

Maize2035: A decadal vision for intelligent maize breeding

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ABSTRACT

Maize, a cornerstone of global food security, has undergone remarkable transformations through breeding, yet further increase in global maize production faces mounting challenges in a changing world. In this Perspective paper, we overview the historical successes of maize breeding that laid the foundation for present opportunities. We examine both the specific and shared breeding goals related to diverse geographies and end-use demands. Achieving these coordinated breeding objectives requires a holistic approach to trait improvement for sustainable agriculture. We discuss cutting-edge solutions, including multi-omics approaches from single-cell analysis to holobionts, smart breeding with advanced technologies and algorithms, and the transformative potential of rational design with synthetic biology approaches. A transition toward a data-driven future is currently underway, with large-scale precision agriculture and autonomous systems poised to revolutionize farming practice. Realizing these futuristic opportunities hinges on collaborative efforts spanning scientific discoveries, technology translations, and socioeconomic considerations in maximizing human and environmental well-being.

Key words: food security, *Zea mays*, genomic prediction, synthetic biology, multi-omics, hologenomics

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INTRODUCTION

If helium flashes, earthquakes, floods, droughts, cold spells, and extreme heat—all these massive fluctuations—have not instantly wiped out our human race, then we, who survive in the narrow crevices left by the universe, still need to bargain with nature, still need agriculture (Inspired by Liu Cixin's “The Wandering Earth”).

The referenced book concisely captures a doomsday perspective of global climate change. Hopefully, as plant scientists, we can contribute to ensuring not only that the worst-case scenario does not occur but also global food security in a changing world. Intensive agriculture practices carry a significant environmental footprint, including high water usage and pollution from over-fertilization and pesticide use. Transitioning to sustainable

agriculture is therefore critical. This Perspective offers a decadal vision for maize breeding, encompassing foundational aspects of maize breeding as well as discussing how modern technologies are being embraced to further this. We will highlight the opportunities afforded by marrying data science to breeding to meet the massive societal challenges. We propose two synergistic approaches as key components of intelligent maize breeding: programmable molecular design and guided selection based on precise trait prediction. These, combined with other system advances, offer holistic solutions. The fact that we are attempting this coincides with a formidable challenge, compounded by rising global food demand, declining arable land availability, and the effects of climate change, underscoring the need for collaborative efforts.

SUCCESS IN MAIZE BREEDING UNDER PARADIGM SHIFT

Originating in central Mexico from the wild grass teosinte approximately 9000 years ago and following the Columbian exchange, maize spread rapidly across the globe, adapting to diverse environments through further human-involved artificial selection and natural selection (Doebley et al., 2006; Yang et al., 2023a). Over the past century, maize yields have increased dramatically, more than six-fold in the US (10 883 kg ha⁻¹ in 2022 vs. 1651 kg ha⁻¹ in 1922) and five-fold in China (6436 kg ha⁻¹ in 2022 vs. 1185 kg ha⁻¹ in 1961)—the two leading producers, together accounting for over half (54% in 2022, with 277.42 million tonnes in China and 348.75 million tonnes in US) of global maize production (1.16 billion tonnes, data from the Food and Agriculture Organization of the United Nations, FAO; Figure 1A). This remarkable achievement stems from a philosophical evolution throughout the breeding history, from empirical farmer selection to a sophisticated science driven by technology and deeper understanding of genetics and molecular biology (Wallace et al., 2018; Ramstein et al., 2019).

Pre-scientific era (before 1900s)

Early maize improvement relied heavily on farmer empirical selection based on observable traits like ear size, kernel type, and maturity. This was characterized by a largely intuitive and localized approach, with farmers saving seeds from the best-performing plants in their fields (Ramstein et al., 2019). Knowledge was passed down through generations, leading to the development of diverse landraces adapted to specific environment. While proving inefficient with the lack of a formal scientific framework, yields stagnated between 1200 and 2000 kg ha⁻¹ for over 70 years prior to hybrid adoption (data from the US Department of Agriculture, USDA). However, this period established the foundation for modern maize diversity (Van Heerwaarden et al., 2011).

Early scientific era (early to late 1900s)

The rediscovery of Mendel's laws of inheritance and the development of quantitative genetics revolutionized maize breeding. The introduction of heterosis through double-cross and then single-cross hybrids in the US dramatically increased yield, climbing steadily from 1814 kg ha⁻¹ in the 1940 to more than 8000 kg ha⁻¹ in the year 2000 (USDA). Maize, with its outcrossing nature and high genetic diversity, shows exceptionally strong

heterosis. Breeding shifted from farmers to commercial companies and toward a more controlled and scientific approach, emphasizing the development of elite inbred lines. This led to germplasm concentration, with many widely used lines derived from only a few foundational inbreds (Mikel and Dudley, 2006).

Gene-focused era (since late 1980s)

Molecular biology and statistics enabled identification of quantitative trait loci (QTLs), genes, and causal variants, paving the way for marker-assisted selection (MAS). A good example is provided in vitamin A biofortification: two genes (*lcyE* and *crtRB1*) were identified for kernel carotenoid content (Harjes et al., 2008; Yan et al., 2010), with *crtRB1* boosting beta-carotene and provitamin A two- to 10-fold (Babu et al., 2013). Over 40 biofortified varieties incorporating these favorable alleles have been released in Africa, improving vitamin A supplementation and visual function in deficient children.

This era also witnessed the rise of transgenic breeding, exemplified by the introduction of *Bacillus thuringiensis* (Bt) maize that expresses crystalline (Cry) proteins toxic to certain insect pests. This technology reduced insecticide use and provided significant economic benefits to farmers (Hutchison et al., 2010). Actually, genetic improvement has driven over 50% of yield gains in major maize-producing countries (Fernández et al., 2022), highlighting the greater effectiveness of breeding informed by functional genomics, MAS, and transgenics.

Systems-thinking era (since 2000s)

High-throughput genotyping and sequencing ushered in the genomics era. Genomic selection, using genome-wide markers to predict breeding values, became powerful for improving complex traits (Crossa et al., 2017a). A systems-biology perspective emerged, moving beyond the focus on individual genes to recognize the interconnectedness of genes, pathways, and the environment. Multi-omics approaches are providing a more holistic understanding of plant function, enabling more targeted breeding strategies (Xiao et al., 2017; Wallace et al., 2018; Ramstein et al., 2019; Scossa et al., 2021).

The contributions of the systems-thinking era to maize breeding and agricultural production are evident through several key advances. Studies have demonstrated that genomic selection can improve prediction accuracy for complex traits compared to conventional and MAS methods and thus reduce the breeding cycle (Crossa et al., 2017b). Additionally, multi-omics approaches have been instrumental in identifying gene networks and metabolic pathways associated with yield improvement and stress resilience (Yamaguchi-Shinozaki and Shinozaki, 2006; Xiao et al., 2017; Yuan et al., 2024; Nolan and Shahan, 2023; Mascher et al., 2024). These advancements highlight the significant impact of systems-based approaches on modern maize breeding.

Intelligent-design era (present and beyond)

Maize has been a highly successful model for applying heterosis, transgenics, and genomic selection. This historical overview highlights the continuous evolution of maize breeding philosophy, driven by scientific advancements and the increasing complexity of breeding targets. Now, facing challenges like a growing global

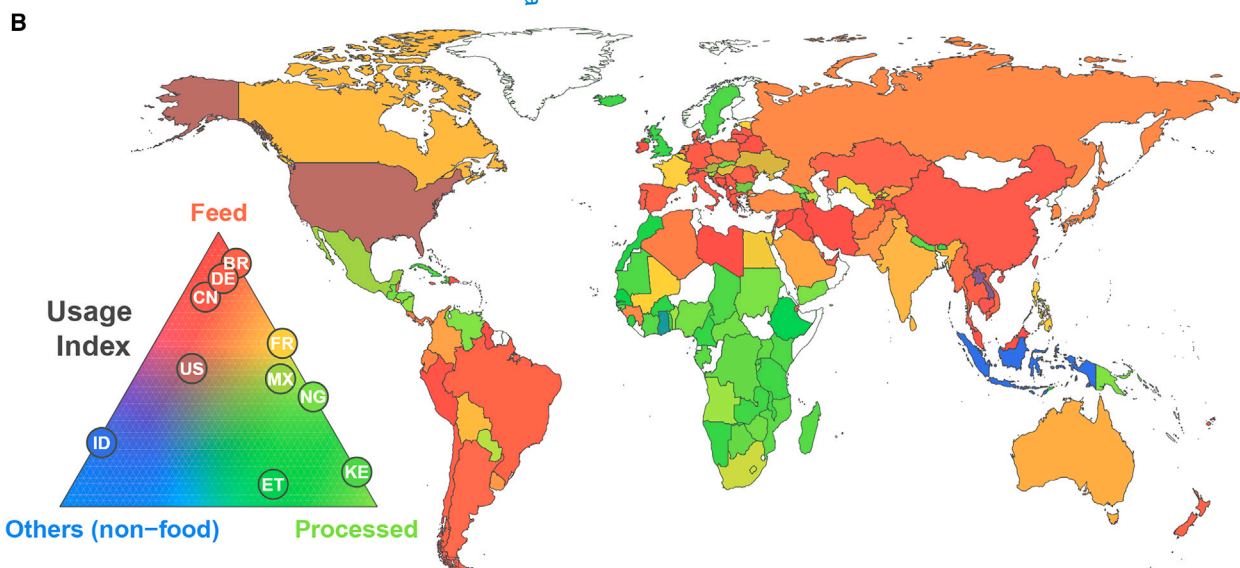
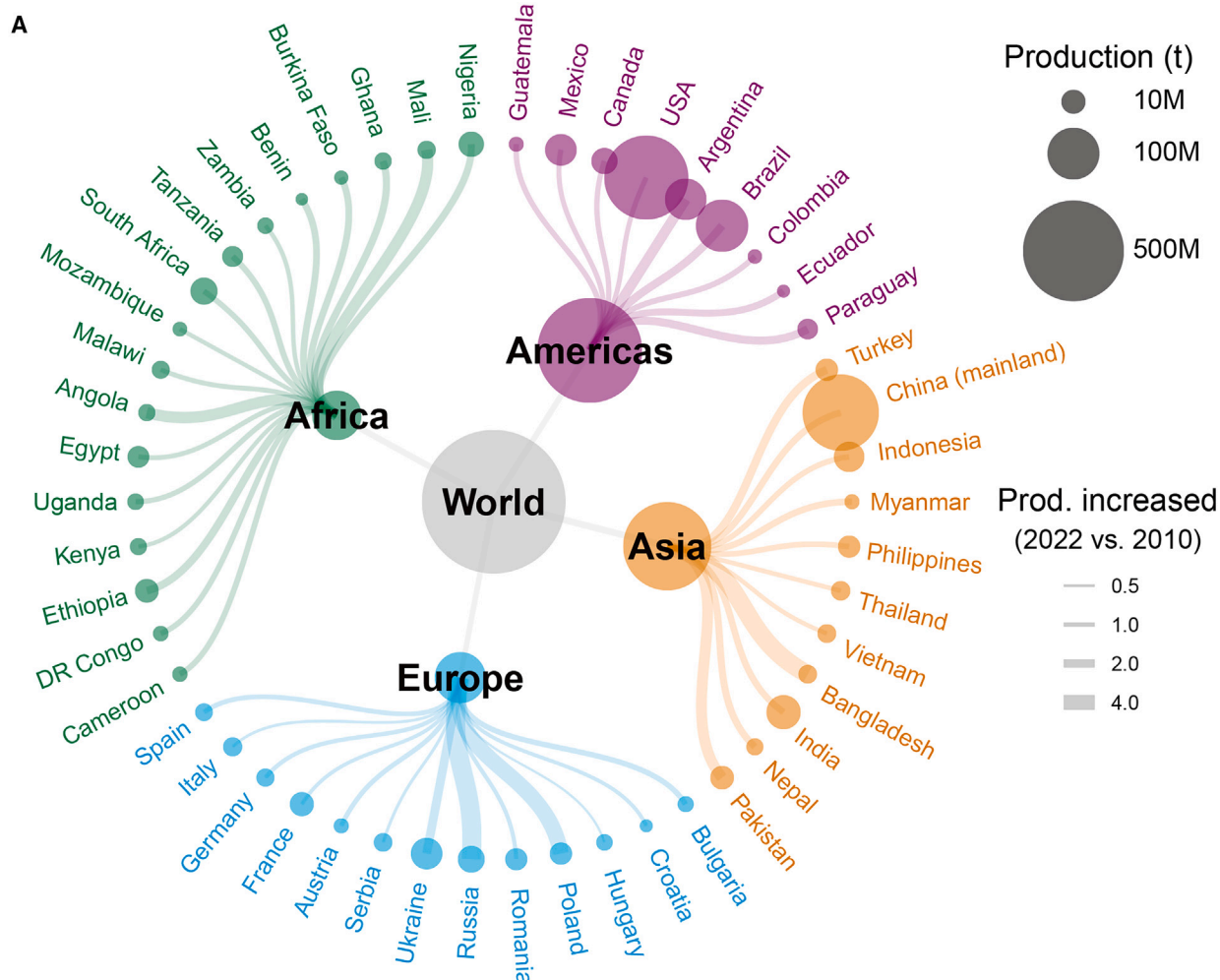


Figure 1. Global maize production and consumption.

(A) Maize production among the top 50 countries, represented by node size. Line thickness shows production change from 2010 to 2022 (2 = double production; 0.5 = half). Data sourced from FAOSTAT.

(B) Maize consumption is categorized into three main uses: feed (red), food processing (green), and non-food uses (such as industrial energy, blue). Ten representative countries were selected to demonstrate varied consumption preferences: CN (China, mainland), ID (Indonesia), US (United States), BR (Brazil), MX (Mexico), NG (Nigeria), ET (Ethiopia), KE (Kenya), FR (France), and DE (Germany).

population, shrinking arable land, and climate change, a paradigm shift toward accelerated, precise, and programmable breeding is essential.

Recent advances in genomics and computation are propelling this transformation. Advancements in doubled-haploid technology, including clearer mechanisms and higher haploid induction rate, accelerate breeding by generating homozygous lines in a single generation (Jacquier et al., 2020; Jiang et al., 2022; Meng et al., 2021; Qu et al., 2024). Automated phenotyping utilizing advanced imaging and sensor technologies provides high-volume phenotypic data for genomic selection (Yang et al., 2020; Alemu et al., 2024). Concurrently, we are entering a data-driven decision-making era. Artificial intelligence (AI) and machine learning are shifting maize breeding from descriptive to predictive biology. AI mines high-dimensional datasets (phenotypic, genotypic, and multi-omics) for comprehensive insights (Liu et al., 2020b; Durand et al., 2024). Genome-informed predictive models guide selection and crosses (Wallace et al., 2018; Farooq et al., 2024). In addition, genome editing allows precise modifications, enabling trait introduction, correction of defects, and fine-tuning of gene expression (Wang and Doudna, 2023; Li et al., 2024a). Synthetic biology offers the potential to create novel genetic circuits and environmentally responsive traits (Khalil and Collins, 2010).

Integrating these two, precise predictions of traits directly from genomic data and precise molecular design with guided targets will further make rational breeding more practical, leading to a holistic, data-driven, and predictive approach. While systems-based approaches laid the groundwork for understanding biological complexity, the intelligent-design era integrates AI and molecular-design technologies to accelerate and enhance breeding precision. We anticipate that, in the coming decades, intelligent maize breeding integrating these advances will move into a rapid, precise, and programmable framework. Before exploring these key components in detail, we next examine current and future demands on maize breeding from both socioeconomic and trait perspectives.

THE DIVERSE AND SHARED DEMANDS

Although global maize production keeps increasing generally, higher increases in the last decade happen mainly in developing countries, particularly in low/lower-middle-income countries (Figure 1A; Erenstein et al., 2022). However, this growth is insufficient to meet projected demand. Global cereal demand is expected to reach 3.28 billion tonnes by 2035, with maize comprising a substantial portion (43.5%, 1.427 billion tonnes) of this total (data from the Organisation for Economic Co-operation and Development and the Food and Agricultural Organization of the United Nations, OECD-FAO Agricultural Outlook, 2024–2033). China and the US alone are anticipated to require approximately 340 million tonnes in 2035. Meeting this growing need presents a considerable challenge, particularly for China, which will require a 23% production increase compared to current levels. The fact that Chinese maize production saw a modest total increase of 5% from 2015 to 2022 highlights the challenge. Closing this yield gap requires a multifaceted strategy. One promising avenue lies in optimizing planting density. Studies suggest that increasing planting density to an

average of 7.8×10^4 plants ha^{-1} (currently at only 77% of this target) is possible to meet the predicted demand in China, highlighting the crucial need for developing high-density-tolerant maize varieties (Luo et al., 2023). These varieties must not only withstand closer spacing but also maintain high yield potential under these conditions. Beyond planting density, achieving future production targets will necessitate concurrent advancements in accelerating breeding cycles, scaling up breeding efforts, and increasing precision.

Diverse usage of maize

The ultimate goals of breeding programs are also shaped by the diverse ways in which maize is utilized across the globe, and the consumption choices matter breeding strategies (Figure 1B). In many countries, such as China, Brazil, most European countries, and North Africa, maize was primarily used for animal feed (>65%, FAO). In Central and South Africa, maize is primarily used as staple (direct or processed) food, providing a substantial portion of daily caloric intake (63% of Africa in 2022). In the US, maize is divided relatively equally between industrial uses (e.g., 38% for ethanol production) and animal feed (40% in 2022; USDA). There are also policies from the European Union to plan to shift more cropland to bio-energy (Searchinger et al., 2022).

These differing utilization patterns drive distinct breeding priorities. While the US may focus on developing high-starch maize for industrial applications, China prioritizes high-yielding, high-protein varieties for animal feed, influenced by the availability of other feed crops like soybeans. In regions where maize is a staple food, nutritional enhancement is a critical breeding goal.

The “high-five” shared demands

Despite differing priorities among countries, some breeding goals remain universally crucial for global food security. We summarize these as five key pillars, reflecting the need to address multiple challenges and capitalize on emerging opportunities simultaneously.

High yield

Meeting global food demand requires continuously increasing maize yield potential. The planting density has trended together with yield per unit area in an increasing fashion over time over the last decades. High-density planting, while potentially reducing individual plant yield, increases overall yield per hectare. For instance, from 1930 to 2010 in the US Corn Belt, maize plant density increased 2.5-fold while yield increased 7.5 times (Mansfield and Mumm, 2014). This necessitates adapting varieties to high-density conditions (Mansfield and Mumm, 2014).

Increased density creates competition for resources. Breeding targets include “smart canopy” traits (Tian et al., 2024; Ort et al., 2015), enhanced photosynthesis and source-sink relationships (Ort et al., 2015; Yan et al., 2024), reduced shade avoidance (Jafari et al., 2024; Liu et al., 2021e), optimized root systems (Ren et al., 2022), and increased stress tolerance (Check et al., 2023). Optimizing planting density requires a holistic assessment of varietal traits, environment, and management practices. Furthermore, the breeding goals outlined below primarily contribute to achieve high and stable yields as well.

High resistance

Protecting yields from biotic stress is paramount. While progress has been made against fungal and viral diseases (Zhong et al., 2024; Li et al., 2019; Chen et al., 2022a; Chen et al., 2023a; Deng et al., 2024; Li et al., 2024b), translating research into effective field solutions remains a challenge. High-density planting can exacerbate disease outbreaks due to elevated humidity and temperature (Check et al., 2023; Chen et al., 2022a), further emphasizing the need for disease-resistant varieties.

Pest management is increasingly challenging due to evolving resistance to Bt toxins and pesticides (Tabashnik and Carrière, 2017) and the rising risk of invasive species (Early et al., 2016). Climate change further alters disease distribution and severity. For example, southern rust has recently expanded northward in China, causing significant losses in the Huang-Huai-Hai region.

A multifaceted approach is needed to address biotic stress, including diversifying resistance genes, pyramiding strategies, understanding pathogen and pest co-evolution, and developing integrated management strategies.

High adaptability

Breeding maize for environmental adaptation is essential, particularly by optimizing flowering time and (suboptimal) temperature tolerance. Latitude significantly influences these traits: tropical maize exhibits short-day flowering, while temperate maize shows long-day or day-neutral responses (Buckler et al., 2009; Liang et al., 2021). Temperature tolerance involves adaptations to both heat and chilling stress when grown in distinct regions (Rezaei et al., 2023; Zeng et al., 2021; Wang et al., 2025). High adaptability relies on genetic diversity and plasticity, enabling variety's broad geographic range.

Climate change poses additional multifaceted threats to maize production. Extreme heat, drought, and waterlogging can severely impact yields (Lesk et al., 2022; Rezaei et al., 2023; Yang et al., 2023b). While elevated CO₂ can benefit C3 crops, its effects on C4 maize are limited and primarily under drought (Rezaei et al., 2023). Climate change impacts vary regionally and temporally; some regions may experience intensified drought, while others face increased precipitation and waterlogging. This change can also happen at one location in different years. In China, projections indicate a northward shift of the temperate zone, potentially redistributing suitable maize-growing areas (Rezaei et al., 2023).

Improving saline-alkali adaptability is additionally crucial for expanding maize cultivation onto marginal lands (Yang et al., 2023b; Cao et al., 2023b). Salinity reduces water uptake and causes ion toxicity, while alkalinity disrupts nutrient availability and impairs root growth. Exploiting tolerance alleles from diverse maize germplasm (Cao et al., 2020; Liu et al., 2024a), understanding physiological mechanisms (Yang et al., 2023b; Cao et al., 2023b), and harnessing the role of beneficial microbes (Liu et al., 2024a; Ali et al., 2023) are multi-pronged approaches to enhancing these tolerances.

Studies in the area of plant stress biology are now beginning to embrace the fact that most crops face multiple stresses if not simultaneously then at least sequentially. Intriguingly, despite

common claims that it is difficult to predict the response of multiple stresses by looking at the stresses individually (Zandalinas and Mittler, 2022; Yang et al., 2023b), studies of the effects of multi-stress in maize at the metabolomic level reveal that this can be achieved (Obata et al., 2015; Yang et al., 2022c).

Breeding climate-resilient maize requires moving beyond static improvements in traits like root architecture, photosynthetic efficiency, stomatal regulation, and senescence. Phenotypic plasticity with intelligent environmental response, leveraging genotype-by-environment (GxE) interactions (Napier et al., 2023) and diverse environmental response elements (EREs) (Yamaguchi-Shinozaki and Shinozaki, 2006), is highly crucial, as shown in the study of *ZmDRO1*, whose constitutive over-expression was detrimental where conditional activation improved drought tolerance without yield penalty (Feng et al., 2022). This responsive practice would optimize resource acquisition based on environmental cues and should be central to future breeding efforts.

High nutrition

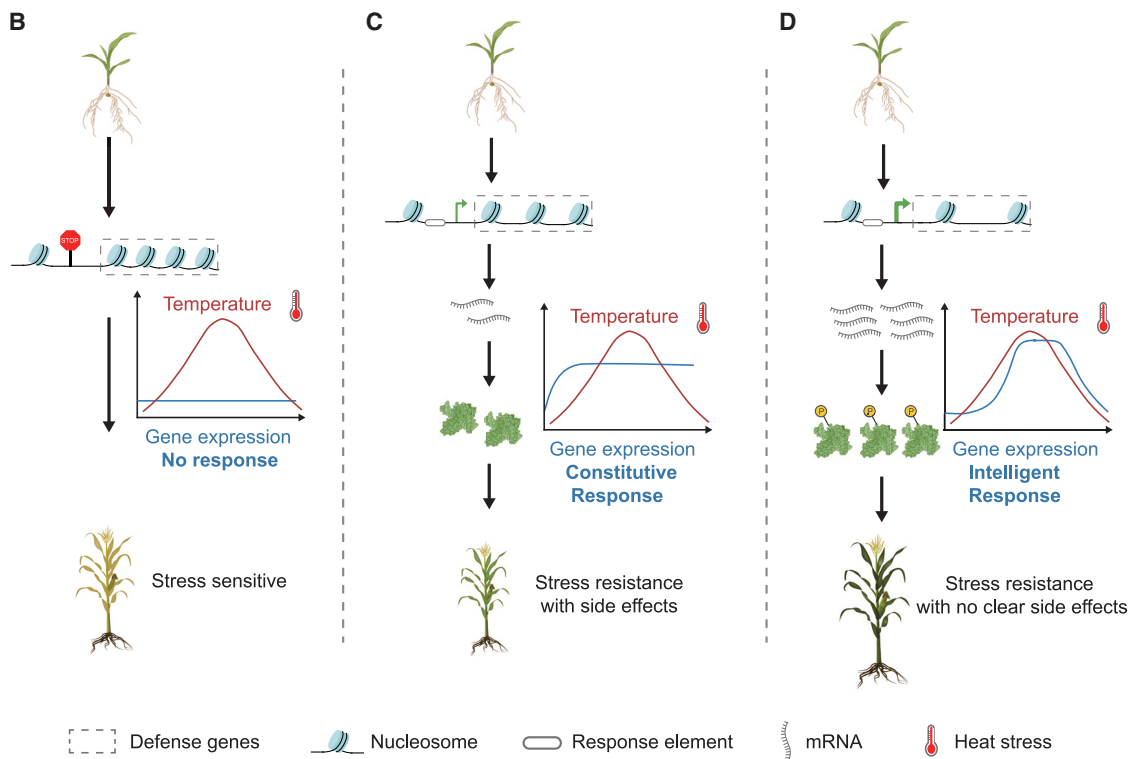
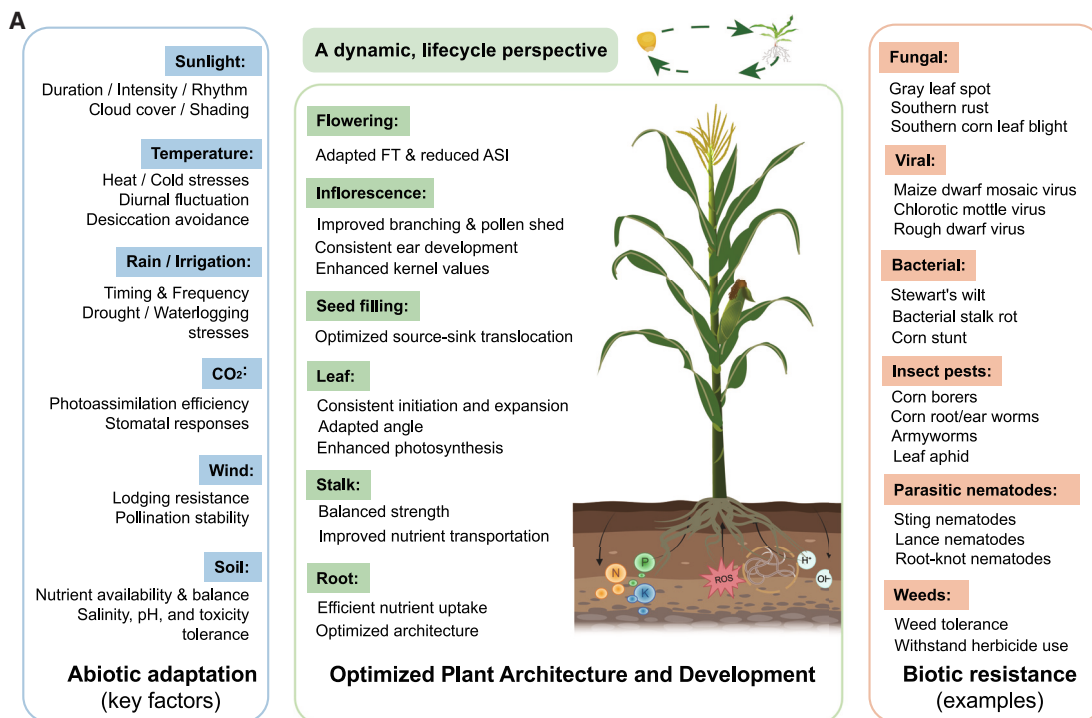
Beyond calories, maize must contribute to a healthy diet. Increasing the protein content and quality of maize will be vital for addressing malnutrition; therefore, enhancing nitrogen and phosphorus use efficiency is vital. *Teosinte High Protein 9 (THP9)* cloned recently has shown the promise for increasing protein content (Huang et al., 2022). Biofortification of micronutrients like vitamins A and E, folate, and iron is also being pursued (Yan et al., 2010; Liu et al., 2024b; Yan et al., 2023). Harnessing these genetic resources through integrated approaches has immense potential for improving human health, particularly in developing countries, which are generally less diverse with respect to the dietary requirements.

Enhancing maize nutritional value should benefit not only humans but also animals, and maize can be tailored to specific needs. Particularly, for livestock, improving feed conversion ratios and reducing reliance on synthetic supplements can improve animal health and lessen the environmental impact. We should be fully aware that, in certain countries and regions, maize may function not only as an energy source but also as a source of protein and other essential elements.

High value

The advancement of sweet and waxy corn demonstrates the market potential for specialty maize with tailored quality traits (Luo et al., 2024). This success can guide commercialization of emerging value-added types, such as anthocyanin-rich, high-folate, and high-oleic corn (Bhushan et al., 2024; Zambelli, 2021).

Expanding industrial applications through value-added traits and advanced bio-product development would maximize maize's economic and societal benefits. This requires tailoring traits, such as modified starch for biofuels (Niu et al., 2023) and increased fiber digestibility for animal feed (Vanhevel et al., 2024). Utilizing maize for pharmaceuticals (Chung et al., 2022) or biomaterials (Marichelvam et al., 2019) further diversifies its applications. Advancing maize as a versatile bio-product platform requires elucidating biosynthetic pathways, improving transformation systems, and applying synthetic biology (Rizzo et al., 2023). This will contribute to a sustainable bio-based economy.



(legend continued on next page)

Importantly, while striving for these “highs” in maize breeding, minimizing inputs is equally crucial. This “low-input” approach is essential for sustainable agriculture, addressing both economic and environmental concerns. It involves developing varieties that thrive with reduced reliance on external resources (like fertilizers and water) and simplified management practices (like those suited for mechanization).

Holistic phenotype optimization for the future

Future phenotypic improvement requires considering the complex interplay of traits, environment, and sustainability (Figure 2A). This necessitates addressing trade-offs like the “growth-defense” dilemma, where resource allocation must balance growth with stress responses (He et al., 2022). While enhancing resistance is achievable, universal solutions for this trade-off remain elusive. Phytohormones play a crucial role, with some promoting growth and others mediating defense (Berens et al., 2017). Precise spatiotemporal control of key genes and the use of environment-responsive elements offer promising approaches to optimize resource allocation through rational design of genetic circuits. A systems approach is essential for sustainably increasing productivity without compromising quality, safety, or environmental integrity (Tester and Langridge, 2010).

Breeding objectives must also balance performance with adaptation to increasingly unpredictable environments. Climate change poses a significant threat to maize production (Yang et al., 2024). Developing tolerance to extreme heat is particularly crucial, as data indicate decreasing heat tolerance in modern hybrids (Kusmec et al., 2023). Furthermore, climate change can exacerbate biotic stresses like diseases and pests (Outhwaite et al., 2022).

Future maize improvement therefore requires a multi-objective perspective, simultaneously addressing nutritional, ecological, and ethical needs. This lies in integrative, inclusive, and foresight-driven innovation, developing varieties that respond intelligently to environmental fluctuations and disease pressures (Tester and Langridge, 2010) (Figures 2B–2D). Such a holistic approach is essential for climate-ready, high-performing, and sustainable maize.

CORE METABOLIC PRINCIPLES IN MAIZE BREEDING

While specific phenotypic traits are important direct targets, understanding the underlying fundamental energetic and metabolic processes driving these objectives is also critical and inspiring. Current challenges in maize breeding include enhancing nitrogen use efficiency (NUE), optimizing photosynthesis and harvest in-

dex, and balancing carbon and nitrogen metabolism. Addressing these requires a deeper understanding of molecular mechanisms and innovative strategies.

NUE

Nitrate serves as both a primary nitrogen source and a signaling molecule regulating plant development (Wang et al., 2004). Efficient nitrate uptake, transport, and translocation are essential for optimal growth (Vidal et al., 2020). Research in *Arabidopsis* has provided insights into nitrate pathways (Wang et al., 2018; Li et al., 2021), but translating this knowledge to maize remains challenging. Comparative genomics has identified related genes, but few underlying QTLs have been cloned (Liu et al., 2022).

Improving NUE is crucial given negative impacts of excess fertilizer. Optimizing nitrogen use under reduced fertilizer input requires identifying key nitrogen transporters and sensors, with progress in *Arabidopsis* (Wang et al., 2018; Liu et al., 2022) outpacing maize. This potentially due to the greater genomic complexity of maize and functional redundancy. While traditional phenotypic analyses are based on biomass or nitrate concentration, new tools like biosensors facilitate direct nitrate visualization (Chen et al., 2022c; Liu et al., 2022), complementing isotopic labeling (Stüeken et al., 2015). Further research should explore regulatory networks, root architecture, microbiome interactions, and nitrogen form's influence on NUE and plant growth.

Photosynthesis and harvest index

Photosynthesis is the primary driver of biomass production. In the US Corn Belt, biomass increased by an estimated 86% from 1970 to 2020, with a 15% increase in the harvest index (Ruiz et al., 2023). Enhancing photosynthetic efficiency remains a high priority in maize breeding. Strategies include engineering Rubisco (Bracher et al., 2017), which could significantly enhance carbon assimilation.

Optimizing light interception through leaf angle and canopy structure is crucial for maximizing photosynthetic efficiency (Tian et al., 2019). Emerging technologies like 3D phenotyping and modeling can facilitate ideotype-based breeding. Furthermore, understanding the interplay between photosynthesis and other metabolic processes (e.g., respiration and photorespiration) is key for holistic yield improvement.

Balancing carbon and nitrogen metabolism

Photosynthesis and nitrogen metabolism are intricately linked. Rubisco synthesis depends on nitrogen availability (Bracher et al., 2017), and numerous carbon metabolism genes are regulated by nitrogen signaling (Wang et al., 2004), including

Figure 2. Holistic view of maize breeding goals. Future improvement requires a holistic, dynamic, environment-responsive approach, considering interactions with other organisms and environmental factors.

(A) Current research often focuses on individual traits or specific biotic/abiotic stresses (as shown for key tissues and relevant developmental processes, biotic stressors, and effects from environmental factors). Future breeding strategies have to integrate these complex interactions, including beneficial microbiome associations, for comprehensive optimization. FT, flowering time; ASI, anthesis-silking interval.

(B–D) Design and advantage of intelligent environmental responses, taking heat stress as an example. **(B)** A case with no stress response, where the gene remains inactive regardless of temperature changes. **(C)** A continuous response with constitutively high expression of the responsive gene, whether the stress is present or not. **(D)** An intelligent response, where the gene's expression increases only when the stress reaches a certain threshold and then decreases or shuts off once the stress disappears.

the interconnectedness between the key energy regulator TOR (Target of Rapamycin) and nitrogen regulation (Fichtner et al., 2021). Optimizing the carbon-nitrogen balance is essential for achieving both high yield and high protein content but is complex. Systems biology approaches, integrating multi-omics and computational modeling, offer promise for unraveling these complex interactions and developing strategies for targeted manipulation. Understanding the dynamic allocation of resources between growth and storage is crucial as well for optimizing yield and quality. Furthermore, considering environmental impacts (e.g., light, temperature, water availability) on carbon-nitrogen interactions is essential for developing climate-resilient maize (Figure 2A).

SOLUTIONS FOR ENHANCED MAIZE BREEDING

Meeting the above-mentioned multifaceted demands of future maize production, alongside the challenges of a burgeoning global population and a changing climate, requires a strategic roadmap of scientific endeavors (Figure 3). This roadmap must harness the full potential of both bio-technology and data technology. We are standing at the tipping point of another technological revolution in maize breeding, where the strategic integration of bio-technology and data technology will be essential for developing resilient, productive, and nutritious varieties adaptable to unpredictable environments. This roadmap focuses on three interconnected areas: deeper biological knowledge, intelligent molecular design, and smart breeding.

Deeper biological knowledge: Unraveling the complexities of trait variation

The future maize breeding lies in effectively utilizing the vast genetic diversity within the species and perhaps also genes/loci from wild relatives. This area focuses on understanding the intricate link between gene function and phenotypic traits under certain environments. Integrating multi-omics for network construction, pan-genomes to capture the complete gene set, and single-cell technologies to dissect cellular heterogeneity would offer synergistic approaches to unlock the full potential of maize genetic resources and accelerate crop improvement.

From allele mining to network construction

Quantitative traits in maize, such as yield and flowering time, are controlled by many genetic loci. Decades of research have identified numerous QTLs and genes associated with key agronomic traits in maize (Liang et al., 2021). Linkage analysis, genome-wide association study (GWAS), and mutant characterization have accelerated gene discovery (Xiao et al., 2017; Liang et al., 2021). Recent advancements in gene-mapping techniques have further improved the identification and validation of favorable alleles.

While our understanding of individual genes and pathways has grown, understanding their coordinated action in complex traits remains a tremendously challenge. Research is shifting from single-gene studies toward exploring gene modules, such as the *ZmNLP3.2-ZmARF19-ZmAux/IAA14* module regulating root biomass under nitrogen deficiency (Wang et al., 2024c). However, deciphering the interplay between different pathways

and the consequences of module perturbation requires intensive further investigation.

Advances in multi-omics approaches offer a holistic view of the complex biological systems governing plant growth and development. This integrative approach can reveal how genetic variations influence phenotypic traits through their effects at multiple systemic levels. While still underutilized in maize, multi-omics studies have demonstrated their potential for constructing genetic networks, identifying key genes and pathways, and improving efficiency of prediction (Gui et al., 2022; Han et al., 2023). Crucially, moving beyond correlation to identify causal relationships (Han et al., 2023) promises a more comprehensive understanding of maize genetics and enabling precision breeding.

Capturing the breadth of diversity with pan-genomes

Genomic analyses relying solely on a single reference genome, such as the B73 inbred line for maize, inherently fail to capture the full spectrum of genetic variations present within the maize species. This limitation hinders a comprehensive understanding of gene function, evolution, and the genetic basis of complex traits. The construction of pan-genomes, encompassing the entire gene set of a species, offers a powerful solution to overcome this reference bias.

Early efforts to develop maize pan-genomes and pan-transcriptomes leveraged Next-Generation Sequencing technologies (Hirsch et al., 2014; Jin et al., 2016; Chen et al., 2022b; Gui et al., 2022). However, the advent of third-generation sequencing technologies like PacBio and Nanopore has recently enabled high-quality *de novo* genome assemblies for a much wider range of maize lines. MaizeGDB currently hosts over 100 high-quality maize genome assemblies, with more under development. This rapid expansion of available genomes would significantly enhance our understanding of maize diversity. For example, assembling a tropical genome enabled the successful cloning of the first maize kernel weight QTL, revealing multiple large InDels spanning tens of kilobases compared to the B73 reference, with an 8.9 kb InDel identified as functional (Yang et al., 2019). Similarly, the drought-tolerant maize genome assembly led to the discovery of a novel H + -pump gene conferring drought resistance and uncovered dozens of favorable alleles contributing to its high drought tolerance (Tian et al., 2023).

A notable recent achievement is the telomere-to-telomere assembly of the Mo17 inbred line using ultralong Nanopore and PacBio HiFi reads (Chen et al., 2023b). This complete assembly unveiled over 1000 previously uncharacterized genes compared to past high-quality assemblies, providing unprecedented access to complex and previously inaccessible “dark-matter” regions of the genome. These regions often harbor crucial regulatory elements and genes involved in adaptation and stress response. Pan-genomes, constructed from complete assemblies, provide complete views of gene content, order, and other complex genomic regions. This facilitates the identification of novel genes, alleles, and regulatory elements that may be absent or misrepresented in a single reference genome. For example, the analysis of the NAM founder lines identified over 103 000 pan-genes, with less than 30% shared across all 26 genomes and nearly 20% being line specific (Hufford et al., 2021).

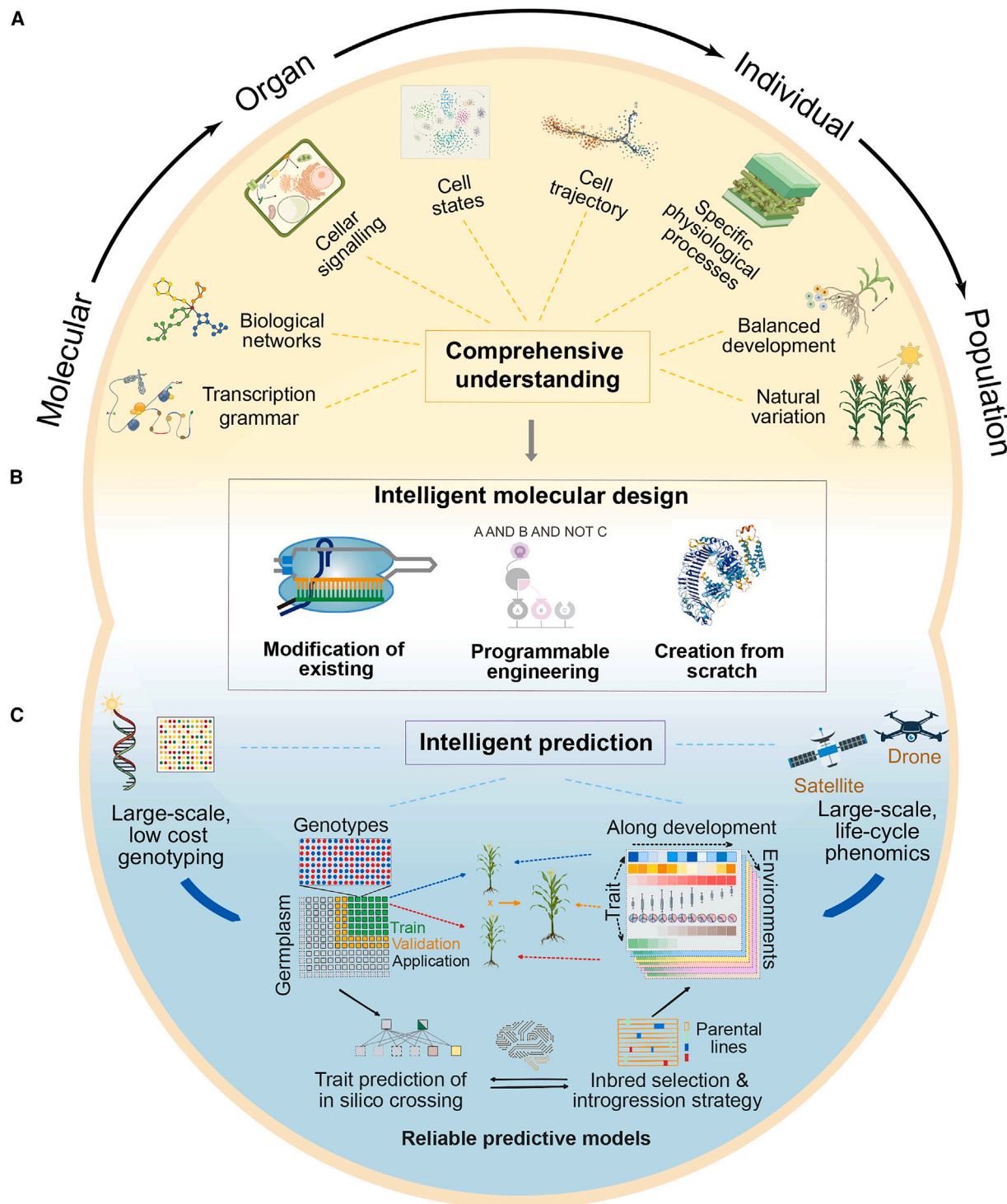


Figure 3. Integrating intelligent molecular design and predictive genomics for holistic maize improvement.

(A) Comprehensive biology understanding. Future maize improvement demands a deeper biology understanding, moving beyond individual traits to a systems-level approach encompassing molecular, cellular, physiological, individual, and population levels, including environmental interactions. This will deepen our understanding of trait variation, developmental dynamics, and environmental responses.

(B) Intelligent molecular design. The comprehensive understanding will inform the foundation of intelligent molecular design, which includes manipulating existing or designing *de novo* genetic circuits and optimizing or creating novel proteins. Essentially, it is about precisely engineering plant traits at the molecular level.

(C) Precise genome prediction provides another strategy on intelligent breeding. This leverages large datasets of genotypic and phenotypic information from diverse germplasms and their corresponding hybrids. Advanced algorithms enhance prediction accuracy, guiding breeding selections effectively. The synergy between intelligent molecular design and predictive genomics offers a holistic solution for future maize improvement.

Interestingly, tropical lines were revealed harboring a greater number of NLR genes compared to temperate lines, highlighting the impact of adaptation on gene content.

Some studies have pinpointed structural variation (SV) as causal variants underlying important traits. Classic examples include the loss of a distal transposable element reducing the expression of *Tb1* and impacting maize tillering. More recent examples involve a *CACTA*-like transposon insertion in *ZmCCT10* affecting flowering time (Hung et al., 2012; Yang et al., 2013), an 8.9-kb insertion in *ZmBAM1d* influencing kernel weight (Yang et al., 2019), SVs in *ZmACO2* contributing to ear length and yield heterosis (Ning et al., 2021; Wang et al., 2023a), and tandem-duplicated *ZmWUS1* leading to defects in meristem size (Chen et al., 2021).

The complete picture of genetic diversity offered by pan-genomes improves the accuracy and power of genetic mapping and trait prediction. Studies in the NAM population have demonstrated the significant general contribution of SVs to trait variation, particularly for disease resistance (Hufford et al., 2021; Gui et al., 2022). Untapped SVs have also been linked to heterosis (Wang et al., 2023a; Jin et al., 2016).

Pan-genomes would further enable haplotype-based association studies (Bradbury et al., 2022) and improve the resolution of multi-omics analyses (Hufford et al., 2021; Sibbesen et al., 2023). This will offer novel targets missing in the B73 reference, enhance understanding of the interplay between genotype and phenotype, and lead to more accurate genomic prediction models for crop improvement (Della Coletta et al., 2021).

ILLUMINATING GENETIC EFFECTS AT THE CELLULAR LEVEL

Traditional genomic approaches typically analyze bulk tissue samples, averaging out the unique characteristics from diverse cell types, thus obscuring the cellular heterogeneity that underlies complex biological processes. Single-cell and spatial technologies provide unprecedented resolution to dissect this heterogeneity within plant tissues, revealing how genetic variations influence gene expression and function at the cellular level, thus providing a more nuanced understanding of plant development and trait architecture.

Single-cell genomics and transcriptomics characterize stage- and cell-type-specific molecular profiles masked in bulk tissue analyses. In maize, single-cell analyses have yielded comprehensive understanding on dynamics and evolution of gene regulatory networks (Marand et al., 2021), revealed the developmental trajectories of root cells and regulators of their identities (Ortiz-Ramírez et al., 2021; Marand et al., 2021) and cell-type-specific response to nitrate and fungal infection (Li et al., 2022; Cao et al., 2023a), transcriptional regulation of developing maize ears and the association with yield traits (Xu et al., 2021b; Sun et al., 2024b; Wang et al., 2024d), regulon-based regulatory coordination during progressive endosperm development (Yuan et al., 2024), major determinants in mesophyll and abaxial bundle-sheath cells and stomata development and their contributions to photosynthesis-related metabolism (Bezruczyk et al., 2021; Sun et al., 2022), and transcriptional dynamics during germ development and meiotic recombination in meiocytes (Nelms and Walbot, 2019). These insights enable fine-tuning developmental processes to improve complex traits and inform strate-

gies for manipulating recombination and generating novel genetic diversity.

GWAS combined with single-cell genomics, a burgeoning field, offers a powerful approach to dissect trait variation at the cellular level (Figure 3A). Combining single-cell transcriptomic or epigenetic data with GWAS allows researchers to identify genetic variants associated with specific cellular phenotypes, deepening our understanding of gene regulation and complex traits and revealing novel targets for breeding and genetic engineering (Marand et al., 2024; Minow et al., 2023).

Advancements in maize genomics and genetics are creating extraordinary possibilities for enhancing crop performance. By incorporating comprehensive approaches like multi-omics, pan-genomes, and single-cell technologies, we are now able to go beyond merely identifying genes. Instead, we can explore how these genes interact within complex networks, behave across various genetic backgrounds, and function at the cellular level. This integrated strategy allows for the creation of predictive models that can accurately engineer and forecast complex traits. Such knowledge is crucial for designing specific breeding interventions, which will expedite the development of new maize varieties. The future of maize breeding depends on our ability to embrace this complexity and utilize these advanced tools to fully tap into the crop's potential.

INTELLIGENT MOLECULAR DESIGN: PRECISE ENGINEERING TRAITS AND RESPONSES

A deeper understanding of the diverse levels of trait variation is opening new avenues for utilizing synthetic biology and genome editing to engineer precise developmental programs and adaptive responses to environmental changes. Single-cell and spatial multi-omics technologies are poised to transform our understanding of maize development and spatiotemporal gene regulation (Nolan and Shahan, 2023; Rhaman et al., 2024). This knowledge can aid the precise engineering of pathways and traits in a developmental stage-specific manner (Borowsky and Bailey-Serres, 2024). Examples include manipulating the *CLAVATA*-*WUSCHEL* circuit for enhanced ear traits (Liu et al., 2021b), using drought-inducible promoters to sense drought conditions without yield penalty (Liu et al., 2021a), and applying stage-specific gene expression engineering to address biotic stresses (Schmitz et al., 2020). Furthermore, elucidating and reprogramming regulatory DNA elements is key to optimize multi-gene pathways, while non-coding sequences like enhancers, silencers, and insulators are valuable targets to modulate complex gene regulatory programs (Yu et al., 2025; Yang et al., 2022a; Liu et al., 2017).

In addition to understanding how gene circuitry is wired to control form and function, other advanced technologies to rewire that circuitry with accelerated build-test cycles are required to ultimately reinvent maize to unlock solutions to our greatest challenges (Figure 3B). While gene editing has matured considerably since its onset, huge advances are still ongoing; in particular, *de novo* genomic and metabolic engineering, empowering researchers to design and build entirely new genetic circuits and metabolic pathways, is paving the way for innovative strategies.

Targeted regulatory control with genome editing

Genome editing technologies, particularly the CRISPR/Cas systems (Wang and Doudna, 2023), have revolutionized our ability to manipulate the maize genome with unprecedented precision and efficiency (Liu et al., 2020a). Precisely targeting and modifying single or multiple genes is rapidly becoming routine, enabling the correction of genetic defects, the introduction of beneficial alleles, and the development of disease-resistant varieties (Li et al., 2024a).

Prime editing allows precise base editing without double-strand DNA breaks, further enhancing the scope of genome editing by facilitating specific nucleotide changes and generating novel genetic variation (Qiao et al., 2023). Beyond single-gene modifications, multiplex editing (Lorenzo et al., 2023), combined with manipulating small or large chromosomal segments (Wang and Doudna, 2023; Li et al., 2024a), allows for the simultaneous modification of multiple genes, accelerating the development of varieties with enhanced complex traits.

The integration of gene editing and *in vivo* doubled-haploid technology has become a powerful approach in maize breeding (Kelliher et al., 2019; Wang et al., 2019; Ye et al., 2024; Tian et al., 2024). This combined strategy offers several key advantages: increased efficiency in obtaining homozygous edited lines, bypassing the low transformation efficiency often encountered in traditional methods, direct generation of transgene-free edited plants, and the ability to rapidly fix recessive alleles, particularly valuable in multiplex editing scenarios (Impens et al., 2023).

Harnessing the power of horizontal gene transfer, a natural process of gene exchange between organisms (Soucy et al., 2015), holds immense potential for introducing novel traits into maize. Targeted knockin of desirable genes or alleles further expands the toolkit for precise trait engineering (Sun et al., 2024a), expanding the genetic toolbox for crop improvement by effectively and precisely transferring desirable genes from diverse organisms into maize.

De novo genome, protein, and metabolic design for programmable development

Alongside plant native regulator elements, the rational design based on *de novo* synthetic regulatory elements with predictable characteristics is highly desirable, since they are revolutionizing the speed and efficiency of genetic circuit design and testing (Figure 3B). Both principles and modular toolkits have been created to engineer plants with orthogonal synthetic systems (Borowsky and Bailey-Serres, 2024; Yasmeen et al., 2023; Yang et al., 2022a; Yaschenko et al., 2022; Bull and Khakhar, 2023). Recent examples include the CRISPR-interference (CRISPRi)-based platform, which demonstrates programmable and reversible logic gate activity (Khan et al., 2024), and the successful implementation of orthogonal regulatory systems derived from yeast to modulate transcription in plants (Belcher et al., 2020). These modular approaches enable rapid prototyping and testing of diverse circuit designs directly in maize.

In parallel with gene regulation, *de novo* protein design offers immense potential for engineering novel proteins with enhanced or entirely new functionalities. Deep learning, particularly genera-

tive AI, is transforming this field by enabling the creation of new-to-nature protein sequences with programmable functions (Huang et al., 2016; Kortemme, 2024). The *de novo* design of photosynthetic reaction centers exemplifies this potential, offering a path toward increasing solar-to-fuel energy-conversion efficiency (Ennist et al., 2022). While application in maize improvement is still prospective, it holds significant promise.

These levels of control also facilitate the precise engineering of metabolic pathways for targeted outcomes, termed metabolic engineering (Birchfield and McIntosh, 2020). Examples include engineering maize kernels for increased oil content, producing value-added compounds (Li et al., 2023; Liu et al., 2021d), and even development of new medicines (Wurtzel and Kutchan, 2016). Reconstituting specialized metabolic networks can enhance defenses, adaptation, and microbiome interactions (Zhou et al., 2022; Yasmin et al., 2024). Furthermore, manipulating nutrient uptake, transport, and utilization offers a path toward improved yield and reduced fertilizer requirements (Babele et al., 2023).

Engineering adaptive responses to environmental cues

In addition, to achieve regulation during maize development in a precise spatiotemporal manner, like all plants, maize has evolved sophisticated mechanisms to perceive and respond to environmental fluctuations. These responses are often mediated by specific regulatory elements within the genome, termed EREs. Harnessing these (both native and exogenous) EREs offers a powerful strategy for engineering targeted responses to specific environmental cues (Figures 2B–D). EREs are specific DNA sequences within the maize genome that regulate gene expression in response to environmental stimuli like drought, heat, salinity, and nutrient availability. Harnessing these native regulatory mechanisms offers a powerful strategy for engineering targeted and efficient responses to environmental challenges.

Well-characterized EREs in various plant species provide a starting point for maize research, including the dehydration responsive element (DRE) and the abscisic acid-responsive element (Yamaguchi-Shinozaki and Shinozaki, 2006). DREs, initially identified in the *RD29A* promoter in *Arabidopsis* (Yamaguchi-Shinozaki and Shinozaki, 1994), are bound by DRE-binding transcription factors that regulate numerous abiotic stress-responsive genes. DREs have been successfully used to enhance diverse stress tolerance in various crops (Agarwal et al., 2017; Liu et al., 2013). Abscisic acid-responsive elements, often coupled with other regulatory elements, play a crucial role in abscisic acid-mediated responses to drought, salinity, seed maturation, and dormancy (Yamaguchi-Shinozaki and Shinozaki, 2006).

Beyond these well-characterized EREs, research has uncovered maize-specific regulatory mechanisms. Studies have revealed instances of transposable element insertions and specific *cis* elements conferring drought tolerance in maize, highlighting the diversity of regulatory mechanisms (Wang et al., 2016). Notably, environmental responses can also occur within a plant, between different organs. A recent discovery found that the gene *ZmPORB1*, encoding a photosynthesis-related enzyme, regulates tocopherol levels in maize kernels. While light enhances *ZmPORB1* activity and

boosts tocopherol production through photosynthesis, low-oxygen conditions can maintain its activity and tocopherol levels through a different metabolic pathway (Liu et al., 2024b). Harnessing the responsiveness to light and oxygen could help breed maize varieties dynamically adapted to various light and hypoxia conditions.

In addition to these *cis* elements, *trans*-acting regulators are also found. For instance, miR393 plays a role in maize responses to nitrate availability (Vidal et al., 2010) and even antibacterial resistance (Navarro et al., 2006). The transposable element-mediated inverted repeat-derived small RNAs contribute to a complex gene regulatory network that influences the trade-off between environmental adaptation and yield-related traits, highlighting the importance of post-transcriptional regulation in environmental response (Sun et al., 2023).

Plant responses to other environmental factors, including nutrient availability, light, temperature, and the crosstalk between these factors, are critical for growth and developmental plasticity (Liu et al., 2021e; Ding et al., 2024). While significant progress has been made in plants, the identification and functional characterization of EREs in maize are still relatively nascent. Challenges include the complexity of regulatory networks, the potential for pleiotropic effects, and the need for robust high-throughput validation methods.

Once identified, these EREs can be incorporated into synthetic promoters or targeted gene editing to drive the expression of desirable genes specifically under the target environmental condition. However, modifying EREs can have unintended consequences on other traits, requiring careful evaluation and selection. This occurs particularly by constitutive activation of stress-responsive genes. Therefore, tissue-specific and stress-inducible promoters are crucial for achieving intelligent responses to environmental stress. As demonstrated by the *ZmDRO1* example, only conditional activation improved drought tolerance without yield penalty (Feng et al., 2022).

These advancements promise a future where maize varieties are not only high yielding but also resilient to climate change, resource limitations, and emerging diseases. By integrating these diverse approaches, we can move beyond incremental improvements and achieve transformative gains in maize productivity and sustainability. The ability to precisely engineer traits and responses will be crucial for ensuring food security in a changing world.

Smart breeding under the rise of machines and algorithms

The next decade of maize research will be defined by the integration of advanced technologies into breeding programs, ushering in an era of unprecedented precision and efficiency. Central to this transformation is the concept of smart breeding, which leverages high-throughput phenotyping, genotyping, robust databases, and predictive modeling to accelerate genetic gain and develop or design maize varieties tailored to specific needs (Liu et al., 2020b; Xu et al., 2022; Wang et al., 2024b). This integrated approach promises to revolutionize maize improvement by enabling researchers to predict phenotypic

performance with greater precision and select superior genotypes from diverse germplasm collections.

Automated phenotyping at scale

Traditional phenotyping methods are labor intensive, time consuming, and often largely subjective. Automated phenotyping platforms, utilizing high-throughput imaging, remote sensing, and robotics, are enabling high-throughput, rapid, and non-destructive characterization of a multitude of traits across large populations and diverse environments (Yang et al., 2020; Mascher et al., 2024). These platforms effectively capture a wide range of traits related to plant architecture, growth dynamics, physiology, and yield components at unprecedented scale and resolution (Figure 3C).

For instance, unmanned aerial vehicles equipped with spectral sensors can rapidly assess canopy traits such as plant height, leaf area index, and stress responses (Wang et al., 2024a). Ground-based platforms equipped with various sensors can generate detailed 3D point clouds to quantify architectural (including root) and yield traits in greater detail (Xu and Li, 2022; Liu et al., 2021c). Furthermore, advances in image analysis and machine-learning algorithms allow for the automated extraction of phenotypic data from images, further enhancing throughput and reducing human error, as exemplified by a recent study on maize drought tolerance (Wu et al., 2021). The development of automated, high-throughput, and precise field-phenotyping technologies will greatly enhance the efficiency of maize breeding. Actually, maize is an ideal crop for developing these technologies, and it will, in turn, benefit genetic improvement efforts in other species as well.

Germplasm banks and cost-effective genotyping

Diverse and well-characterized germplasm collections are the bedrock of realizing the full potential of smart breeding (Mascher et al., 2024). Large-scale efforts to collect, conserve, and characterize maize genetic resources from diverse geographical origins and wild relatives serve as valuable resources for identifying novel alleles and genetic variation for important traits (Chen et al., 2022b; Tian et al., 2019; Huang et al., 2022). With these collections, coupled with advances in sequencing and array technologies (Rasheed et al., 2017), high-throughput genotyping has become increasingly affordable and accessible. One could envisage that this will enable the rapid characterization of vast germplasm collections. Together with high-throughput phenotyping, the large amount of genotypic data will enable us to uncover the genetic architecture underlying valuable traits, providing more details, developmental dynamics, and physiological responses for multiple traits at once. The power of this approach has already been demonstrated to be instrumental in identifying key genes and genomic regions associated with important agronomic traits. Large-scale genotyping of diverse germplasm provides a rich source of genetic variation for breeding and the development of accurate genomic prediction models.

Putting predictions to the field

The vast amounts of phenotypic and genotypic data generated by automated phenotyping and genotyping platforms require robust database systems for efficient storage, management, and analysis. While the centralized databases that integrate phenotypic, genotypic, and environmental data are crucial, the true power of smart breeding lies in integrating large-scale phenotypic and genotypic data to develop robust predictive models (Figure 3C).

While algorithms that directly predict hybrid performance from parental genotypes are emerging (Xu et al., 2022; Farooq et al., 2024; Yang et al., 2022b; Wang et al., 2023b), it remains equally, if not more, crucial to create large, standardized, representative datasets documenting genotypic and phenotypic variation. Such foundational work, akin to the impact of the ImageNet database (Deng et al., 2009) in the field of computer vision, has the potential to ignite a new wave of advances. Machine-learning algorithms, trained on massive datasets, would predict the performance of new genetic combinations with remarkable accuracy, even for complex traits such as yield that are influenced by multiple genes and environmental factors.

Rigorous evaluation and validation are additionally essential to ensure the accuracy and reliability of predictive models (Xu et al., 2022; Mascher et al., 2024). This involves testing model predictions in diverse environments and genetic backgrounds. Continuous evaluation and refinement of predictive models are crucial to improve their accuracy and predictive power and to identify the most promising genotypes with desirable combinations for specific target environments. By leveraging the power of data analytics, breeders can make more informed decisions, accelerate genetic gain with largely reduced time and resources, and guide the development of tailored varieties for specific needs, all with high precision.

Smart breeding marks a paradigm shift in maize improvement, focusing on harnessing advanced technologies and data-driven strategies. This approach enables us to rapidly develop maize varieties that are not only higher yielding but also more resilient and nutritionally enhanced. With smart breeding, the use of data and algorithms opens up new possibilities, allowing us to tailor crops specifically for future needs. This method holds the promise of securing food supply and enhancing the resilience of agricultural systems, ensuring a sustainable future for agriculture.

Microbiome-informed hologenomic breeding

The holobiont concept recognizes the host and its associated microbiota as an ecological unit, with “hologenomics” encompassing both genomes (Xu et al., 2021a). While high-throughput sequencing has yielded extensive data on plant microbiome composition (Cordovez et al., 2019), a systematic understanding of maize hologenomics remains nascent.

Plant-associated microbes participate in various physiological processes, enhancing stress resistance (Wang and Song, 2022). For example, specific bacterial taxa contribute to maize salt stress tolerance through mechanisms involving exopolysaccharide production, volatile organic compound emission, and antioxidant activity (Ali et al., 2023). Synthetic bacterial communities can enhance disease resistance (e.g., against oomycete pathogens; Durán et al., 2018), and root-associated bacteria can suppress pathogenic fungi (Carrion et al., 2019). Microbes also play crucial roles in nutrient (e.g., phosphorus) acquisition (Castrillo et al., 2017; Shi et al., 2021).

Plant-microbe interaction studies have expanded from immunity and symbiosis to commensalism (Escudero-Martinez and Bulgarelli, 2023). Plant genetic elements contribute to

navigating microbe-rich environments. Pattern-triggered immunity maintains plant health (Chen et al., 2020). Plant genes related to the salicylic acid pathway, phosphate starvation response, and NUE can also shape microbial community composition and function (Lebeis et al., 2015; Castrillo et al., 2017; Zhang et al., 2019).

Forward genetic approaches (e.g., mGWAS, QTL mapping) have identified “M genes” regulating microbe associations (Zhan and Wang, 2024), including maize genes regulating beneficial *Massilia* and Oxalobacteraceae under nitrogen stress (Yu et al., 2021; He et al., 2024). These findings underscore the importance of investigating plant-microbe interactions using both reverse and forward genetic approaches for developing microbe-based breeding strategies (Wang et al., 2022).

Focusing on beneficial plant-microbe interactions, rather than solely engineering nitrogen-fixing microbes, holds greater promise for near-term maize advancements. Dissecting the complex maize-microbiome interplay—identifying key microbial players, understanding interaction mechanisms, and characterizing involved maize genes (de Vries et al., 2020)—will enable targeted strategies for enhancing maize health, productivity, and environmental resilience sustainably.

CONCLUDING REMARKS AND PERSPECTIVES

A paradigm shift and deepening focus

The future of maize research is poised for a transformative leap, driven by a convergence of cutting-edge technologies and a commitment to sustainability. The integration of high-throughput phenotyping, advanced genomics, and genome editing alongside machine learning and algorithm-driven analytics will revolutionize breeding practices (Qu et al., 2024; Durand et al., 2024; Farooq et al., 2024; Alemu et al., 2024; Li et al., 2024a). These technologies enable rapid trait discovery and the development of maize varieties with enhanced precision and reduced environmental impact, necessitating a shift toward big data and systems-level approaches in research.

Given the convergence of the formidable pressures of rising global food demand, shrinking arable land, and the pervasive impacts of climate change (Rezaei et al., 2023; Lesk et al., 2022), the future of maize research appears both daunting and promising. Our review has charted a course for the next decade of maize research, highlighting the critical areas that will likely shape the trajectory of agricultural advancements. Facing the challenges, maize research must pursue holistic and sustainable solutions. Our review highlights the need to consider maize phenotypes and their responses to stress in a comprehensive manner rather than focusing on individual traits in isolation. We also stress the importance of enhancing fundamental metabolic processes, including NUE, photosynthesis, and carbon-nitrogen balance, to improve crop efficiency and adaptability (Bracher et al., 2017; Liu et al., 2022; Fichtner et al., 2021). Genomic advances present significant opportunities for maize improvement. Techniques such as allele mining and the exploration of pan-genomes will deepen our understanding of maize genetics, leading to varieties that are finely adapted to their environments

(Bevan et al., 2017). Synthetic biology, including genome editing and *de novo* genome design, will allow for the enhancement of traits and the introduction of new capabilities, such as adaptive responses to environmental changes—critical for coping with climate variability (Borowsky and Bailey-Serres, 2024; Belcher et al., 2020; Li et al., 2023). Smart breeding techniques will enhance the efficiency of breeding programs through automated phenotyping and cost-effective genotyping, supported by predictive models that streamline the selection process (Xu et al., 2022; Farooq et al., 2024; Palani et al., 2023). Moreover, microbiome-informed hologenomic breeding offers a novel approach to enhance crop resilience and productivity by exploiting the synergistic interactions between maize and its microbiome (Ali et al., 2023; Wang and Song, 2022; Xu et al., 2021a). Integration of these interdisciplinary approaches is crucial for addressing global challenges and securing the future of maize as a staple food source.

Embracing data-driven farming and management

Beyond the realm of genetics and breeding, innovations in maize production and management are set to transform the field through AI, robotics, and advanced sensing technologies. These tools will enhance resource efficiency and support data-driven decision making (Zhang et al., 2021; Xu et al., 2022; Farooq et al., 2024).

Drones equipped with multi-spectral cameras and sensors will provide high-resolution aerial imagery, enabling real-time monitoring of crop health, nutrient status, and water stress (Wang et al., 2024a). This information will be fed into AI algorithms to generate actionable insights for precise and timely interventions. Envision fields managed by intelligent machines will autonomously perform tasks like planting, weeding, fertilizing, and harvesting. This is becoming a reality with sophisticated robots featuring advanced sensors, guidance from global navigation and positioning systems, and AI-powered decision-making capabilities (Gackstetter et al., 2023). Certainly, it is necessary to consider systemic factors and risks related to security, culture, and economy in addition to technologies (Tzachor et al., 2022).

Machine-learning models trained on historical weather data, pest life cycles, and disease epidemiology will offer early warnings of potential outbreaks, enabling proactive management such as targeted pesticide use or biological control measures (Palani et al., 2023). The recent desert locust outbreak in East Africa, linked to climate change (Salih et al., 2020), underscores the value of such predictive capabilities. By integrating real-time soil moisture data, weather forecasts, and crop growth models, farmers can anticipate drought stress and optimize irrigation, maximizing water-use efficiency and protecting yields (Zhang et al., 2021). The future of maize farming is smart, sustainable, and increasingly automated, where real-time insights empower farmers to make informed decisions.

Fostering collaboration from germplasm to global impact

Addressing the complex challenges facing maize production demands collaborative efforts beyond geographical and disciplinary boundaries. International partnerships will be crucial,

particularly in (1) establishing global networks for the exchange and conservation of maize genetic resources that will ensure the long-term sustainability of breeding efforts; (2) developing open-access platforms for sharing genomic, phenotypic, and environmental data to speed up research progress and facilitate the development of globally relevant solutions; and (3) fostering collaborations among researchers, breeders, farmers, and industry stakeholders to translate scientific discoveries into tangible benefits worldwide.

Global hunger demands urgent action, and collaborative efforts like the TELA maize project (“tela” meaning “protection” in Latin) are yielding promising solutions. Nigeria is facing historic food insecurity exacerbated by recent price surges. Under supports by the TELA project and the African Agricultural Technology Foundation, a local institute developed four genetically modified drought- and pest-resistant varieties, which were commercially released in January 2024. These varieties offer an average yield increase of 25% and can produce up to 10 tonnes per hectare under good practices (Oyekunle et al., 2023). This empowers Nigerian smallholder farmers to reduce pesticide use, boost yields, enhance food security, and adapt to climate change, ultimately contributing to national self-sufficiency and economic growth.

Socioeconomic considerations and engaging consumers

The benefits of maize research must reach all stakeholders, particularly smallholder farmers in developing countries who play a vital role in global food production. Ensuring equitable access and benefits includes (1) tailoring innovations to the specific needs and constraints of smallholder farming systems, considering factors such as resource availability, local knowledge, and market access; (2) empowering farmers with the knowledge and skills to adopt new technologies and best practices through training programs, extension services, and farmer-to-farmer learning networks and creating an enabling policy environment that incentivizes innovation, promotes technology transfer, and ensures equitable access to markets.

Consumer preferences and perceptions play a crucial role in shaping the future of maize. Educating the public on the benefits of new technologies, addressing concerns about genetically modified organisms, and promoting maize’s nutritional value are essential for fostering public acceptance and driving market demand for improved varieties.

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REFERENCES

- Agarwal, P.K., Gupta, K., Lopato, S., and Agarwal, P. (2017). Dehydration responsive element binding transcription factors and their applications for the engineering of stress tolerance. *J. Exp. Bot.* **68**:2135–2148.
- Alemu, A., Åstrand, J., Montesinos-López, O.A., Isidro y Sánchez, J., Fernández-González, J., Tadesse, W., Vetukuri, R.R., Carlsson, A.S., Ceplitis, A., Crossa, J., et al. (2024). Genomic selection in plant breeding: Key factors shaping two decades of progress. *Mol. Plant* **17**:552–578.
- Ali, B., Hafeez, A., Afridi, M.S., Javed, M.A., Sumaira, Suleman, F., Nadeem, M., Ali, S., Alwahibi, M.S., Elshikh, M.S., et al. (2023). Bacterial-Mediated Salinity Stress Tolerance in Maize (*Zea mays* L.): A Fortunate Way toward Sustainable Agriculture. *ACS Omega* **8**:20471–20487.
- Babele, P.K., Srivastava, A., Selim, K.A., and Kumar, A. (2023). Millet-inspired systems metabolic engineering of NUE in crops. *Trends Biotechnol.* **41**:701–713.
- Babu, R., Rojas, N.P., Gao, S., Yan, J., and Pixley, K. (2013). Validation of the effects of molecular marker polymorphisms in LcyE and CrtRB1 on provitamin A concentrations for 26 tropical maize populations. *Theor. Appl. Genet.* **126**:389–399.
- Belcher, M.S., Vuu, K.M., Zhou, A., Mansoori, N., Agosto Ramos, A., Thompson, M.G., Scheller, H.V., Loqué, D., and Shih, p.m. (2020). Design of orthogonal regulatory systems for modulating gene expression in plants. *Nat. Chem. Biol.* **16**:857–865.
- Berens, M.L., Berry, H.M., Mine, A., Argueso, C.T., and Tsuda, K. (2017). Evolution of hormone signaling networks in plant defense. *Annu. Rev. Phytopathol.* **55**:401–425.
- Bevan, M.W., Uauy, C., Wulff, B.B.H., Zhou, J., Krasileva, K., and Clark, M.D. (2017). Genomic innovation for crop improvement. *Nature* **543**:346–354.
- Bezruczyk, M., Zöllner, N.R., Kruse, C.P.S., Hartwig, T., Lautwein, T., Köhrer, K., Frommer, W.B., and Kim, J.Y. (2021). Evidence for phloem loading via the abaxial bundle sheath cells in maize leaves. *Plant Cell* **33**:531–547.
- Bhushan, B., Kumar, S., Kaur, C., Devi, V., Chaudhary, D.P., Singh, A., Dagla, M.C., Karjagi, C.G., Saleena, L.A.K., Chandran, D., et al. (2024). Beyond colors: The health benefits of maize antho-cyanins. *Applied Food Research* **4**:100399.
- Birchfield, A.S., and McIntosh, C.A. (2020). Metabolic engineering and synthetic biology of plant natural products - A minireview. *Current Plant Biology* **24**:100163.
- Borowsky, A.T., and Bailey-Serres, J. (2024). Rewiring gene circuitry for plant improvement. *Nat. Genet.* **56**:1574–1582.
- Bracher, A., Whitney, S.M., Hartl, F.U., and Hayer-Hartl, M. (2017). Biogenesis and metabolic maintenance of Rubisco. *Annu. Rev. Plant Biol.* **68**:29–60.
- Bradbury, P.J., Casstevens, T., Jensen, S.E., Johnson, L.C., Miller, Z.R., Monier, B., Romay, M.C., Song, B., and Buckler, E.S. (2022). The Practical Haplotype Graph, a platform for storing and using pangenomes for imputation. *Bioinformatics* **38**:3698–3702.
- Buckler, E.S., Holland, J.B., Bradbury, P.J., Acharya, C.B., Brown, P.J., Browne, C., Ersoz, E., Flint-Garcia, S., Garcia, A., Glaubitz, J.C., et al. (2009). The genetic architecture of maize flowering time. *Science* **325**:714–718.
- Bull, T., and Khakhar, A. (2023). Design principles for synthetic control systems to engineer plants. *Plant Cell Rep.* **42**:1875–1889.
- Cao, Y., Ma, J., Han, S., Hou, M., Wei, X., Zhang, X., Zhang, Z.J., Sun, S., Ku, L., Tang, J., et al. (2023a). Single-cell RNA sequencing profiles reveal cell type-specific transcriptional regulation networks conditioning fungal invasion in maize roots. *Plant Biotechnol. J.* **21**:1839–1859.
- Cao, Y., Zhang, M., Liang, X., Li, F., Shi, Y., Yang, X., and Jiang, C. (2020). Natural variation of an EF-hand Ca²⁺-binding-protein coding gene confers saline-alkaline tolerance in maize. *Nat. Commun.* **11**:186.
- Cao, Y., Zhou, X., Song, H., Zhang, M., and Jiang, C. (2023b). Advances in deciphering salt tolerance mechanism in maize. *Crop J.* **11**:1001–1010.
- Carrión, V.J., Perez-Jaramillo, J., Cordovez, V., Tracanna, V., de Hollander, M., Ruiz-Buck, D., Mendes, L.W., van Ijcken, W.F.J., Gomez-Exposito, R., Elsayed, S.S., et al. (2019). Pathogen-induced activation of disease-suppressive functions in the endophytic root microbiome. *Science* **366**:606–612.
- Castrillo, G., Teixeira, P.J.P.L., Paredes, S.H., Law, T.F., de Lorenzo, L., Feltcher, M.E., Finkel, O.M., Breakfield, N.W., Mieczkowski, P., Jones, C.D., et al. (2017). Root microbiota drive direct integration of phosphate stress and immunity. *Nature* **543**:513–518.
- Check, J.C., Byrne, a.m., Singh, M.P., Steinke, K., Widdicombe, W.D., and Chilvers, M.I. (2023). Effects of Nitrogen Application Rate and Plant Density on Severity of Tar Spot of Corn. *Plant Health Prog.* **24**:416–423.
- Chen, G., Zhang, B., Ding, J., Wang, H., Deng, C., Wang, J., Yang, Q., Pi, Q., Zhang, R., Zhai, H., et al. (2022a). Cloning southern corn rust resistant gene RppK and its cognate gene AvrRppK from *Puccinia polysora*. *Nat. Commun.* **13**:4392.
- Chen, G., Xiao, Y., Dai, S., Dai, Z., Wang, X., Li, B., Jaqueth, J.S., Li, W., Lai, Z., Ding, J., et al. (2023a). Genetic basis of resistance to southern corn leaf blight in the maize multi-parent population and diversity panel. *Plant Biotechnol. J.* **21**:506–520.
- Chen, J., Wang, Z., Tan, K., Huang, W., Shi, J., Li, T., Hu, J., Wang, K., Wang, C., Xin, B., et al. (2023b). A complete telomere-to-telomere assembly of the maize genome. *Nat. Genet.* **55**:1221–1231.
- Chen, L., Luo, J., Jin, M., Yang, N., Liu, X., Peng, Y., Li, W., Phillips, A., Cameron, B., Bernal, J.S., et al. (2022b). Genome sequencing reveals evidence of adaptive variation in the genus *Zea*. *Nat. Genet.* **54**:1736–1745.
- Chen, T., Nomura, K., Wang, X., Sohrabi, R., Xu, J., Yao, L., Paasch, B.C., Ma, L., Kremer, J., Cheng, Y., et al. (2020). A plant genetic network for preventing dysbiosis in the phyllosphere. *Nature* **580**:653–657.
- Chen, Y.-N., Cartwright, H.N., and Ho, C.-H. (2022c). In vivo visualization of nitrate dynamics using a genetically encoded fluorescent biosensor. *Sci. Adv.* **8**:eabq4915.

- Chen, Z., Li, W., Gaines, C., Buck, A., Galli, M., and Gallavotti, A. (2021). Structural variation at the maize WUSCHEL1 locus alters stem cell organization in inflorescences. *Nat. Commun.* **12**:2378.
- Chung, Y.H., Church, D., Koellhoffer, E.C., Osota, E., Shukla, S., Rybicki, E.P., Pokorski, J.K., and Steinmetz, N.F. (2022). Integrating plant molecular farming and materials research for next-generation vaccines. *Nat. Rev. Mater.* **7**:372–388.
- Cordovez, V., Dini-Andreote, F., Carrión, V.J., and Raaijmakers, J.M. (2019). Ecology and Evolution of Plant Microbiomes. *Annu. Rev. Microbiol.* **73**:69–88.
- Crossa, J., Pérez-Rodríguez, P., Cuevas, J., Montesinos-López, O., Jarquín, D., de Los Campos, G., Burgueño, J., González-Camacho, J.M., Pérez-Elizalde, S., Beyene, Y., et al. (2017a). Genomic Selection in Plant Breeding: Methods, Models, and Perspectives. *Trends Plant Sci.* **22**:961–975.
- Crossa, J., Pérez-Rodríguez, P., Cuevas, J., Montesinos-López, O., Jarquín, D., de Los Campos, G., Burgueño, J., González-Camacho, J.M., Pérez-Elizalde, S., Beyene, Y., et al. (2017b). Genomic selection in plant breeding: Methods, models, and perspectives. *Trends Plant Sci.* **22**:961–975.
- Della Coletta, R., Qiu, Y., Ou, S., Hufford, M.B., and Hirsch, C.N. (2021). How the pan-genome is changing crop genomics and improvement. *Genome Biol.* **22**:3.
- Deng, J., Dong, W., Socher, R., Li, L.J., Li, K., L, F.-F., et al. (2009). ImageNet: A large-scale hierarchical image database. In 2009 IEEE Conference on Computer Vision and Pattern Recognition (Miami, FL: IEEE), pp. 248–255.
- Deng, S., Jiang, S., Liu, B., Zhong, T., Liu, Q., Liu, J., Liu, Y., Yin, C., Sun, C., and Xu, M. (2024). ZmGDI α -hel counters the RBSDV-induced reduction of active gibberellins to alleviate maize rough dwarf virus disease. *Nat. Commun.* **15**:7576.
- Ding, Y., Shi, Y., and Yang, S. (2024). Regulatory Networks Underlying Plant Responses and Adaptation to Cold Stress. *Annu. Rev. Genet.* **58**:3–65.
- Doebley, J.F., Gaut, B.S., and Smith, B.D. (2006). The molecular genetics of crop domestication. *Cell* **127**:1309–1321.
- Durán, P., Thiergart, T., Garrido-Oter, R., Agler, M., Kemen, E., Schulze-Lefert, P., and Hacquard, S. (2018). Microbial Interkingdom Interactions in Roots Promote Arabidopsis Survival. *Cell* **175**:973–983.e14.
- Durand, M., Besseau, S., Papon, N., and Courdavault, V. (2024). Unlocking plant bioactive pathways: omics data harnessing and machine learning assisting. *Curr. Opin. Biotechnol.* **87**:103135.
- Early, R., Bradley, B.A., Dukes, J.S., Lawler, J.J., Olden, J.D., Blumenthal, D.M., Gonzalez, P., Grosholz, E.D., Ibañez, I., Miller, L.P., et al. (2016). Global threats from invasive alien species in the twenty-first century and national response capacities. *Nat. Commun.* **7**:12485.
- Ennist, N.M., Zhao, Z., Stayrook, S.E., Discher, B.M., Dutton, P.L., and Moser, C.C. (2022). De novo protein design of photochemical reaction centers. *Nat. Commun.* **13**:4937.
- Erenstein, O., Jaleta, M., Sonder, K., Mottaleb, K., and Prasanna, B. (2022). Global maize production, consumption and trade: trends and RD implications. *Food Secur.* **14**:1295–1319.
- Escudero-Martinez, C., and Bulgarelli, D. (2023). Engineering the Crop Microbiota Through Host Genetics. *Annu. Rev. Phytopathol.* **61**:257–277.
- Farooq, M.A., Gao, S., Hassan, M.A., Huang, Z., Rasheed, A., Hearne, S., Prasanna, B., Li, X., and Li, H. (2024). Artificial intelligence in plant breeding. *Trends Genet.* **40**:891–908.
- Feng, X., Jia, L., Cai, Y., Guan, H., Zheng, D., Zhang, W., Xiong, H., Zhou, H., Wen, Y., Hu, Y., et al. (2022). ABA-inducible *DEEPER ROOTING 1* improves adaptation of maize to water deficiency. *Plant Biotechnol. J.* **20**:2077–2088.
- Fernández, J.A., Messina, C.D., Salinas, A., Prasad, P.V.V., Nippert, J.B., and Ciampitti, I.A. (2022). Kernel weight contribution to yield genetic gain of maize: a global review and US case studies. *J. Exp. Bot.* **73**:3597–3609.
- Fichtner, F., Dissanayake, I.M., Lacombe, B., and Barbier, F. (2021). Sugar and nitrate sensing: A multi-billion-year story. *Trends Plant Sci.* **26**:352–374.
- Gackstetter, D., von Bloh, M., Hannus, V., Meyer, S.T., Weisser, W., Luksch, C., and Asseng, S. (2023). Autonomous field management - An enabler of sustainable future in agriculture. *Agric. Syst.* **206**:103607.
- Gui, S., Wei, W., Jiang, C., Luo, J., Chen, L., Wu, S., Li, W., Wang, Y., Li, S., Yang, N., et al. (2022). A pan-Zea genome map for enhancing maize improvement. *Genome Biol.* **23**:178.
- Han, L., Zhong, W., Qian, J., Jin, M., Tian, P., Zhu, W., Zhang, H., Sun, Y., Feng, J.W., Liu, X., et al. (2023). A multi-omics integrative network map of maize. *Nat. Genet.* **55**:144–153.
- Harjes, C.E., Rocheford, T.R., Bai, L., Brutnell, T.P., Kandianis, C.B., Sowinski, S.G., Stapleton, A.E., Vallabhaneni, R., Williams, M., Wurtzel, E.T., et al. (2008). Natural genetic variation in lycopene epsilon cyclase tapped for maize biofortification. *Science* **319**:330–333.
- He, X., Wang, D., Jiang, Y., Li, M., Delgado-Baquerizo, M., McLaughlin, C., Marcon, C., Guo, L., Baer, M., Moya, Y.A.T., et al. (2024). Heritable microbiome variation is correlated with source environment in locally adapted maize varieties. *Nat. Plants* **10**:598–617.
- He, Z., Webster, S., and He, S.Y. (2022). Growth-defense trade-offs in plants. *Curr. Biol.* **32**:R634–R639.
- Hirsch, C.N., Foerster, J.M., Johnson, J.M., Sekhon, R.S., Muttoni, G., Vaillancourt, B., Peñagaricano, F., Lindquist, E., Pedraza, M.A., Barry, K., et al. (2014). Insights into the Maize Pan-Genome and Pan-Transcriptome. *Plant Cell* **26**:121–135.
- Huang, P.-S., Boyken, S.E., and Baker, D. (2016). The coming of age of de novo protein design. *Nature* **537**:320–327.
- Huang, Y., Wang, H., Zhu, Y., Huang, X., Li, S., Wu, X., Zhao, Y., Bao, Z., Qin, L., Jin, Y., et al. (2022). THP9 enhances seed protein content and nitrogen-use efficiency in maize. *Nature* **612**:292–300.
- Hufford, M.B., Seetharam, A.S., Woodhouse, M.R., Chougule, K.M., Ou, S., Liu, J., Ricci, W.A., Guo, T., Olson, A., Qiu, Y., et al. (2021). De novo assembly, annotation, and comparative analysis of 26 diverse maize genomes. *Science* **373**:655–662.
- Hung, H.-Y., Shannon, L.M., Tian, F., Bradbury, P.J., Chen, C., Flint-Garcia, S.A., McMullen, M.D., Ware, D., Buckler, E.S., Doebley, J.F., et al. (2012). *ZmCCT* and the genetic basis of day-length adaptation underlying the postdomestication spread of maize. *Proc. Natl. Acad. Sci. USA* **109**:E1913–E1921.
- Hutchison, W.D., Burkness, E.C., Mitchell, P.D., Moon, R.D., Leslie, T.W., Fleischer, S.J., Abrahamson, M., Hamilton, K.L., Steffey, K.L., Gray, M.E., et al. (2010). Area-wide Suppression of European Corn Borer with Bt Maize Reaps Savings to Non-Bt Maize Growers. *Science* **330**:222–225.
- Impens, L., Lorenzo, C.D., Vandeputte, W., Wytynck, P., Debray, K., Haeghebaert, J., Herwegh, D., Jacobs, T.B., Ruttink, T., Nelissen, H., et al. (2023). Combining multiplex gene editing and doubled haploid technology in maize. *New Phytol.* **239**:1521–1532.
- Jacquier, N.M.A., Gilles, L.M., Pyott, D.E., Martinant, J.P., Rogowsky, p.m., and Widiez, T. (2020). Puzzling out plant reproduction by haploid induction for innovations in plant breeding. *Nat. Plants* **6**:610–619.

- Jafari, F., Wang, B., Wang, H., and Zou, J. (2024). Breeding maize of ideal plant architecture for high-density planting tolerance through modulating shade avoidance response and beyond. *J. Integr. Plant Biol.* **66**:849–864.
- Jiang, C., Sun, J., Li, R., Yan, S., Chen, W., Guo, L., Qin, G., Wang, P., Luo, C., Huang, W., et al. (2022). A reactive oxygen species burst causes haploid induction in maize. *Mol. Plant* **15**:943–955.
- Jin, M., Liu, H., He, C., Fu, J., Xiao, Y., Wang, Y., Xie, W., Wang, G., and Yan, J. (2016). Maize pan-transcriptome provides novel insights into genome complexity and quantitative trait variation. *Sci. Rep.* **6**:18936.
- Kelliher, T., Starr, D., Su, X., Tang, G., Chen, Z., Carter, J., Wittich, P.E., Dong, S., Green, J., Burch, E., et al. (2019). One-step genome editing of elite crop germplasm during haploid induction. *Nat. Biotechnol.* **37**:287–292.
- Khalil, A.S., and Collins, J.J. (2010). Synthetic biology: applications come of age. *Nat. Rev. Genet.* **11**:367–379.
- Khan, M.A., Herring, G., Zhu, J.Y., et al. (2024). CRISPRi-based circuits to control gene expression in plants. *Nat. Biotechnol.* <https://doi.org/10.1038/s41587-024-02236-w>.
- Kortemme, T. (2024). De novo protein design—From new structures to programmable functions. *Cell* **187**:526–544.
- Kusmec, A., Attigala, L., Dai, X., Srinivasan, S., Yeh, C.T.E., and Schnable, P.S. (2023). A genetic tradeoff for tolerance to moderate and severe heat stress in US hybrid maize. *PLoS Genet.* **19**:e1010799.
- Lebeis, S.L., Paredes, S.H., Lundberg, D.S., Breakfield, N., Gehring, J., McDonald, M., Malfatti, S., Glavina del Rio, T., Jones, C.D., Tringe, S.G., et al. (2015). Salicylic acid modulates colonization of the root microbiome by specific bacterial taxa. *Science* **349**:860–864.
- Lesk, C., Anderson, W., Rigden, A., Coast, O., Jägermeyr, J., McDermid, S., Davis, K.F., and Konar, M. (2022). Compound heat and moisture extreme impacts on global crop yields under climate change. *Nat. Rev. Earth Environ.* **3**:872–889.
- Li, B., Sun, C., Li, J., and Gao, C. (2024a). Targeted genome-modification tools and their advanced applications in crop breeding. *Nat. Rev. Genet.* **25**:603–622.
- Li, L., Liu, K.-H., and Sheen, J. (2021). Dynamic nutrient signaling networks in plants. *Annu. Rev. Cell Dev. Biol.* **37**:341–367.
- Li, H., Fernie, A.R., and Yang, X. (2023). Using systems metabolic engineering strategies for high-oil maize breeding. *Curr. Opin. Biotechnol.* **79**:102847.
- Li, N., Lin, B., Wang, H., Li, X., Yang, F., Ding, X., Yan, J., and Chu, Z. (2019). Natural variation in ZmFBL41 confers banded leaf and sheath blight resistance in maize. *Nat. Genet.* **51**:1540–1548.
- Li, X., Zhang, X., Gao, S., Cui, F., Chen, W., Fan, L., and Qi, Y. (2022). Single-cell RNA sequencing reveals the landscape of maize root tips and assists in identification of cell type-specific nitrate-response genes. *The Crop Journal* **10**:1589–1600.
- Li, Z., Chen, J., Liu, C., He, S., Wang, M., Wang, L., Bhaduria, V., Wang, S., Cheng, W., Liu, H., et al. (2024b). Natural variations of maize ZmLecRK1 determine its interaction with ZmBAK1 and resistance patterns to multiple pathogens. *Mol. Plant* **17**:1606–1623.
- Liang, Y., Liu, H.J., Yan, J., and Tian, F. (2021). Natural Variation in Crops: Realized Understanding, Continuing Promise. *Annu. Rev. Plant Biol.* **72**:357–385.
- Liu, B., Zhang, B., Yang, Z., Liu, Y., Yang, S., Shi, Y., Jiang, C., and Qin, F. (2021a). Manipulating *ZmEXPA4* expression ameliorates the drought-induced prolonged anthesis and silking interval in maize. *Plant Cell* **33**:2058–2071.
- Liu, H.-J., Jian, L., Xu, J., Zhang, Q., Zhang, M., Jin, M., Peng, Y., Yan, J., Han, B., Liu, J., et al. (2020a). High-Throughput CRISPR-Cas9 Mutagenesis Streamlines Trait Gene Identification in Maize. *Plant Cell* **32**:1397–1413.
- Liu, H., Luo, X., Niu, L., Xiao, Y., Chen, L., Liu, J., Wang, X., Jin, M., Li, W., Zhang, Q., et al. (2017). Distant eQTLs and Non-coding Sequences Play Critical Roles in Regulating Gene Expression and Quantitative Trait Variation in Maize. *Mol. Plant* **10**:414–426.
- Liu, J., Li, J., Wang, H., and Yan, J. (2020b). Application of deep learning in genomics. *Sci. China Life Sci.* **63**:1860–1878.
- Liu, J., Yang, B., Chen, X., Zhang, T., Zhang, H., Du, Y., Zhao, Q., Zhang, Z., Cai, D., Liu, J., Chen, H., Zhao, L., et al. (2024a). ZmL75 is required for colonization by arbuscular mycorrhizal fungi and for saline-alkali tolerance in maize. *J Genet Genomics.* <https://doi.org/10.1016/j.jgg.2024.12.015>.
- Liu, L., Gallagher, J., Arevalo, E.D., Chen, R., Skopelitis, T., Wu, Q., Bartlett, M., and Jackson, D. (2021b). Enhancing grain-yield-related traits by CRISPR-Cas9 promoter editing of maize CLE genes. *Nat. Plants* **7**:287–294.
- Liu, N., Du, Y., Yan, S., Chen, W., Deng, M., Xu, S., Wang, H., Zhan, W., Huang, W., Yin, Y., et al. (2024b). The light and hypoxia induced gene ZmPORB1 determines tocopherol content in the maize kernel. *Sci. China Life Sci.* **67**:435–448.
- Liu, Q., Wu, K., Song, W., Zhong, N., Wu, Y., and Fu, X. (2022). Improving crop nitrogen use efficiency toward sustainable Green Revolution. *Annu. Rev. Plant Biol.* **73**:523–551.
- Liu, S., Wang, X., Wang, H., Xin, H., Yang, X., Yan, J., Li, J., Tran, L.S.P., Shinozaki, K., Yamaguchi-Shinozaki, K., et al. (2013). Genome-Wide Analysis of ZmDREB Genes and Their Association with Natural Variation in Drought Tolerance at Seedling Stage of Zea mays L. *PLoS Genet.* **9**:e1003790.
- Liu, S., Barrow, C.S., Hanlon, M., Lynch, J.P., and Bucksch, A. (2021c). DIRT/3D: 3D root phenotyping for field-grown maize (*Zea mays*). *Plant Physiol.* **187**:739–757.
- Liu, X., Ma, X., Wang, H., Li, S., Yang, W., Nugroho, R.D., Luo, L., Zhou, X., Tang, C., Fan, Y., et al. (2021d). Metabolic engineering of astaxanthin-rich maize and its use in the production of biofortified eggs. *Plant Biotechnol. J.* **19**:1812–1823.
- Liu, Y., Jafari, F., and Wang, H. (2021e). Integration of light and hormone signaling pathways in the regulation of plant shade avoidance syndrome. *aBIOTECH* **2**:131–145.
- Lorenzo, C.D., Debray, K., Herwegh, D., Develtere, W., Impens, L., Schaumont, D., Vandeputte, W., Aesaert, S., Coussens, G., De Boe, Y., et al. (2023). BREEDIT: a multiplex genome editing strategy to improve complex quantitative traits in maize. *Plant Cell* **35**:218–238.
- Luo, J., He, C., Yan, S., Jiang, C., Chen, A., Li, K., Zhu, Y., Gui, S., Yang, N., Xiao, Y., et al. (2024). A metabolic roadmap of waxy corn flavor. *Mol. Plant* **17**:1883–1898.
- Luo, N., Meng, Q., Feng, P., Qu, Z., Yu, Y., Liu, D.L., Müller, C., and Wang, P. (2023). China can be self-sufficient in maize production by 2030 with optimal crop management. *Nat. Commun.* **14**:2637.
- Mansfield, B.D., and Mumm, R.H. (2014). Survey of Plant Density Tolerance in U.S. Maize Germplasm. *Crop Sci.* **54**:157–173.
- Marand, A.P., Chen, Z., Gallavotti, A., and Schmitz, R.J. (2021). A cis-regulatory atlas in maize at single-cell resolution. *Cell* **184**:3041–3055.e21.
- Marand, A.P., Jiang, L., Gomez-Cano, F., Minow, M.A., Zhang, X., Mendieta, J.P., Luo, Z., Bang, S., Yan, H., Meyer, C., et al. (2024). The genetic architecture of cell-type-specific cis-regulation in maize. Preprint at bioRxiv. <https://doi.org/10.1101/2024.08.17.608383>.
- Marichelvam, M.K., Jawaaid, M., and Asim, M. (2019). Corn and Rice Starch-Based Bio-Plastics as Alternative Packaging Materials. *Fibers* **7**:32.

- Mascher, M., Jayakodi, M., Shim, H., and Stein, N.** (2024). Promises and challenges of crop translational genomics. *Nature* **636**:585–593.
- Meng, D., Liu, C., Chen, S., and Jin, W.** (2021). Haploid induction and its application in maize breeding. *Mol. Breed.* **41**:20.
- Mikel, M.A., and Dudley, J.W.** (2006). Evolution of North American Dent Corn from Public to Proprietary Germplasm. *Crop Sci.* **46**:1193–1205.
- Minow, M.A.A., Marand, A.P., and Schmitz, R.J.** (2023). Leveraging Single-Cell Populations to Uncover the Genetic Basis of Complex Traits. *Annu. Rev. Genet.* **57**:297–319.
- Napier, J.D., Heckman, R.W., and Juenger, T.E.** (2023). Gene-by-environment interactions in plants: Molecular mechanisms, environmental drivers, and adaptive plasticity. *Plant Cell* **35**:109–124.
- Navarro, L., Dunoyer, P., Jay, F., Arnold, B., Dharmasiri, N., Estelle, M., Voinnet, O., and Jones, J.D.G.** (2006). A Plant miRNA Contributes to Antibacterial Resistance by Repressing Auxin Signaling. *Science* **312**:436–439.
- Nelms, B., and Walbot, V.** (2019). Defining the developmental program leading to meiosis in maize. *Science* **364**:52–56.
- Ning, Q., Jian, Y., Du, Y., et al.** (2021). An ethylene biosynthesis enzyme controls quantitative variation in maize ear length and kernel yield. *Nat. Commun.* **12**:5832.
- Niu, L., Liu, L., Zhang, J., Scali, M., Wang, W., Hu, X., and Wu, X.** (2023). Genetic Engineering of Starch Biosynthesis in Maize Seeds for Efficient Enzymatic Digestion of Starch during Bioethanol Production. *Int. J. Mol. Sci.* **24**:3927.
- Nolan, T.M., and Shahan, R.** (2023). Resolving plant development in space and time with single-cell genomics. *Curr. Opin. Plant Biol.* **76**:102444.
- Obata, T., Witt, S., Lisec, J., Palacios-Rojas, N., Florez-Sarasa, I., Youf, S., Araus, J.L., Cairns, J.E., and Fernie, A.R.** (2015). Metabolite profiles of maize leaves in drought, heat and combined stress field trials reveal the relationship between metabolism and grain yield. *Plant Physiol.* **169**:2665–2683.
- Ort, D.R., Merchant, S.S., Alric, J., Barkan, A., Blankenship, R.E., Bock, R., Croce, R., Hanson, M.R., Hibberd, J.M., Long, S.P., et al.** (2015). Redesigning photosynthesis to sustainably meet global food and bioenergy demand. *Proc. Natl. Acad. Sci. USA* **112**:8529–8536.
- Ortiz-Ramírez, C., Guillotin, B., Xu, X., Rahni, R., Zhang, S., Yan, Z., Coqueiro Dias Araujo, P., Demesa-Arevalo, E., Lee, L., Van Eck, J., et al.** (2021). Ground tissue circuitry regulates organ complexity in maize and *Setaria*. *Science* **374**:1247–1252.
- Outhwaite, C.L., McCann, P., and Newbold, T.** (2022). Agriculture and climate change are reshaping insect biodiversity worldwide. *Nature* **605**:97–102.
- Oyekunle, M., Adamu, R.S., Ndou, E., Beyene, Y., Abdulmalik, M.M., and Oikeh, S.O.** (2023). Efficacy of drought-tolerant and insect-protected transgenic TELA® maize traits in Nigeria. *Transgenic Res.* **32**:169–178.
- Palani, H.K., Ilangovan, S., Senthilvel, P.G., Thirupurasundari, D.R., Kumar, R., et al.** (2023). AI-Powered Predictive Analysis for Pest and Disease Forecasting in Crops. In *2023 International Conference on Communication, Security and Artificial Intelligence (ICCSAI)*. Greater Noida (India: IEEE), pp. 950–954.
- Qiao, D., Wang, J., Lu, M.H., Xin, C., Chai, Y., Jiang, Y., Sun, W., Cao, Z., Guo, S., Wang, X.C., et al.** (2023). Optimized prime editing efficiently generates heritable mutations in maize. *J. Integr. Plant Biol.* **65**:900–906.
- Qu, Y., Fernie, A.R., Liu, J., and Yan, J.** (2024). Doubled haploid technology and synthetic apomixis: Recent advances and applications in future crop breeding. *Mol. Plant* **17**:1005–1018.
- Ramstein, G.P., Jensen, S.E., and Buckler, E.S.** (2019). Breaking the curse of dimensionality to identify causal variants in Breeding 4. *Theor. Appl. Genet.* **132**:559–567.
- Rasheed, A., Hao, Y., Xia, X., Khan, A., Xu, Y., Varshney, R.K., and He, Z.** (2017). Crop Breeding Chips and Genotyping Platforms: Progress, Challenges, and Perspectives. *Mol. Plant* **10**:1047–1064.
- Ren, W., Zhao, L., Liang, J., Wang, L., Chen, L., Li, P., Liu, Z., Li, X., Zhang, Z., Li, J., et al.** (2022). Genome-wide dissection of changes in maize root system architecture during modern breeding. *Nat. Plants* **8**:1408–1422.
- Rezaei, E.E., Webber, H., Asseng, S., Boote, K., Durand, J.L., Ewert, F., Martre, P., and MacCarthy, D.S.** (2023). Climate change impacts on crop yields. *Nat. Rev. Earth Environ.* **4**:831–846.
- Rhaman, M.S., Ali, M., Ye, W., and Li, B.** (2024). Opportunities and Challenges in Advancing Plant Research with Single-cell Omics. *Dev. Reprod. Biol.* **22**:qzae026.
- Rizzo, P., Chavez, B.G., Leite Dias, S., and D'Auria, J.C.** (2023). Plant synthetic biology: from inspiration to augmentation. *Curr. Opin. Biotechnol.* **79**:102857.
- Ruiz, A., Trifunovic, S., Eudy, D.M., Sciarresi, C.S., Baum, M., Danalatos, G.J., Elli, E.F., Kalogeropoulos, G., King, K., dos Santos, C., et al.** (2023). Harvest index has increased over the last 50 years of maize breeding. *Field Crops Res.* **300**:108991.
- Salih, A.A.M., Baraibar, M., Mwangi, K.K., and Artan, G.** (2020). Climate change and locust outbreak in East Africa. *Nat. Clim. Change* **10**:584–585.
- Schmitz, L., Kronstad, J.W., and Heimel, K.** (2020). Conditional gene expression reveals stage-specific functions of the unfolded protein response in the *Ustilago maydis*-maize pathosystem. *Mol. Plant Pathol.* **21**:258–271.
- Scossa, F., Alseekh, S., and Fernie, A.R.** (2021). Integrating multi-omics data for crop improvement. *J. Plant Physiol.* **257**:153352.
- Searchinger, T., James, O., Dumas, P., Kastner, T., and Wirsenius, S.** (2022). EU climate plan sacrifices carbon storage and biodiversity for bioenergy. *Nature* **612**:27–30.
- Shi, J., Zhao, B., Zheng, S., et al.** (2021). A phosphate starvation response-centered network regulates mycorrhizal symbiosis. *Cell* **184**:5527–5540.e18.
- Sibbesen, J.A., Eizenga, J.M., Novak, a.m., Sirén, J., Chang, X., Garrison, E., and Paten, B.** (2023). Haplotype-aware pantranscriptome analyses using spliced pangenome graphs. *Nat. Methods* **20**:239–247.
- Soucy, S.M., Huang, J., and Gogarten, J.P.** (2015). Horizontal gene transfer: building the web of life. *Nat. Rev. Genet.* **16**:472–482.
- Stüeken, E.E., Buick, R., Guy, B.M., and Koehler, M.C.** (2015). Isotopic evidence for biological nitrogen fixation by molybdenum-nitrogenase from 3.2 Gyr. *Nature* **520**:666–669.
- Sun, C., Lei, Y., Li, B., Gao, Q., Li, Y., Cao, W., Yang, C., Li, H., Wang, Z., Li, Y., et al.** (2024a). Precise integration of large DNA sequences in plant genomes using PrimeRoot editors. *Nat. Biotechnol.* **42**:316–327.
- Sun, G., Xia, M., Li, J., Ma, W., Li, Q., Xie, J., Bai, S., Fang, S., Sun, T., Feng, X., et al.** (2022). The maize single-nucleus transcriptome comprehensively describes signaling networks governing movement and development of grass stomata. *Plant Cell* **34**:1890–1911.
- Sun, X., Xiang, Y., Dou, N., Zhang, H., Pei, S., Franco, A.V., Menon, M., Monier, B., Ferebee, T., Liu, T., et al.** (2023). The role of transposon inverted repeats in balancing drought tolerance and yield-related traits in maize. *Nat. Biotechnol.* **41**:120–127.
- Sun, Y., Dong, L., Kang, L., Zhong, W., Jackson, D., and Yang, F.** (2024b). Progressive meristem and single-cell transcriptomes reveal

- the regulatory mechanisms underlying maize inflorescence development and sex differentiation. *Mol. Plant* **17**:1019–1037.
- Tabashnik, B.E., and Carrière, Y.** (2017). Surge in insect resistance to transgenic crops and prospects for sustainability. *Nat. Biotechnol.* **35**:926–935.
- Tian, J., Wang, C., Xia, J., Wu, L., Xu, G., Wu, W., Li, D., Qin, W., Han, X., Chen, Q., et al.** (2019). Teosinte ligule allele narrows plant architecture and enhances high-density maize yields. *Science* **365**:658–664.
- Tester, M., and Langridge, P.** (2010). Breeding Technologies to Increase Crop Production in a Changing World. *Science* **327**:818–822.
- Tian, J., Wang, C., Chen, F., Qin, W., Yang, H., Zhao, S., Xia, J., Du, X., Zhu, Y., Wu, L., et al.** (2024). Maize smart-canopy architecture enhances yield at high densities. *Nature* **632**:576–584.
- Tian, T., Wang, S., Yang, S., Yang, Z., Liu, S., Wang, Y., Gao, H., Zhang, S., Yang, X., Jiang, C., et al.** (2023). Genome assembly and genetic dissection of a prominent drought-resistant maize germplasm. *Nat. Genet.* **55**:496–506.
- Tzachor, A., Devare, M., King, B., Avin, S., and Ó hÉigeartaigh, S.** (2022). Responsible artificial intelligence in agriculture requires systemic understanding of risks and externalities. *Nat. Mach. Intell.* **4**:104–109.
- Van Heerwaarden, J., Doebley, J., Briggs, W.H., Glaubitz, J.C., Goodman, M.M., de Jesus Sanchez Gonzalez, J., Ross-Ibarra, J., et al.** (2011). Genetic signals of origin, spread, and introgression in a large sample of maize landraces. *Proc. Natl. Acad. Sci. USA* **108**:1088–1092.
- Vanhevel, Y., De Moor, A., Muylle, H., Vanholme, R., and Boerjan, W.** (2024). Breeding for improved digestibility and processing of lignocellulosic biomass in *Zea mays*. *Front. Plant Sci.* **15**:1419796.
- Vidal, E.A., Alvarez, J.M., Araus, V., Riveras, E., Brooks, M.D., Krouk, G., Ruffel, S., Lejay, L., Crawford, N.M., Coruzzi, G.M., et al.** (2020). Nitrate in 2020: Thirty years from transport to signaling networks. *Plant Cell* **32**:2094–2119.
- Vidal, E.A., Araus, V., Lu, C., Parry, G., Green, P.J., Coruzzi, G.M., and Gutiérrez, R.A.** (2010). Nitrate-responsive miR393/AFB3 regulatory module controls root system architecture in *Arabidopsis thaliana*. *Proc. Natl. Acad. Sci. USA* **107**:4477–4482.
- de Vries, F.T., Griffiths, R.I., Knight, C.G., Nicolitch, O., and Williams, A.** (2020). Harnessing rhizosphere microbiomes for drought-resilient crop production. *Science* **368**:270–274.
- Wallace, J.G., Rodgers-Melnick, E., and Buckler, E.S.** (2018). On the road to breeding 4.0: Unraveling the good, the bad, and the boring of crop quantitative genomics. *Annu. Rev. Genet.* **52**:421–444.
- Wang, B., Zhu, L., Zhao, B., Zhao, Y., Xie, Y., Zheng, Z., Li, Y., Sun, J., and Wang, H.** (2019). Development of a Haploid-Inducer Mediated Genome Editing System for Accelerating Maize Breeding. *Mol. Plant* **12**:597–602.
- Wang, B., Hou, M., Shi, J., Ku, L., Song, W., Li, C., Ning, Q., Li, X., Li, C., Zhao, B., et al.** (2023a). De novo genome assembly and analyses of 12 founder inbred lines provide insights into maize heterosis. *Nat. Genet.* **55**:312–323.
- Wang, B., Yang, C., Zhang, J., You, Y., Wang, H., and Yang, W.** (2024a). IHUP: An Integrated High-Throughput Universal Phenotyping Software Platform to Accelerate Unmanned-Aerial-Vehicle-Based Field Plant Phenotypic Data Extraction and Analysis. *Plant Phenomics* **6**:0164.
- Wang, J.Y., and Doudna, J.A.** (2023). CRISPR technology: A decade of genome editing is only the beginning. *Science* **379**:eadd8643.
- Wang, K., Abid, M.A., Rasheed, A., Crossa, J., Hearne, S., and Li, H.** (2023b). DNNGP, a deep neural network-based method for genomic prediction using multi-omics data in plants. *Mol. Plant* **16**:279–293.
- Wang, P., Li, Z., Li, H., Zhang, D., Wang, W., Xu, X., Xie, Q., Duan, Z., Xia, X., Guo, G., et al.** (2024b). SMART CROPS. *New Crops* **1**:100007.
- Wang, R., Tischner, R., Gutiérrez, R.A., Hoffman, M., Xing, X., Chen, M., Coruzzi, G., and Crawford, N.M.** (2004). Genomic analysis of the nitrate response using a nitrate reductase-null mutant of *Arabidopsis*. *Plant Physiol.* **136**:2512–2522.
- Wang, R., Zhong, Y., Han, J., Huang, L., Wang, Y., Shi, X., Li, M., Zhuang, Y., Ren, W., Liu, X., et al.** (2024c). NIN-LIKE PROTEIN3.2 inhibits repressor Aux/IAA14 expression and enhances root biomass in maize seedlings under low nitrogen. *Plant Cell* **36**:4388–4403.
- Wang, T., Wang, F., Deng, S., Wang, K., Feng, D., Xu, F., Guo, W., Yu, J., Wu, Y., Wuriyangan, H., et al.** (2025). Single-cell transcriptomes reveal spatiotemporal heat stress response in maize roots. *Nat. Commun.* **16**:177.
- Wang, X., Wang, H., Liu, S., Ferjani, A., Li, J., Yan, J., Yang, X., and Qin, F.** (2016). Genetic variation in ZmVPP1 contributes to drought tolerance in maize seedlings. *Nat. Genet.* **48**:1233–1241.
- Wang, Y., Wang, X., Sun, S., Jin, C., Su, J., Wei, J., Luo, X., Wen, J., Wei, T., Sahu, S.K., et al.** (2022). GWAS, MWAS and mGWAS provide insights into precision agriculture based on genotype-dependent microbial effects in foxtail millet. *Nat. Commun.* **13**:5913.
- Wang, Y., Luo, Y., Guo, X., Li, Y., Yan, J., Shao, W., Wei, W., Wei, X., Yang, T., Chen, J., et al.** (2024d). A spatial transcriptome map of the developing maize ear. *Nat. Plants* **10**:815–827.
- Wang, Y.-Y., Cheng, Y.H., Chen, K.E., and Tsay, Y.F.** (2018). Nitrate transport, signaling, and use efficiency. *Annu. Rev. Plant Biol.* **69**:85–122.
- Wang, Z., and Song, Y.** (2022). Toward understanding the genetic bases underlying plant-mediated “cry for help” to the microbiota. *iMeta* **1**:e8.
- Wu, X., Feng, H., Wu, D., Yan, S., Zhang, P., Wang, W., Zhang, J., Ye, J., Dai, G., Fan, Y., et al.** (2021). Using high-throughput multiple optical phenotyping to decipher the genetic architecture of maize drought tolerance. *Genome Biol.* **22**:185.
- Wurtzel, E.T., and Kutchan, T.M.** (2016). Plant metabolism, the diverse chemistry set of the future. *Science* **353**:1232–1236.
- Xiao, Y., Liu, H., Wu, L., Warburton, M., and Yan, J.** (2017). Genome-wide association studies in maize: Praise and stargaze. *Mol. Plant* **10**:359–374.
- Xu, R., and Li, C.** (2022). A Review of High-Throughput Field Phenotyping Systems: Focusing on Ground Robots. *Plant Phenomics* **2022**:9760269.
- Xu, L., Pierroz, G., Wipf, H.M.L., Gao, C., Taylor, J.W., Lemaux, P.G., and Coleman-Derr, D.** (2021a). Holo-omics for deciphering plant-microbiome interactions. *Microbiome* **9**:69.
- Xu, X., Crow, M., Rice, B.R., Li, F., Harris, B., Liu, L., Demesa-Arevalo, E., Lu, Z., Wang, L., Fox, N., et al.** (2021b). Single-cell RNA sequencing of developing maize ears facilitates functional analysis and trait candidate gene discovery. *Dev. Cell* **56**:557–568.e6.
- Xu, Y., Zhang, X., Li, H., Zheng, H., Zhang, J., Olsen, M.S., Varshney, R.K., Prasanna, B.M., and Qian, Q.** (2022). Smart breeding driven by big data, artificial intelligence, and integrated genomic-environmental prediction. *Mol. Plant* **15**:1664–1695.
- Yamaguchi-Shinozaki, K., and Shinozaki, K.** (1994). A novel cis-acting element in an *Arabidopsis* gene is involved in responsiveness to drought, low-temperature, or high-salt stress. *Plant Cell* **6**:251–264.
- Yamaguchi-Shinozaki, K., and Shinozaki, K.** (2006). Transcriptional regulatory networks in cellular responses and tolerance to dehydration and cold stresses. *Annu. Rev. Plant Biol.* **57**:781–803.
- Yan, J., Kandianis, C.B., Harjes, C.E., Bai, L., Kim, E.H., Yang, X., Skinner, D.J., Fu, Z., Mitchell, S., Li, Q., et al.** (2010). Rare genetic

- variation at *Zea mays* crtRB1 increases β -carotene in maize grain. *Nat. Genet.* **42**:322–327.
- Yan, P., Du, Q., Chen, H., Guo, Z., Wang, Z., Tang, J., and Li, W.X.** (2023). Biofortification of iron content by regulating a NAC transcription factor in maize. *Science* **382**:1159–1165.
- Yan, Y., Duan, F., Li, X., Zhao, R., Hou, P., Zhao, M., Li, S., Wang, Y., Dai, T., and Zhou, W.** (2024). Photosynthetic capacity and assimilate transport of the lower canopy influence maize yield under high planting density. *Plant Physiol.* **195**:2652–2667.
- Yang, L., Zhang, P., Wang, Y., Hu, G., Guo, W., Gu, X., and Pu, L.** (2022a). Plant synthetic epigenomic engineering for crop improvement. *Sci. China Life Sci.* **65**:2191–2204.
- Yang, N., Liu, J., Gao, Q., Gui, S., Chen, L., Yang, L., Huang, J., Deng, T., Luo, J., He, L., et al.** (2019). Genome assembly of a tropical maize inbred line provides insights into structural variation and crop improvement. *Nat. Genet.* **51**:1052–1059.
- Yang, N., Wang, Y., Liu, X., Jin, M., Vallebuena-Estrada, M., Calfee, E., Chen, L., Dilkes, B.P., Gui, S., Fan, X., et al.** (2023a). Two teosintes made modern maize. *Science* **382**:eadg8940.
- Yang, Q., Li, Z., Li, W., Ku, L., Wang, C., Ye, J., Li, K., Yang, N., Li, Y., Zhong, T., et al.** (2013). CACTA-like transposable element in *ZmCCT* attenuated photoperiod sensitivity and accelerated the postdomestication spread of maize. *Proc. Natl. Acad. Sci. USA* **110**:16969–16974.
- Yang, W., Feng, H., Zhang, X., Zhang, J., Doonan, J.H., Batchelor, W.D., Xiong, L., and Yan, J.** (2020). Crop Phenomics and High-Throughput Phenotyping: Past Decades, Current Challenges, and Future Perspectives. *Mol. Plant* **13**:187–214.
- Yang, W., Guo, T., Luo, J., Zhang, R., Zhao, J., Warburton, M.L., Xiao, Y., and Yan, J.** (2022b). Target-oriented prioritization: targeted selection strategy by integrating organismal and molecular traits through predictive analytics in breeding. *Genome Biol.* **23**:80.
- Yang, X., Zhu, X., Wei, J., Li, W., Wang, H., Xu, Y., Yang, Z., Xu, C., and Li, P.** (2022c). Primary root response to combined drought and heat stress is regulated via salicylic acid metabolism in maize. *BMC Plant Biol.* **22**:417.
- Yang, Y., Tilman, D., Jin, Z., Smith, P., Barrett, C.B., Zhu, Y.G., Burney, J., D'Odorico, P., Fantke, P., Fargione, J., et al.** (2024). Climate change exacerbates the environmental impacts of agriculture. *Science* **385**:eadn3747.
- Yang, Z., Cao, Y., Shi, Y., Qin, F., Jiang, C., and Yang, S.** (2023b). Genetic and molecular exploration of maize environmental stress resilience: Toward sustainable agriculture. *Mol. Plant* **16**:1496–1517.
- Yaschenko, A.E., Fenech, M., Mazzoni-Putman, S., Alonso, J.M., and Stepanova, A.N.** (2022). Deciphering the molecular basis of tissue-specific gene expression in plants: Can synthetic biology help? *Curr. Opin. Plant Biol.* **68**:102241.
- Yasmeen, E., Wang, J., Riaz, M., Zhang, L., and Zuo, K.** (2023). Designing artificial synthetic promoters for accurate, smart, and versatile gene expression in plants. *Plant Commun.* **4**:100558.
- Yasmin, F., Cowie, A.E., and Zerbe, P.** (2024). Understanding the chemical language mediating maize immunity and environmental adaptation. *New Phytol.* **243**:2093–2101.
- Ye, H., Louden, M., and Reinders, J.A.T.** (2024). A novel in vivo genome editing doubled haploid system for *Zea mays* L. *Nat. Plants* **10**:1493–1501.
- Yu, P., He, X., Baer, M., Beirinckx, S., Tian, T., Moya, Y.A.T., Zhang, X., Deichmann, M., Frey, F.P., Bresgen, V., et al.** (2021). Plant flavones enrich rhizosphere Oxalobacteraceae to improve maize performance under nitrogen deprivation. *Nat. Plants* **7**:481–499.
- Yu, Y., Li, W., Liu, Y., Liu, Y., Zhang, Q., Ouyang, Y., Ding, W., Xue, Y., Zou, Y., Yan, J., et al.** (2025). A *Zea* genus-specific micropeptide controls kernel dehydration in maize. *Cell* **188**:44–59.e21.
- Yuan, Y., Huo, Q., Zhang, Z., Wang, Q., Wang, J., Chang, S., Cai, P., Song, K.M., Galbraith, D.W., Zhang, W., et al.** (2024). Decoding the gene regulatory network of endosperm differentiation in maize. *Nat. Commun.* **15**:34.
- Zambelli, A.** (2021). Current Status of High Oleic Seed Oils in Food Processing. *J. Americ. Oil Chem. Soc.* **98**:129–137.
- Zandalinas, S.I., and Mittler, R.** (2022). Plant responses to multifactorial stress combination. *New Phytol.* **234**:1161–1167.
- Zeng, R., Li, Z., Shi, Y., Fu, D., Yin, P., Cheng, J., Jiang, C., and Yang, S.** (2021). Natural variation in a type-A response regulator confers maize chilling tolerance. *Nat. Commun.* **12**:4713.
- Zhan, C., and Wang, M.** (2024). Disease resistance through M genes. *Nat. Plants* **10**:352–353.
- Zhang, J., Liu, Y.X., Zhang, N., Hu, B., Jin, T., Xu, H., Qin, Y., Yan, P., Zhang, X., Guo, X., et al.** (2019). NRT1.1B is associated with root microbiota composition and nitrogen use in field-grown rice. *Nat. Biotechnol.* **37**:676–684.
- Zhang, P., Guo, Z., Ullah, S., Melagraki, G., Afantitis, A., and Lynch, I.** (2021). Nanotechnology and artificial intelligence to enable sustainable and precision agriculture. *Nat. Plants* **7**:864–876.
- Zhong, T., Zhu, M., Zhang, Q., et al.** (2024). The *ZmWAKL-ZmWIK-ZmBLK1-ZmRBOH4* module provides quantitative resistance to gray leaf spot in maize. *Nat. Genet.* **56**:315–326.
- Zhou, S., Ma, Y., Shang, Y., Qi, X., Huang, S., and Li, J.** (2022). Functional diversity and metabolic engineering of plant-specialized metabolites. *Life Metabolism* **1**:109–121.