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TARGETING THE PLANT KINOME: FROM MAPK CASCADES TO RECEPTOR-LIKE KINASE EDITING FOR STRESS RESILIENCE

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ABSTRACT

Plants rely on complex and highly coordinated signaling networks to perceive and respond to fluctuating environmental conditions. Central to these networks is the plant kinome, comprising large families of protein kinases that regulate growth, development, and stress adaptation. Major kinase groups, including mitogen-activated protein kinases (MAPKs), receptor-like kinases (RLKs), calcium-dependent protein kinases (CDPKs), and SNF1-related kinases (SnRKs), function as interconnected hubs that integrate extracellular stimuli, calcium dynamics, hormonal signals, and cellular energy status. Through tightly regulated phosphorylation events, these kinases orchestrate transcriptional reprogramming, metabolic adjustments, and physiological responses to abiotic stresses such as drought, salinity, and heat, as well as biotic challenges like pathogen attack. Recent advances in phosphoproteomics, interactomics, and systems biology have revealed that stress signaling is governed by dynamic, multilayered kinase networks characterized by feedback regulation and extensive cross-talk. Parallel progress in genome editing, particularly CRISPR/Cas-based approaches, along with structural biology, computational modeling, and artificial intelligence, has enabled precise functional interrogation and rational modification of kinase genes. These integrative strategies provide new opportunities to fine-tune stress-responsive signaling while maintaining growth and yield. Collectively, kinome-centered approaches offer a promising framework for developing climate-resilient crops capable of sustaining productivity under increasingly variable environmental conditions.

***Keywords*:** Plant kinome, Protein kinase signaling, Stress-responsive pathways, MAPK cascades, Receptor-like kinases, Calcium signaling, SNF1-related kinases, Abiotic and biotic stress, CRISPR-based genome editing, Climate-resilient crops.

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1. INTRODUCTION

The plant kinome encompasses the full complement of protein kinases encoded within a plant genome, typically ranging from 1,000 to 1,500 in higher plants (Yan et al., 2024). This expansive superfamily, which includes receptor-like kinases (RLKs), mitogen-activated protein kinases (MAPKs), SNF1-related protein kinases (SnRKs), and calcium-dependent protein kinases (CDPKs), acts as a central hub for regulating growth, development, and responses to environmental stimuli. Through targeted phosphorylation events, these kinases perceive signals such as hormones, light, drought, and pathogen attack, translating them into coordinated cellular and physiological responses (Lehti-Shiu & Shiu, 2012).

Within this network, RLKs function as primary receptors that sense extracellular cues and activate downstream MAPK cascades, which amplify and fine-tune signaling to modulate gene expression and stress responses. SnRKs integrate metabolic and abscisic acid (ABA)-dependent pathways, helping plants adapt to water deficit, salinity, and other environmental stresses (Dekomah et al., 2022). Similarly, CDPKs decode transient calcium fluctuations into phosphorylation signals that regulate development, nutrient assimilation, and adaptive stress responses (Pandey, 2021). Together, these kinase families form an interconnected signaling system that balances growth, defense, and metabolism, positioning the plant kinome as a critical orchestrator of resilience.

Despite the central role of kinases, traditional breeding approaches face significant constraints in manipulating these complex networks (Bradshaw, 2017). Dependence on phenotypic selection and natural recombination limits the precision with which multigenic and highly interdependent pathways can be modified (Nayeri et al., 2019). Additional factors, including epistasis, linkage drag, and long breeding cycles, reduce the efficiency of improving multiple traits simultaneously, while limited genetic diversity in elite germplasm further constrains targeted modifications (Gordley et al., 2016). These challenges underscore the need for advanced biotechnological strategies that allow precise engineering of signaling modules.

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Open Access Journal

In this context, genome editing technologies, particularly CRISPR-Cas9, combined with structural biology, offer powerful tools to reprogram plant kinases for enhanced stress resilience. Structural insights into kinase domains, regulatory motifs, and substrate interactions guide rational genome modifications, enabling precise alterations of key residues, regulatory regions, or negative regulators without compromising plant growth. Editing drought-responsive genes involved in ABA signaling, transcriptional regulation, and other stress pathways has demonstrated improvements in water-use efficiency, root architecture, and antioxidant defenses. By enabling modular and targeted rewiring of multigenic signaling networks, these approaches mark a paradigm shift from conventional breeding toward precision engineering of crops capable of thriving under challenging environmental conditions.

Functional Atlas of Plant Kinases and Phosphatases in Stress Signaling

Plant responses to environmental stress are known to be mostly regulated by MAPK cascades, which are made up of MAPKKKs, MAPKKs, and MAPKs. Importantly, these pathways function within a larger signaling network rather than independently, according to the Functional Atlas of Plant Kinases and Phosphatases. Within this network, phosphatases, especially PP2Cs, regulate MAPK activity, allowing for quick but balanced reactions without compromising development. For example, the MAPKKK17/18–MKK3–MPK1/2/7 module, which involves several overlapping mechanisms to preserve cellular stability, enhances Abscisic acid (ABA) signaling, modifies stomatal behavior, and supports ROS management under drought stress (He et al., 2020).

On the other hand, heat stress primarily causes the generation of ROS, which in turn quickly activates MPK3 and MPK6, resulting in the induction of heat-shock proteins and the stabilization of membranes. Studies in wheat further confirm that ROS-activated TaMPK3/6 can impair photosynthesis and grain filling at high temperatures. Moreover, MPK3 is one of the defense mechanisms that are activated by MAPKs in response to abiotic stresses; collectively, MPK3/MPK6 activate PR genes, fortify the cell wall, and regulate the responses mediated through SA, JA, and ET. To prevent overactivation, these defensive mechanisms rely on tightly coordinated kinase–phosphatase interactions. Overall, MAPK cascades act as flexible signaling hubs that integrate a range of stress stimuli, enabling plants to adjust effectively while preserving membrane integrity and growth (Kumar et al., 2020). This versatility likely explains their broad conservation in cereals and horticultural crops.

Receptor-like kinases (RLKs), which include important subfamilies including LRR-RLKs, CrRLK1Ls, and WAKs, are important membrane-bound sensors that go beyond MAPK cascades (Passricha et al., 2019). They let plants to sense environmental stressors while keeping a careful balance between defense and development. A broad range of signals, such as peptides, hormones, pathogen-associated chemicals, and indications of abiotic stress, are detected by RLKs via their varied extracellular domains. The intracellular kinase domains start regulated signaling cascades that combine environmental data with developmental programs as soon as these cues are detected (Q. Zhu et al., 2023). RLKs function as molecular hubs that coordinate plant responses across several biological levels. Similar to this, overexpression of SENESCENCE-RELATED RECEPTOR KINASE 1 (SENRK1) delays senescence, illustrating how RLKs affect both developmental time and stress response. By identifying bacterial flagellin (flg22) and triggering downstream defense pathways, LRR-RLKs like FLS2 demonstrate accurate pathogen identification in the immunological domain. By transforming extracellular stress signals into intracellular adaptive responses, certain RLKs take part in abiotic stress sensing in addition to biotic stress, such as drought, salt, cold, and heavy metal toxicity. When considered collectively, these findings demonstrate that RLKs serve as integrative signaling nodes, coordinating stress adaption and growth control to preserve homeostasis in the face of changing environmental circumstances (Gandhi & Oelmüller, 2023).

Calcium (Ca^{2+}) functions as a quick and adaptable second messenger inside the cell, especially when ABA levels concurrently rise during drought. Plants need specific systems to decipher these overlapping signals since dryness causes both ABA buildup and cytosolic Ca2+ increases (Aliniaeifard, Shomali, Seifikalhor, & Lastochkina, 2020). At this point, CDPKs and SnRKs become major decoding modules that convert signals generated from Ca2+ and ABA into coordinated responses. With their intrinsic kinase activity and Ca2+-binding regulatory domains, CDPKs immediately translate calcium signals into phosphorylation events that control transcription factors, metabolic enzymes, and ion channels for quick stress adaptation (Edel & Kudla, 2016). Simultaneously, ABA sensing through PYR/PYL/RCAR receptors triggers SnRK2 kinases, which phosphorylate important transcription factors and ion transporters to enhance drought signaling. Notably, CDPKs and SnRKs can function in a complimentary and occasionally convergent way thanks to the ABA-induced Ca2+ increase, which provides an extra layer of integration. Stomatal closure, ROS generation, and the transcriptional activation of drought-responsive genes are all fine-tuned by this interaction. As such, instead of separate pathways, the Ca2+-ABA network provides a network of immediate modifications in physiological behavior and an initiation of long-term programs in stress tolerance (Kiselev & Dubrovina, 2025).

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)
Open Access Journal

Protein phosphatases, especially PP2Cs and MAPK phosphatases (MKPs), offer crucial feedback and signaling reset to preserve signaling equilibrium. The level of phosphorylation rapidly increases upon the activation of immunological or abiotic stress signaling; however, these signals must be tightly controlled since overreaction is often detrimental (Bhaskara et al., 2019). By dephosphorylating active MAPKs, MKPs operate as crucial brakes on MAPK cascades, reducing immunological signals once the danger has been neutralized. This guarantees that normal development is not disrupted by MAPK-driven defenses. Similarly, through their interaction with SnRK2 kinases, PP2Cs play a key role in ABA and stress signaling. By continuously dephosphorylating SnRK2s, PP2Cs sustain basal signaling in the absence of stress (Kaushik, 2025). In non-stress situations, PP2Cs sustain basal signaling by continuously dephosphorylating SnRK2s. PYR/PYL/RCAR receptors block PP2Cs in response to stress or ABA perception, which permits SnRK2 activation. After stress has passed, PP2Cs become reactivated, thus resetting the pathway. These methods of reversible dephosphorylation enable quick activation of stress responses while guaranteeing a prompt return to equilibrium. When combined, MKPs and PP2Cs offer a well-balanced regulatory framework in which phosphatases function as accurate modulators, limiting excessive phosphorylation buildup and returning signaling states to baseline (Deng et al., 2024; Li et al., 2025).

Finally, systems biology methods that include interactomics and phosphoproteomics have greatly improved our comprehension of plant kinase–substrate networks under stress. Phosphoproteomic databases, such as P3DB, provide large-scale datasets of in vivo phosphorylation events and, thus, enable the identification of kinases and substrates that are changed under particular stress conditions (Xiao, Chen, & Yang, 2023). Temporal phosphorylation waves are captured by high-resolution phosphoproteomics, which shows how MAPKs, CDPKs, SnRKs, and RLKs coordinate their actions during adaptation. Mapping physical kinase-substrate interactions, reconstructing signaling nodes, and identifying cross-talk between pathways are all made possible by combining these phosphorylation patterns with interactomics. (Li et al., 2025) With feedback loops, hierarchical regulation, and network hubs that would be obscured by conventional single-gene methods, our studies show that plant stress signaling is arranged into densely linked modules (Cai et al., 2025). When taken as a whole, these integrative methods show that plants use intricate kinase–substrate networks to preserve resistance in the face of biotic and abiotic stress (Shi et al., 2021).

CRISPR/Cas-Mediated Editing of Kinases in Model and Crop Species

Protein kinases are excellent targets for CRISPR/Cas-mediated genome editing in both model and crop species because they are key regulators of development, plant growth and stress responses. In order to analyze kinase functions and signaling cascades, loss-of-function editing with CRISPR/Cas9-induced frame-shift mutations was first extensively used in Arabidopsis, rice, maize, and tomato (Lu et al., 2020). However, there are drawbacks to depend solely on gene knockouts, especially in polyploid crops like wheat. A wheat tandem kinase mutation that provide resistance to powdery mildew is an example of how recent research has evolved toward gain-of-function editing, where precise in-frame deletions or targeted amino-acid changes improve kinase activity and yield dominant characteristics (Huang et al., 2021). Moreover, the advances of base and prime editing methods has made it possible to modify kinase domains and regulatory areas on a fine scale without introducing foreign DNA. When combined, loss- and gain-of-function CRISPR techniques offer a flexible and efficient framework for enhancing, maximizing plant architecture, disease resistance and raising yield potential in a variety of plant species (Fig. 1) (Zhu & Qian, 2020).

Building upon these approaches, advances in base and prime editing have revolutionized the ability to modify kinase genes with unprecedented precision. Base editors enable targeted single-nucleotide substitutions without generating double-strand breaks, which is ideal for altering phosphorylation motifs, ATP-binding pockets, or activation loops that are central to kinase regulation (Belli et al., 2024). These precise changes allow researchers to fine-tune kinase activity and explore the functional consequences of specific amino acid substitutions. Prime editors complement base editors by enabling insertions, deletions, and transversions, thereby allowing the introduction of more complex sequence modifications (Dorighi et al., 2024). When combined in multimodal strategies, base and prime editing allow systematic targeting of multiple functional elements within kinases, providing a platform for high-resolution functional mapping and rational protein engineering. Furthermore, the development of optimized mutagenic platforms equipped with enhanced deaminases and tailored guide RNA libraries enables the generation of diverse allelic variants, facilitating exploration of protein-coding regions at scale and uncovering subtle changes that influence activity, stability, and regulatory dynamics (Li et al., 2025).

In addition, multiplex CRISPR editing strategies have enabled simultaneous modification of multiple kinases within complex signaling networks, such as the MAPKKK–MAPKK–MAPK cascades in rice and other crops. Using polycistronic tRNA-gRNA (PTG) systems, researchers can express multiple guide RNAs from a single transcript, allowing co-targeting of several homologous or functionally related kinases in a single transformation event (Fig. 1). Consequently, this approach permits the generation of single, double, and even quadruple mutants,

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Open Access Journal

facilitating functional analysis of redundant gene families and enabling dissection of network interactions that would remain hidden if genes were edited individually (Minkenberg, 2017). By perturbing multiple nodes across MAPK cascades, researchers can effectively rewire signaling networks, providing insights into kinase hierarchies, cross-talk between pathways, and their roles in development and stress adaptation.

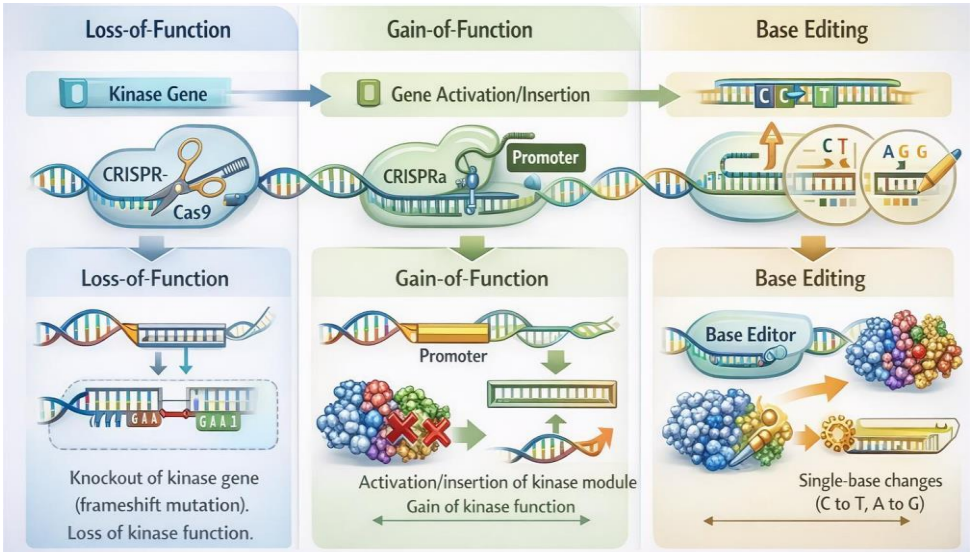

Fig. 1: CRISPR editing strategy for kinase modules (loss/gain-of-function and base editing); Note: The figure illustrates CRISPR-based editing strategies for plant kinase modules, including loss-of-function, gain-of-function, and base-editing approaches, highlighting their potential to precisely modulate kinase activity for improved stress responses and crop traits (Brito et al., 2025).

Furthermore, CRISPR-based transcriptional regulation, including CRISPR activation (CRISPRa) and interference (CRISPRi), has extended the utility of CRISPR beyond genome editing by enabling tunable control of gene expression (Fontana et al., 2024). These systems utilize a catalytically inactive Cas protein (dCas) fused to transcriptional activators or repressors to upregulate or downregulate target genes in a programmable manner. Advances in guide RNA design and scaffold engineering now allow combinatorial CRISPRa programs capable of independently controlling multiple genes, producing graded and orthogonal expression patterns (Bendixen, Jensen, & Bak, 2023). Such tunable regulation is particularly valuable for kinases, where subtle adjustments in transcript levels can optimize signaling cascades, enhance stress tolerance, and prevent adverse effects associated with constitutive overexpression or complete knockdown. Thus, CRISPRa/i provides a flexible framework for dynamically regulating kinase expression, enabling precise exploration of gene function and network engineering in plants (Srinivasa & Escobar, 2025).

Finally, one of the major challenges in CRISPR-based editing is off-target activity and functional redundancy, especially in polyploid crops or large gene families with closely related paralogs. Moreover, reliance on a single reference genome may overlook sequence variation across cultivars, leading to mismatches in guide RNA binding and unintended edits (Singer et al., 2021). To overcome these issues, researchers now utilize pangenome references to capture the full spectrum of genomic diversity, enabling the design of paralog-specific guides that precisely target individual gene copies while minimizing off-target effects. Consequently, integrating pangenome information with paralog-aware guide design enhances editing precision, resolves functional redundancy, and allows accurate functional characterization of kinases in complex plant genomes (Graham et al., 2020).

Taken together, these strategies—spanning loss- and gain-of-function edits, base and prime editing, multiplexed targeting, RNA-guided transcriptional modulation, and pangenome-informed guide design—provide a comprehensive and flexible framework for CRISPR/Cas-mediated manipulation of kinases (Zhao & Wolt, 2017). Collectively, they enable researchers to dissect kinase signaling networks, rewire functional cascades, fine-tune gene expression, and ultimately improve plant architecture, stress resistance, and yield potential across a wide range of model and crop species.

Case Studies

OsMPK5 and OsMPK6 in Rice Stress Responses

To begin with, rice MAP kinases such as OsMPK5 and OsMPK6 have been shown to participate in responses to both abiotic and biotic stresses through activation in MAPK cascades. Although classical early work on OsMPK5 demonstrated its induction by drought, salt, and cold treatments in plants and that kinase activity increases under these stresses, recent research has broadened the understanding of MAPK roles in stress signaling. For example, studies have revealed that non-canonical regulatory modules in rice involving MAPK cascades actively contribute

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Open Access Journal

to stress tolerance: upstream kinases such as OsCPK5 and OsCPK13 directly activate OsMPK3 and OsMPK6 under salt stress, and this activation enhances salt tolerance by facilitating stress-responsive signaling and ROS control, indicating that OsMPK6 functions as a positive regulator in salinity responses in rice alongside other MAPKs (Su et al., 2024). Moreover, the OsCRK14-OsRLCK57-MKK4-OsMPK6 signaling module has been demonstrated to enhance drought resistance in recent work through phosphorylation of downstream transcription factors (such as OsbZIP66), illustrating that OsMPK6 integrates upstream receptor kinase signals into drought-responsive gene expression. Together, these findings indicate that MAPKs including OsMPK5/6 are not only activated in drought and salt stresses but also participate in crosstalk with calcium-dependent kinases and receptor kinases to modulate stress tolerance in rice (Bhavani & Chatterjee, 2020). Representative examples of CRISPR/Cas-mediated editing of kinase genes in major crop species and their associated phenotypic outcomes are summarized in Table 1.

Table 1: Key plant kinase editing studies (2020–2025) and phenotypic outcomes (Li et al., 2022; Wang et al., 2024)

Gene	Kinase Family	Crop Species	Editing Approach(2020–2025)	Phenotypic Outcomes
OsCPK18 / OsCPK4 phosphorylation motif	CDPK (Calcium-dependent protein kinase)	*Oryza sativa* (rice)	CRISPR/Cas9-mediated precise editing of phosphorylation motifs to disrupt MAPK-dependent regulation	Enhanced disease resistance and increased grain yield growth–defence trade-off
TaMKP1 (MAP kinase phosphatase 1)	MAPK phosphatase (negative regulator of MAPKs)	*Triticum aestivum* (wheat)	CRISPR/Cas9-mediated loss-of-function mutation	Enhanced resistance diseaes, yield traits improved under non-stress conditions
GhCPK33 / GhCPK74	CDPK	*Gossypium hirsutum* (cotton)	CRISPR/Cas9 CDPK mutant library generation	ghcpk33 and ghcpk74 mutants exhibited enhanced insect resistance
TaRPK1	RLK (Receptor-like kinase)	*Triticum aestivum* (wheat)	CRISPR/Cas9-mediated targeted mutagenesis	Altered root system architecture accompanied by higher effective tiller number and grain weight

AtMPK6 in *Arabidopsis* Stress Regulation

Similarly, in Arabidopsis thaliana, AtMPK6 is widely recognized as a multifunctional MAP kinase mediating responses to diverse environmental stresses (Kumar et al., 2020). AtMPK6 participates in hormone-mediated stress signaling and is activated by abiotic stressors such as salt and drought, as well as by pathogen-associated signals. Studies show that AtMPK6 contributes to salt stress signaling by phosphorylating targets involved in ROS detoxification and transcriptional reprogramming, and its homolog activity in other crops (e.g., GmMPK6 in soybean) supports a conserved positive role for MPK6 in abiotic stress tolerance across species. Functionally, AtMPK6 modulates downstream stress markers and may participate in ABA-dependent and independent signaling pathways, helping plants adjust osmotic balance, regulate stomatal movements, and enhance pathogen defense when challenged by biotic stressors (Li et al., 2017).

TaSnRK2.8 in Wheat Abiotic Stress Tolerance

Moving to cereal SnRKs (SNF1-related protein kinases), wheat TaSnRK2.8 has been experimentally shown to confer enhanced drought, salt, and cold tolerance when overexpressed in Arabidopsis under controlled conditions. TaSnRK2.8 localizes to multiple cellular compartments and enhances physiological resilience under stress, including increased root growth, higher relative water content, stronger membrane stability, and altered ABA signaling and stress-responsive gene expression (Yanfei Zhang et al., 2023). This supports its role as a regulatory factor in multi-stress adaptation pathways, particularly within ABA-mediated stress signaling. In addition, broader analyses of SnRK2 gene family members in cereals highlight that several SnRK2s are activated by both drought and salt stress and may contribute to ROS homeostasis and stress tolerance, indicating that TaSnRK2.8 is part of a conserved mechanism across species (Yanyang Zhang et al., 2025).

GhRLK1 in Cotton Stress Responses

Finally, receptor-like kinases (RLKs) in cotton such as GbRLK, though older in publication origin, remain critical case studies for stress signal transduction. GbRLK from Gossypium barbadense exhibited inducible expression under drought, high salinity, ABA, and pathogen stimuli, and transgenic expression in Arabidopsis enhanced drought and salinity tolerance by activating ABA-dependent stress signaling and reducing water loss (Sadau et al., 2021). These functional reports show that RLK family members can serve as adaptive sensors that translate extracellular stress cues into downstream stress signaling pathways, including kinase networks involved in drought and salt resistance. While direct recent functional studies specifically on GhRLK1 per se (e.g., focused on

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pathogen resistance) are still limited, broader reviews of RLKs confirm that RLK family members play important roles in integrating biotic and abiotic stimuli across plant species, including cotton (Zhang et al., 2022).

Structural and Computational Insights for Kinase Engineering

Recent advances in structural biology have profoundly expanded our understanding of kinase activation domains, largely through the complementary application of X-ray crystallography and cryo-electron microscopy (Rygiel & Elkins, 2023). Initially, X-ray crystallography provided high-resolution snapshots of tyrosine kinases, revealing conserved regulatory elements such as the activation loop, αC-helix, and catalytic spine, and clarifying how phosphorylation stabilizes the active conformation. These studies have also helped identify subtle differences between inactive and active kinase conformations, enabling rational drug design targeting specific kinase states. Nevertheless, the rigid requirements of crystal formation often limit the capture of flexible or transient states, particularly in large multi-domain or membrane-associated kinases. In contrast, cryo-electron microscopy enables structural determination under near-native conditions without crystallization, making it particularly effective for resolving GPCR–kinase complexes, large protein assemblies, and transient signaling states (García-Nafría & Tate, 2021). High-resolution cryo-EM studies of the human CDK-activating kinase complex reveal how interactions among CDK7, cyclin H, and MAT1 stabilize the activation domain and correctly position the activation loop for catalysis, illustrating the importance of structural plasticity in kinase regulation. Collectively, integrating X-ray crystallography and cryo-EM provides a dynamic and comprehensive view of kinase activation, which is critical for kinase engineering and therapeutic targeting (Fig. 2) (Greber, 2024).

Building upon these structural insights, in silico modeling and molecular docking have become indispensable for understanding phosphorylation-induced allostery and conformational dynamics. Computational approaches, including molecular dynamics simulations, allow detailed mapping of structural fluctuations, inter-domain communication, and allosteric pathways that are difficult to capture experimentally (SarathKumar & Lakshmi, 2019). Studies on glycogen phosphorylase demonstrate that phosphorylation induces long-range allosteric effects, resulting in coordinated domain movements that reshape the global conformational landscape. Similarly, molecular docking and MD simulations of protein tyrosine phosphatase 1B have identified non-catalytic allosteric pockets where natural compounds preferentially bind, inducing conformational shifts that impair enzymatic activity. These approaches facilitate the discovery of allosteric inhibitors and modulators, guiding rational design of targeted molecules and expanding the potential for selective kinase regulation (Huang et al., 2022).

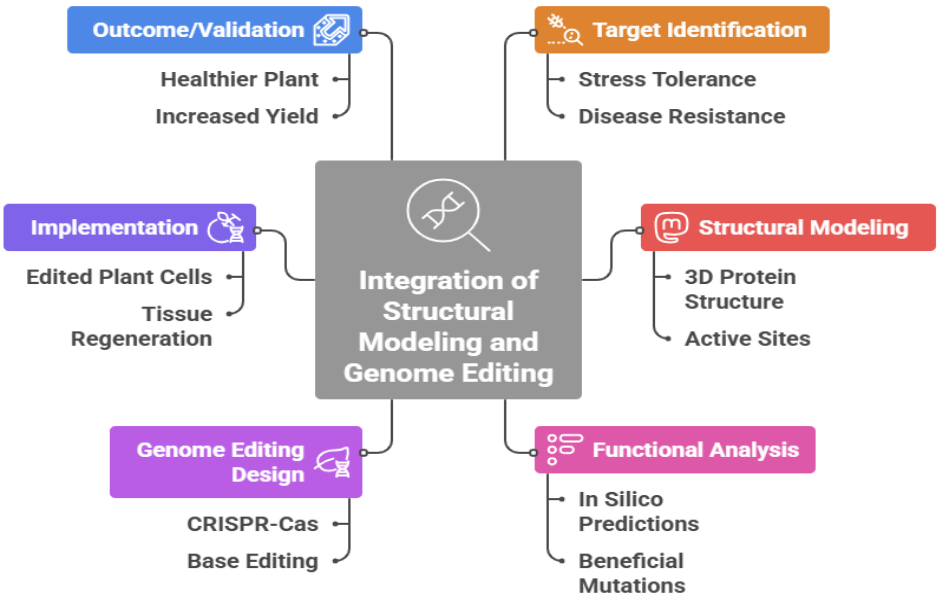

Fig. 2: Integration of structural modeling and genome editing.
Note: The figure illustrates the integration of structural modeling and genome editing, showing how predicted protein structures guide precise gene modifications to enhance plant stress tolerance, metabolic traits, and overall crop improvement (Chen, Liu, & Zhang, 2024).

Computational mutagenesis complements these approaches by predicting gain- or loss-of-function variants and dominant-negative mutations. Systematic in silico mutational scanning evaluates the effects of missense variants on protein stability, active-site geometry, and interaction networks (Gerasimavicius, Livesey, & Marsh, 2022). Loss-of-function variants typically destabilize the protein core or disrupt catalytic residues, whereas gain-of-function mutations stabilize active conformations, enhance ligand or substrate binding, or reinforce allosteric signaling. Dominant-negative mutations maintain structural integrity while selectively disrupting protein–protein interactions in multimeric assemblies, interfering with normal complex

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function. By integrating sequence conservation, energetic analysis, and molecular dynamics simulations, computational mutagenesis improves predictive accuracy, enabling functional classification of variants, guiding experimental validation, and informing rational engineering strategies.

Beyond classical structural and computational methods, AI-based structural prediction has become transformative for kinase and crop protein engineering, particularly in non-model organisms. Platforms such as AlphaFold2, coupled with deep learning algorithms and bioinformatics pipelines, allow accurate prediction of protein structures, domain interactions, and stress-responsive regulatory networks, even in species lacking experimental structural data (Peng & Rajjou, 2024). This capability enables researchers to identify conserved motifs, predict functional residues, and prioritize mutagenesis targets for enzyme optimization or stress resilience. Integrating AI predictions with experimental and computational workflows allows a seamless pipeline for protein engineering, accelerating the development of stress-tolerant crops and novel kinase variants with improved specificity and activity (Zhang et al., 2024). Additionally, AI-based approaches support large-scale functional annotation, enabling breeders and researchers to translate structural predictions into practical crop improvement strategies (Li et al., 2025).

Finally, structure-guided design has substantially enhanced CRISPR base-editing technologies, creating precise and efficient genome editing tools. Studies on sgBE show that detailed structural insights into the Cas–sgRNA complex allow optimization of sgRNA architecture, specifying base-editing windows and enabling simultaneous conversion of cytosine and adenosine within target sequences (Yanhong Wang et al., 2020). Structure-guided engineering of adenine base editors has minimized RNA off-target activity while maintaining high editing efficiency. By leveraging atomic-level knowledge of protein–nucleic acid interactions, these approaches refine targeting specificity, expand the editable sequence space, and reduce unintended edits. Integrating structure-guided design with computational modeling and AI predictions can further accelerate the development of highly precise genome editing tools for both model and non-model species, including crops where base editing can improve stress tolerance, yield, or nutritional quality (Giner et al., 2023).

In conclusion, the integration of structural biology, in silico modeling, computational mutagenesis, AI-based structural prediction, and structure-guided genome editing offers a comprehensive and synergistic framework for kinase engineering and protein functional optimization. Together, these approaches provide detailed mechanistic insights into activation, allostery, and functional regulation, while enabling the rational design of enzymes, signaling modulators, and genome editing tools. By bridging computational predictions with experimental validation, they advance both fundamental biology and practical applications in therapeutic development and crop improvement.

Chemical and Peptidic Modulation of Kinase Activity

Protein kinases are central regulators of cellular signaling and serve as prominent targets in both biomedical and agricultural research. These enzymes orchestrate a multitude of cellular processes, including cell proliferation, differentiation, stress responses, and immune signaling (Attwood et al., 2021). Given their pivotal roles, accurate functional validation of kinases is critical before permanent genetic interventions such as CRISPR/Cas-mediated editing. Misinterpretation of kinase function can lead to incorrect conclusions or undesirable phenotypes. Chemical and peptidic modulation provides a rapid, reversible, and precise approach to interrogate kinase activity, enabling researchers to establish causal links between signaling alterations and downstream biological effects, while avoiding irreversible genetic perturbation in the early stages of research (Wang et al., 2021).Recent advances in kinase drug discovery have broadened the target landscape beyond traditional oncology applications.

Kinases involved in inflammatory, metabolic, and neurodegenerative diseases are increasingly recognized as critical therapeutic targets. This expansion highlights the context-dependent nature of kinase signaling, as the same kinase may exert different effects depending on cell type, tissue, or environmental conditions (Wilbie et al., 2025). To dissect such complexities, researchers rely on selective chemical and peptidic modulators to interrogate specific signaling pathways, evaluate target dependency, and explore therapeutic potential. Small-molecule inhibitors, including allosteric and covalent compounds, have become essential tools to validate kinase targets. Meanwhile, kinase activators are employed to probe gain-of-function effects, revealing how increased kinase activity may influence cellular behavior or stress responses.

A cornerstone of chemical validation is the development and application of well-characterized chemical scaffolds. Staurosporine analogs, pyridine-based inhibitors, and quinazoline derivatives have each played critical roles in kinase-targeted drug discovery (Das et al., 2021). Staurosporine, a natural pan-kinase inhibitor, provided foundational structural insights into kinase inhibition but suffered from poor selectivity and significant toxicity. Medicinal chemistry efforts produced staurosporine analogs with improved selectivity, allowing researchers to study kinase function with fewer off-target effects. These analogs elucidated key principles of kinase inhibition,

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Open Access Journal

such as the importance of hinge-region binding, hydrophobic pocket interactions, and the orientation of the ATP-binding site (Rahaman & Chaudhary, 2024). Expanding upon these principles, researchers developed simpler synthetic scaffolds to improve pharmacological properties and optimize selectivity.

Pyridine-based inhibitors emerged as highly versatile molecules capable of engaging the kinase hinge region while allowing flexible chemical modifications to fine-tune both selectivity and pharmacokinetics (Duncan, 2020). Pyridine scaffolds facilitated scaffold-hopping strategies, which enable chemists to explore new chemical space while retaining critical molecular interactions. This evolution led to the adoption of quinazoline scaffolds, which closely emulate ATP interactions and provide extensive opportunities for structure–activity relationship (SAR) optimization. Quinazoline-based inhibitors have been central to the development of clinically successful therapies, particularly in targeting EGFR-driven cancers with drugs such as gefitinib and erlotinib. Continuous refinements within this chemical family have further enhanced potency, reduced resistance, and improved pharmacological profiles (Zayed, 2023). Together, the progression from staurosporine to pyridine and quinazoline derivatives illustrates the power of scaffold-hopping and SAR-guided design in developing selective and effective kinase inhibitors.

Beyond classical inhibitors, small molecules have proven invaluable in exploring plant hormone signaling pathways. Plant growth, development, and stress responses are tightly regulated by hormones such as abscisic acid (ABA) and brassinosteroids (BR). Small-molecule agonists that mimic ABA or BR provide reversible and precise modulation of these pathways without the need for genetic manipulation (Rigal et al., 2014). ABA-mimicking compounds engage PYR/PYL/RCAR receptors, inhibit PP2C phosphatases, and activate downstream SnRK2 kinases. These molecules reproduce ABA-mediated physiological responses, including stomatal closure, enhanced drought tolerance, osmotic stress adaptation, and improved survival under adverse conditions (Yadav et al., 2024). Compared to natural ABA, synthetic ABA agonists often exhibit enhanced chemical stability, prolonged activity, and greater ease of application, making them practical tools for both research and agricultural implementation. Similarly, BR-mimicking small molecules activate the BRI1 receptor complex, promoting cellular elongation, vascular differentiation, biomass accumulation, and overall plant growth. In addition to supporting growth, BR agonists enhance tolerance to abiotic stresses by modulating gene expression associated with the balance between growth and stress responses (Lepri et al., 2023). The ability to precisely regulate hormone signaling with these compounds has significantly advanced the understanding of phytohormone networks while providing potential strategies for crop improvement under challenging environmental conditions. Examples of small-molecule kinase inhibitors and activators that have been evaluated in plant systems, together with their biological effects, are presented in Table 2.

Table 1: Notable small-molecule kinase inhibitors/activators tested in plants (Balasubramanyam, Swaminathan, Ranganathan, & Kundu, 2003)

Compound	Target Kinase / Pathway	Plant System	Effect / Outcome
Bikinin	GSK3-like kinases (BIN2)	Arabidopsis	Activates brassinosteroid signaling; promotes growth
Reversine	FERONIA (RLK)	Rice, tomato, tobacco	Enhances root immunity without affecting growth
Staurosporine	Broad-spectrum kinases	Arabidopsis, crops	Inhibits multiple kinases; modulates root development
Lavendustin A	Kinases (ATP-binding site)	Rice, tomato, tobacco	Enhances root defense responses
Compound 991	SnRK1 (AMPK-like)	Rice	Activates SnRK1; modulates germination and metabolism
INH1	SnRK2	Arabidopsis	Inhibits ABA-responsive SnRK2 activity

In addition to small molecules, peptidic regulators and nanobodies have emerged as highly selective tools for modulating kinase activity in both animal and plant systems. While small molecules primarily target conserved ATP-binding sites, peptidic and nanobody-based approaches exploit unique conformational epitopes, enabling highly specific modulation with minimal off-target effects (Singh et al., 2022). For instance, in Parkinson's disease research, nanobodies targeting LRRK2 have been shown to stabilize inactive or signaling-biased conformations, demonstrating that allosteric modulation can achieve pathway-specific effects without directly competing with ATP. This highlights a generalizable strategy for precise intervention in complex kinase networks. Similar strategies are being applied in plant systems, particularly with receptor-like kinases (RLKs) (Galindo-Trigo et al., 2020). Short peptidic regulators and engineered nanobodies can selectively influence RLK activation, receptor complex assembly, and downstream phosphorylation events. One notable example is the fusion of pathogen-targeting nanobodies with NLR immune receptors, which enables plants to selectively activate RLK-mediated immune responses. This strategy enhances disease resistance while minimizing unintended perturbations to growth-related signaling, illustrating the potential of peptidic and nanobody-based tools for precise, functional modulation of kinase signaling in agriculture (Kourelis et al., 2023).

Finally, the integration of chemical genetics with CRISPR-based screening provides a comprehensive framework for functional validation of kinase targets. By combining small-molecule interventions with genome-

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Open Access Journal

wide or targeted CRISPR perturbations, researchers can systematically identify genetic factors that influence compound activity, validate therapeutic targets, and uncover mechanisms of resistance (Yan et al., 2022). For example, in *Mycobacterium tuberculosis*, CRISPRi combined with chemical-genetic profiling has revealed essential genes and pathways that modulate drug sensitivity. Similarly, large-scale CRISPR-Cas9 chemical-genetic screens in eukaryotic systems have linked DNA damage–inducing compounds to repair and stress-response genes (Lin et al., 2024). When integrated with computational drug profiling, these approaches predict compounds that enhance or suppress specific genetic phenotypes, providing a powerful tool for target validation. Together, chemical modulation and CRISPR-based functional genomics accelerate drug discovery, clarify mechanisms of action, and ensure that only rigorously validated targets advance to permanent genetic editing.

In conclusion, chemical and peptidic modulation of kinase activity offers a multifaceted and versatile toolkit for both biomedical and agricultural research (Shen et al., 2017). The combination of small-molecule inhibitors and activators, synthetic chemical scaffolds, peptidic regulators, nanobodies, and CRISPR-based functional screens enables precise, reversible, and context-specific interrogation of kinase signaling. This integrated approach ensures robust target validation, facilitates the development of selective therapeutics, and advances our understanding of complex signaling networks in diverse biological systems.

Integration of Multi-Omics to Decipher Kinase Regulatory Networks

Phosphoproteomics has emerged as a powerful tool for dynamic kinase activity profiling, enabling the detection of stimulus-dependent changes in protein phosphorylation across complex cellular signaling networks (Tan et al., 2017). Unlike static proteomic analyses, phosphoproteomics captures the temporal and context-specific activity of kinases, offering insights into signaling pathways that control cell fate, metabolism, and stress responses. Integrated proteomic and phosphoproteomic studies of immune cells have revealed that macrophage polarization and T cell activation are governed by rapid kinase-mediated rewiring of phosphorylation networks (Arshad et al., 2019). In macrophages, pro-inflammatory and alternative phenotypes are characterized by differential activation of MAPKs, CDKs, mTOR, and metabolic kinases, which coordinate signal transduction with bioenergetic adaptation. In T cells, temporal dynamics of phosphorylation, rather than changes in protein abundance alone, determine early signaling events, metabolic reprogramming, and effector differentiation, with kinases such as LCK, ZAP70, AKT, and AMPK playing central roles (Wu et al., 2025). In cancer, combined tumor phosphoproteome and proteome analyses reveal functional kinase dependencies and signaling vulnerabilities that are not apparent from gene expression data alone, highlighting the utility of phosphoproteomics in identifying therapeutic targets and understanding disease-specific signaling landscapes (Piersma et al., 2024).

Transcriptomics and co-expression network analyses provide a complementary approach to link kinase signaling with stress-responsive gene networks. Weighted gene co-expression network analysis and similar network-based methods allow the identification of functionally coordinated gene modules and their regulatory hubs under various stress conditions (He et al., 2018). In crops such as barley, large-scale transcriptome profiling under cold stress identified co-expression modules enriched in receptor-like kinases, MAPKs, and calcium-dependent protein kinases. These kinases act upstream of transcription factors and protective genes involved in membrane stabilization, osmolyte biosynthesis, redox homeostasis, and energy metabolism, demonstrating a tight coupling between kinase signaling and adaptive transcriptional responses (Panahi & Shahi, 2024). Similarly, in cotton roots subjected to potassium-regulated salt stress, kinase hub genes were found to integrate ion transporters, hormone signaling components, and transcriptional regulators within salt-responsive modules. In fungal systems such as Beauveria bassiana, kinase-centered stress-responsive modules coordinate cell wall remodeling, oxidative stress defense, autophagy, and metabolic adaptation, showing a conserved mechanism for stress adaptation across organisms (Ju et al., 2023). Transcriptomics combined with network analysis provides a systems-level view of how kinase signals are translated into coordinated transcriptional and physiological responses.

Interactomics integrated with phosphoproteomics further enhances understanding of kinase regulatory networks by mapping kinase–substrate–phosphatase complexes and elucidating the structural and spatial organization of signaling modules. Perturbation-based phosphoproteomic experiments, temporal profiling, and motif enrichment analyses capture dynamic phosphorylation events, but their mechanistic interpretation is strengthened when combined with protein–protein interaction data (Wei et al., 2018). Large-scale mapping of the human tyrosine phosphatase interactome has shown that phosphatases are not general signal erasers; they interact with specific kinases, substrates, and adaptor proteins to confer spatial and temporal specificity to dephosphorylation events. Scaffolding proteins, such as Numb, stabilize these complexes by linking kinases to their substrates and associated signaling components, fine-tuning the duration and amplitude of signaling events. Integration of interactomics and phosphoproteomics enables systematic identification of kinase–substrate–phosphatase assemblies and reveals how phosphorylation networks achieve robustness, specificity, and dynamic regulation (Narushima et al., 2016).

Machine learning and deep learning approaches are now essential for predicting key kinase nodes and synthetic

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)
Open Access Journal

circuit points within complex regulatory networks (Invergo et al., 2020). Machine learning models trained on phosphoproteomic, interactomic, and temporal signaling data can reconstruct signed kinase regulatory circuits, inferring both kinase–substrate relationships and the directionality of regulation. Graph-based learning, Bayesian networks, and causal inference models efficiently identify hub kinases whose perturbation leads to widespread changes in cellular behavior, prioritizing targets for experimental validation (Palacios et al., 2025). In synthetic biology, machine learning guides the design of gene circuits by predicting optimal intervention points, such as promoter–kinase couplings, feedback loops, and signaling thresholds. Supervised and reinforcement learning models can predict how kinase activity affects downstream gene expression dynamics, stability, and noise (Goshisht, 2024). Deep neural networks and recurrent architectures further model nonlinear and context-dependent kinase regulation, facilitating the rational design of robust synthetic circuits capable of functioning reliably across varying cellular states. Integrating predictive modeling with experimental validation accelerates the identification of critical kinase nodes and synthetic circuit points, enhancing mechanistic understanding and engineering potential (Rai et al., 2024).

Finally, multi-omics integration enables prioritization of targets for genome editing or chemical intervention in crops, fungi, and other biological systems (Gogolev et al., 2021). Genomics, including GWAS and QTL mapping, identifies candidate genes linked to yield, stress tolerance, and nutritional quality, while transcriptomics and phosphoproteomics reveal genes, kinases, and enzymes consistently responsive to environmental stimuli (Kumar et al., 2025). Metabolomics validates these molecular targets by connecting gene and protein activity to functional biochemical outcomes such as osmolyte accumulation, antioxidant production, and metabolic adaptation. Epigenomics adds another layer by highlighting DNA methylation patterns, histone modifications, and chromatin accessibility that can be manipulated for targeted or reversible modifications. Together, these integrated omics approaches provide a systems-level roadmap for rational target selection, allowing precise modulation of kinase regulatory networks to enhance stress resilience, metabolic efficiency, and crop improvement while informing the design of synthetic circuits and chemical targeting strategies (Hassan & Ganai, 2023).

By combining phosphoproteomics, transcriptomics, interactomics, machine learning, and multi-omics integration, researchers can achieve a holistic and dynamic understanding of kinase regulatory networks, bridging molecular signaling, transcriptional control, and functional adaptation (Varadharajan et al., 2025). This integrative framework reveals fundamental principles of cellular signaling and provides actionable insights for crop improvement, synthetic biology, and therapeutic intervention, representing a new era of data-driven and mechanistically informed biological engineering (Ijaz et al., 2024).

Translational Perspectives: From *Arabidopsis* to Crops

Arabidopsis thaliana has long served as a pivotal model for dissecting kinase signaling networks due to its well-annotated genome, ease of genetic manipulation, and extensive functional characterization of kinases (Alam et al., 2022). Studies in Arabidopsis have provided foundational insights into kinase-mediated regulation of development, stress responses, and metabolic pathways, offering mechanistic knowledge that can be translated to crop species. Many kinase families, including MAPKs, CDPKs, SnRKs, and RLKs, are highly conserved between Arabidopsis and major cereal and legume crops, allowing functional inference and guiding target prioritization in translational kinome pipelines (Hu et al., 2025). In cereals such as rice, wheat, and maize, these pipelines typically begin with the identification of candidate kinases based on Arabidopsis functional data. Multi-omics approaches—including transcriptomics, phosphoproteomics, and co-expression network analyses—are employed to prioritize kinases that regulate stress responses, growth, and yield (Singh et al., 2024). Candidate genes are then validated using functional assays, comparative genomics, or heterologous expression systems before being targeted for genome editing. CRISPR/Cas9 and its variants are applied to generate targeted knockouts, knock-ins, or allelic modifications, producing lines with enhanced stress tolerance, optimized flowering, improved nutrient use efficiency, or modified plant architecture. For example, kinases implicated in drought and salinity responses in Arabidopsis have guided editing strategies in rice, resulting in modifications that enhance osmotic adjustment and root system development without negatively affecting yield.

In legumes such as soybean, chickpea, and common bean, translational kinome pipelines integrate panomics data encompassing genomics, transcriptomics, proteomics, and metabolomics (Baloglu et al., 2022). Functional modules identified in Arabidopsis under stress or symbiotic conditions are often conserved, facilitating cross-species inference of candidate kinases involved in nodulation, nitrogen fixation, seed development, and pathogen defense. CRISPR/Cas-mediated editing of these kinases has successfully improved stress adaptation, root architecture, and disease resistance. Co-expression network analyses under stress or symbiotic conditions further refine the identification of key kinase hubs, ensuring that editing affects target traits while minimizing off-target effects. A typical translational workflow involves candidate identification through multi-omics datasets and Arabidopsis-based functional insights, in silico and experimental validation of kinase function, CRISPR-mediated

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)
Open Access Journal

genome editing, and comprehensive phenotypic evaluation under controlled and field conditions. Integration of machine learning and predictive modeling enhances this process by forecasting downstream effects of kinase modifications and facilitating rational prioritization of targets, ultimately ensuring predictable improvements in stress tolerance, growth, and productivity.

One major challenge in crop kinome editing is regulatory and technical constraints associated with stable transgene integration. Traditional DNA-based delivery of CRISPR components often results in permanent insertion of Cas9 or guide RNA sequences, raising concerns about off-target effects, regulatory compliance, and public acceptance (Kocsisova & Coneva, 2023). To overcome these limitations, transient delivery strategies, particularly CRISPR ribonucleoprotein (RNP) complexes, have emerged as a highly effective alternative. RNP-mediated editing involves introducing pre-assembled Cas9 protein and guide RNA directly into plant cells, allowing immediate editing activity and natural degradation of the complex over time (Zhang et al., 2021). This approach enables precise genome modifications without permanent transgene integration, significantly reducing the likelihood of off-target mutations and simplifying regulatory approval. RNP delivery has been successfully applied across cereals, legumes, and even woody perennials using techniques such as protoplast transfection, particle bombardment, and emerging nanoparticle-based methods (Kaupbayeva et al., 2024). By bypassing transgene integration, transient RNP editing accelerates the generation of edited lines, facilitating rapid breeding cycles and enhancing public acceptance of genome-edited crops (Ramakrishnan et al., 2025).

Translational applications of kinome editing are exemplified by several case studies in cereals and legumes, highlighting how insights from Arabidopsis can guide targeted improvements in stress resilience. In rice, the receptor-like kinase OsRLK1 has been identified as a critical regulator of salinity tolerance (Alam et al., 2022). Functional characterization in model systems revealed that OsRLK1 modulates ionic homeostasis, maintains membrane integrity under salt stress, and triggers downstream signaling cascades that activate stress-responsive genes (Yue, Cao, & Liu, 2020). Guided by these mechanistic insights, CRISPR/Cas-mediated editing of OsRLK1 in rice cultivars has been used to enhance sodium exclusion, optimize root architecture, and improve overall growth under saline conditions, without negatively affecting yield potential. Multi-omics analyses, including transcriptomics and phosphoproteomics, were crucial in prioritizing OsRLK1 alleles that confer optimal stress response while minimizing pleiotropic effects (Zhang et al., 2021).

In wheat, TaMAPK4, a member of the mitogen-activated protein kinase family, has been functionally characterized as a key mediator of osmotic stress and reactive oxygen species (ROS) management (Hou et al., 2024). Overexpression or targeted modification of TaMAPK4 enhances root system architecture, antioxidant enzyme activity, and nutrient acquisition under drought and osmotic stress. While its role in heat tolerance has not been fully validated, MAPK cascades broadly regulate pathways that intersect with thermal stress responses, including ROS detoxification, hormonal signaling, and transcriptional reprogramming (Ling et al., 2024). Editing or allele selection for TaMAPK4 variants therefore offers a promising strategy to improve thermotolerance in wheat and other cereals by stabilizing physiological and cellular processes under high temperatures (Li et al., 2024).

Similarly, members of the SnRK2 kinase family, including TaSnRK2.4, TaSnRK2.8 in wheat, and GhSnRK2 variants in cotton, exemplify the conserved nature of kinase-mediated stress adaptation across species. SnRK2 kinases are central regulators of abscisic acid (ABA)-dependent signaling and mediate stomatal regulation, osmotic adjustment, and activation of stress-responsive transcription factors (Luo et al., 2024). Functional studies indicate that targeted modifications of these kinases improve root growth, water retention, and membrane stability under drought, salinity, and osmotic stresses, providing indirect benefits for heat tolerance by maintaining cellular homeostasis and signaling integrity. In cotton, GhSnRK2 editing guided by Arabidopsis functional data has demonstrated enhanced resilience to water-deficit conditions, highlighting the potential for cross-species translation of kinase-based interventions.

Collectively, these case studies illustrate the practical utility of kinome editing in crops (Uauy et al., 2025). They demonstrate how candidate kinases can be selected using multi-omics datasets and functional insights from Arabidopsis, validated through comparative and experimental approaches, and subsequently modified through precision genome editing to enhance specific stress responses. Importantly, these studies highlight the need to consider redundancy, pleiotropy, and network-level interactions when editing kinases in polyploid or complex crop genomes (Springer et al., 2019). By combining targeted editing of OsRLK1, TaMAPK4, and SnRK2 variants with multi-environment phenotyping and advanced breeding pipelines, researchers can achieve predictable improvements in stress resilience, root system architecture, and physiological performance, thereby advancing the development of climate-smart, high-yielding crop varieties. These examples underscore the translational potential of Arabidopsis-informed kinome editing and illustrate a framework for rational, mechanism-based crop improvement that integrates signaling biology with precision breeding technologies.

To address these challenges, modern breeding programs increasingly integrate kinome editing with speed breeding and precision phenotyping (Rai, 2022). Speed breeding accelerates generation turnover by optimizing

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)
Open Access Journal

environmental conditions, allowing multiple crop generations per year and rapid fixation of favorable kinase alleles (Imam et al., 2024). When combined with CRISPR-based kinome editing, this approach enables rapid introduction and testing of stress-responsive variants. Precision phenotyping platforms, incorporating high-throughput imaging, robotics, and drone-based sensors, capture dynamic traits such as growth, canopy temperature, chlorophyll content, and morphological responses to stress (Naqvi et al., 2024). Integration of machine learning and artificial intelligence allows analysis of these multi-dimensional datasets alongside genotypic information, predicting trait outcomes and prioritizing promising edited lines (de Farias et al., 2025). The synergy of kinome editing, speed breeding, and precision phenotyping thus establishes a feedback-driven pipeline that accelerates crop improvement, enhances selection accuracy, and enables the development of climate-smart varieties with improved stress resilience, yield stability, and nutritional quality (Varshney et al., 2021).

Breeding and Evolutionary Implications of Kinome Engineering

Comparative analyses of plant kinomes across angiosperms reveal that protein kinase families have undergone extensive expansion, contraction, and functional diversification in close association with environmental pressures (Yan et al., 2018). Genome-wide characterization of crop and model plant kinomes, including sunflower, highlights pronounced lineage-specific duplications within receptor-like kinases, mitogen-activated protein kinases, calcium-dependent protein kinases, and SnRK families. These kinase groups play essential roles in stress perception, signal amplification, and downstream transcriptional regulation. Their diversification is largely driven by whole-genome duplication and tandem duplication events, which are recurrent throughout angiosperm evolution and provide the raw genetic material for functional divergence (Cohen et al., 2023). From an evolutionary perspective, the emergence and elaboration of complex kinome architectures parallel major transitions in plant history, most notably the conquest of land and the subsequent radiation of flowering plants into diverse ecological niches. Early terrestrial plants faced unprecedented challenges such as desiccation, ultraviolet radiation, nutrient limitation, and temperature fluctuations, necessitating robust and adaptable signaling systems (Wang et al., 2025). Selective retention and refinement of stress-responsive kinase modules enabled plants to integrate environmental cues with developmental programs, laying the foundation for the ecological success of angiosperms.

Over evolutionary timescales, kinase-mediated signaling pathways increased in complexity through subfunctionalization and neofunctionalization of duplicated genes, allowing plants to fine-tune growth–defense trade-offs and optimize fitness under variable conditions. Comparative studies among angiosperms adapted to contrasting climates suggest that, while a conserved core of kinase families has been maintained due to strong evolutionary constraints, lineage-specific expansions and regulatory rewiring have contributed to local adaptation (Kumar et al., 2023). In cold-adapted species, for example, modest but targeted expansions of kinases involved in cold perception, membrane stability, and transcriptional control reflect similar selective pressures acting independently across evolutionary lineages. This limited but recurring convergence highlights the central role of kinases as integrative hubs that connect environmental sensing with physiological and developmental responses, reinforcing their evolutionary importance in plant adaptation.

Beyond deep evolutionary patterns, genome-wide analyses across diverse taxa consistently demonstrate that expansion of kinase gene families serves as a major driver of stress plasticity (Ali et al., 2025). In crop species such as sugarcane, large-scale identification of MAP kinase cascade components reveals that duplication-driven expansion of MAPKKKs, MAPKKs, and MAPKs enhances the capacity to perceive, transmit, and integrate abiotic stress signals (Kesawat et al., 2022). Many of these duplicated kinases exhibit stress-inducible expression under drought, salinity, heat, and oxidative stress, suggesting functional diversification that enables rapid and context-specific signaling responses in complex polyploid genomes. Similarly, expansion of the proline-rich extensin-like receptor kinase gene family in wheat—largely resulting from polyploidization and segmental duplication contributes to developmental regulation and environmental responsiveness (Wang et al., 2025). Differential expression of PERK paralogs across tissues, developmental stages, and stress conditions indicates subfunctionalization, allowing precise modulation of cell wall signaling, growth transitions, and stress responses under adverse environments.

Evidence from invasive plant species such as *Mikania micrantha* further strengthens the link between kinase family expansion and adaptive plasticity. Genomic analyses reveal that expansion of kinase-related gene families, often accompanied by increased transposable element activity, promotes genomic variability and regulatory innovation. These features enable rapid transcriptional reprogramming in response to environmental fluctuations, contributing to invasiveness and ecological success (Cui et al., 2021). Comparable patterns observed in non-plant systems, such as the Chinese mitten crab, indicate that kinase expansion represents a conserved evolutionary strategy across kingdoms. In these systems, expanded kinase families involved in hormonal signaling, stress response, and developmental regulation exhibit dynamic expression across life stages and environmental contexts, underscoring the universal role of kinases in enhancing regulatory capacity and phenotypic flexibility.

REVIEW ARTICLE
TRENDS IN BIOTECHNOLOGY AND PLANT SCIENCE
ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)
Open Access Journal

Within the context of crop improvement, these evolutionary and functional insights highlight the potential of kinome engineering as a powerful tool for reprogramming complex quantitative traits. Traits such as yield stability, stress tolerance, and nutritional quality are governed by intricate genetic architectures shaped by pleiotropy and epistatic interactions among multiple loci (Soyk et al., 2020). Advances in quantitative genetics have revealed that these non-additive interactions often involve regulatory genes rather than structural components, limiting the effectiveness of traditional selection strategies focused on individual alleles. Protein kinases, due to their hierarchical positions within signaling networks, exert broad control over transcriptional programs, metabolic fluxes, and developmental processes (Mackay & Anholt, 2024). Consequently, targeted modification of kinase activity offers a systems-level approach to reshaping epistatic relationships, allowing breeders to influence entire networks rather than isolated trait components.

The integration of OMICs technologies has greatly enhanced the feasibility of kinome-based strategies for crop improvement. Transcriptomics, proteomics, phosphoproteomics, and epigenomics provide high-resolution insights into kinase-centered interaction networks and their dynamic responses to environmental cues (Gogolev et al., 2021). These datasets reveal how kinase signaling interfaces with chromatin state, epigenetic regulation, and metabolic pathways, enabling identification of kinases that act as convergence points for multiple quantitative trait loci. Genome editing technologies, particularly CRISPR-based tools, now allow precise modulation of kinase genes through promoter editing, allelic replacement, or domain-specific modification rather than complete loss-of-function. Such fine-tuned interventions are essential for managing pleiotropy, as subtle adjustments in kinase signaling can reprogram epistatic interactions without disrupting core developmental functions (Mackay & Anholt, 2024). When combined with epigenetic editing approaches, these strategies offer the potential to stabilize favorable gene interactions across environments, enhancing trait predictability and resilience.

Looking forward, these advances collectively support the emergence of kinome-assisted selection as a new breeding paradigm. By integrating kinome-level information with high-throughput genotyping, expression profiling, and phosphorylation dynamics, breeders can identify functional kinase signatures associated with superior performance under diverse environmental conditions. Incorporation of these signatures into genomic prediction models has the potential to improve selection accuracy, particularly for complex traits influenced by environmental variability. Furthermore, the convergence of kinome-assisted selection with precision genome editing and speed breeding offers a powerful framework for accelerating crop improvement. Favorable kinase alleles identified through selection can be rapidly validated and fine-tuned, enabling the development of climate-resilient, high-performing crops grounded in an evolutionary informed understanding of signaling networks that control complex quantitative traits.

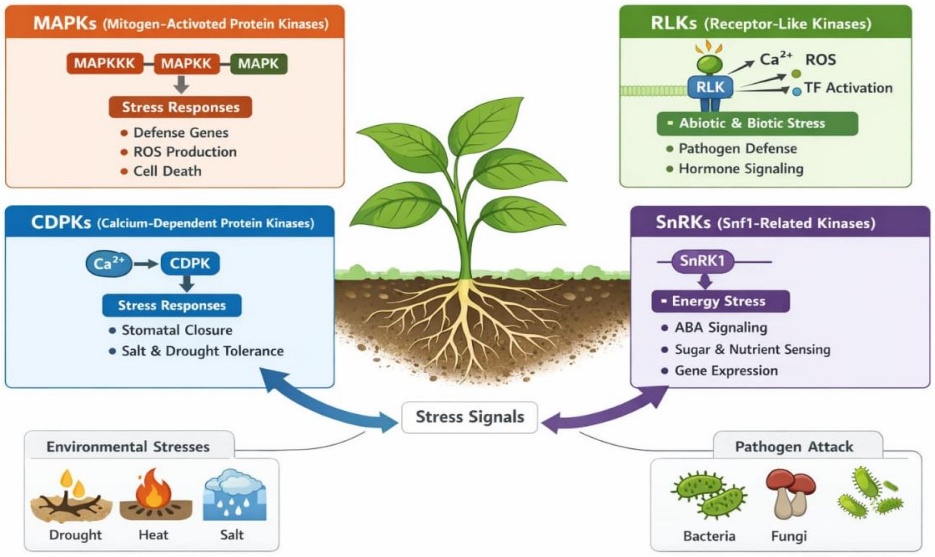

Fig. 3: Overview of major kinase families and their stress pathways (MAPKs, RLKs, CDPKs, SnRKs).
Note: The figure illustrates the major plant kinase families, including MAPKs (MPKs), CDKs, RLKs, and SnRKs, showing their classification, evolutionary relationships, and functional roles in regulating cellular processes and stress signaling. The classification follows established kinome analyses and plant-specific reviews (Sharma et al., 2020).

Future Outlook: Toward Rational Design of Stress-Smart Crops

The future of stress-smart crop development is poised to benefit from the convergence of genome editing, structural biology, and artificial intelligence, enabling the predictive engineering of crucial signaling components such as protein kinases. By integrating high-resolution structural data with AI-driven modeling, researchers can design precise interventions that enhance plant resilience to abiotic and biotic stresses (Yaxin Wang et al., 2022). The development of comprehensive digital kinome atlases, combined with multi-omics datasets including

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)
Open Access Journal

transcriptomics, proteomics, and metabolomics, provides a detailed map of stress-response networks, allowing identification of key regulatory nodes and predictive modeling of plant responses under varying environmental conditions. Synthetic biology approaches offer prospects for creating programmable kinases or synthetic signaling modules capable of dynamically responding to external cues, thereby improving adaptability and efficiency (Roychowdhury et al., 2023). However, these innovations must be balanced with careful consideration of ethical, ecological, and regulatory challenges, such as gene flow, biosafety, and potential impacts on ecosystems. Ultimately, the integration of kinome mapping, computational modeling, and molecular breeding pipelines aims to translate these insights into field-ready strategies, enabling the development of high-yielding, resilient crops capable of thriving in changing climates and contributing to global food security (Xu et al., 2022).

Conclusion

The plant kinome plays a central role in coordinating responses to biotic and abiotic stresses through interconnected kinase families, including MAPKs, RLKs, CDPKs, and SnRKs. These signaling modules function as integrative hubs that translate environmental cues into precise physiological and transcriptional responses while maintaining growth–defense balance. Advances in multi-omics, phosphoproteomics, and network biology have revealed that stress signaling is governed by dynamic kinase–phosphatase interactions and extensive pathway cross-talk rather than linear cascades. The integration of genome editing technologies with structural, computational, and AI-based approaches now enables precise modulation of kinase activity for crop improvement. Together, these strategies position kinome engineering as a powerful framework for developing stress-resilient, climate-smart crops with improved adaptability and yield stability.

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