

Postprint of the Innovative System for Molecular Module Design Breeding

Authors: Institute of Genetics and Developmental Biology, Chinese Academy of Sciences

Date: 2017-02-08T00:00:00+00:00

Abstract

China is a major agricultural nation, and the sustained and stable production of major agricultural products such as rice, wheat, and fish is of significant practical and strategic importance for ensuring the sustainable development of agriculture in China. In recent years, the yield and quality of major agricultural products have been stagnating, making it difficult to meet China's food security requirements. Therefore, enhancing the level of breeding science and technology and developing a new generation of breeding theories and technical systems is an urgent requirement for the development of modern seed industry. The development of emerging disciplines such as genomics, computational biology, systems biology, and synthetic biology has brought opportunities for deciphering the genetic regulatory networks of complex biological traits, and has also laid a scientific foundation for breeding technology innovation. Most agronomic (economic) traits are regulated by multiple genes and possess “modular” characteristics. The Pioneer Program on Innovative System of Molecular Module Design Breeding focuses primarily on rice, with wheat, carp, and others as supplementary subjects, comprehensively employing genomics, computational biology, systems biology, synthetic biology, and other means to dissect the molecular modules underlying important agronomic (economic) traits such as high yield, stable yield, superior quality, and high efficiency, reveal the principles of systematic dissection and coupling of molecular modules, optimize the optimal strategies for variety design through multi-module assembly, and establish a modern biotechnology breeding innovation system from “molecular modules” to “designer varieties.”

Full Text

Preamble

Strategic Priority Research Programs (Category A) of the Chinese Academy of Sciences

ChinaXiv Partner Journal: Molecular Module Design Breeding Innovation System

1. Background and Significance

China is a major agricultural nation, and the sustained and stable production of staple crops such as rice, wheat, and fish is of tremendous practical and strategic importance for ensuring the country's agricultural sustainability. In recent years, both the yield and quality of major agricultural products have plateaued, struggling to meet China's food security demands. Therefore, enhancing breeding technology and developing a new generation of breeding theories and technical systems represents an urgent need for modern seed industry development. Advances in emerging disciplines including genomics, computational biology, systems biology, and synthetic biology have created opportunities to decipher the genetic regulatory networks underlying complex biological traits, while also establishing a scientific foundation for breeding technology innovation. Most agronomic (economic) traits are regulated by multiple genes and exhibit "modular" characteristics. The Molecular Module Design Breeding Innovation System pilot program, focusing primarily on rice with wheat and carp as secondary targets, integrates genomic, computational, systems, and synthetic biology approaches to dissect molecular modules controlling important agronomic (economic) traits such as high yield, stable production, superior quality, and high efficiency. The program aims to reveal the principles of molecular module system analysis and coupling, optimize strategies for multi-module assembly in variety design, and establish a modern biotechnology breeding innovation system that progresses from "molecular modules" to "designer varieties."

2. Overall Progress and Breakthroughs

Over three years of implementation, the program has accomplished collection, curation, and preservation of 20,000 germplasm resources including rice, wheat, soybean, maize, and carp. Seventy-six molecular modules controlling high yield, stable production, superior quality, and high efficiency have been identified and characterized, among which 33 modules show significant application potential. Additionally, 43 molecular module systems have been obtained, 2 new coupling models developed, and coupling effect analysis conducted for 6 molecular modules. Thirty-two primary module-based new lines have been developed and are currently undergoing regional and production trials. Infrastructure and service capabilities have been enhanced at six molecular breeding bases in Northeast, North, East, Central, Southwest China, and Hainan. With the program reaching its halfway point, a series of important interim achievements and break-

throughs have been achieved in frontier basic theories, core scientific issues, and key breeding technologies.

2.1 Major Breakthroughs in Frontier Basic Theory Research

2.1.1 Elucidating the Molecular Mechanism of Cold Perception in Rice

Rice originated in tropical and subtropical regions and is highly sensitive to low temperatures. The Kang Chong research group at the Institute of Botany, Chinese Academy of Sciences, and collaborators utilized a genetic population constructed from the indica rice 93-11 and japonica rice Nipponbare to identify COLD1, an important cold tolerance QTL gene in japonica rice. During cold treatment, COLD1 interacts with the G-protein α subunit RGA1, participating in G-protein-dependent signal transduction that activates Ca^{2+} channels and triggers downstream cold defense responses, thereby conferring cold tolerance to japonica rice. The characterization of the COLD1 module facilitates the molecular design of cold-tolerant rice varieties and can be directly applied to improve cold tolerance in super hybrid rice parent 93-11 and other indica and japonica rice varieties, expanding their cultivation areas and ensuring food supply security [FIGURE:1].

The related research was published as a cover article in *Cell* and selected as one of *Cell*'s Best Papers of 2015 and Best Papers by Chinese Authors. It was also chosen as one of the Top Ten Advances in Chinese Life Sciences for 2015. International mainstream journals including *Cell*, *Science Signaling*, and *Molecular Plant* published special commentaries on the COLD1 research, which received extensive coverage from Xinhua News Agency, *Guangming Daily*, *China Science Daily*, *Hong Kong South China Morning Post*, and *Wenhui Daily*.

2.1.2 Breaking the “High Yield but Not High Quality” Bottleneck

For a long time, China's rice breeding has primarily focused on ensuring yield improvement, often resulting in relatively poor grain quality in high-yielding varieties. The Fu Xiangdong research team at the Institute of Genetics and Developmental Biology successfully isolated and cloned GW7, a key gene controlling rice grain shape and improving grain quality, from the high-quality hybrid rice sterile line Taifeng A. This gene alters cell division patterns, making rice grains slender and effectively reducing chalkiness, thereby improving appearance, taste, and other quality aspects. By pyramiding superior allelic variations of GW7 and GS3 genes in China's high-yielding indica rice, simultaneous genetic improvement of both quality and yield can be achieved. This breakthrough was published in the internationally renowned journal *Nature Genetics*.

In a news report on this achievement, *Nature* quoted Professor Susan McCouch of Cornell University, who stated that no one has yet successfully addressed both high yield and high quality simultaneously in rice breeding, calling it “a hugely impactful research outcome.”

2.1.3 Major Breakthrough in Rice Nitrogen Use Efficiency Improvement

Nitrogen fertilizer is the most critical factor for increasing crop yields. China applies over 60 million tons of chemical fertilizer annually. Heavy nitrogen application not only increases agricultural production costs but also causes environmental disasters including climate change, soil acidification, and water eutrophication. The key to solving these problems lies in developing new crop varieties with high nitrogen use efficiency. The Chengcai Chu research team at the Institute of Genetics and Developmental Biology cloned the high nitrogen use efficiency gene NRT1.1B from indica rice. Introducing the indica-type NRT1.1B into japonica rice varieties can increase yield by 8–10% under normal nitrogen conditions, with nitrogen use efficiency improved by approximately 10%. Under half-rate nitrogen application, yield increases by 30–33% compared to controls, with nitrogen use efficiency improved by 30%. This research provides an important molecular module for the “molecular module design breeding” and “green super rice” concepts proposed by Chinese scientists, holding tremendous application value. The results were published in *Nature Genetics* [FIGURE:2].

Nature Plants published a special commentary stating that “this work solves the long-standing mystery of nitrogen utilization efficiency differences between indica and japonica rice and provides important genetic resources for nitrogen-efficient rice improvement.” This achievement was also selected as one of the Top Ten Advances in Chinese Life Sciences for 2015.

2.1.4 Providing New Ideas for “Green Agriculture” Statistics show that rice nitrogen fertilizer use efficiency is very low, with approximately 63–72% of nitrogen being released into the environment as nitrogen gas, nitrous oxide, and other forms, causing atmospheric pollution and eutrophication of rivers and lakes. The Fu Xiangdong research team discovered that DEP1, a key rice yield-increasing gene cloned previously, also plays an important role in nitrogen-efficient utilization. The DEP1 allelic mutant shows reduced sensitivity to nitrogen during the vegetative growth stage but improved nitrogen uptake and utilization efficiency during reproductive development, ultimately enabling higher yields under appropriately reduced nitrogen fertilizer conditions. This finding identifies a new pathway for sustainable “green agriculture” development that can simultaneously increase total grain output, improve nitrogen use efficiency, reduce production costs, and minimize environmental pollution. The related research was published in *Nature Genetics*.

2.2 Major Breakthroughs in Core Breeding Technology Research

2.2.1 Systematic Analysis of Heterosis in Rice Yield Traits Heterosis results from parental genome interactions and represents a complex biological phenomenon, yet its underlying genetic mechanisms have long remained unclear. The Bin Han research team at the Institute of Plant Physiology and Ecology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, and collaborators collected 1,495 hybrid rice variety materials and conducted ge-

omic analysis and field evaluation of yield traits on 17 representative genetic populations. By comprehensively applying cutting-edge techniques from genomics, quantitative genetics, and computational biology, they systematically identified the major genetic loci controlling rice heterosis and ultimately elucidated its molecular mechanisms. This research holds significant implications for advancing precision molecular design breeding practices in both hybrid and conventional rice. The related study was published online in *Nature* on September 8, 2016.

Following publication, *Nature* also featured a special commentary by Professor James Birchler, who stated that the paper “deciphers the genetic basis of heterosis and will help guide future crop genetic improvement strategies,” calling it “a tour de force study” in crop heterosis research.

2.2.2 Using Population Genetics to Analyze Rice Grain Size and High-Yield Regulation Mechanisms Rice grain size is an important factor affecting both yield and quality, yet the genetic mechanisms controlling this typical grain trait difference between tropical and temperate japonica rice varieties remain unclear. Academician Bin Han’s research team developed an integrated genome-wide association analysis approach to conduct GWAS on grain length and thousand-grain weight in 40 tropical japonica and 341 temperate japonica rice accessions. They identified a key quantitative trait locus, QTL-GLW7, that controls both grain length and thousand-grain weight, and successfully cloned the key gene GLW7 controlling rice grain length and weight. This research not only refines the gene identification method for rice complex traits based on genome-wide association analysis but also elucidates a new molecular mechanism regulating rice grain size. More importantly, this gene provides crucial genetic resources for high-yield and high-quality breeding of japonica rice, with broad application prospects. The related research was published in *Nature Genetics* on March 7, 2016.

2.2.3 Systematic Analysis of Genetic Basis of Soybean Domestication and Improvement The Zhixi Tian research team at the Institute of Genetics and Developmental Biology and collaborators conducted deep resequencing ($>10\times$) and genomic analysis of 302 representative soybean germplasm accessions. The results indicate that genetic polymorphism in soybean decreased significantly during domestication and improvement, suggesting a clear selection bottleneck effect

. Using the XP-CLR method, 121 strong selection signals were identified during the domestication stage (wild soybean $\rightarrow$ landrace) and 109 during the improvement stage (landrace $\rightarrow$ cultivated variety). Genome-wide association studies (GWAS) on seed size, coat color, growth habit, and oil content revealed that oil content traits have undergone intensive artificial selection, forming a complex regulatory network controlling oil metabolism. The study also mapped regulatory loci for important agronomic traits and clarified the role of specific

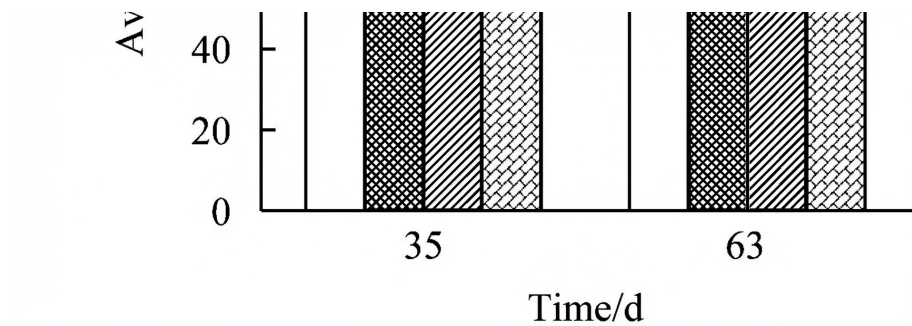


Figure 1: Figure 3

genes in regional selection, such as E1 controlling flowering time, Dt1 controlling growth habit, and T controlling pubescence color. This work provides an important foundation for studying the regulatory networks of key agronomic traits in soybean. The related research was published in *Nature Biotechnology* in 2015.

2.3 Important Breakthroughs in Core Breeding Key Technologies

As President Xi Jinping stated, “With grain in hand, there is no panic.” Food security concerns national stability. The Food and Agriculture Organization (FAO) predicts that global food demand will need to double by 2050, requiring crop yields to maintain an annual growth rate of over 2.4%. Currently, annual yield growth rates for rice, maize, wheat, and soybean are only 1.0%, 1.6%, 0.9%, and 1.3%, respectively. With China’s population increasing by 6.5 million annually, requiring an additional 2.6 billion kilograms of grain, meeting the rigid demand for food remains a formidable task.

Addressing major strategic needs for China’s food security and strategic emerging industry development, the program focuses on rice with wheat and carp as supplementary targets. Through dissection of important molecular modules, it establishes a molecular module design breeding innovation system for multi-module coupling and assembly, cultivating designer new varieties with high yield, superior quality, stable production, and high efficiency suited to modern agriculture. Since its launch over three years ago, the program has developed 13 new rice lines, 11 new wheat lines, 1 new crucian carp line, 6 new soybean lines, and 1 new maize line, which are undergoing national and provincial variety registration trials. Seven new varieties have already been approved.

Taking rice as an example, in the middle and lower Yangtze River region, the Jiayou Zhongke 3 new line developed by the Jiayang Li research team using the IPA1 new allele gene WS8 achieved over 10% yield increase compared to controls in both regional and production trials of single-crop japonica hybrid rice in Zhejiang Province (19.4% increase in 2014) and has passed Zhejiang provincial

variety approval. In Northeast China, using the high-quality rice variety Dao-huaxiang 2 as the chassis variety and introducing blast resistance and lodging resistance modules, over 200 intermediate materials with significantly improved blast resistance, compact plant architecture, and strong lodging resistance have been obtained, enabling coordinated improvement of quality, lodging resistance, and yield in recipient varieties. Using the main cultivar Kongyu 131 as the chassis variety, over 1,000 multi-module pyramiding materials with blast resistance and long-grain genes have been obtained, laying a foundation for further selection of molecular module-based new varieties meeting breeding objectives. These interim achievements have broken the long-standing plateau in China's major crop breeding and opened a new chapter in Chinese design breeding.

3. Originality

Addressing current bottlenecks in breeding technology development, this program applies the concept and approach of module design breeding, integrating genomics, computational biology, systems biology, and synthetic biology. Through systematic analysis of molecular regulatory networks underlying complex traits such as high yield, superior quality, stable production, and high efficiency in animals and plants, the program proposes a theory of superimposed molecular module control of complex traits. Leveraging the Chinese Academy of Sciences' advantages in multidisciplinary integration and technology convergence, the program overcomes key technical bottlenecks in efficient molecular module dissection and coupling, establishing an agricultural biological molecular breeding theory and technology innovation system from molecular module analysis to assembly. This aims to achieve a leapfrog development of molecular design breeding technology from "molecular modules" to "designer varieties" for crops within 10 years, promoting the formation of China's modern seed industry and upgrading major agricultural biological varieties.

4. Significance for Industry

The successful implementation of this program has guided the launch of the National Key R&D Program "7 Major Crops Breeding Special Project." Among the 16 pilot projects initiated in 2016, 6 were led by core backbone members from this program, demonstrating its leading and driving role in national major scientific research program planning.

5. Recommendations for Future Deployment

(1) Establish a talent cultivation and evaluation system aligned with disciplinary characteristics and laws. Currently, a "one-size-fits-all" talent and discipline evaluation mechanism oriented toward publications commonly exists in China. It is essential to establish corresponding evaluation systems for talent cultivation and disciplinary development guided by the "three orientations": facing world science and technology frontiers, facing major national

needs, and facing the main battlefield of national economy.

(2) Establish a variety registration and approval system suited to China's agricultural production. The current variety approval system constrains the sustainable development of breeding science and technology. A variety registration and approval system that accommodates both conventional and molecular breeding technology development and meets market demands needs to be established.

(3) Establish an industry system aligned with variety promotion. Currently, there is a disconnect between variety approval and promotion in China, with many approvals but few promotions. A policy system centered on market entities is needed to promote the healthy development of the seed industry.

(Host Institution: Institute of Genetics and Developmental Biology, Chinese Academy of Sciences)

Source: ChinaXiv — Machine translation. Verify with original.