiting scientist at MIT and Harvard. His work has been published in prestigious journals such as Nat. Mach. Intell, Nat. Biomed. Eng., Nat. Commu. and presented at leading conferences like NeurIPS and KDD. His work has been recognized by numerous awards, including the Asian Young Scientist Fellowship, Young Elite Scientists Sponsorship by CAST, Forbes 30 Under 30 Asia, and the WAIC Rising Star Award.

Reaction Enzyme Mining and Evaluation Based on Pre-Trained Protein and Reaction Language Models

Xiaoping Liao(廖小平)
Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences

Abstract

The pursuit of designing novel metabolic pathways for synthesizing industrially important chemicals stands as a pivotal research frontier. Central to this endeavor is the formidable challenge of identifying suitable enzymes capable of catalyzing reactions within these engineered pathways, which dictates the rate and selectivity of chemical transformations, particularly when faced with non-natural reactions. Synthetic biologists navigate this challenge by integrating principles of enzyme mining, experimental validation and enzyme engineering, leveraging computational tools and experimental techniques to unlock the potential of enzymes in novel contexts. Existing enzyme mining approaches mainly rely on reaction similarity computations, but current tools struggle to locate the most similar reactions and face limitations in the subsequent enzyme screening and evaluation, making further experimental validation difficult.

To address this need, in 2024, we developed the REME platform (https://reme.biodesign.ac.cn), which combines atom-to-atom mapping and reaction similarity computation based on multiple reaction representations. REME enables rapid ranking of similar reactions and convenient visualization. Additionally, REME allows users to filter similar reactions and associated proteins based on atom type changes and specific functional groups, and assess them using tools such as ESP, DLKcat/TurNup/UniKP, DeepET, and EpHod, helping experimental scientists quickly identify potential candidate enzymes.

Brief Biography

Liao Xiaoping, Ph.D., is a researcher at the Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences. He graduated with a bachelor's degree from the University of Science and Technology of China in 2006 and earned his Ph.D. from the Academy of Mathematics and Systems Science, Chinese Academy of Sciences, in 2011. From 2011 to 2014, he conducted postdoctoral research at the University of Alberta in Canada. In 2014, he joined the Tianjin Institute of Industrial Biotechnology, where he focuses on intelligent analysis of industrial biological big data and develops core databases, algorithms, and tools.

He has constructed several industrial biology-specific databases, including the glycosyltransferase database pUGTdb and the Escherichia coli regulatory landscape ERMer. Additionally, he has developed a series of bio-design software, such as the automated editing sequence design platform AutoESD and the pathway design platform CAVE. He has also advanced AI tools, including the protein function prediction algorithm HDMLF, the enzyme mining and evaluation tool REME, and the protein homomeric state prediction algorithm DeepSub.

In recent years, he has published over 50 papers in high-impact journals such as *Nucleic Acids Research*, *Science Advances*, *Molecular Plant*, and *Research*, with more than 2,000 citations. He has led several national and provincial-

level projects, including key interdisciplinary projects funded by the National Natural Science Foundation of China, the Strategic Priority Research Program of the Chinese Academy of Sciences, the Tianjin Synthetic Biotechnology Innovation Capacity Improvement Project, and the Innovation Fund of Haihe Laboratory of Synthetic Biology.

Artificial General Intelligence for Protein Engineering Based on Pre-Training

Liang Hong (洪亮)
Shanghai Jiao Tong University

Abstract

AlphaFold has solved the challenge of predicting the three-dimensional structure of proteins and their complexes, but having the correct three-dimensional structure does not necessarily imply that a protein has a specific function. Our team has spent the past 3 years developing a general-purpose artificial intelligence platform for protein engineering – the Pro series – based on pre-trained models. Unlike AlphaFold, the Pro series groundbreaking achieves precision protein design directly from sequence to function. Through pre-training, the large model can learn the known protein sequence and structural characteristics in nature, and explore and understand the mapping law of protein sequence and function in nature. As a result, we have developed a set of general large model that can efficiently design various protein products with enhanced stability, activity and function. Using this method in just one year, we have successfully designed and modified more than 20 proteins , with experimental validation completed in wet labs (including nucleic acid polymerases, gene editing enzymes, IVD enzymes, antibodies, etc.). Among these, two proteins have been scaled up for production and applied in industrial production.

Brief Biography

Professor Hong received his bachelor's degree in physics from the University of Science and Technology of China in 2004, his master's degree in physics from the Chinese University of Hong Kong in 2006, and his doctorate degree in polymer science from the University of Akron in 2010. He did his postdoctoral research in computational biology at Oak Ridge National Laboratory in 2010 and joined Shanghai Jiao Tong University in December 2014. He is currently a distinguished professor of Academy of Natural Sciences/School of Physics and Astronomy/School of Pharmacy, Shanghai Jiao Tong University, and director of Artificial Intelligence Biomedical Center, Zhang Jianggao Institute of Research, Shanghai Jiao Tong University. Engages in computational, artificial intelligence, and experimental approaches to molecular biophysics and protein design research. In 2016, he was selected as a national high-level talent Young expert, and in 2021, he was selected as a Changjiang Scholar of the Ministry of Education. He has published more than 70 SCI papers in nature, science, PNAS and other journals. Participated in and led the development of several innovative algorithms to improve the research and development efficiency of functional proteins.

Π-primenovo: An Accurate and Efficient Non-Autoregressive Deep Learning Model for De Novo Peptide Sequencing

Siqi Sun (孙思琦)
Fudan University

Abstract

Peptide sequencing via tandem mass spectrometry (MS/MS) is fundamental in proteomics data analysis, playing a pivotal role in unraveling the complex world of proteins within biological systems. In contrast to conventional database searching methods, deep learning models excel in de novo sequencing peptides absent from existing databases, thereby facilitating the identification and analysis of novel peptide sequences. Current deep learning models for peptide sequencing predominantly use an autoregressive generation approach, where early errors can cascade, largely affecting overall sequence accuracy. And the usage of sequential decoding algorithms such as beam search suffers from the low inference speed. To address this, we introduce π-PrimeNovo, a non-autoregressive Transformer-based deep learning model designed to perform accurate and efficient de novo peptide sequencing. With the proposed novel architecture, π-PrimeNovo achieves significantly higher accuracy and up to 69x faster sequencing compared to the state-of-the-art methods.

Brief Biography

Siqi Sun is a Young PI at Fudan University and the AI For Science Group at Shanghai AI Lab. He completed his Ph.D. at the TTIC under Professor Jinbo Xu and earned his Bachelor's from Fudan University. Between 2018 and 2022, he contributed to research on language model and its applications at Microsoft Research. Siqi's work in deep learning spans life sciences and natural language processing, and has published numerous papers on top conferences and journals.

Combining Multi-Omics and Metabolic Modelling to Decipher Cellular Stress Mechanisms for Antimicrobial Pharmacology and Biomanufacturing Applications

Yan Zhu (朱岩)
Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences

Abstract

Multidrug resistance presents a critical challenge to global health, with the emergence of widespread superbugs urgently demanding novel antimicrobial treatments. Concurrently, the escalating climate crisis and the pressing need for sustainable development underscore the importance of biomanufacturing through synthetic microbial cell factories to produce biochemicals, biofuels, and biomaterials. While microbial pathogens are targeted by antimicrobials that specifically disrupt their cellular machinery or structure, microbial cell factories are exposed to industrial stresses that impose a broader spectrum of detrimental impacts. However, the underlying cellular mechanisms governing these responses are intricate and remain only partially understood. Recent advances in mass spectrometry, sequencing technologies, and data science have enabled the integration of multi-omics approaches with computational modelling to effectively unravel the cellular dynamics underlying responses to these diverse stresses. In this context, I utilise polymyxin treatment against Gram-negative superbugs as a model, combining multi-omics analyses and computational approaches to decipher the mechanisms of antimicrobial action, drug synergy, resistance development, and nephrotoxicity. For industrial applications, I integrate correlative multi-omics approaches with metabolic modelling to elucidate the mechanisms by which *Corynebacterium glutamicum* cell factory responds to various industrial stresses, including methanol exposure, low pH, hydrogen peroxide, furfural, high osmolarity, and heat. Our integrated omics and metabolic modelling analyses consistently revealed a reduction in central metabolism, alongside perturbations in redox homeostasis and energy biogenesis under multiple stress conditions. Ultimately, the combination of multi-omics and metabolic modelling provides a powerful framework for deciphering the complex interplay of biological pathways in response to both antimicrobial and industrial stresses, offering valuable insights for the development of more effective antimicrobial treatments targeting superbugs, as well as for optimising microbial cell factories for biomanufacturing.

Brief Biography

Dr Zhu received his PhD in Microbiology in 2013 from the University of the Chinese Academy of Sciences (UCAS). He subsequently joined the University of Queensland and Monash University, where he worked on food microbiology and systems pharmacology. In 2022, he accepted a full-time professorship at the Tianjin Institute of Industrial Biotechnology (TIB), CAS, where he focuses on systems biotechnology. His research is well-supported through funding from TIB, CAS, and the Ministry of Science and Technology (MOST). Dr Zhu has published two book chapters and 96 peer-reviewed papers to date. His recent first-authored research on polymyxin dependence was featured on the front cover of Advanced Science in 2020. Additionally, his work on a novel synthetic lipopeptide antibiotic, published in Nature Communications in 2022, was selected as an Editorial Highlight. Dr Zhu serves as a member of the Technical Committee of Computational Synthetic Biology at the Chinese Bioinformatics Society and as an Associate Editor for the International Journal of Antimicrobial Agents.

Understanding and Engineering Proteins with Geometric Deep Learning

Bingxin Zhou (周冰心)
Shanghai Jiao Tong University

Abstract

Protein engineering plays a pivotal role in addressing global challenges, from healthcare to sustainability. Recent research leverages deep learning methods, such as language models and graph neural networks, to analyze protein sequences, structures, and functions. This emerging biotechnology significantly reduces the cost and complexity of studying and modifying proteins. This talk introduces our recent deep learning solutions for protein engineering, aimed at enhancing protein functionality and properties to meet practical needs. We address a range of challenges faced by biologists, including zero-shot mutations, deep mutations, few-shot dry-wet experimental iterations, and patent blockades. The reliability and generalizability of our solutions have been validated through wet lab experiments on a variety of proteins and protein assays.

Brief Biography

Bingxin Zhou is currently a Research Scientist at Shanghai Jiao Tong University. She obtained her Ph.D. from the University of Sydney, Australia, in 2022, and was also a visiting scholar at the University of Cambridge. Her research primarily focuses on the development of deep learning techniques, especially geometric deep learning, to address challenges in biology such as enzyme engineering, metabolic gene networks, and proteome-wide evolutionary analysis. For model development, she has published useful Graph Neural Network models for static, dynamic, heterophilic, and noisy graphs in IEEE TPAMI, JMLR, ICML, NeurIPS, etc. In the field of protein analysis and application, she has established general deep learning frameworks for protein engineering and sequence design, with promising experimental evaluations. Some results have been published in eLife, Chem. Sci., JCIM, etc.

Exploration of the Biological Diversity of RNA-guided Miniature Cas12 Genome Editors

Quanjiang Ji (季泉江)
ShanghaiTech University

Abstract

CRISPR-Cas9/Cas12a genome editing systems have been widely harnessed for genetic engineering and gene therapeutics. However, the large sizes of these CRISPR effector nucleases restrict their flexibility in therapeutic applications that use the cargo-size-limited adeno-associated virus delivery vehicle. We recently developed miniature CRISPR-Cas12f and -Cas12n systems for efficient genome editing. We studied the detailed DNA recognition and cleavage mechanisms of the two systems. Moreover, we engineered a CRISPR-Cas12f variant with enhanced editing activity using structure-guided protein engineering. The small sizes of the nucleases offer advantages for cellular delivery, and characterizations of the nucleases will facilitate engineering more compact genome-manipulation technologies.

Brief Biography

Dr. Quanjiang Ji is a Professor at ShanghaiTech University and his research focuses on the mining and engineering of new CRISPR-Cas systems and the development of CRISPR-based gene therapeutics. He received his bachelor's degree from Nanjing University in 2009, and PhD from University of Chicago in 2014. He pursued his postdoctoral training from University of California, Berkeley from 2014 to 2016. He has developed two miniature genome editing systems, CRISPR-Cas12f and -Cas12n. Moreover, he has developed facile CRISPR-based genetic manipulation methods in pathogenic bacteria.

High-Precision Base Editing Technology

Erwei Zuo (左二伟)
Institute of Agricultural Genomics, Chinese Academy of Agricultural Sciences

Abstract

Base editing technology is a cutting-edge genome editing tool that has emerged in recent years. By combining the CRISPR/Cas editing system with deaminases, it merges the catalytic efficiency of these enzymes with the precise targeting capabilities of CRISPR/Cas. This approach enables deamination reactions at specific sites on DNA or RNA strands, facilitating accurate base substitutions. Because base editors do not induce double-strand breaks (DSBs) and do not rely on the host's non-homologous end joining or homologous recombination pathways, they significantly reduce DSB-related byproducts, such as small insertions or deletions. Nevertheless, base editing still faces challenges, including low editing efficiency, a limited number of editable sites, and off-target effects. Researchers are actively exploring effective strategies, such as optimizing Cas proteins or deaminases through rational design or continuous evolution, and developing various enhanced versions of base editors, thereby providing powerful tools for disease treatment and molecular breeding.

Brief Biography

Zuo Erwei is a researcher at the Institute of Agricultural Genomics, Chinese Academy of Agricultural Sciences. In recent years, he has concentrated on enhancing the precision and efficiency of gene editing technologies, engaging in the research and application of high-performance techniques while actively advocating for the establishment of a safety evaluation system for these applications. He has developed various technologies to detect off-target effects and has demonstrated that base editors can lead to completely random and unpredictable off-target effects across the genome. Furthermore, he proposed a scientific hypothesis regarding the molecular mechanisms underlying these off-target effects and created several base editing tools designed to minimize such issues. His contributions have been acknowledged in prestigious listings, including the "Top Ten Advances in Life Sciences in China 2019," "Major Medical Advances in China 2019," the "Major Scientific Discoveries of the Chinese Academy of Agricultural Sciences 2020," and the "2022 Youth Science and Technology Innovation Award." He has published numerous research papers in top scientific journals, including Science, Nature, Nature Methods, Cell Research, and Nature Communications.

fficient Genome-Editing tools to Engineer the Recalcitrant Non-model Industrial Microorganism

Binan Geng (耿碧男)
Hubei University

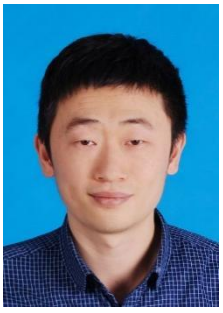
Abstract

Current biotechnology relies on a few well-studied chasses such as *Escherichia coli* and *Saccharomyces cerevisiae*, which have abundant information and efficient toolkits for genetic manipulation, but lack industrial characteristics. Instead, non-model industrial microorganisms usually possess excellent features but do not have effective and efficient genome-engineering toolkits, which hampers the development of microbial cell factories to meet the fast-growing bioeconomy. In this study, using the non-model ethanologenic bacterium *Zymomonas mobilis* as an example, we developed a workflow to mine and temper the elements of Restriction-Modification, CRISPR-Cas, Toxin-Antitoxin systems, and native plasmids that are hidden within industrial microorganisms themselves as efficient genome-editing toolkits, and established a Genome-Wide Iterative and Continuous Editing (GW-ICE) system for continuous genome-editing with high-efficiency**.** This research not only provides tools and pipelines for engineering the non-model polyploid industrial microorganism *Z. mobilis* efficiently, but also sets a paradigm to overcome biotechnological limitations in other genetically recalcitrant non-model industrial microorganisms.

Brief Biography

Binan Geng works as a postdoctoral researcher in school of life sciences from Hubei university. She got her bachelor's degree and followed by her Ph.D. training from Hubei university. Her research focuses on synthetic biology, genome-editing, and biotechnology, aimed at developing efficient genome-editing technology for non-model industrial microorganisms. Up to now, Dr. Geng has published more than 11 academic papers and holds 4 patents in China.

Engineering Prime Editors for Versatile and High Efficient Editing in Rice



Pengcheng Wei (魏鹏程)
Anhui Agricultural University

Abstract

The efficiencies of plant prime editing systems are frequently lower than those of mammalians. To improve plant PE activity, we engineered two types of prime editors, PE5a/b/c and PE6s, for plants, and their editing ability was examined with different types of mutations in rice. Compared to previously established plants PEs, ePE5c-Cre and ePE6d exhibited superior capability on short mutation editing as well as fragment insertions. Our engineering on plant prime editors provided reliable and easy-to-use toolbox for plant functional genomic research and for genome structural variants manipulations of practical breeding.

Brief Biography

Wei Pengcheng, Professor of Anhui agricultural University, college of agronomy. He seeks the engineering precise breeding tools and manipulation methods for plants. He especially is interested in the germplasm innovation of rice industrial production traits, e.g. herbicide resistance, mechanized seed production, through genome editing strategies. The recent publications included Nature plants, genome biology, Molecular plant, Plant Biotechnology Journal, etc.

Development of Novel Gene Editing Tools Using A Data-driven Approach

Zhenghe Li (李正和)
Zhejiang University

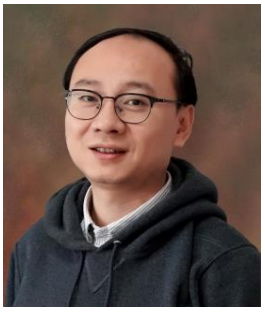
Abstract

Emerging genome editing tools such as CRISPR/Cas nucleases, base editors, and prime editors enable targeted precise changes to a cell's genome and facilitate fundamental biological research. Adaption and refinement of these technologies in plant science have also opened up new opportunities for rapid and precise trait improvement of a myriad of crops. Despite the potential, challenges remain for most plant species/genotypes in delivering the CRISPR/Cas reagents into plant cells and subsequent recovery of genetically modified plants from edited cells. Plant viral vectors have emerged as promising tools for gene delivery, but the generally small packaging capacities constrain their utilities in delivering the large CRISPR/Cas enzymes. Here, we compare the biological properties of various plant viral vectors and highlight the unparalleled cargo capacities of a group of segmented or nonsegmented, negative-stranded RNA viruses. Our work addressed issues related to strategies for viral vector designing, recovery of edited plants, heritability of virus-induced mutations, viral vector clearance etc. Using these RNA viral vectors, we demonstrate efficient delivery of the commonly used genome-editing enzymes (CRISPR/Cas9, CRISPR/Cas12a, adenosine and cytosine base editors) and DNA-free genome editing of several crop species and varieties. The viral delivery systems promise to overcome gene delivery bottlenecks for genome-editing some recalcitrant plant species and elite crop varieties.

Brief Biography

Zhenghe Li is currently a professor at Institute of Biotechnology, Zhejiang University, China. Zhenghe graduated at Zhejiang University with a Ph.D. degree in plant pathology in 2005 and then moved to University of Kentucky, USA for a postdoctoral training during 2005-2011, where he studies plant positive-strand RNA virus replication. Since 2011, Zhenghe has been employed as a faculty member in Zhejiang University. Current work in Zhenghe's laboratory focuses on molecular plant virology studies, viral vector development and applications in genome editing. His research group has developed the first reverse genetics systems for any plant negative-strand RNA viruses and engineered several viral vectors for transformation-free genome editing in plants.

Plant Synthetic Biology Promotes the Development of Future Functional Food Crops



Qinlong Zhu (祝钦泷)
South China Agricultural University

Abstract

Functional and nutritious food crops are beneficial to human health. Refined grains are mainly starch of endosperm and lack nutrients. Therefore, using plant biodesign and synthetic biology methods to synthesize nutrients and bioactive components in crops has important research significance. The development of plant synthetic biology has opened up opportunities to germplasm innovation of future functional food crops, which have multiple functions and high nutritional density. In previous studies, we have developed TAC-based TransGene Stacking (TGSII) systems, TGSII and TGSII-UNiE, through Cre/*loxP* irreversible recombination and unique nucleotide sequence-guided nicking endonuclease (UNiE)-mediated DNA assembly. Furthermore, a series of high-efficiency plant multiplex genome editing systems and base editors with a wide range have been developed for synthetic metabolic engineering. Utilizing these tools, we have successfully developed "Purple endosperm rice (called Zijingmi in Chinese) ", "Astaxanthin rice 1.0 (AR, called Chijingmi 1.0 in Chinese)" and new high-quality rice germplasm with suitable amylose content. On this basis, we have further developed new DNA assembly tools and strategies that enable effective multigene stacking and multiplex gene editing at the same time. As a result, we have developed the AR2.0 germplasm with higher astaxanthin content and enhanced stability. And successful heterologous biosynthesis of crocins was obtained in rice callus and plants. Additionally, effective synthesis of melatonin was also achieved in rice callus. These studies provide valuable tools and examples for the genetic engineering operations of complex metabolic pathways, the biosynthesis of essential bioactive substances, and enhancement of important agronomic traits involving multiple genes.

Brief Biography

Dr. Zhu is a professor of plant synthetic biology and molecular breeding at College of Agriculture, South China Agricultural University, and previously served as a visiting associate professor at Cornell University. His research mainly focuses on using plant synthetic biology strategies to develop new functional food crops for addressing the challenges in human health by synthesizing bioactive compounds and improving nutritional quality. His research program is centered on developing DNA assembly methods, TransGene Stacking system, and genome engineering tools for plant biosynthetic biology and crop breeding application. He has developed the first endosperm anthocyanin-rich Purple Endosperm Rice (Zijingmi in Chinese) and the first endosperm astaxanthin-rich Astaxanthin Rice (AR, Chijingmi in Chinese). He supervised the students to win the first Best Plant Synthetic Biology Award of iGEM in 2016. He won the Best Youth Outstanding Paper Award of CSBT in 2019.

High-Throughput, Label-Free Sorting of High DHA-Content Single-Cells from Genome-Wide Random Mutagenesis Libraries by Flowracs

Jian Xu (徐健)
Qingdao Institute of Bioenergy and Bioprocess Technology, Chinese Academy of Sciences

Abstract

A full spontaneous single-cell Raman spectrum captures the metabolic phenome in a label-free and non-invasive manner, however Raman-activated cell sorting (RACS) of rare target cells from highly heterogeneous systems has remained a concept. Here, we present a positive dielectrophoresis-induced deterministic lateral displacement (pDEP-DLD)-based flow-mode RACS (FlowRACS), where a modulated pDEP-DLD force is exerted to focus, trap, and sort the fast-moving single cells in a wide channel. In pigment- and oil-producing yeasts, FlowRACS shows high sorting accuracy (>90%), high throughput (>600 events per min), high yield (>85%), long running time (>10 hours), and therefore is capable of sorting rare cells while preserving full cellular vitality. As an example, direct label-free sorting of a genome-wide random mutagenesis library containing 10^5 *Aurantiochytrium* sp. mutants via intracellular docosahexaenoic acid (DHA) content produced mutant cells with 58% higher DHA productivity in just two FlowRACS runs completed within two days, representing two orders of magnitude improvement in time- and cost-efficiency over conventional approaches. The superior trait is attributed to global remolding of transcriptome, including enhanced carbon metabolism, reduced intracellular NADPH synthesis rate, and increased triacylglycerol (TAG) synthesis. FlowRACS emerges as a powerful platform for synthetic biology by enabling the direct screening of metabolic traits from genome-wide mutagenesis libraries.

Brief Biography

XU Jian (xujian@qibebt.ac.cn) currently serves as Director of Single-Cell Center and Director of BioEnergy Division at CAS-QIBEBT. Jian has published over 170 papers on leading journals such as *Science, Cell Host Microbe* etc with ~17,000 citations (H-index 62). He is a founding senior editor of *mSystems*. His contribution was recognized by career awards from NSFC, MOST and CAS, including National Distinguished Young Scholars Award (2014), National Young-Scientist Award for Science and Technology (2016) and VCANBIO Award for Biosciences and Medicine (2016). Single-Cell Center (http://www.single-cell.cn/) has invented the Ramanomics Instrument Series (RACS-Seq, FlowRACS, EasySort, etc; http://www.singlecellbiotech.com/) to support industrial biotechnology, precision medicine, environmental remediation and synthetic biology.

Pioneering Bioingredient Production

Congqiang Zhang (张聪强)
Singapore Institute of Food and Biotechnology Innovation

Abstract

The worldwide shift away from fossil fuels toward more environmentally friendly resources and technologies has opened up significant opportunities for biomanufacturing, particularly through microbial fermentation. Isoprenoids represent the largest classes of natural products, numbering over 110,000 compounds. Their structural diversity contributes to a wide range of applications, including pharmaceuticals (e.g., Taxol), nutraceuticals (e.g., astaxanthin), flavours and fragrances (e.g., linalool), polymer molecules (e.g., isoprene), and biofuels (e.g., farnesene). To enhance isoprenoid production, our approach involves mining novel terpene synthases from fungi using bioinformatics. We also refine synthetic biology tools and explore novel microaerobic fermentation bioprocess to maximize the product yields and titres. Leveraging pathway design and our recently identified novel enzymes, we have successfully engineered *Escherichia coli* to produce high-value flavour, fragrance, and nutraceutical molecules at near-theoretical yields (up to 90%) and high titers (17-30 g/L) for several sesquiterpenes and monoterpenes, a challenging task for microorganisms. We also engineer microbes to produce carotenoids and vitamin A at “g/L” levels. We also engineer a filamentous fungus for diterpenoid production reaching “g/L” level in flasks.

Brief Biography

Dr. Congqiang Zhang earned his PhD in 2014 from a joint program at the National University of Singapore and the Massachusetts Institute of Technology. He joined the Biotransformation Innovation Platform at A*STAR in 2015 as a founding member and is now a Principal Investigator and a group leader at SIFBI, A*STAR. His research focuses on metabolic engineering, synthetic biology, and enzyme engineering, with a particular emphasis on industrial production of isoprenoids, carotenoids, and lipids. He has authored >40 publications and holds >10 international patents (4 granted) in this area. He collaborates closely with both local and multinational corporations on translational research. He serves as the Secretary of the BioEnergy Society of Singapore and is an editor for Frontiers in Bioengineering and Biotechnology and Advanced Biotechnology. Dr. Zhang was awarded the prestigious Singapore Young Investigator Research Grant in 2019 and has secured multiple national-level competitive grants as Principal Investigator or Co-Principal Investigator, like Singapore-France and Singapore-Australia Bilateral grants.

XianLiang Zheng (郑贤良)
Angel Yeast Company

Brief Biography

Dr. Xian-Liang Zheng graduated from the University of Chinese Academy of Science, completed 3-year postdoctoral research at Denmark Technical University and University of Tennessee. he is currently the vice general manager of Center for Biocatalysis and Enzyme Technology at Angel Yeast Company, China. Mainly responsible for the development of special enzyme strains, protein engineering, bio-manufacturing and other related work. He also serves as a corporate supervisor for graduate student at Shandong University, Hubei University and Three Gorges University. In recent years, as the project leader and participant, he undertakes multiple key research and development projects. He and his team developed various new enzyme preparation products, annual sales exceeding 20 million yuan. He is currently a council member of the Hubei Society of Synthetic Biology, he has been awarded multiple honorary titles, such as Innovative Talent, Mount Taishan Industrial Leading Talents, Model of Innovation and Entrepreneurship and so on.

High-throughput and Low-cost DNA Synthesis on Semiconductor Biochip

Dan Wu (吴丹)
XinSu Technology (Suzhou) Co., Ltd.

Abstract

DNA synthesis and sequencing are complementary processes that form a critical feedback loop in synthetic biology and genomics. While the past decade has seen an extraordinary reduction in the cost of DNA sequencing—approximately six orders of magnitude—this rapid progress has not been mirrored in DNA synthesis. The growing demand for large-scale DNA production in fields like synthetic biology, personalized medicine, and biomanufacturing calls for more efficient and cost-effective synthesis techniques, yet existing methods fall short of meeting these needs.

In this talk, I will present the cutting-edge development of next-generation DNA synthesis technology, leveraging semiconductor bio-chips to transform the way DNA is synthesized. This innovative approach promises to overcome current limitations, offering scalable, precise, and economical DNA synthesis. Additionally, I will explore the exciting potential of this technology in DNA data storage, an emerging field poised to revolutionize information storage for the digital age.

Brief Biography

Dan Wu is a seasoned biomedical engineer and entrepreneur with extensive experience in end-to-end development of biomedical systems, including biomedical imaging, single-cell detection, and protein testing technologies. He holds a Bachelor's degree in Electrical Engineering and a Master's degree in Acoustics from Nanjing University, as well as a Ph.D. in Mechanical Engineering and Computation from MIT. Currently, Dan is the co-founder and CTO of Atantares, a leading company pioneering next-generation DNA synthesis technology.

Application and Prospects of DNA Biosynthesis Technology

Jun Sun (孙隽)
Tianjin Zhonghe Gene Technology Co., Ltd.

Abstract

DNA synthesis technology is the fundamental key technology of synthetic biology, and its update and iteration will promote giant development of synthetic biology research and industry, guide the revolution of life science research methods, and have great scientific research and industrial application value. Traditional DNA synthesis technology is based on solid phase phosphoramidite chemical synthesis, and has undergone two generations of technological changes, but there are still some technical defects such as short synthetic fragments, serious environmental pollution, and high cost, which can not meet the growing needs of gene and even genome synthesis. DNA biosynthesis technology is a new generation of DNA synthesis technology, which exploits terminal deoxynucleotidyl transferase (TdT) as a DNA synthesis tool. The current development of DNA synthesis equipment based on biosynthesis by Zhonghe Gene will be introduced. Based on the current progress of Zhonghe Gene, the application and prospects of DNA biosynthesis will be discussed in this presentation.

Brief Biography

Dr. Xiaoyun Lu is the Deputy General Manager of Zhonghe Gene and previously worked at the Tianjin Institute of Industrial Biotechnology under the Chinese Academy of Sciences. Her research focuses on developing DNA biosynthesis technology and equipment, which holds the potential to overcome the current limitations of DNA synthesis based on phosphoramidite chemistry. Dr. Lu has published numerous papers in high-impact journals, including Nature Communications, ACS Catalysis, PNAS, and Plant Communications. She holds 23 international and domestic patents, several of which are pioneering patents in DNA biosynthesis. With extensive experience in this field, she is a recognized leader in advancing DNA biosynthesis technology.

High Throughput, Fully Integrated, and Low Cost DNA Storage System

Hong Liu (刘宏)
Southeast University

Abstract

DNA has been considered as a compelling candidate for digital data storage due to advantages such as high coding density, long retention time, and low energy consumption. Despite many works reported, the development of a DNA-based database of full integration, high efficiency, and practical applicability is still challenging. In this talk, firstly I summarize the general procedures of the state-of-the-art DNA-based digital data storage methods, highlighting the uncertainties involved (Nucleic Acids Res. 2021). Then, synthesis and sequencing of DNA on a single electrode with scalability for an integrated DNA-based data storage system is presented (Sci. Adv. 2021). Next, a high throughput, and fully integrated CMOS chip specifically designed for DNA storage is introduced. Lastly, I will present a flexible paradigm by recombining already synthesized DNA to build cost-effective and intelligent DNA data storage systems (ACS Appl. Mater. Inter. 2023), and the quasi-solid-state electrochemical DNA synthesis based on gels (Chem. Eng. J. 2024).

Brief Biography

Hong Liu, Professor and doctoral supervisor in Southeast University, Associate Dean of School of Biological Science and Medical Engineering. He got his Bachelor and Master degree in Nanjing University, and PhD degree in University of Texas, Austin. He developed origami paper analytical device (oPAD) during his PhD, and the device was permanently kept in NIH history museum. His current research interest is large scale microelectrode array for DNA synthesis and sequencing with applications on data storage, and point-of-care testing. He is the recipient of ‘Wanren’ project and ‘Qianren’ project, and PI of two National Key R&D Program of China, and two Key R&D Program of Jiangsu. He published more than 80 papers on Nat. Rev. Bioeng., Nat. Commun., Sci. Adv., J. Am. Chem. Soc., Angew. Chem. Int. Ed. and others.

Development and Application of Integrated DNA Data Storage Device

Chunyang Geng (耿春阳)
Southern University of Science and Technology

Abstract

As the demand for data generation and storage skyrockets, traditional storage technologies encounter significant challenges related to capacity, durability, and reliability. DNA data storage, an emerging and advanced technology, offers a potential solution by harnessing the high-density storage capabilities of DNA. Our group employs microfluidic technology to achieve DNA synthesis, mineralization preservation, random accessing, sequencing and reading within a single device, integrating the processes of DNA data storage and advancing the automation and device-based implementation of DNA data storage.

Brief Biography

Visiting research student at Southern University of Science and Technology, under the supervision of Prof. Xingyu Jiang. The research focuses on DNA data storage and biomolecular detection using microfluidic technology.

Research progress on information model theory and application tools for DNA storage

Xin Chen (陈鑫)
Tianjin University

Abstract

DNA information storage is a cutting-edge interdisciplinary research topic. Our team rise the characteristics of mathematical research to assist the experimental team in advancing the development of DNA information storage technology. Relying on the interdisciplinary platform within Tianjin University and collaborative efforts with leading domestic institutions, our team has completed a series of work on the foundational mathematical principles of DNA information storage, the development of application tools tailored to the biochemical properties of applicable DNA information storage, and coding methods designed to address specific scientific challenges. Here, we provide a brief introduction to our team's work and attempt to raise some general considerations regarding mathematical modeling issues and biochemical technology issues in DNA information storage.

Brief Biography

Chen Xin is an Associate Professor at Tianjin University - Tianjin National Center for Applied Mathematics. He holds a degree in Bioinformatics from Jilin University. His main research direction is the application of mathematical methods in biological data and software development. He has published more than 20 papers in the fields of bioinformatics and DNA storage. Chen Xin has led several sub-projects under the Fundamental Strengthening Project of the Science and Technology Committee of the Central Military Commission and the Ministry of Science and Technology's Key Research and Development Plan. He currently serves as the Project Secretary for the Ministry of Science and Technology's Key Research and Development Plan porject "Combinatorial Methods in DNA Storage"

DNA Storage Empowered by Soft-Decision Decoding

Lulu Ding (丁璐璐)
Shenzhen University

Abstract

DNA storage (DS) is an emerging technology with significant potential due to its exceptional density, long-term stability, and low maintenance costs. However, high error rates during DNA synthesis, amplification, sequencing, and preservation pose severe challenges, complicating data recovery and reducing storage density. To address these challenges, our study focuses on enhancing the error-correcting capabilities of error-correcting codes for DS systems. We analyzed the error characteristics and developed prediction models to quantify the DS channel. By introducing the soft-decision strategy from the communications field, we devised the *Derrick* algorithm for four nucleotide-based DS and *Derrick_cp* for composite letter-based DS. *In vitro* experiments demonstrated that *Derrick* doubled the error-correcting capability of the Reed-Solomon code compared to previous algorithms that lacked soft-decision, and *Derrick_cp* achieved the highest information density in DS systems.

Brief Biography

Lulu Ding received the Ph.D. degree in bioinformatics from the Chinese Academy of Agricultural Sciences in 2023, then she joined the National Engineering Laboratory for Big Data System Computing Technology at Shenzhen University. Her research focuses on DNA storage, multiple sequence alignments in third-generation sequencing, and pangenome construction. Dr. Ding's work in the field of DNA storage has been published as the first author (including co-first author) in journals such as *National Science Review* and *Advanced Science*.

DNA-based On-chip Classifiers

Xiaolei Zuo (左小磊)
Shanghai Jiao Tong University

Abstract

So far, as chip circuits continue to become more complex and Moore's Law approaches its limits, the development of silicon-based computers has hit a bottleneck, leading to the emergence of biocomputation and quantum computation. However, biocomputation strictly follows traditional design principles (e.g. binary system) of digital electronics, which could reach their limits when assembling gene circuits of higher complexity. Here, we introduce a DNA-encoded molecular classifier that can physically implement the computational classification of molecular data with module-n system. To produce unified sensing signals across heterogeneous molecular recognition events, we exploit DNA-framework-based programmable atom-like nanoparticles with n valence to develop valence-encoded signal reporters that enable linearity in translating virtually any biomolecular recognition events to signal gains. Multidimensional molecular information in computational classification is thus precisely assigned weights for bioanalysis. We demonstrate the implementation of a molecular classifier based on programmable atom-like nanoparticles to perform biomarker panel screening and analyze a panel of six biomarkers across three-dimensional data types for a near-deterministic molecular taxonomy of prostate cancer patients.

Brief Biography

Xiaolei Zuo received his Ph.D. degree from Shanghai Institute of Applied Physics, Chinese Academy of Science (2008). He was a postdoctoral fellow at University of California, Santa Barbara, USA (2008-2010), and at Los Alamos National Laboratory, USA (2010-2012). Now he is a professor of the Institute of Molecular Medicine, Renji Hospital, School of Medicine, Shanghai Jiao Tong University. His research interests include DNA electrochemical biosensors, 3D DNA probes, and DNA memory.

DNA Data Storage: A Revolutionary Paradigm for Future Data Storage

Wen Wang (王雯)
BGI Research

Abstract

The global explosion of digital information presents significant challenges for data storage. DNA, with its remarkable durability and space-efficient storage, emerges as a highly promising medium for this purpose. DNA data storage technology involves encoding digital information into artificially designed sequences of DNA molecules. Its high storage density and low energy consumption make it an extremely promising solution to the growing demands of data storage. As an interdisciplinary frontier, DNA data storage bridges biotechnology and information technology. This presentation will provide a systematic overview of DNA data storage, discussing recent progress and future application prospects.

Brief Biography

Dr. Wen Wang got her bachelor's degree from Zhejiang University and PhD degree from the Hong Kong University of Science and Technology. After postdoctoral training at Tsinghua University, she joined BGI Research in 2022 as a research scientist of DNA storage. Her research interests include DNA nanotechnology and its related applications in DNA storage, multiplexed imaging and detection, and self-assembly of functional materials. She has published 10 related papers in high level journals such as *Nucleic Acids Research, Nature Communications* and *Angewandte Chemie*.

DNA Nanodevices for Nongenetically Controlled Cellular Behaviors and Their Cell Therapeutic Applications

Zhou Nie (聂舟)
Hunan University

Abstract

Nucleic acids, as crucial biological functional molecules, are not only the primary carriers of genetic information but also have increasingly gained widespread attention for their non-genetic functions in recent years. The development of emerging technologies such as functional nucleic acids, self-assembly of DNA nanostructures, and dynamic DNA nanotechnology has made it possible to construct intelligent DNA nanomaterials with complex functions. Benefiting from the precise programmability of DNA sequence complementarity, high structural controllability, and the convenience of synthesis, modification, and functionalization, intelligent DNA nanomaterials are gradually becoming an important tool for biological function regulation, with broad application prospects in biomedical research. Here, we propose a new concept of non-genetic reprogramming of cell receptor functions for regulating cellular behaviors based on intelligent DNA nanomaterials. By using various de novo designed DNA intelligent nanodevices, we can precisely regulate and reprogram the molecular recognition and activation patterns of important receptor families on the cell membrane surface, thereby rewiring cellular signaling pathways to achieve precise control over downstream cellular behaviors. Utilizing dynamic DNA nano-assembly technology, we have successfully reprogrammed the molecular recognition targets of the receptor tyrosine kinases (RTKs) from native protein ligands to customized small molecules, extracellular miRNA, near-infrared light, and specific cell types. We have also achieved automated control and precise nanoscale clustering regulation of RTK receptor activation through DNA nanorobots and DNA origami techniques. In addition, we have developed a novel CAN-TE technology based on DNA-antibody chimeras, enabling multi-target intelligent logical recognition of antigens on the surface of tumor cells and regulating the activation efficiency of immune cells through multivalent effects, greatly enhancing the specificity of tumor cell recognition in T cell engagement techniques. We have also targeted integrins to construct a molecular tension sensing unit, creating an artificial mechanoreceptor that can specifically respond to the cellular mechanical action mediated by individual adhesion proteins at the piconewton (pN) scale, and successfully used it for the maintenance of stemness in neural stem cells mediated by cellular adhesion force.

Brief Biography

Zhou Nie is a professor at College of Chemistry and Chemical Engineering, Hunan University. He obtained bachelor degree from Nankai University in 2002, and obtained Ph.D. degree from Institute of Chemistry, Chinese Academy of Science in 2007. Since 2007, He started his career at State Key Laboratory of Chemo/Biosensing and Chemometrics at Hunan University. From 2011 to 2012, he received his postdoctoral training at Purdue University. His current research is focused on the development of new chemical-biological tools for detection and regulation of key factors in crucial biological events, such as cellular signal transduction and transcription regulation. In recent 5 years, he has published 90+ papers as correspondence author in high impact journals, including Nat. Chem. Biol., J. Am. Chem. Soc., Angew. Chem. Int. Ed., Science Advances. He was awarded by the National Science Fund for Distinguished Young Scholars in 2017, the "Cheung Kong Scholar" for Young Scholars in 2015, the Ten Thousand Talent Program for Young Top-notch Talent in 2014, the National Science Fund for Excellent Young Scholars in 2012, and Chinese Chemical Society Award for

Outstanding Young Chemist in 2015.

Engineering Long-Lived T Cells to Cure Chronic Diseases

Min Peng (彭敏)
Tsinghua University

Abstract

Engineered T cells represent a cornerstone of immunotherapy. The long-term therapeutic efficacy of engineered T cells depends on their functional persistence in vivo. Recently, we have demonstrated the induction of CAR T cells into an immortal-like and functional state, termed T_{IF}. These reprogrammed T_{IF} cells possess near-infinite stemness, akin to induced pluripotent stem cells, while retaining the functionality of mature T cells, representing a novel synthetic state of T cells. I will discuss the induction, mechanism, and application of T_{IF} cells in cancer and noncancerous diseases.

Brief Biography

Dr. Peng received his bachelor's degree in clinical medicine from West China School of Medicine, Sichuan University in 2005, and a Ph.D. in immunology from Peking Union Medical College in 2010. He conducted postdoctoral research at Memorial Sloan Kettering Cancer Center from 2010 to 2017, focusing on mTORC1 regulation and immunometabolism, with first-author publications in Cell, Science, and Nature. In 2017, Dr. Peng joined Tsinghua University, where he leads research on T cell biology. His work has been published in Nature Immunology, Journal of Experimental Medicine, among others.

Precise Engineering of Immune Cells for Therapeutics

Jie Sun (孙洁)
Zhejiang University

Abstract

Genetic engineering of immune cells, such as cytotoxic T and NK cells, to express chimeric antigen receptors (CARs) enables them to recognize and eliminate tumor cells. Currently, the most common way to efficiently delivery exogenous CAR gene into primary T and NK cells is through integrating viral vectors, such as retrovirus or lentivirus. However, these viral vectors integrate CAR gene into the immune cell genome in a random way, resulting in risk of carcinogenesis. Here we utilize CRISPR/Cas9 gene editing tools to precisely integrate CAR gene at designated genetic loci in T and NK cells. This precise engineering strategy has allowed us to reduce the fratricide of CAR-T cells as well as to develop allogeneic CAR-T and CAR-NK cells to treat cancer.

Brief Biography

Dr. Jie Sun is a principal investigator at School of Medicine, Zhejiang University. She obtained her Bachelor's degree from Hong Kong University and PhD degree from University of Illinois at Urbana Champaign. She was a Beckman Postdoctoral Fellow at Beckman Institute for Advanced Science, developing biosensors for live cell imaging. Then she was trained to develop novel CAR-T therapies in Michel Sadelain's lab at Memorial Sloan Kettering Cancer Center. Her current research focuses on developing tools and strategies to enhance the anti-tumor functions of CAR-T and CAR-NK cells for both hematological and solid tumors as well as revealing the molecular mechanisms underlying the cytotoxicity, proliferation and exhaustion of CAR-T cells.

Immune Cell Engineering and Cellular Immunotherapy

Lupeng Ye (叶露鹏)
Nanjing University

Abstract

Immunotherapy has achieved remarkable success in treating certain cancers, but its effectiveness remains limited for most solid tumors, with an overall response rate of approximately 15-20% in clinical settings. In addition, current methods for producing therapeutic immune cells (e.g. CAR-T cells) still face various obstacles, including low efficiency, uncertain cell quality, and safety concerns. These limitations hinder the development of high-quality, cell-based cancer therapies like CAR-T. Therefore, advancing new immunotherapies and engineering improved methods or platforms for producing therapeutic immune cells are critical to enhancing cancer immunotherapy and cell therapy.

In the past few years, we have developed high-throughput genetic screening platforms in primary CD8+ T cells to overcome technological limitations in identifying gene targets that may improve cancer immunotherapy. For instance, we created a novel gene editing system for efficiently manipulating the genome of mouse T cells: the adeno-associated virus (AAV)-SB transposon-CRISPR (AAV-SB-CRISPR) system (*Nature Biotechnology*, 2019). The advantage of this system over most other current systems is more efficacious editing of primary immune cells and other hard-to-gene-edit cell types. Using this system, we have identified promising membrane gene targets, such as Pdia3 and Mgat5, that could improve therapies for glioblastoma multiforme and other solid tumors. We also applied this technology to primary NK cell editing and identified a genetic checkpoint, CALHM2, which enhances CAR-NK therapy (*Nature Biotechnology*, 2024).

Recently, we established the first gain-of-function screening platform in primary T cells, leading to the discovery of immune boosters such as Prodh2 (proline dehydrogenase). Over-expressing *Prodh2/PRODH2* substantially enhanced TCR-T and CAR-T cells' anti-tumor activity by re-programming T cell proline metabolism (*Cell Metabolism*, 2022). To further enhance the safety and efficiency of immune cell engineering, we developed a novel technology called MAJESTIC (mRNA AAV-Sleeping-Beauty Joint Engineering of Stable Therapeutic Immune Cells) (*Nature Biomedical Engineering*, 2023). This innovative technology allows us to engineer cancer-fighting immune cells - such as CAR-T, CAR-NK, TCR-T, CAR-Macrophages, and CAR-iPSCs - more efficiently, with reduced cellular toxicity and genotoxicity, compared to conventional systems like lentivirus, retrovirus, CRISPR-based gene editing, plasmid transposon electroporation, and minicircle transposon electroporation.

Brief Biography

Dr. Ye received his Ph.D. in Biochemistry and Molecular Biology from Zhejiang University in 2015, after which he began his postdoctoral training at Zhejiang University College of Pharmaceutical Sciences. In 2017, he joined Dr. Sidi Chen's lab at Yale University School of Medicine for further postdoctoral training. His research mainly focuses on new tech development, cancer immunotherapy, and cell therapy. Since 2018, Dr. Ye has published over ten first-author and corresponding author papers in leading journals, including Nature Biotechnology (2019, 2024), Nature Biomedical Engineering (2023, cover story), Cell Metabolism (2022), Cell (2019), Nature Methods (2019), Journal of Hematology & Oncology (2022), Cancer Immunology Research (2023), Cell Discovery (2018). In 2022, Dr. Ye joined Nanjing University Institute of Modern Biology as a Tenure-track Assistant Professor and Principal Investigator.

Production of Steroids by Synthetic Biology

Jingwen Zhou (周景文)
Jiangnan University

Abstract

Steroids are the second largest class of drugs after antibiotics and are currently widely used in the treatment of cancer, inflammation, and heart disease. However, existing synthetic biology technologies for steroid production face several challenges, including the promiscuity and efficiency of heterologous enzymes required for post-modification of active steroid functions, the metabolic pathway balance in synthetic cell factories, and the tolerance to exogenous steroids. Thus, advanced novel synthetic biology strategies need to be developed for overcoming multiple electron-requiring rate-limiting steps in the biosynthesis of steroids. Our study focuses on engineering efficient heterologous enzymes for steroid post-modification, constructing novel synthetic pathways for steroid production, and ultimately developing artificial cell factories capable of high-yield steroid production. The specific contents include: 1) Based on the post-modification characteristics of target steroids, evolutionary analysis techniques were employed to deeply explore related heterologous enzymes. Computational simulations were used to elucidate their catalytic mechanisms and guide their rational modification. 2) Efficient integration targets and heterologous expression systems were developed. By combining subcellular regionalization engineering, the expression and functional adaptation of heterologous enzymes were achieved. Cofactor and electron transfer engineering were utilized to enhance and balance the energy-driven pathways. 3) the metabolic transport network of cell factories was rationally regulated, and biosensors and microfluidic technologies were employed to achieve rapid, high-throughput screening of strains with high steroid production and tolerance. This approach has successfully achieved the efficient *de novo* biosynthesis of various important steroid compounds, including ergosterol, campesterol, 7-dehydrocholesterol, cholesterol, pregnenolone, and progesterone. Additionally, new synthetic pathways for some important steroid hormones, such as cortisone and hydrocortisone have been developed.

Brief Biography

Prof. Jingwen Zhou is a Professor of School of Biotechnology, and the Vice Dean of Science Center for Future Foods at Jiangnan University. His research areas include metabolic engineering of microorganisms to produce natural products and vitamins, development of strategies related to fine-tuning of metabolic pathway, high-throughput screening, and AI-dependent protein/pathway design. He has over 300 peer reviewed publications and invited reviews with a H-index 43 (Web of Science). He has been awarded with National Award for Technological Invention 2nd Prize, WIPO-SIPO Award for Chinese Outstanding Patented Invention, and ACS Membership Award. He has been serving as the Editor-in-Chief of 3 Biotech from 2023.

Yeast Cell Factories Facilitate the Biomanufacturing of Lipophilic Compounds

Shuobo Shi (史硕博)
Beijing University of Chemical Technology

Abstract

Lipophilicity describes a chemical compound's ability to dissolve in fats, oils, lipids, and non-polar solvents like hexane. Lipophilic compounds have a wide range of applications, with fatty acid derivatives and terpenoids being two of the most important groups. For example, many natural products belonging to terpenoids are vital for human nutrition and health, while fatty acids can be converted into biofuels such as biodiesel, which are considered more environmentally friendly and sustainable alternatives to traditional fossil fuels. However, current production methods for certain lipophilic compounds face challenges and complexities.

Recognizing the significance of constructing artificial microbial cell factories for efficient biological manufacturing, both the scientific and industrial communities have embraced this approach. Nonetheless, there are still many challenges in developing microbial cell factories that are highly efficient and robust. In this report, the speaker presents recent laboratory work focused on the analysis and optimization of biosynthesis pathways using synthetic biology techniques. Additionally, the development of efficient CRISPR technology is explored to achieve the biological manufacturing of lipophilic compounds such as fatty acids and carotenoids. This research provides valuable insights and serves as a reference for related studies.

Brief Biography

Dr. Shuobo Shi is now a professor at Beijing University of Chemical Technology. He obtained his Ph.D. degree in Biochemical Engineering from Tianjin University in 2009. Dr. Shi's primary scientific interests lie in metabolic engineering and synthetic biology. His research encompasses metabolic engineering of microbial cell factories, specifically for the production of lipids and terpenoids. Additionally, he focuses on the development of tools for genome engineering and synthetic biology, as well as the advancement of automation systems for synthetic biology applications. To date, he has authored over 70 peer-reviewed papers in well-known journals such as Nature Communications and Metabolic Engineering, including four highly cited papers in the ESI (Essential Science Indicators) category.

Green Biomanufacturing of Functional Chemicals Via Biocatalyst Engineering and Biological Circuit Design

Jinsong Gong (龚劲松)
Jiangnan University

Abstract

The green biomanufacturing of functional chemicals is a disruptive technology that has rapidly developed in recent years as an alternative to chemical processes. Employing non-food biomass and other biological carbon resources as raw materials, and building biocatalysts with independent intellectual property rights, as well as establishing a modern biomanufacturing industry technology system, are at the core of solving the supply issues in the biomanufacturing industry. Our research group starts with the performance requirements of biological circuit design and key biocatalysts (cells or enzymes) for bioprocessing, focusing on solving the core issue of poor performance in industrial applications. Through the construction of metabolic network models, modularization of synthetic pathways, virtual-real screening and bidirectional evolution of key enzymes, semi-automatic design and efficient expression of difficult-to-express proteins, and industrial technology integration, several typical biosynthetic processes have been established. We have achieved the green biomanufacturing of functional chemical products such as niacin, membrane proteins, functional sugars, and polyamino acids, and have gained comparative advantages in cost and environmental friendliness over traditional chemical processes.

Brief Biography

Dr. Jin-Song Gong is currently a Professor of biopharmaceutical engineering at Jiangnan University, China. He received Ph.D. degree in Fermentation Engineering from Jiangnan University in 2014. And joined School of Life Sciences and Health Engineering of Jiangnan University in 2014. His research interests mainly focused on the biomanufacturing of functional chemicals and pharmaceutical intermediates via protein engineering, synthetic biology, material chemistry, fermentation engineering strategies. He published more than 80 papers in the international academic journal, including ACS catalysis, Biotechnology Advances, Metabolic Engineering, ACS Synthetic Biology, Applied and Environmental Microbiology, and so on. Also, he obtained 75 authorized national invention patents and 3 US patents. He also serves the scientific community as the editor of international journals such as Frontiers in Bioengineering and Biotechnology, BioDesign Research.

AI-driven Enzyme Discovery for Synthetic Biology Innovative R&D Models

Qiannan Hu (胡黔楠)
Shanghai Institute of Nutrition and Health, Chinese Academy of Sciences

Abstract

Identifying functional enzymes for the catalysis of specific biochemical reactions is a major bottleneck in the de novo design of biosynthesis and biodegradation pathways. Conventional methods based on microbial screening and functional metagenomics require long verification periods and incur high experimental costs; recent data-driven methods apply only to a few common substrates. To enable rapid and high-throughput identification of enzymes for complex and less-studied substrates, we propose a robust enzyme's substrate promiscuity prediction model based on positive unlabeled learning. We anticipate that this model will serve as a useful tool for identifying new functional enzymes and understanding the nature of biocatalysis, thereby advancing the fields of synthetic biology, metabolic engineering, and pollutant biodegradation.

Furthermore, Dr. Qian-Nan Hu will report a novel data-driven one-stop biosynthetic/biodegradation design technology system: (1)Cell2Chem: Mining Explored and Unexplored Biosynthetic Chemical Spaces. (2) BCSExplorer: A Customized Biosynthetic Chemical Space Explorer with Multifunctional Objective Function Analysis. (3)Bio2Rxn: Sequence-Based Enzymatic Reaction Predictions by a Consensus Strategy. (4) RxnBLAST: Molecular Scaffold and Reactive Chemical Environment Feature Extractor for Biochemical Reactions. (5) PrecursorFinder: a customized biosynthetic precursor explorer. (6) CF-Targeter: a rational biological cell factory targeting platform for biosynthetic target chemicals. (7)novoPathFinder: a webserver of designing novel-pathway with integrating GEM-model. (8) Data-Driven Rational Biosynthesis Design: From Molecules to Cell Factories.

Brief Biography

Prof. Hu received Ph.D. degree in applied chemistry from Central South University in 2004. He joined Computer Chemistry Center at University of Erlangen Nurnberg as a Postdoctoral Research Associate in 2004. Dr. Hu joined School of Informatics and Computer Sciences University of California Irvine in 2007 as a Postdoctoral Research Associate, and then Bioinformatics Center at Kyoto University as a staff Scientist in 2008. He joined Wuhan University as Associate Professor of School of Pharmacy in 2010. Then, Dr. Hu joined in Chinese Sciences of Academy as Full Professor since 2014, and his research interest focuses on data-driven synthetic biology for solving global health challenges.

Protein Engineering Facilitates in Vitro Synthetic Enzymatic Biosystem

Chun You (游淳)
Zhejiang University

Abstract

The in vitro synthetic enzymatic biosystem (ivSEB) operates on the basis of a meticulously designed multi-enzyme catalytic pathway. This pathway is intricately composed of a diverse array of biological enzyme components, each playing a crucial role in the overall functionality of the system. The ivSEB is capable of transforming specific substrates into desired target compounds, all within an environment that is external to living organisms. One of the most notable characteristics of this biosystem is its modularity, which provides researchers with a high degree of freedom when it comes to the design, assembly, and regulation of the system. Our research team has adopted a strategic approach that focuses on the ATP-independent energy activation of glycosidic bonds. This innovative strategy leverages the use of inexpensive and renewable biomass materials, such as starch, cellulose, glucose, and carbon dioxide, as substrates for the purpose of biomanufacturing. These substrates serve as the foundational building blocks from which a variety of valuable compounds can be synthesized. However, within these biosystems, certain enzymes that are rate-limiting in nature often fall short of meeting the demands of the ivSEB, resulting suboptimal product yields and titers. To address this challenge, We have employed protein engineering to enhance the activity, thermostability, and substrate specificity of these rate-limiting enzymes within the ivSEBs. These advanced ivSEBs have been instrumental in the efficient synthesis of a range of valuable compounds, such as myo-inositol, glucosamine, rare sugars, disaccharides, bio-materials, and even biomimetic coenzyme regeneration. Through continuous research and development, we are committed to further refining these biosystems to unlock even greater possibilities in the realm of in vitro synthetic biology.

Brief Biography

Chun You got his PhD degree in Fudan University, and then worked as postdoctoral in Virginia Tech from 2010-2015. He join Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences as Principal Investigator since 2016, and join Zhejiang University as Principal Investigator since 2024. His research focused on the construction, optimization and application of in vitro synthetic enzymatic biosystems from renewable biomass, including improving enzyme engineering, switching coenzyme preference, constructing enzyme complex, elucidating substrate channeling mechanism, and figuring out the suitability of enzymes/modules. He has published more than 50 scientific papers in Nat. Commun, ACS Catal, Angew Chem Int Ed, Proc Natl Acad Sci USA, ChemSusChem et. al.

Artificial Enantioselective Photoenzymes with Unnatural Amino Acids

Yuzhou Wu (吴钰周)
Huazhong University of Science and Technology

Abstract

Designing artificial enzyme that could catalyze unnatural reaction is of great interest for expanding enzymatic reactions and could be highly useful for biosynthesis of unnatural products. Particularly, taking the advantages of enzyme's extraordinary enantioselectivity, developing unnatural enzymes for asymmetric synthesis is highly valuable. For instance, stereochemical control of photochemical reactions remains a formidable challenge with the existing small molecule catalysts. Therefore, we developed a method to create artificial photoenzymes with desired reactivity for unnatural reactions. The genetically encoded, chemically evolved triplet photoenzymes were developed which embedded with a benzophenone synthetic photosensitizer via genetic code expension. Structural optimization through four founds of rational mutagenesis afforded proficient variants. They promoted enantioselective intramolecular [2+2] photocycloaddition of indole derivatives with good substrate generality and excellent enantioselectivites (up to 99% enantiomeric excess). X-ray crystal structure of photoenzyme-substrate complex elucidated the important multiple noncovalent interactions that work synergistically to induce high enantioselectivity. This study shows that by merging the empowering mechanism of triplet energy transfer catalysis with the delicate supramolecular cavity of proteins, the triplet photoenzymes artificially expand the fundamental reactivity with respect to enzyme catalysis and unlock an integrated approach to valuable enantioselective photochemical synthesis that are not accessible with either the synthetic or the biological world alone.

Brief Biography

Prof. Yuzhou Wu is a professor at Huazhong University of Science and Technology (HUST). She graduated from Zhejiang University, obtained a master's degree and a doctor's degree from the National University of Singapore and Ulm University in Germany respectively, supervised by Professor Tanja Weil. She has been worked as the project leader in Ulm University and Max Planck Institute of Polymers in Germany. Since 2017, she was appointed as Professor in HUST, and was also selected as the leader of the Max Planck Society Overseas Partner Group. Her research interests laid in the development of unnatural enzymes and biomacromolecules for biosynthesis and biomedical applications, and has published more than 100 papers in Nature, J Am. Chem. Soc., Angew. Chem. Int. Ed., Adv. Func. Mater., ACS Nano, Nano Lett. , Nano Res., Chem. Rev.. She has received four national and provincial research projects, including the National Key R&D Program of China, the Key R&D Program of Hubei province, and projects from National Natural Science Foundation of China.

Machine Learning to Engineer Trna Synthetase Activity for Improved Incorporation of Noncanonical Amino Acids

Haoran Yu (于浩然)
Zhejiang University

Abstract

The pyrrolysyl-tRNA synthetase (PylRS) and *Methanocaldococcus jannaschii* tyrosyl-tRNA synthetase (MjTyrRS) are most widely used enzymes for the incorporation of noncanonical amino acids (ncAAs) into proteins at specific positions. Although directed evolution of these enzymes have enabled over 400 ncAAs to be incorporated into proteins, most of the ncAA containing proteins are expressed in a limited yield due to low activities of the variants. To further improve the activities of these enzymes, we first applied machine learning (ML) to engineer the tRNA-binding domain of PylRS with a fast fourier transformation-partial least square regression (FFT-PLSR) model and three zero-shot prediction ML models. A variant Com2-IFRS was obtained from a sequence space containing 11520 mutations, which showed a 30-fold increase in activity. Transplantation of the evolved mutations into other 7 PylRS-derived synthetases improved yields of proteins containing six types of ncAAs including Phe derivatives, Tyr derivatives, Trp derivatives, Cys derivatives, His derivatives and Lys derivatives, by up to 1149.7-fold. We also devised a protein language model-enabled automatic evolution (PLMeAE) platform, a closed-loop system for automated protein engineering within the Design-Build-Test-Learn (DBTL) cycle. The protein language model (PLM) ESM-2 makes zero-shot prediction of 96 variants to initiate the cycle. Then the biofoundry constructs and evaluates these variants, and feeds the results back to a multi-layer perceptron to train a fitness predictor, which then makes prediction of second round of 96 variants with improved fitness. With the application of PLMeAE platform, four-rounds of *in vitro* continuous directed evolution was carried out to engineer MjTyrRS within half a month. The mutants obtained increased the enzyme activity by up to 12.0-fold.

Brief Biography

Dr. Haoran Yu is now a principal investigator in Zhejiang University. He received his PhD in 2019 from the University College London for work on protein engineering of transketolase. After that, he worked as a research associate in Department of Chemistry, UCL, to incorporate unnatural amino acids into proteins using the expanding genetic codes method. He joined Zhejiang University as a PI since 2020, and the research interest of his group focuses on developing advanced protein engineering methods to improve enzyme properties for industrial applications. He has published more than 30 papers in the journals such as PNAS, Angew. Chem. Int. Ed.

Toward Better Utilization of Nicotinamide Biomimetics: Coupled Photo-Enzymatic Approach

Ye Ni (倪晔)
Jiangnan University

Abstract

As potential substitutes for natural cofactors, nicotinamide cofactor biomimetics (NCBs) have been extensively explored due to their cost-efficiency and easy synthesis. *Ss*GDH is the first enzyme identified to utilize oxidized NCBs, enabling NCBs-based in situ cofactor regeneration. However, *Ss*GDH remains limited in cofactor scope, and the catalytic efficiency is inadequate. Here, a series of totally synthetic NCBs were designed. *Ss*GDH was engineered by modification of interface residues. M2-IG showed a 47.2-fold increase in catalytic efficiency when utilizing newly synthesized *p*-BNNA$^+$. Beneficial variants were coupled with XenA-catalyzed reaction to demonstrate their universality as NCBs regenerative enzymes. Based on all-atom MD simulation, more flexible conformation of F279 and widened cofactor entry tunnel are conducive to the entry and binding of NCBs. In addition, photocatalytic regeneration of NADH and NCBs using g-C3N4 was developed. The highest regeneration yield of 48.32% was achieved with BANA+, outperforming the natural cofactor NAD+. A coupled photo- XenA system was explored. Among all the NCBs and NAD+, the highest conversion ratio of over 99% was obtained with BANA$^+$. After recycled for 8 times, g-C3N4 maintained over 93.6% catalytic efficiency.

Brief Biography

Prof. Ye NI is a Chang Jiang Distinguished Professor, Ministry of Education. Her expertise is biocatalysis and protein engineering. Prof. Ni is a Chief Scientist of National key research and development program. She has published over 100 original paper in top journals including JACS, ACS Catal. She has over 30 authorized Chinese patents and 6 US patents, and has received Science & Technology Progress Award from Ministry of Education of China. She also serves as an Associate Editor of Applied Biochemistry and Biotechnology.

FRISM-A Powerful Method for Protein Engineering

Qi Wu (吴起)
Zhejiang University

Abstract

Directed evolution has emerged as the most productive enzyme engineering method, with stereoselectivity playing a crucial role when evolving mutants for application in synthetic organic chemistry and biotechnology. In order to reduce the screening effort (bottleneck of directed evolution), an improved method dubbed focused rational iterative site-specific mutagenesis (FRISM), has been developed. It involves the identification of hotspots, which is usually rationalized through computer-aided technologies, followed by the generation of a focused mutant library. By reducing the size of the mutation library and the screening efforts, the FRISM strategy has been successfully employed in engineering a wide range of enzymes with enhanced catalytic performance, improved enantio-, regio-, and chemoselectivities.

Brief Biography

Wu Qi is a full professor of chemistry and principal investigator at Zhejiang University. His research mainly focuses on biocatalysis and protein engineering. In the past five years, he has published more than 40 papers as the first and corresponding author in journals such as *J. Am. Chem. Soc*., *Angew*. *Chem*. *Int*. *Ed*., and *Nature Commun*.

AI-BT-Chem Assisted 1C Assimilation

Yajie Wang (王雅婕)
Westlake University

Abstract

Biocatalysts offer advantages like self-regeneration, renewability, and environmental friendliness compared to traditional chemical catalysts. They are increasingly used in agriculture, chemical engineering, pharmaceuticals, and energy. McKinsey estimates that biomass manufacturing could account for 60-70% of chemical production, becoming a major economic market. Despite their potential, biocatalysts face challenges such as low activity and stability. Directed evolution has improved these aspects but is not a complete solution. Our lab has developed high-efficiency enzyme discovery tools and platforms, including "ESM-Ezy," a deep learning tool for identifying superior enzymes. This tool has discovered multi-copper oxidases with enhanced performance in dye decolorization and biotoxin degradation. We also develop a cooperative bioelectrochemical system featuring a bifunctional rhodium-based catalyst for simultaneous CO_2 and NAD^+ electroreduction for the first time, and enzymatic cascades for the direct synthesis of C3 and C4 from CO_2 in a “one pot” manner.

Brief Biography

Dr. Yajie Wang joined the Westlake University in the fall of 2021 and established WangSynbio lab. Wang lab focuses on integrating protein engineering, synthetic biology, chemistry, material sciences, and machine learning to establish a “Design-Build-Test-Learn” platform to design and construct artificial chemo-bio hybrid systems to harness the synthetic power from both chemistry and biology, and synthesize value-added compounds from the renewable sources, waste, and even air. Her research has been published in Nature, Nature Chemical Biology, ACS Catalysis, Chemical Review, Natural Product Report, etc. Dr. Wang was the recipient of Singapore National Scholar and the recipient of “35 Innovators Under 35 (TR35)” in China 2022.

Chemo-biocatalytic Synthesis of Valuable Chiral Pharmaceutical Intermediates

Bo Yuan (袁波)
Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences

Abstract

Biocatalysis is an important technology for green synthesis and aligns with the long-term goals set by China during the 14th Five-Year Plan. To achieve the biosynthesis of key pharmaceuticals and fine chemicals using biocatalysis, it is necessary to integrate chemoenzymatic, photoenzymatic, and metal-enzyme cascade reactions. Meanwhile, in recent years, enzyme engineering techniques combining directed evolution and rational design have developed rapidly, promoting the significant application of enzyme catalysis methods in green biomanufacturing industries. This talk will introduce the team's research achievements in the synthesis of chiral compounds, including the synthesis of axially chiral compounds via biocatalysis, chemoenzymatic cascade reactions, the directed evolution of enzymes for the synthesis of intermediates for cephalosporin antibiotics, and their industrial applications. With the advancement of directed evolution technology, the design of new enzyme-catalyzed reactions, and the emergence of new enzymatic processes, it is expected that full-chain R&D routes for important pharmaceutical intermediates will be established in the future, contributing to the development of China's green bioeconomy.

Brief Biography

Bo Yuan graduated from the University of Manchester with a PhD in biochemistry. She is currently an associate professor at Tianjin Institute of Industrial Biotechnology at Chinese Academy of Sciences. Previously, she obtained her BSc from Sun Yat-Sen University and MSc from the University of Manchester. She also worked in Xi'an Jiaotong University during 2016-2021. Her main research interests lie in the applications of protein engineering and chemoenzymatic cascade methodologies in biocatalytic synthesis of pharmaceutical intermediates. In the recent 5 years she has been hosting more than 5 national and provincial programs including the National Natural Science Foundation of China General and Youth programs and Tianjin Synthetic Biotechnology Innovation Capacity Improvement Project. She has published more than 20 papers, and 2 book chapters.

Constructing Microbial Cell Factories to Produce Pharmaceuticals

Qipeng Yuan (袁其朋)
Beijing University of Chemical Technology

Abstract

The production of pharmaceutical chemicals plays an important role in ensuring people's health, but traditional production processes have problems such as large pollution emissions and low efficiency. Green biomanufacturing of pharmaceutical chemicals is an important pathway for achieving sustainable development of human society. High-efficiency cell factories are the core of green biomanufacturing and will greatly promote the development of the bioeconomy. This report introduces the scientific and technical problems and challenges in the current construction of cell factories, and presents new technologies and strategies for constructing high-efficiency cell factories from the perspectives of the discovery and application of new enzyme functions, the design and construction of non-natural pathways, the enhancement of cell factory synthesis capacity through drive force, the construction of stable self-regulating co-culture systems, and the principles and applications of quorum sensing regulation. It also demonstrates the infinite potential of synthetic biology through the construction of cell factories for three-seven-sulfate and paracetamol, and the industrial application of arbutin, to provide strategies for the green biomanufacturing of pharmaceutical chemicals.

Brief Biography

Qipeng, Yuan, Distinguished Professor of Changjiang Scholars of the Ministry of Education, winner of the 11th China Youth Science and Technology Award, one of the top 100 Leading Talents in Beijing. The main research areas are synthetic biology and metabolic engineering, large-scale preparation of high purity natural products and study of their bioactivities. In recent years, it has undertaken key research and development tasks of the Ministry of Science and Technology, key and general programs of the National Natural Science Foundation, provincial and ministerial level and enterprise cooperation projects. He has published more than 300 SCI papers as the corresponding author, and authorized more than 60 PCT and Chinese invention patents. A number of results have been achieved in industrial production, creating good economic benefits. As the first contributor, he won 1 second prize of National Science and Technology Progress, 1 special prize, 2 first prizes and 2 second prizes of provincial and ministerial science and technology progress.

Reprogramming Methylotrophic Yeast for Chemical Overproduction from Methanol

Yongjin Zhou (周雍进)
Dalian Institute of Chemical Physics, Chinese Academy of Sciences

Abstract

Methanol is an ideal feedstock for bio-manufacturing that can be beneficial for global carbon neutrality. However, the toxicity of methanol limits the efficiency of methanol metabolism toward biochemical production, and it is still challenging in engineering this non-conventional yeast due to serious lack of genetic editing tools and unclear methanol metabolism. In this talk, we will show our recent progress in establishing CRISPR-Cas9 based genome editing tools and enhancing the homologous recombination in methylotrophic yeast *Ogataea polymorpha* and *Pichia pastoris*. With this genetic platform, we tried to engineer cellular metabolism for fatty acid production from methanol. We found that engineering overproduction of free fatty acids (FFA) from sole methanol resulted cell death with a decreased cellular phospholipid in O. polymorpha, and the cell growth was restored by adaptive laboratory evolution (ALE). Multi-moic analysis showed that phospholipid metabolism homeostasis is very essential for methanol tolerance. Enhancing the methanol tolerance and engineering cellular metabolism enabled methanol biotransformation for high level production of a variety of chemicals such as FFA (20 g/L) and lactic acids (35 g/L).

Brief Biography

Yongjin Zhou is a Chair Professor at Dalian Institute of Chemical Physics, Chinese Academy of Sciences. His research areas include synthetic microbiology for cell factory construction, yeast genetics and metabolic engineering. He co-authored more than 100 peer reviewed papers on prestigious journal such as Cell, Nature Energy, Nature Metabolism, Nature Chemical Biology, JACS, PNAS, Nature Communications with >6800 citations and hold 15 patents. He serves as Editor-in-Chief of Biotechnology Journal, Associate Editor of Synthetic and Systems Biotechnology and editor board member for 5 other journals. He was honored several awards includes Outstanding Young Scholar Grant from NSFC (2024), Agilent “ACT-UR” Award (2023), and Excellent Youth Scholars from NSFC (2019) etc.

Developing The Reading and Writing Toolbox for Nucleic Acid Modifications

Guanzheng Luo (骆观正)
Sun Yat-sen University

Abstract

Nucleic acids harbor over 150 distinct chemical modifications, expanding their functional roles beyond the genetic code. These "epigenetic codes" are implicated in diverse biological processes, ranging from bacterial immunity to mammalian development, highlighting the importance of deciphering their intricate functions. Recent advances in third-generation nanopore direct sequencing (DRS) have revolutionized the field by enabling simultaneous detection of canonical and modified bases across long DNA/RNA molecules. This disruptive technology provides unprecedented opportunities for studying epigenetic modifications at single-molecule resolution. We have developed a high-precision algorithm for identifying nucleic acid modifications based on DRS data, generating detailed single-molecule modification maps. This approach has been successfully applied to investigate various biological processes across multiple species, providing valuable insights into the dynamic nature of epigenetic regulation. Furthermore, we are actively developing novel tools for "writing" modifications, enabling the targeted installation or editing of nucleic acid modifications in vivo. These tools offer the ability to modulate biological functions and track RNA and DNA dynamics with spatiotemporal precision. The reading and writing technologies provide a powerful toolbox for understanding the fundamental roles of nucleic acid modifications and unlocking their application potential.

Brief Biography

Dr. Luo Guanzheng is currently a professor at the School of Life Sciences, Sun Yat-sen University. He received his Bachelor's degree in Biomedical Engineering from Southeast University and his bioinformatics PhD from the Institute of Genetics and Development, Chinese Academy of Sciences. Following his doctoral studies, he pursued postdoctoral research at the University of Chicago before joining Sun Yat-sen University in 2017. His research focuses on understanding the fundamental principles of genome coding and complex life phenomena through the lens of nucleic acid modifications. His work is characterized by a multidisciplinary and methodology-driven approach, integrating theoretical innovation with scientific discovery. He has contributed to the field by developing novel reading and writing technologies to systematically investigate the biological significance of diverse DNA and RNA modifications. He has published numerous articles as a corresponding author in prestigious journals, including *Nature Methods*, *Science Advances*, and *Cell Research*.

Rapid Genome Evolution of the *Corynebacterium Glutamicum* Via the Dual Genetic Level Editing

Meijuan Xu (徐美娟)
Jiangnan University

Abstract

As an industrial microorganism, *Corynebacterium glutamicum* plays a pivotal role in the amino acid industry. This study proposes a practical, efficient, and controllable evolutionary tool (oMut-Cg^{ts}) for *Corynebacterium glutamicum* based on dual genetic level modification engineering, which facilitates the creation and optimization of *C. glutamicum* cell factories. Initially, endogenous RNA polymerase α-subunit and DNA helicase Cgl0854 were utilized as "docks" for cytosine deaminase (pmCDA1) in transcription and replication level modification engineering, respectively. This significantly enhanced the genomic mutation rate, demonstrating that the localization of pmCDA1 around transient ssDNA is a necessary condition for achieving efficient genomic mutations. Subsequently, the combined modification and optimization of both genetic levels elevated the spontaneous mutation rate of *C. glutamicum* by 1.02×10^4-fold, while maintaining a relatively low background mutation rate (approximately 2.62-fold that of the wild-type strain). This represents the highest mutation rate reported so far for *C. glutamicum* evolutionary tools. Whole-genome sequencing of the mutation library revealed the "breadth" and "depth" of genome mutations mediated by oMut-Cg^{ts}, which achieved uniform and efficient C:G → T:A transitions across the entire genome without evident strand preference or base background bias. Furthermore, the rapid evolution of stresses (low pH, oxidative stress, and high ethanol concentration) tolerance phenotypes mediated by oMut-Cg^{ts} demonstrates the tool's powerful capabilities in multi-dimensional bioengineering, including rapid phenotype evolution, gene function mining, and protein evolution

Brief Biography

Professor Xu Meijuan, from the School of Biological Engineering at Jiangnan University, has presided over more than ten national and provincial projects and been selected for the National Special Support Program for high-level Talents Youth Top Program. Professor Xu's research primarily focuses on synthetic biology and industrial enzyme engineering, with a specialization in constructing microbial cell factories that efficiently produce target amino acids and their high-value derivatives.

Cisencoder: Integrating Massively Parallel Reporter Assays and Artificial Intelligence for *De Novo* Design of Cis-Regulatory Elements

Yuwen Liu (刘毓文)
Institute of Agricultural Genomics, Chinese Academy of Agricultural Sciences

Abstract

In synthetic biology, artificially designed cis-regulatory elements (CREs), such as enhancers, can be used to precisely control the yield of target products, playing a critical role in cost reduction and efficiency enhancement. However, our understanding of CRE nucleic acid syntax remains limited, and *de novo* design of these elements is still in its infancy. To address this challenge, we are developing CisEncoder, a platform that integrates Massively Parallel Reporter Assays (MPRAs), which provide high-quality, large-scale quantification of CREs, with DREAM (DNA cis-Regulatory Elements with controllable Activity design platforM), an innovative deep learning framework designed to unravel the nucleic acid syntax of CREs. To demonstrate the capabilities of CisEncoder, we achieved state-of-the-art sequence-based enhancer activity prediction in Drosophila S2 cells and identified key sequence features that are crucial for strong enhancer activity. Leveraging this predictive power, we designed DreaMer001, a synthetic enhancer with 3.6 times the activity of the strongest natural enhancer in the Drosophila genome. Remarkably, DreaMer001 not only showed high activity in Drosophila S2 cells but also demonstrated significant activity across multiple species' cell lines. In mammals like humans, mice, and pigs, DreaMer001 averaged over twice the activity of the CMV enhancer. In SF9 cells, its activity was 15.7 times higher than the Hr5 enhancer, and it exhibited 7.6 times and 26.6 times higher activity than the CMV enhancer in chicken DF1 cells and fish spermatogonial cells, respectively. Additionally, using MPRA-derived data, we developed the ultra-strong silencer DreaMer002, which reduced gene expression by 44.7-fold. Our study not only introduces an efficient platform for enhancer design but also establishes a general framework applicable to other CRE types, offering significant potential for designing gene expression circuits in synthetic biology.

Brief Biography

Yuwen Liu is a Principal Investigator, PhD supervisor, and Deputy Director of the Animal Genome Research Center at the Agricultural Genomics Institute at Shenzhen (AGIS), Chinese Academy of Agricultural Sciences. Dr. Liu earned his bachelor's degree from Tsinghua University in 2006 and completed his PhD at the University of Chicago in 2014. Since joining AGIS in 2019, Dr. Liu has been recognized with several prestigious awards, including the National Major Talent Project (Youth), Guangdong High-Level Talent (Youth), “Agricultural Leading Talent” by the Chinese Academy of Agricultural Sciences, Shenzhen High-Level Talent, and the Shenzhen "Youth May Fourth Medal." With over 20 years of research experience in genetics and functional genomics, Dr. Liu specializes in developing experimental and computational methods to decipher the regulatory code of natural non-coding cis-regulatory elements (CREs) and in the de novo design of synthetic CREs. His research has been published in leading journals such as Genome Biology, American Journal of Human Genetics, JACS, Bioinformatics, and Genetics Selection Evolution, and his work has been cited over 1,700 times. Dr. Liu is also actively advancing the industrial application of the recently developed CisEncoder platform, which provides a comprehensive suite of synthetic CREs tailored to fine-tune gene expression in synthetic biology.

Design Strategy for "Genetic Software" Based on Engineered Tristate Logics

Jiawei Shao (邵佳伟)
Zhejiang University

Abstract

Bio-computation strictly follows traditional design principles of digital electronics, which could reach their limits when assembling gene circuits of higher complexity. By creating genetic variants of tristate buffers instead of using conventional logic gates as basic signal processing units, we introduce a tristate based logic synthesis (TriLoS) framework for resource-efficient design of multi-layered gene networks capable of performing complex Boolean calculus within single-cell populations. This sets the stage for simple, modular, and low-interference mapping of various arithmetic logics of interest and an effectively enlarged engineering space within single cells. We not only construct computational gene networks running full adder and full subtractor operations at a cellular level but also describe a treatment paradigm building on programmable cell-based therapeutics, allowing for adjustable and disease-specific drug secretion logics in vivo. This work could foster the evolution of modern biocomputers to progress toward unexplored applications in precision medicine.

Brief Biography

Jiawei Shao is a young Principal Investigator (PI) at the International School of Medicine, Zhejiang University, and the Fourth Affiliated Hospital of Zhejiang University School of Medicine. He employs synthetic biology techniques to construct gene switches by leveraging the transcription initiation, translation processes, and post-translational modifications of gene expression. Shao designs artificial gene circuits and develops smart cell and gene therapies to enhance the precision and effectiveness of disease treatment. His primary research outcomes have been published in international academic journals such as Cell, Science Translational Medicine, PNAS, Cell Research, Science, Science Advances, and Nature Communications, and he has been granted over 10 PCT and Chinese patents.

Synthetic Designer Bacteria-Based Anti-Tumor Therapies with Customizable Outputs and Precise Dosage Control

Ningzi Guan (管宁子)
East China Normal University

Abstract

Bacteria-based therapies offer significant potential for cancer treatment due to their ability to selectively colonize tumors and deliver therapeutic proteins. However, clinical application has been limited by the lack of safe, tunable systems to regulate therapeutic protein expression. Recent advances in remote-control technologies have enabled precise spatial and temporal control of these therapies. We developed two distinct platforms to address this need. The first is a sono-activatable gene circuit (SINGER), based on the thermosensitive repressor TlpA39. In various tumor models, engineered bacteria expressing apoptotic Azurin and the immune checkpoint inhibitor PD-L1 nanobody, when activated by US, significantly suppressed tumor growth. The second platform employs a NIR-mediated PadC-based photoswitch (NETMAP) system, which controls protein expression in engineered bacteria via NIR light. In murine tumor models with varying immunogenicity, bacteria colonized tumors and selectively produced immunomodulators and cytotoxic proteins. In highly immunogenic A20 lymphoma models, NIR-induced CTLA-4 and PD-L1 nanobodies enhanced adaptive immune responses, while in low-immunogenic colon and breast cancer models, NIR-induced Azurin and ClyA triggered apoptosis. These platforms demonstrate precise, remote-controlled bacterial therapies for cancer, offering customizable therapeutic outputs with enhanced safety and efficacy.

Brief Biography

Dr. Ningzi Guan is an Associate Researcher at the School of Life Sciences, East China Normal University. She earned her Ph.D. in Fermentation Engineering from Jiangnan University in 2016 and conducted postdoctoral research at the Georgia Institute of Technology from 2016 to 2018. Since 2018, she has been working at East China Normal University. Her research focuses on the application of metabolic engineering and microbial synthetic biology in disease treatment, with particular emphasis on the development and application of probiotic sensors, optogenetics, and cancer immunotherapy. Her work has been published in Nature Communications, Cell Reports Medicine, Science Advances, Nature Biotechnology, ACS Synthetic Biology, and other journals.

Efficient Biosynthesis of Poly(3-Hydroxybutyrate-*Co*-Lactate) in Metabolically Engineered *Escherichia Coli*

Hui Wu (吴辉)
Dalian University of Technology

Abstract

With the wide application of traditional plastic products, the harm of "white pollution" caused by these products has become increasingly serious. Application of bio-based degradable plastics are the main solution for plastic pollution. Compared to petroleum-based plastics, bio-based degradable plastics have a lower carbon footprint and contribute to a more sustainable life cycle. Polyhydroxyalkanoates (PHAs) synthesized by microorganisms have excellent degradation properties and are important alternatives to petroleum-based plastics. Poly(3-hydroxybutyrate-*co*-lactate) [P(3HB-*co*-LA)] is a high-molecular-weight biomaterial with excellent biocompatibility and biodegradability. The material properties of P(3HB-*co*-LA) are mainly determined by its lactate fraction. Here different strategies of metabolic engineering were applied in this study, including electron transfer chain based metabolic transistor regulation, engineered LA-CoA biosynthesis, and cofactor engineering. The lactate fraction in P(3HB-*co*-LA) synthesized by the engineered strain ranged from 6.2 to 52.84 mol%. Furthermore, when a 5 L bioreactor was used for fermentation utilizing xylose as a carbon source, the titer of P(3HB-*co*-41.3 mol% LA) reached 8.57 g/L.

Brief Biography

Dr. Hui Wu is a professor in Dalian University of Technology (DUT), China, and a member of State Key Lab of Bioreactor Engineering of China. He received Ph.D in East China University of Science and Technology (ECUST) in 2009. Then he joined Shanghai Institutes for Biological Sciences, CAS (2009-2011) and Department of Bioengineering, Rice University (2011-2014) as Postdoc. He joined ECUST in 2014 and moved to DUT in 2024. His recent research focuses on microbial metabolic engineering, metabolic regulation, and synthetic biology. He published more than 60 papers. He also serves the scientific community as an editor of international journals such as *Frontiers in Bioengineering and Biotechnology, Journal of Industrial Microbiology & Biotechnology, Journal of Chemical Technology and Biotechnology, Bioresources and Bioprocessing*, and is the associate editor of *Frontiers in Microbiology* and *BioDesign Research*.

Construction of methanol-tolerant yeast cell factories and synthesis of fine chemicals

Shuangyan Han (韩双艳)
South China University of Technology

Abstract

Yeast can be empowered to produce a variety of chemicals through metabolic engineering and synthetic biology, thereby aiding in the sustainable creation of bioproducts via a clean and renewable approach. Methanol stands out as both a copious and eco-friendly substance, and as a viable candidate for clean energy. The development of microorganisms that can thrive solely on methanol make it is possible to circumvent the food issue of competition with people. *Pichia pastoris* is one of the natural methylotrophic yeast. However, poor tolerance at higher methanol concentrations as well as low carbon atom economy caused by methanol dissimilating into CO_2 have become bottlenecks restricting its efficient utilization and conversion of methanol. Addressing these challenges, our group used kinds of strategies such as knockout of the dissimilation pathway, strengthening of methanol assimilation pathway, along with the construction of the substrate channels and rebalancing of cofactors. These modifications prompted *P. pastoris* into more efficient chassis cells, elevating its methanol utilization by 10%-30%. Furthermore, through iterative evolution and multi omics combination, the high tolerance mechanism of evolutionary strains was analyzed while multiple membrane related tolerance elements were excavated, which helps the construction of multiple high tolerant engineering yeast strains growing well in 10% liquid methanol medium. Based on the above research, our group successfully constructed and obtained several *P. pastoris* cell factories using methanol as the sole carbon source, which were used to synthesize of multiple high-value chemicals high-efficiency, such as linolenic acid (72.2 g/L) and β-arbutin (128.6 g/L), etc.

Brief Biography

Han Shuangyan, a female scholar born in 1976, holds the distinguished title of level-3 professor as well as serving as a doctoral supervisor at South China University of Technology. Her research endeavors focus on microbial utilization and efficient conversion of methanol, microbial cell factory construction and fine chemicals biosynthesis and so on. In the past five years, she has published upwards of 30 scholarly articles in esteemed journals such as *Green chemistry, Food Hydrocolloids, International Journal of Biological Macromolecules*, etc., and authorized more than 20 patents. She has presided over more than 10 scientific research projects, including the National Key R&D Program of China, the National Natural Science Foundation of China, and the Key Technologies R&D Program of Guangdong Province. The book "Enzyme Engineering" edited by her has been awarded the "14th Five Year Plan" undergraduate planning textbook for general higher education by Science Press. She was also ever honored with the China Outstanding Patent Award and the Second Prize of Guangdong Provincial Science and Technology Progress Award.

Plant-based Meat Processing: Fundamentals, Progress, and Industrialization

Xiaonan Sui (隋晓楠)
Northeast Agricultural University

Abstract

With the concepts of sustainable development and "big food" gaining popularity, plant-based meat, as a typical representative of plant-based food, have been widely favored by consumers and is gradually becoming a major trend in the future development of the food industry. Accordingly, following the current research progress in the field of plant-based meat at home and abroad, this report will summarize and discuss the key scientific issues that need to be broken through in the field of plant-based meat, and provide an outlook on the future development of plant-based meat.

Brief Biography

Dr. Xiaonan Sui, a full professor at the College of Food Science, Northeast Agricultural University, is also the vice dean of the Heilongjiang Green Food Science Research Institute. He earned his Ph.D. from the National University of Singapore (NUS) and is a recipient of the Distinguished Young Scientists Fund and Excellent Young Scientists Fund from the National Natural Science Foundation of China (NSFC). Dr. Sui's primary research focuses on soy protein, specifically molecular structure analysis, conformational relationships, and regulatory mechanisms. His goal is to uncover the fundamental scientific principles governing protein molecule alteration, assembly, and rearrangement in food processing to promote green processing and high-value utilization of soy proteins. He has received research grants from various organizations, including NSFC, the Ministry of Human Resources and Social Security's High-level Talents Fund, the Fok Ying Tung Education Foundation's Young Teachers Fund, and the China Association for Science and Technology's Young Talent Promotion Project. Dr. Sui serves as an associate editor for *Sustainable Food Proteins* and is a member of the academic editorial board for *Journal of Food Biochemistry*, *Food Science* and *Future Food Science*. He has authored nearly 200 SCI papers published in respected journals including *Biomaterials*, *Annual Review of Food Science and Technology*, and *ACS Sustainable Chemistry & Engineering*, with nearly 6000 citations to his name. He has also published three English books. His exceptional research contributions have earned him numerous awards, including the Distinguished Young Scientists from Chinese Institute of Food Science and Technology (CIFST), Young Scientist Award from the Division of Agricultural and Food Chemistry of the American Chemical Society (ACS), the Young Scientist Award from the International Union of Food Science and Technology (IUFoST), the Young Scientist Research Award from the American Oil Chemists' Society (AOCS), the Springer Thesis Award.

Synthetic Biology-driven Alternative Protein/Fatty Acids Manufacturing

Demao Li (李德茂)
Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences

Abstract

With the improvement of living standards and the growth of the global population, the consumption of protein continues to increase, which puts enormous pressure on the global food supply. In order to meet the dietary needs of global consumers, it is necessary to produce protein and other food resources in a sustainable manner to address the severe challenges brought by population growth, climate change, and other environmental factors. Microbial protein has the advantages of high production efficiency, no occupation of farmland, and the ability to use one carbon gas as raw material. It is a sustainable and low-carbon protein manufacturing method with unique advantages in replacing proteins. It is an important path to achieve "protein demand from microorganisms" through biotechnology, which can effectively fill the rigid demand for edible and feed protein in China. Oils and fats are important food ingredients that play a crucial role in food flavor, texture, and other aspects. The report introduces in detail the research progress in cell factory construction, process optimization, safety evaluation and food technology of microbial protein/oil production in Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences, and puts forward its key bottleneck problems and future solutions.

Brief Biography

Demao Li, Ph.D., a professor of the Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences, doctoral supervisor, PI of the Industrial Biosystem Engineering Research Group, a candidate for a distinguished research post of the Chinese Academy of Sciences, a member of the Youth Innovation Promotion Association of the Chinese Academy of Sciences, coordinator of the bioenergy joint research group of COMSATS Industrial Biotechnology Joint Center, a member of the Industrial Fermentation Sub technical Committee of the National Technical Committee for Food Industry Standardization, a member of the Beijing Tianjin Hebei Food Nutrition, Health and Safety Innovation Platform, and an editorial board member of the magazine Fermentation. Dedicated to low-carbon biomanufacturing research of microbial proteins/oils. Hosted more than 20 provincial and ministerial level projects, obtained more than 20 authorized national invention patents, and published over 100 SCI papers in internationally renowned journals such as Applied Catalysis B: Environment and Energy, Nature Communication, Biotechnology Advances, Journal of Agricultural and Food Chemistry, Sustainable Energy&Fuels, Reviews in Aquaculture, etc. As the main contributor, won the second prize of the National Oceanic Administration Ocean Engineering Award and the second prize of the National Oceanic Administration Ocean Science and Technology Award.

Biological Upcycling of Waste for Sustainable Development

Jinjin Diao (刁进进)
Washington University in St. Louis

Abstract

More than 70 million tons of poly(ethylene terephthalate) (PET) are manufactured worldwide every year. The accumulation of PET waste has become a global pollution concern, motivating the urgent development of technologies to valorize post-consumer PET. The development of chemocatalytic and enzymatic approaches for depolymerizing PET to its corresponding monomers opens up new opportunities for PET upcycling through biological transformation. However, there are only a handful of reports demonstrating non-model microbes capable of growing on both TPA and EG generated from PET as sole carbon sources. Moreover, the scarcity of synthetic biology tools specifically designed for these non-model species, limiting the development of the corresponding microbial cell factories for upcycling of the post-consumer PET. To overcome the aforementioned limitations, we performed strain screening to discover a Rhodococcus strain RPET (RPET) that can grow well on the alkaline hydrolysis products of PET as the sole carbon source. Notably, this strain can grow on a mixture of TPA and EG at extremely high concentrations (up to 0.6M) and high osmolarity resulting from alkaline hydrolysis and pH neutralization. The resultant media supported RPET's growth without any purification and sterilization step except for their dilution. To expand the repertoire of bioproducts from post-consumer PET, we described the development of potent genetic tools in RPET, including: (1) two inducible and titratable expression systems for tunable gene expression, (2) Serine Integrase based Recombinational Tools (SIRT) for genome editing. Using these tools, we systematically engineer the RPET strain to ultimately establish microbial supply chains of multiple chemicals, producing the highest titers of chemicals ever reported thus far, including lycopene, lipids, and succinate, from post-consumer PET waste bottles (e.g., 22.6 mg/L of lycopene, about 10,000-fold higher than that of the wild-type strain). This work highlights the great potential of plastic upcycling as a generalizable means of sustainable production of diverse chemicals.

Brief Biography

Dr. Jinjin Diao is a Senior Scientist in the Department of Energy, Environment, and Chemical Engineering at Washington University in St. Louis. Dr. Diao received his PhD from Tianjin University in Biochemical Engineering in 2019. In his PhD, Dr. Diao demonstrated how microbes can be reprogrammed to produce value-added chemicals through synthetic biology. Dr. Diao finished his postdoc training under Prof. Tae Seok Moon at Washington University in St. Louis, where he focused on elucidating the metabolic and regulatory mechanisms of aromatic catabolism in Rhodococcus opacus PD630. Now, Served as CO-PIs of three US federal funded grants, Dr. Diao mainly focused on the development of robust microbial chassis for the goal of "Green Biomanufacturing" by using alternative feedstocks. So far, Dr. Diao has published 25 peer-reviewed papers, and of them, 8 first-author papers have been published in the prestigious journals including Cell Reports, Nature Communications Biology, Metabolic Engineering, et al. In recognition of his outstanding research, he has received Johns Hopkins University Conference Travel Fellowship and IMES Travel Award, been invited to join the Early Career Reviewer Board of the BMC journals in Biotechnology, and also been invited to give oral presentations in multiple international conferences.

Biosynthesis Strategies of Sweetener Rebaudioside D

Yuanyuan Ma (马媛媛)
Tianjin University

Abstract

Rebaudioside D (Reb D) is a promising sweetener due to its zero calorie and high sweetness, but its content in stevia leaves is extremely low. Here, I will briefly discuss two biological conversion strategies established to convert the low-value Rebaudioside A to Reb D. The first strategy involves constructing an expression system for glycosyltransferase EUGT11 using *Pichia pastoris* and *E. coli*. The effects of different hosts on the activity of the recombinant enzyme were examined. Reb D was synthesized in a one-pot reaction using the engineered *Pichia pastoris*. A two-step temperature control method was subsequently developed, achieving a conversion rate of 95.31% at 28/35 °C. The second strategy involves identifying a new enzyme StUGT, which can convert Reb A to generate Reb D. The characteristics of this enzyme were characterized, and a cell catalytic system was developed using the StUGT *E. coli* strain. The highest yield of 98.08% was obtained by enhancing cell permeability and optimizing conditions statistically. A cascade process was further established using this StUGT strain and *E. coli* expressing sucrose synthase to reduce costs by replacing expensive UDPG with sucrose. These studies pave the way for cost-effective and sustainable synthesis of scarce, high-value sweeteners.

Brief Biography

Dr. Ma received Ph.D. degree from Nankai University in Dec 2006. She joined "Biomass conversion Lab, R&D Center for Petrochemical Technology, Tianjin University" as an assistant professor in Mar 2007, and then she became an associate professor and the head of biomass conversion Lab in 2012. In 2012, she also worked as a visiting scholar in the Industrial Biotechnology Lab at the Institute of Chemical & Engineering Sciences (ICES) in Singapore for one month. Subsequently, she worked at the School of Marine Science and Technology at Tianjin University. Her research interest focuses on synthetic biology, biocatalysis and exploration of functional genes from marine. She has published papers in journals including Metab Eng, Biotechnol Biofuels, Int J Biol Macromol, Applied Microbiol Biotechnol, and Front Microbiol. And she has undertaken numerous National level research projects as well as the projects from central State-owned enterprises.

Establishing cell factories for value-added food protein bioproduction

Yanfeng Liu (刘延峰)
Jiangnan University

Abstract

Cell factories-based efficient biosynthesis of value-added food protein is a sustainable approach for protein supply. However, efficient protein expression tools and chassis cell hamper economic protein bioproduction in large-scale. In this talk, recent advances in developing protein expression regulatory elements and strategies for engineering production host are discussed. Specifically, continues evolution and antibiotic free-recombinant protein expression tools are developed for improving protein expression regulatory tools. Next, single stranded DNA annealing protein-guided CRISPR genome editing method and protein secretory pathway engineering strategies are developed for modifying chassis cell for protein production. Finally, the developed protein expression regulatory elements and strategies for engineering production host are used for establishing cell factories for bioproduction of value-added food protein, such as -lactalbumin and ovalbumin. The proposed protein expression tools and engineering approach may be useful for enhancing bioproduction of other food protein.

Brief Biography

Yanfeng Liu is a Professor of School of Biotechnology in Jiangnan University. He focuses on using synthetic biology tools to construct cell factories for biosynthesis of important nutraceuticals and food ingredients. As the first or corresponding author, his research has been published in journals such as Nature Chemical Biology, Nature Communications and Metabolic Engineering. As the first inventor, 15 invention patents were authorized. He is the project leader of National Excellent Youth Fund, National Natural Science Foundation. He is currently a member of Industrial Microbiology Committee of the Chinese Society of Microbiology and an editorial board member of Frontiers in Bioengineering and Biotechnology.

Construction of Bioinspired Multi-enzyme Molecular Machines and the Application for Functional Sugars Biosynthesis

Wei Liu (刘伟)
Nanjing Tech University

Abstract

To address the challenges of multi-enzyme adaptation and coupling in the current enzymatic synthesis of functional sugars, this work developed various substrate-channeling and compartmentalized multi-enzyme molecular machines based on protein-peptide pairs, self-assembling proteins, nucleic acids, and phase-separated proteins. These molecular machines provided mild and efficient assembly tools for multi-enzyme cascade catalysis, which were applied to the enzymatic preparation of typical functional sugars, including trehalose, tagatose, and psicose, achieving enhanced multi-enzyme catalytic efficiency.

Brief Biography

Wei Liu, Entrepreneurship and Innovation Doctoral Talent of Jiangsu Province, associate professor at college of Food Science and Light Industry, Nanjing Tech University. His primary research focuses on enzyme engineering and synthetic biology, with a particular emphasis on the construction of in vivo/in vitro multi-enzyme cascade systems and the creation of cell factories for food nutrients. He has successively led several national and provincial/ministerial projects, including the Youth Fund Project of the National Natural Science Foundation of China and subprojects of the National Key Research and Development Program. He has published over 20 papers in academic journals, including Metabolic Engineering, Food Research International, Journal of Agricultural and Food Chemistry, and applied for 14 invention patents and 3 PCT patents. His research achievements have garnered one First Prize for Scientific and Technological Progress awarded by the China National Light Industry Council and one Special Prize for Scientific and Technological Progress awarded by the China General Chamber of Commerce.

Current Situation and Future Prospect of the Bio-manufacturing on Human Milk Oligosaccharides

Zhengqiang Jiang (江正强)
China Agricultural University

Abstract

The strategy for “Healthy China” not only promotes the development of healthy industry, but also brings the golden opportunity for the development of functional oligosaccharides. Human milk oligosaccahrides (HMOs) as a kind of oligosaccharides naturally exist in human milk. Their monosaccharide compositions are simple, while the structures are complex. HMOs play an important role in the growth and development of infants. USA and European Union have approved seven HMOs as the novel foods to be applied in infants formula. So far, the global market of HMOs has reached up to 380 million dollars. Chemical synthesis and biosynthesis can be used to produce HMOs. The biosynthesis including enzymatic and whole cell synthesis is the principal method. As the representative HMOs, the productivity of 2'-fucosyllactose (2'-FL) and lacto-N-neotetraose (LNnT) has been more than 100 g/L via the whole cell synthesis based on precision fermentation. With the aim to facilitate the industrial development of HMOs, our research team has focused on the production of HMOs using enzymatic method and whole cell synthesis. The novel α-L-fucosidases, β-N-acetylhexosaminidases, and β-galactosidases were exploited to produce 2'-FL, 3-fucosyllactose (3-FL), LNnT, and lacto-N-tetraose (LNT) via enzymatic method. Many of them were modified to increase the yield. Also, the novel α-1,2-fucosyltransferases and β-1,4-galactotransferases were introduced to the engineered Escherichia coli for the efficient synthesis of 2'-FL, 3-FL, difucosyllactose (DFL), LNT, and LNnT. In the future, we will enhance the study on the biomanufacturing and downstream purification of HMOs, which will provide technological and theoretical foundation for the industrial development of HMOs.

Brief Biography

Jiang Zhengqiang, member of the Communist Party of China, born in June, 1971. He was graduated from China Agricultural University with doctorate in Food Science and gained “One Hundred Outstanding Doctoral Dissertation” in 2001. Since 1995, he worked in China Agricultural University and was promoted as Professor in 2004. He has been the Winner of “The National Science Fund for Distinguished Young Scholars” and the distinguished professor of “The Yangtze River Scholar”. Moreover he has been selected as young and middle-aged expert contribution to “The National People’s Ten Thousand Talents Program”, the leading talent of “The National Ten Thousand People Plan”, and received the state council special allowance. Also, he has won “The Young and Middle-Aged Leading Talents in Technological Innovation” of the ministry of science and technology, and obtained the agricultural bioprocessing technology innovation team” of “Outstanding Agricultural Research Talents and Innovation Teams” approved by the ministry of agriculture. In addition, he was served as the president of “Agricultural Processing Branch of Chinese Society of Agricultural Engineering”, the vice president of “Enzyme Branch of Chinese Society of Food Science and Technology” and “Enzyme Preparations and Prebiotics Branch of Chinese Fermentation Industrial Association”. The editorial board member of more than ten journals, such as “Food Chemistry”, “Food Science”. He focus on food biotechnology, food enzyme, and fermentation engineering. More than 300 academic papers (including more than 200 SCI papers) and 6 monographs were published during the past 20 years. More than 70 invention patents were authorized. He has won two awards for “Second Class Prizes of National Science and Technology Progress (named first and second)”, one award for “Second Prize of National Science and Technology”, and one award for “China Youth Science and Technology”, two awards for “Guanghua

Engineering Science and Technology Prize", and two international academic awards.

Yeast Metabolism Adaptation for Efficient Terpenoids Synthesis Via Isopentenol Utilization

Wenyong Lou (娄文勇)
South China University of Technology

Abstract

Terpenoids, also known as isoprenoids, are abundant natural compounds found in animals, plants, and microorganisms, playing a crucial role in maintaining normal biological activities. These compounds have extensive applications, including use in fragrances, biofuel, colorants, micronutrients, cosmetics, and medicine. However, conventional extraction methods are insufficient to meet the growing market demand for terpenoids. Synthetic biology technology has enabled the design and construction of microbial cell factories, offering a sustainable and scalable solution for terpenoid production. Several valuable terpenoids have been successfully synthesized by engineered microorganisms such as retinol, carotenoid, ursolic acid, and rebaudiosides. Recently, a two-step isopentenol utilization (IU) pathway relying solely on ATP as the cofactor has been proposed as an alternative to the mevalonate (MVA) pathway, streamlining the synthesis of the common terpenoid precursors. Herein, we find that isopentenol inhibits energy metabolism, leading to reduced efficiency of the IU pathway in *Saccharomyces cerevisiae*. To overcome this, we engineer an IU pathway-dependent (IUPD) strain, designed for growth-coupled production. The IUPD strain is compelled to enhance the ATP supply, essential for the IU pathway, and incorporates a high-throughput screening method for enzyme evolution. The refined IU pathway surpasses the MVA pathway in synthesizing complex terpenoids. Our work offers valuable insights into developing growth-coupled strains adapted to efficient natural product synthesis.

Brief Biography

He is currently Vice president and Deputy Party Secretary of the School of Food Science and Engineering, South China University of Technology. He received numerous honors including the National Excellent Doctoral Dissertation Award, the National Outstanding Youth Science Foundation (the first batch of Outstanding Youth), the Ministry of Education's New Century Excellent Talents Award, and the Leading Talent of Guangdong Province's "Hundred, Thousand, and Ten Thousand Talents Project". In 2023, ranked among the top 100,000 scholars globally for academic impact (Lifetime Academic Influence Rankings).Research focuses on food biotechnology, regulation and application of biocatalytic processes, exploration and biomanufacturing of food functional factors, and encapsulation and targeted delivery of nutrients. Led and participated in over 30 research projects, including the National Key R&D Program, the National Natural Science Foundation of China, the Guangdong Key R&D Program, and industry-university collaborative projects. Published over 150 SCI papers in prestigious journals such as Nature Communications, Microbiome, Coordination Chemistry Reviews, Biotechnology Advances, and Small, with more than 6,000 citations and an h-index of 46. Serves as associate editor for Frontiers in Bioengineering and Biotechnology and Frontiers in Microbiology, and on the editorial boards of Bioresources and Bioprocessing and the Chinese Journal of Food Science. Holds 56 Chinese invention patents, 3 international PCT patents (USA), and has transferred 10 patents to industry, with many research outcomes successfully commercialized.

Crystaline Immobilization Platform for Biocatalysis

Yao Chen (陈瑶)
Nankai University

Abstract

Biomacromolecules, such as enzymes, are ubiquitous in nature and essential for maintaining basic life activities. Apart from the fundamental biological functions, biomacromolecules are also of great values in industrial applications, especially in food and pharmaceutical production. However, their industrial applications are often handicapped by low operational stability, poor robustness, difficult recovery and reuse. Incorporation of biomolecules within protective exteriors has been proved to be an effective method to promote their stabilities and applications. As new classes of crystalline solid-state materials, covalent-organic frameworks (COFs), feature high surface area, tunable pore size, high stability, and easily tailored functionality, which entitle them as ideal supports for encapsulation of biomolecules to form novel composite materials for various applications. Moreover, the formed composites can combine the properties of both constitutes, where crystalline frameworks materials and biomolecules are indeed mutually beneficial. Our researches mainly focus on the development of novel functional carriers, and their efficient assemble/cascade with biomacromolecules. This novel crystalline platform composed of biomolecules-incorporation and framework materials exhibited various functionality and superior poteintials in catalysis and separation.

Brief Biography

Yao Chen is a professor and doctoral supervisor of Nankai University and Institute of Process Engineering, China. She received the master's degree from Nanjing University of technology in 2009, and then the doctor's degree from the University of South Florida in 2014, and engaged in postdoctoral research at the UCSD from 2014 to 2016. She joined Nankai University in July 2016 and established independent research group that focuses on the precise immobilization and functional formulation of biomacromolecules. In 2024, she also joined Institute of Process Engineering, CAS. She has published 130 SCI papers. As the corresponding/first author she has published 60 papers including Nat Commun、Nat Protoc、Nat Rev Chem, JACS, Angew Chem, Adv Mater, Chem, Chem Soc Rev. 14 papers have been selected as ESI highly-cited paper. She has 41 authorized/applied Chinese patents and 3 U.S. patents. She became the member of the council of The Chemical Industry and Engineering Society of China (2022) and received the National Excellent Youth Science Fund (2020)

Designing Enzyme-producing Cell Factories for Green Production of Chemicals

Yaping Xue (薛亚平)
Zhejiang University of Technology

Abstract

The evolution of industrial enzyme-producing cell factories marks a notable progress in biotechnology, providing novel solutions for diverse industrial applications. These factories leverage genetically engineered microorganisms to synthesize enzymes at scale, thereby enhancing the efficiency and sustainability of industrial processes through genetic and metabolic optimizations. The progress in industrial enzyme production signifies an exciting frontier in biotechnological innovation, promising to enhance efficiency across multiple sectors. We have engineered a suite of tools and synthetic biology elements, including genome-editing technologies, promoters, signal peptides, and molecular chaperones. These tools have been instrumental in constructing industrial enzymes or whole-cell biofactories for the efficient production of functional chemicals such as pesticides, pharmaceuticals, and nutrition additives

Brief Biography

Dr. Ya-Ping Xue is a distinguished Professor from Zhejiang University of Technology. His research interests include biopharmaceutical, biocatalysis and transformation, enzyme engineering, synthetic biology, and green bio-manufacturing. He has successfully developed several green bio-manufacturing industrialization technologies for the production of pharmaceuticals or their intermediates, pesticides or their intermediates, and nutritional additives, resulting in enormous profits in both economy and society. He has published more than 100 papers in academic journals and authorized more than 100 patents for invention.

Biosynthesis of Bioactive Cyclic Peptides

Huan Wang (王欢)
Nanjing University

Abstract

Cyclic peptides represent a unique family of bioactive compounds. Our group aims to develop chemical and biochemical methods to synthesize cyclic peptides with structural and functional diversity. This presentation will introduce our efforts in elucidation of the biosynthesis of a family of natural peptide natural products named lanthipeptides, specifically on the enzymology involved in the biosynthetic process and attempts to engineering biosynthetic enzymes for enhanced catalytic activities.

Brief Biography

Huan Wang is a Professor in the Department of Chemistry and Chemical Engineering at Nanjing University, China. Wang received a BS in Chemistry from Peking University, PhD in Chemistry from Univ. of Maryland, and completed postdoctoral work at UIUC. Wang joined Nanjing University in 2014. Wang's research focuses on the chemical synthesis and biosynthesis of bioactive peptides and related chemical biology.

Molecular Evolution of Baeyer-villiger Monooxygenases for Synthesis of Chiral Sulfoxide Pharmaceuticals

Huilei Yu (郁惠蕾)
East China University of Science and Technology

Abstract

A unique and typical Baeyer Villiger monooxygenase library was constructed by gene mining and cluster analysis. The crystal structure of cyclohexanone monooxygenase from *Acinetobacter* was successfully resolved for the first time. We successfully switched the substrate preference from small molecule cyclohexanone to bulky lazole sulfide substrate through semi rational design. The molecular mechanism affecting the substrate selectivity of thioether monooxygenase for sulfide and sulfoxide was clarified and the precise regulation of substrate selectivity was realized. Finally, the chiral sulfoxides, such as (*S*)-omeprazole, (*R*)-lansoprazole can be synthesized efficiently and controllably in large-scale, achieving a reform in the production mode of chiral sulfoxide drugs.

Brief Biography

Professor. Huilei Yu obtained her Ph.D. on Biochemical Engineering from East China University of Science and Technology in 2008. She was appointed as Assoc. Professor in 2010, and subsequently Professor in 2017 at State Key laboratory of Bioreactor Engineering of ECUST. During 2013-2014, she worked as a Visiting Professor in Laboratory of Bioinformatics and Metabolic Engineering at MIT. Her research focuses on elucidating the structure-activity relationship of enzyme, designing new biochemical reactions, and expanding the space for enzyme catalyzed synthesis of functional molecules. The enzymatic synthesis technologies of chiral hydroxyl acid, chiral sulfoxide and chiral alcohol have been applied in industry, which greatly deceased the production waste generation and promoted the technology renovation of pharmaceutical industry. She was also the executive editor of *Bioresources and Bioprocessing*. She was awarded Outstanding academic leader of Shanghai, Outstanding young enzymologist, First Level Technical Innovation Award of Shanghai City and so on.

Boosted Enzyme Activity by Engineering Microenvironment

Yongqin Lyn (吕永琴)
Beijing University of Chemical Technology

Abstract

For successful industrial applications, high activity and stability are the necessary characteristics for enzymes. However, industrial operational conditions often differ significantly from the natural environment in which enzymes function, such as variations in pH, temperature, and the presence of organic co-solvents. These disparities can lead to a significant reduction in enzyme activity. One effective approach to address this challenge is the immobilization of enzymes onto heterogeneous supports or carriers. This immobilization strategy not only stabilizes enzymes but also facilitates their easy recovery and continuous use. However, traditional immobilization methods often result in a reduced apparent enzyme activity compared to their native counterparts. This is primarily due to the distortion of the enzyme's tertiary structure and the obstruction of substrate access during the immobilization process.

In this study, we have developed novel enzyme immobilization carriers that serve a dual purpose. These carriers not only enhance enzyme activity but also function as "artificial" chaperones to assist in the refolding of denatured enzymes. We achieve this by carefully engineering the local chemical microenvironment of enzymes, which involves modifying pore sizes, pore shapes, and functionalities of solid supports. Furthermore, by replicating the active sites found in native enzymes, we have also successfully created structural mimics of carbonic anhydrase and laccase. These enzyme mimics have demonstrated exceptional catalytic capabilities in the processes of CO_2 hydration and lignin degradation.

Brief Biography

Prof. Yongqin Lv received her Bachelor degree from Department of Materials Science and Engineering in 2005, and Ph.D. degree from the College of Life Science and Technology both at Beijing University of Chemical Technology in December of 2010. From 2008 to 2010 she studied at the Materials Science Division of Commonwealth Scientific and Industrial Research Organization (CSIRO) in Australia. For 2 years from 2011, she was a postdoctoral fellow at the Department of Chemistry, University of California, Berkeley. She is currently a professor at College of Life Science and Technology at Beijing University of Chemical Technology, and deputy directors of International Joint Laboratory for Bioenergy of Ministry of Education and Beijing Key Laboratory of Bioprocess. Her research interests include microenvironment regulation to enhance biocatalysis, photo- and electrically-driven biocatalytic carbon fixation, and synthetic antibody engineering. She has published 76 papers in SCI-index journals including P. Natl. Acad. Sci. USA., J. Am. Chem. Soc., Matter, Nano Lett., Adv. Sci., Prog. Energ. Combust., Biotechnol. Adv., and etc. She also applied more than twenty patents. Her leadership is evident in overseeing more than 10 research projects, including 9 national initiatives. She has presented academic presentations at over 50 domestic and international conferences, with over 30 being invited talks. Beyond her academic contributions, she actively participates in professional committees, serving as a member of the One Carbon Biotechnology Committee of the Chinese Society of Biotechnology and a member of the Youth Work Committee of the Chemical Industry and Engineering Society of China. Moreover, she serves in various editorial roles, including guest editor for Biotechnology Advances, editorial board member and guest editor for Synthetic and Systems Biotechnology, young editorial board member and guest editor for Frontiers of Chemical Science & Engineering, editorial board member for Microchimica Acta, and young editorial board member for Bioresources and Bioprocessing, among others. She also contributes her expertise as an expert reviewer for the National Natural Science Foundation of China, a

reviewer for the Beijing Natural Science Foundation, and an expert reviewer for European Commission projects.

Biotransformation of Lignocellulosic and Waste Plastic Upgraded by Computer-assisted Enzyme Engineering

Xiujuan Li (李秀娟)
Nanjing Normal University

Abstract

Considering the demand in the Chinese market for enzyme preparations, it is essential to strengthen the research and development of new technologies, address issues such as low industrial enzyme performance, establish key technologies including independently owned proprietary technologies and strains, and promote the application of enzyme preparations in the industrial sector. The past few years have witnessed the development of protein engineering, achieved a series of significant advancements and breakthroughs, and became a powerful tool for improving enzyme catalytic performance. In recent years, we have explored and designed several cutting-edge enzyme strategies that combine computational techniques with synthetic biology. These efforts aim to provide methods for the preparation of higher-performance enzyme components. 1) utilized intelligent computing to assist in obtaining highly robust cellulase enzymes to enhance lignocellulosic conversion efficiency, 2) developed BHETase mining strategy and the enzyme engineering strategy guided by kinetic calculation to improve the anchoring rate and catalytic efficiency, and to find new breakthroughs for the biological degradation of plastics to achieve plastic recycling economy.

Brief Biography

Xiujuan Li professor at Nanjing Normal University has long been engaged in deeply integrating cutting-edge technologies such as enzyme engineering, computational biology, and AI into the waste resource recycling research, helping to achieve the goal of carbon neutrality and carbon peak. In the past five years, as the first/corresponding author, she has published more than 30 SCI academic papers in *Nat Commun*, *Angew Chem* and other journals, and applied for more than 20 invention patents. The relevant achievements won the grand prize and the second prize of the China General Chamber of Commerce in 2023, and the first prize of the Jiangsu Agricultural Society technology innovation Award.

Application of Metabolic Pathway Compartmentalization Engineering Strategy in the Construction of Yeast Cell Factories

Aiqun Yu (于爱群)
Tianjin University of Science and Technology

Abstract

Yeast offers a complete and organized production line for compound synthesis and storage, which relies on a variety of organelles and membranous structures, including the endoplasmic reticulum (ER), Golgi, lipid droplets (LDs), peroxisomes, mitochondria, and plasma membrane. Because excessive accumulation of various compounds can cause cytotoxicity, compartmentalization protects the intracellular environment by concentrating detoxifying enzymes and metabolites within a limited and closed space. At the same time, such arrangement improves the catalytic efficiency of enzymes. In recent years, researchers have begun to use this subcellular compartmentalization engineering strategy to construct cell factories that can more effectively produce value-added chemicals, and have achieved good production efficiency. We have repositioned the synthetic pathway of a terpenoid natural product, bisabolene, to the cytoplasm, mitochondria, and peroxisomes of of the yeast *Yarrowia lipolytica*. The findings revealed a significant increase in production for organelle engineering strains compared to cytoplasmic engineering strains, marking the highest bisabolene titer in microbial chassis to date. This highlights the effectiveness of compartmentalizing metabolic pathways as an optimal strategy for bisabolene synthesis in yeast cell factories. However, the molecular mechanisms underlying the strategy's enhancement of product yield remain unexplored, and we herein conduct preliminary analysis and discussion on this.

Brief Biography

Aiqun Yu, Bachelor's degree from Shandong Normal University (2002-2006), Master's degree from Fujian Normal University (2006-2009, supervised by Professor Jianzhong Huang), and PhD from Nankai University (2009-2012, supervised by Professor Mingchun Li); I conducted postdoctoral research at Nanyang Technological University and National University of Singapore from 2012 to 2016, with Professor Matthew Chang as my co-supervisor; Selected for the Overseas Young Scientist Program of Tianjin in 2017. He is now a professor of the State Key Laboratory of Food Nutrition and Safety at Tianjin University of Science and Technology, and the deputy director of Tianjin Microbial Metabolism and Fermentation Process Control Technology Engineering Center. At present, my main research interest lies in yeast cell factories, green biomanufacturing, modern brewing technology, etc. I have published 36 first/corresponding author papers in well-known domestic and foreign journals in the field of biotechnology; applied for/authorized 10 national invention patents as the first inventor; been invited to serve as a young editorial board member for SCI journal Microbial Biotechnology and guest editor for Journal of Fungi, Frontiers in Bioengineering and Biotechnology, and Food Science.

Drug Delivery by Synthetic Probiotic Bacteria

Yun Yang (杨昀)
Beihang University

Abstract

An overwhelming number of studies have reported the correlation of decreased abundance of butyrate-producing commensals with a wide range of diseases. However, the molecular-level mechanisms whereby gut butyrate causally affects the host physiology were poorly understood. We engineered a commensal bacterium to delivery butyrate at the intestinal mucosal surface, and implemented it to dissect the causal role of gut butyrate in microbe-host interaction.

Brief Biography

Dr. Yang is an associate professor at the School of Engineering Medicine, Beihang University. She got her Bachelor and Master degree from Tsinghua University, and received a Ph.D. degree from Nanyang Technological University in Singapore. Dr. Yang has conducted a series of studies on rational design and engineering of bacteria for biocatalysis and drug delivery.

Mechanistic Study and Modification of Depolymerases for Synthetic Polyesters

Yu Yang (杨钰)
Hubei University

Abstract

Bio-based degradation using renewable biological entities, i.e., enzymes or microorganisms, is an ideal and environmentally benign approach to reduce and recycle plastics. Thus, significant effort has been made to develop a PBAT biodegradation strategy. However, the lack of in-depth investigation into their potency and mechanism of action hampers their applications. In this work, we investigate the PBAT hydrolysis potency of cutinases and PET-degrading enzymes, and find that cutinases outcompete other reported enzymes. Significantly, engineering cutinases with the DM strategy results in higher activity such that PBAT polymers can be decomposed to their monomeric constituents. We apply biochemical and structural analyses to investigate the hydrolytic intermediates/products and substrate-binding features to propose its mechanism of action. Taken together, this study illustrates the potential application of engineered cutinase in PBAT biodegradation. These results provide an important basis to guide the development of biodegradation/bio-recycling of PBAT as well as other aliphatic-aromatic co-polyesters.

Brief Biography

Dr. Yu Yang obtained his Ph.D. of biotechnology at Jiangnan University in 2014. After that, he worked as a postdoc at Georgia State University and the University of Texas at San Antonio. Currently, he joined in at Hubei University as an associate professor. He has a broad interest in studying biocatalysis's structural-functional relationship related to the degradation of polyesters and neurological diseases, including hydrolase, decarboxylase, dehydrogenase, and dioxygenase. He has solved over 100 protein structures and published around 20 papers like *Nat. Commun.*, *J. Hazard. Mater.*、*J. Med. Chem.*, *J. Biol. Chem. et al*.

Synthetic Biology with Single-cell Precision: From Enzyme Development to Technology Development and Application

Jia Zhang (张佳)
Qingdao Institute of Bioenergy and Bioprocess Technology, Chinese Academy of Sciences

Abstract

Synthetic biology, an interdisciplinary frontier of science, amalgamates the essence of numerous research areas and directions, emerging as a pivotal force in exploring the mysteries of life and innovating biotechnologies. In recent years, my research team has focused on the innovative development of single-cell Raman technology, skillfully integrating it into the grand blueprint of synthetic biology, aiming to establish a new paradigm of synthetic biology research centered on single-cell precision.

Our journey of exploration began with the meticulous construction of a comprehensive Single-cell Raman technology pipeline: from precise Single-cell sorting and efficient gene amplification to seamless coupling with Single-cell sequencing or Single-cell culture. During this process, we astutely identified that the high efficiency and low cost of enzyme reagents were critical bottlenecks in the entire technology chain. To address this, we successfully developed a high-efficiency, low-cost HotJa single-cell whole-genome enzyme kit based on advanced enzyme engineering technology. This breakthrough not only overcame technical barriers but also endowed our single-cell Raman technology pipeline with distinctive technical features and strong industry competitiveness.

As the technology matured, we applied this innovative achievement across multiple fields: in the targeted discovery of functional gut strains, our technology enables precise identification and selection of strains with specific functions; in the fermentation process of strains, it offers the possibility of real-time monitoring, ensuring the stability and efficiency of the production process; and in the rapid detection technology of integrated probiotic products, it demonstrates rapid and accurate detection capabilities. These applications not only prove the immense potential of single-cell Raman technology but also facilitate our horizontal collaborations with Moutai Group, COFCO Group, and Yili Group, paving new paths for the practical application of synthetic biology and heralding a new era of more precise and efficient biotechnology.

Brief Biography

Jia Zhang is currently the group leader/associate researcher of the Enzyme Research Group at the Qingdao Institute of Bioenergy and Bioprocess Technology, Chinese Academy of Sciences, and a founding young editorial board member of BioDesign Research. Her main research areas include gene synthesis, metabolic engineering, enzyme engineering, and the development and application of single-cell Raman technology, all related to synthetic biology. To date, she has published a total of 15 SCI papers, with 9 as the first author or corresponding author. She has led 9 research projects, including the National Key R&D Program Young Scientist Project, National Defense Science and Technology Projects, National Natural Science Foundation Youth Projects, Shandong Province General Projects, and various horizontal projects (including COFCO Group, Moutai Group, Yili Group, etc.), with a total funding of 10.26 million RMB. She has applied for 33 patents, with 32 granted, and has been awarded the title of "Qingyuan Scholar" Young Talent.

Phosphoantigens Glue Butyrophilin 3A1 and 2A1 to Activate VΓ9VΔ2 T Cells

Yunyun Yang (杨云云)
Hubei University

Abstract

In both cancer and infections, diseased cells are presented to human Vγ9Vδ2 T cells through an “inside-out” signaling process wherein structurally diverse phosphoantigen (pAg) molecules are sensed by the intracellular domain of butyrophilin BTN3A1. Here, we show how—in both human and alpaca—multiple pAgs function as “molecular glues” to promote heteromeric association between the intracellular domains of BTN3A1 and the structurally similar butyrophilin BTN2A1. X-ray crystallographic studies visualized that BTN3A1 engagement with pAgs forms a composite interface for direct binding to BTN2A1, with various pAg molecules each positioned at the center of the interface and gluing the butyrophilins with distinct affinities. Our structural insights guided mutagenesis experiments that led to disruption of the intracellular 3A1-2A1 association, abrogating pAgs-mediated Vγ9Vδ2 T cell activation. Structure-based MD simulations, ^{19}F-NMR investigations, chimeric receptor engineering, and direct measurement of intercellular binding force revealed how pAgs-mediated 2A1 association drives 3A1 intracellular fluctuations outwards in a thermodynamically favorable manner, thereby allowing 3A1 to “push off” from the 2A1 ectodomain to initiate TCR-mediated γδ T cell activation. Practically, we harnessed the molecular glue model for immune-therapeutics design, demonstrating chemical principles for developing both small molecule activators and inhibitors of human γδ T cell function.

Brief Biography

Yang Yunyun, Ph.D., graduated from Tsinghua University and is currently an associate professor at Hubei University. Her research primarily focuses on the structural biology and biochemical mechanisms of (1) disease-related proteins and (2) the enzymatic reaction mechanisms involved in the biosynthesis of antitumor natural products. She has published 17 articles in international journals, including Nature, Cell, Immunity, Angewandte Chemie International Edition, and ACS Catalysis. Dr. Yang has led eight national and provincial-level projects, including a National Key R&D Program of China, and National Natural Science Foundation of China. Additionally, she has been recognized as a candidate for the Hubei Province Future Female Scientist Program and has received exceptional support as a “Chutian Scholar” in Hubei Province.

Reprogramming Unconventional Yeast Cell Factories for The Low-ph Biomanufacturing of Succinic Acid

Zhiyong Cui (崔志勇)
Shandong University

Abstract

Succinic acid (SA) is an important metabolic intermediate and platform compound for organic synthesis, with broad market prospects. It is expected that by 2025, the domestic SA market potential will reach 200,000 tons per year, and the output value is expected to exceed 500 million US dollars/year. The development of green and sustainable SA fermentation technology is not only helpful to solve the problem of plastic pollution, but also in line with low-carbon development strategy. Due to its excellent acid tolerance, *Yarrowia lipolytica* has attracted much attention as a novel chassis for synthetic biology. In our previous study, we obtained a series of recombinant engineered strains of *Y. lipolytica* by inactivating succinate dehydrogenase and enhancing oxidative TCA cycle, and achieved high SA production at low pH for the first time. However, the yields of these strains are too low to meet the needs of industrial production. To address this bottleneck, a reductive SA synthetic pathway was created in strictly aerobic yeast to improve carbon source utilization efficiency. Adaptive evolution and cofactor engineering were used to enhance the adaptability of heterologous metabolic pathways to chassis. Eventually SA titer, yield, and productivity could reach to 111.9 g/L, 0.79 g/g glucose, and 1.8 g/L/h, respectively. Furthermore, the engineered *Y. lipolytica* strain was proved to produce 45.34 g/L SA using undetoxified lignocellulose hydrolysates. This study will help to reveal the metabolic regulation mechanism of SA biosynthesis in aerobic yeast, and lay the foundation for the development of bio-based materials industry in China.

Brief Biography

Zhiyong Cui is an associate researcher at the State Key Laboratory of Microbial Technology, Shandong University. He has long been engaged in the research of unconventional yeast synthetic biotechnology and bulk chemicals bio-manufacturing. Based on the development of large-scale DNA genome integration and high-throughput mutant library construction technology on the platform of important industrial microorganisms, efficient biosynthesis of high-value chemicals such as succinic acid, 3-hydroxypropionic acid, and itaconic acid has been realized. The low pH succinic acid fermentation technology based on unconventional yeast cell factory developed by him is the first in China, which broke the technological monopoly of multinational companies such as DSM, Reverdia, and Cargill. These achievements have been published in Nat Commun, Metab Eng, Biotechnol Biofuels, ACS Synth Biol and other journals, and have been cited more than 800 times.

Unveiling Cryptic Microbial Biosynthesis Towards Unprecedented Classes of Ribosomal Peptides

Hengqian Ren (任恒千)
Dalian University of Technology

Abstract

Secondary metabolism, widely present in numerous microorganisms, produces natural products that serve as invaluable resources for drug development. Ribosomally synthesized and post-translationally modified peptides (RiPPs) constitute an emerging family of natural products since the 21st century. With vast structural diversity and myriad biological functions, such as antimicrobial, anticancer, and antiviral activities, RiPPs are notable for their therapeutic potentials. The rapid growth of genome sequencing data, along with advances in bioinformatics, has led to a significant expansion of predicted RiPP biosynthetic pathways. However, most of these pathways are transcriptionally silent or sparingly expressed under standard laboratory growth conditions, rendering the corresponding products cryptic.

Here I present using synthetic biology to rapidly uncover the biosynthetic potential of cryptic RiPP pathways. To bypass the cryptic transcriptional regulation, we developed a plug-and-play genetic assembly workflow that reconstructs pathway expression systems using well-characterized regulatory elements. For pathways with complex gene arrangements, we employed the direct cloning strategy to achieve heterologous expression in genetically tractable model microbes. Integration of these technologies to an automation platform has significantly expanded the discovery scale. In total, we identified 38 cryptic RiPPs across 8 RiPP classes, including two unprecedented classes: daptides and lipoavitides. Daptides represent the first example of ribosomal peptides bearing two amino termini, with one formed via a novel biosynthetic route involving decarboxylation, transamination, and demethylation. While lipoavitides are a class RiPP/fatty-acid hybrid lipopeptides that display an amino terminus modified by a distinct short-chain fatty acid. Further investigation of lipoavitide biosynthesis revealed an acyltransferase that connects the fatty acid and RiPP substructures with promiscuous activity, affording potential application in lipopeptide bioengineering. Overall, our work showcases the scalable pathway activation, biosynthetic machinery elucidation, and enzymatic tool generation for RiPPs via synthetic biology approaches.

Brief Biography

Dr. Hengqian Ren received his B.S. in Chemical Engineering from Tianjin University in 2013, and Ph.D in Chemical Engineering from University of Illinois at Urbana-Champaign (UIUC) in 2019 under the guidance of Dr. Huimin Zhao. He joined the School of Bioengineering, Dalian University of Technology in the summer of 2024. Dr. Ren focuses on developing synthetic biology strategies to uncover cryptic biosynthetic pathways of ribosomally synthesized and post-translationally modified peptides (RiPPs), an emerging family of natural products with vast pharmaceutical potential. His research has been published in *Nature Chemistry*, *Nature Communications*, *Biotechnology and Bioengineering*, *ACS Chemical Biology*, etc.

The Innovation of Study on Anti-tumor Active Compounds

Mengyao Li (李梦尧)
Shanghai Cancer Institute

Abstract

The disease of tumors poses a grave threat to human wellness, thus the pursuit of novel molecules exhibiting anti-tumor activity remains an enduring concern for medicinal chemists and biologists. It is of paramount importance to devise innovative molecular skeletons, achieve efficient synthesis of active compounds, and select appropriate pharmacodynamic validation models to enhance the clinical value of research. Dr. Li will present the recent researches in the above three fields, encompassing: 1) Employing solvent-free and catalyst-free reactions for synthesizing active molecules against gallbladder and pancreatic cancer; 2) Investigating the efficacy of multi-substituted alkenes against biliary pancreatic tumors; 3) Utilizing patient-derived organoids (PDOs), patient-derived explants (PDEs), and patient-derived xenografts (PDXs) models to assess the *in vitro* and *in vivo* anti-tumor effects of these active molecules.

Brief Biography

Dr. Meng-Yao Li is currently serving as an assistant professor at Renji Hospital Affiliated to Shanghai Jiao Tong University School of Medicine/Shanghai Cancer Institute. He obtained his graduate degree from the prestigious Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, under the esteemed guidance of Prof. Guo-Qiang Lin. Li has made significant contributions to various scientific publications in renowned journals such as Aggregate, Sci. China Chem., Green Chem., iScience, Org. Lett., and Chem. Commun. His research output comprises 19 SCI papers that have garnered a total citation count of 300, resulting in a personal H-index value of 10. His research interests involve investigating the anti-tumor activity and mechanisms of traditional Chinese medicine; exploring drug design, synthesis, and their antitumor properties; developing and utilizing patient-derived organoid models as well as patient-derived tumor xenografts; studying drug resistance mechanisms in biliary and pancreatic tumors.

Engineering Carbon Source Division of Labor for Efficient A-carotene Production in *Corynebacterium Glutamicum*

Kai Li (李凯)
Shanghai Jiao Tong University

Abstract

Effective utilization of glucose, xylose, and acetate, common carbon sources in lignocellulose hydrolysate, can boost biomanufacturing economics. However, carbon leaks into biomass biosynthesis pathways instead of the intended target product remain to be optimized. This study aimed to enhance α-carotene production by optimizing glucose, xylose, and acetate utilization in a high-efficiency *Corynebacterium glutamicum* cell factory. Heterologous xylose pathway expression in *C. glutamicum* resulted in strain m4, exhibiting a threefold increase in α-carotene production from xylose compared to glucose. Xylose utilization was found to boost the biosynthesis of pyruvate and acetyl-CoA, essential precursors for carotenoid biosynthesis. Additionally, metabolic engineering including *pck, pyc, ppc*, and *aceE* deletion, completely disrupted the metabolic connection between glycolysis and the TCA cycle, further enhancing α-carotene production. This strategic intervention directed glucose and xylose primarily towards target chemical production, while acetate supplied essential metabolites for cell growth recovery. The engineered strain *C. glutamicum* m8 achieved 30 mg/g α-carotene, 67% higher than strain m4. In fed-batch fermentation, strain m8 produced 1,802 mg/L of α-carotene, marking the highest titer reported to date in microbial fermentation. Moreover, it exhibited excellent performance in authentic lignocellulosic hydrolysate, producing 216 mg/L α-carotene, 1.75 times higher than the initial strain (m4). These labor-division strategies significantly contribute to the development of clean processes for producing various valuable chemicals from lignocellulosic resources.

Brief Biography

Dr. Kai Li received his Ph.D. degree from the Shanghai Jiao Tong University (SJTU) in 2021. As a visiting scholar, Dr. Li studied at the Massachusetts Institute of Technology (MIT) during 2020-2021. He subsequently worked as a postdoctoral fellow and Assistant Professor at SJTU from 2021 to 2023. He also worked as a Visiting Professor at department of biology of MIT from June 2024.

Bioprocess Design to Enhance Lignin Bioaccessibility and Biotransformation

Zhimin Zhao (赵志敏)
Tianjin University

Abstract

Biological lignin valorization represents an emerging green approach to upgrading lignin for sustainable and economic biorefineries. However, due to the organic macromolecular structure, lignin generally exhibits poor water solubility and inhomogeneous distribution in an aqueous medium, significantly limiting its bioconversion efficiency. Herein, we developed a novel alkali sterilization (AS) strategy to enhance the dispersion and fermentation performance of lignin substrates effectively. AS enhanced the ionization process of acidic groups in lignin colloids, reducing the volume of colloidal lignin particles dramatically compared with conventional thermal sterilization. By providing more uniformly distributed and readily degraded lignin substrates, the AS strategy facilitated both *Rhodococcus opacus* PD630 growth and lipids production during fermentation. Furthermore, Cosolvent enhanced lignocellulosic fractionation (CELF) pretreatment was employed to tailor lignin chemistry, which enhanced lignin bioaccessibility at a molecular level and further upgraded lignin bioconversion. Therefore, this work presents a facile and effective strategy to overcome inhomogeneous lignin distribution in aqueous media, showing great potential as a platform technique to promote biological lignin valorization.

Brief Biography

Zhi-Min Zhao is an associate professor from Tianjin University. He received his Ph.D. degree in biochemical engineering from Institute of Process Engineering, Chinese Academy of Sciences. He was trained as a postdoctoral researcher at Oak Ridge National Laboratory, United States. His research focuses on designing advanced processes to tailor lignin chemistry and depolymerize lignin, aiming to facilitate lignin bioconversion and biorefinery. He has published over 30 peer-reviewed papers in biorefinery and bioprocess design fields.

Design And Construction of Microbial Cell Factory for the Efficient Synthesis of High-value Amino Acid Derivatives

Xuewei Pan (潘学玮)
Jiangnan University

Abstract

The amino acid industry, including amino acids and their derivatives, is one of the pillar industries of China's fermentation industry, with significant application value in the fields of food, pharmaceutical, feed, and chemical industry. China is a large production nation of amino acids, but not a strong producer of amino acids. The main factors restricting the development of China's amino acid industry are: (1) severe overcapacity of bulk amino acid production capacity; (2) a significant gap existed in some production strains compared to the advanced level abroad; (3) lack of independent intellectual property in some production strains, leading to the risk of “bottleneck”. Therefore, there is an urgent need to develop high-value amino acid derivative cell factories with independent intellectual property rights and competitiveness to enhance the international competitiveness of China's amino acid industry. This report introduces the advancement of our research group in the construction of high-value amino acid derivative cell factories in recent years, using high-value chemicals such as prodigiosin, deoxyviolacein, L-carnosine, and α-arbutin as examples.

Brief Biography

Xuewei Pan, Associate Researcher and Master Supervisor at the School of Biotechnology, Jiangnan University, is mainly engaged in research on the construction of efficient synthetic cell factories for high-value amino acid derivatives. As the first/corresponding author, he has published 15 SCI papers in authoritative journals in the fields of synthetic biology and metabolic engineering, such as Nucleic Acids Res, Appl Environ Microbiol, and Bioresour Technol. He has presided over and undertaken 8 national and provincial-level scientific research projects, including the General Program of National Natural Science Foundation of China (No. 32470067), the Youth Fund of National Natural Science Foundation of China (No. 32100055), the National Key Research and Development Program of China (No. 2023YFA0914500), and the Natural Science Foundation of Jiangsu Province (No. BK20210464). He was awarded the title of 2021 Jiangsu Youth Science and Technology Innovation "U35 Exploration" candidate.

Acetate as A Potential Platform Feedstock for Future Biomanufacturing

Guiping Gong (龚贵平)
Biogas Institute of Ministry of Agricultural and Rural Affairs

Abstract

The production of biofuels and biochemicals derived from microbial fermentation has received a lot of attention and interest considering concerns about the depletion of fossil fuel resources and climatic degeneration. However, the economic viability of feedstocks for biological conversion remains a barrier, urging researchers to develop renewable and sustainable low-cost carbon sources for future bioindustries. In concerns of food security, what will be the potential feedstock for future next-generation biomanufacturing? Owing to the numerous advantages, acetate has been regarded as a promising two-carbon building block feedstock targeting the production of acetyl-CoA-derived chemicals in industrial biotechnology. Here, we introduced our latest progress in bioconversion of acetate to produce biomacromolecules, such as single cell protein and microbial lipids in oleaginous microorganisms including yeast and algae. Different alternative approaches and routes for renewable acetate generation based both on biogas and ethanol will be described. Challenges and future development for acetate generation and assimilation as well as chemicals production from acetate will be also discussed.

Brief Biography

Dr. Guiping Gong received his PhD degree from Beijing University of Chemical Technology (BUCT) in 2021. During his PhD career, he got a scholarship from China Scholarship Council (CSC) and went to the lab of **Jens Nielsen** (Foreign academicians of Chinese Academy of Sciences) at Chalmers University of Technology. After graduated from PhD in 2021, he now works in the team of Microbial Synthetic Biology and Bioconversion (mSynBio) at Biogas Institute of Ministry of Agriculture and Rural Affairs (BIOMA). His current research focused on yeast metabolic engineering and acetate bioconversion. Based on the theme of “acetate bioconversion”, he has published more than 10 peer-reviewed papers in leading journals, including *Biotechnology Advances*, *Bioresource Technology* (x5), *Science of the Total Environment*, *ACS Synthetic Biology*, *Engineering Microbiology*, etc.

Bioconversion of Methane to C50 Carotenoid Bacterioruberin Using Soil-enriched Microbial Consortia

Shuqi Guo (郭树奇)
Xi'an Jiaotong University

Abstract

Bacterioruberin is widely used in medicine, food, and cosmetics, owing to its prominent antioxidant and bioactivity characteristics. In this study, we aimed to upcycle methane to bacterioruberin using microbial consortia. Microbial consortia consisting of *Methylomonas* and *Methylophilus*, which are capable of synthesizing carotenoids from methane, were first enriched in paddy soil. Through this microbial community, methane was successfully converted to C50 bacterioruberin for the first time. The bioconversion process was then optimized using response surface methodology. Finally, the methane-derived bacterioruberin reached a yield of 280.88 ± 2.94 μg/g dry cell weight. This study presents a cost-effective and eco-friendly approach for producing long-carbon chain carotenoids from methane, offering significant advancement in the direct conversion of greenhouse gases into value-added products.

Brief Biography

Dr. Shuqi Guo is now an associate professor at the School of Chemical Engineering and Technology of Xi'an Jiaotong University, China. Guo graduated from Shanghai Jiao Tong University in 2020. He then joined the School of Chemical Engineering and Technology of Xi'an Jiaotong University and has been engaged in research on the bioconversion of methane and metabolic engineering of methanotrophic bacteria.

Computation-driven Virtual Screening and Design of Carboxylic Acid Reductase for Nylon Monomers Biosynthesis

Kun Shi (石焜)
East China University of Science and Technology

Abstract

Nonribosomal peptide synthetases (NRPSs) are large multienzyme machineries that produce many valuable pharmaceutical compounds. However, engineering these megaenzymes is challenging due to the complex interactions between modules and domains, which require a deep understanding of protein-protein interactions and substrate specificities. In this work, we reported a computational redesign of the “gate-keeper” adenylation domain of the model NRPS-like enzyme carboxylic acid reductases (CARs). In particular, we proposed a strategy to screen the *in silico* mutant library through approximate mechanism-based geometric criteria and the Rosetta energy score. This approach effectively predicts the catalytic efficiency (k_{cat}/K_M) bypassing the need for specialized molecular dynamics and quantum mechanics simulations. With relatively little and high-efficiency experimental effort, only 72 mutants of *Mab*CAR3 were screened, from which 50 positive mutants were identified with a 70% positive rate. *Mab*CAR3 was efficiently engineered to generate a series of tailored enzymes. The refined biocatalytic system yielded a wide spectrum of nylon monomers (C6-C12) with outstanding yields (up to 88%), loading capacities (up to 100 mM), and productivities (up to 46 g L^{-1} d^{-1}), demonstrating the broad applicability of the system.

Brief Biography

I graduated with a master's degree in microbiology from Nanjing Tech University (Prof. He Huang/ Prof. Xiao-Jun Ji team), and obtained a Ph.D. in biochemical engineering from East China University of Science and Technology (Prof. Jian-He Xu/ Prof. Hui-Lei Yu team). I am currently working as a postdoctoral researcher at East China University of Science and Technology, with Prof. Jian-He Xu as my co-advisor. My research focuses on the computationally driven rational design of enzymes and artificial intelligence-based *de novo* design of multi-enzyme molecular machines. I am presently the principal investigator of a project funded by the National Natural Science Foundation of China (32401276) and am also involved in a project under the Shanghai Commission of Science and Technology (23HC1400200). As the first author, I have published a total of five papers in SCI journals, including *Science Advances*, *ChemSusChem*, *Biotechnology and Bioengineering*, and *Chemical Engineering Science*.

Computation-driven Virtual Screening and Design of Carboxylic Acid Reductase for Nylon Monomers Biosynthesis

Lingling Zhang (张玲玲)
Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences

Abstract

The increasing emission of CO_2 has resulted in severe climate problems, calling for carbon-fixation actions. CO_2 biotransformation through biochemical reactions catalyzed by enzymes and microbes provides a promising and sustainable way for not only reducing CO_2 emission but also producing various chemicals. Key steps in CO_2 biotransformation includes CO_2 activation and energy conversion. By utilizing electricity as activator and energy input, we have successfully established several systems, including CO_2-formate enzymatic conversion sytem, CO_2-single cell protein system, and ATP regeneration system, validating the effective and efficient CO_2 activation and transformation, paving the way for CO_2-based green biomanufacturing.

Brief Biography

Lingling Zhang is now a team leader in Tianjin Institute of Industrial Biotechnology (TIB), Chinese Academy of Sciences (CAS). She got her PhD degree in Changchun Institute of Applied Chemistry, Chinese Academy of Sciences (CAS) in 2016. After that, she did her postdoc in Aarhus University, Denmark and RWTH-Aachen University, Germany. In 2020, she joined in TIB. Her research interests focus on bioelectrocatalysis and electrochemical energy conversion, mainly on bioelectrocatalytic CO2 reduction, electro-assisted ATP regeneration, and intramolecular/heterogeneous electron transfer mechanism understanding.

About *BioDesign Research*

《生物设计研究》（*BioDesign Research*）是由南京农业大学主办，与美国科学促进会（AAAS | *Science* 出版方）合作出版的开放获取（Open Access）英文学术期刊。

期刊刊发高质量的重大研究进展论文、综述、社论、观点和见解，重点关注计算生物系统设计、遗传或表观遗传修饰以及生物基因组编写或重写等领域的研究。刊载范围包括：(1) 科学维度，包括生物设计理论、原则、方法、工具和应用；(2) 生物维度，包括动物、人类、微生物、植物和新生生物设计；(3) 社会责任维度，包括生物设计安全和伦理。

期刊旨在为生物设计这个多学科交叉领域提供国际化的信息交流平台，将致力于生物设计和评估，为解决健康、农业和环境等方面的全球性挑战提供新的视野。

期刊主编由美国橡树岭国家实验室 Xiaohan Yang 高级研究员和英国华威大学 / 西班牙综合系统生物学研究所（I^{2}SysBio）Alfonso Jaramillo 教授担任，执行主编为湖北大学**杨世辉**教授和南京农业大学**程宗明**教授。

期刊已被 ESCI、PubMed Central、Scopus、DOAJ、CAB Abstracts 等数据库收录，将于 2025 年获得首个影响因子。入选 2021 年中国科技期刊卓越行动计划高起点新刊。

期刊官网：spj.science.org/bdr

联系我们：office@biodesignresearch.com

扫码关注微信公众号