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Histidine Kinases and Cytokinin Signaling: Molecular Architecture, Evolution, and Functional Roles in Plant Development and Environmental Adaptation

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Abstract

Histidine kinases (HKs) represent a core component of plant two-component signaling systems and serve as primary receptors for cytokinins, enabling plants to perceive developmental cues and respond to environmental stress. Recent studies have substantially expanded the understanding of HK diversification, receptor evolution, ligand-binding properties, and downstream signaling mechanisms, revealing their essential roles in regulating organogenesis, meristem activity, senescence, root–shoot communication, and responses to abiotic stresses. CHASE-domain-containing receptors have emerged as critical sensors with specialized cytokinin-binding capacities across species, while novel work has clarified the broad distribution and functional specificity of sensor HKs in eukaryotes. Additionally, receptor-like protein kinases (RLKs) have been implicated in complementary and overlapping functions during abiotic stress acclimation, further integrating hormonal, metabolic, and environmental signals. This review synthesizes current advances in HK biology, cytokinin receptor evolution, molecular structure, physiological functions, and their involvement in developmental processes such as shoot organogenesis, leaf aging, embryonic patterning, and environmental adaptation. By consolidating findings across Arabidopsis, maize, apple, and other model systems, this paper highlights new insights into the complexity of HK signaling pathways and proposes future research directions for developmental biology and stress physiology.

Keywords: Cytokinin signaling, Histidine kinases, Two-component systems, Plant development, Abiotic stress response, Receptor evolution

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1. Introduction

Histidine kinases constitute one of the most evolutionarily conserved molecular signaling families across both prokaryotic and eukaryotic organisms. In plants, they are central components of the two-component system (TCS), serving as sensors for environmental cues and hormonal signals that modulate growth and development. The foundational understanding of plant HKs can be traced to early models of TCS signaling, which were later expanded through molecular and genomic analyses that identified multiple subfamilies of HK genes in land plants (Schaller 2000). With the discovery that cytokinin receptors are HK-type proteins containing CHASE (Cyclase/Histidine kinase-associated sensory extracellular) domains, the field progressed toward a detailed structural and functional understanding of hormone perception (Heyl et al. 2012). These receptors, including AHK2, AHK3, and CRE1/AHK4 in Arabidopsis, were shown to mediate cytokinin-dependent phosphorylation cascades essential for regulating meristem function, shoot formation, and developmental plasticity (Kieber & Schaller 2018).

As research expanded, comparative genomics and biochemical analyses revealed that plant HKs are far more diverse than initially assumed, spanning multiple functional categories such as osmosensors, ethylene receptors, and cytokinin receptors (Hoang et al. 2021). Studies in maize and apple demonstrated species-specific expansions of receptor families, divergent ligand affinities, and variations in CHASE-domain configurations, reflecting evolutionary adaptations to ecological conditions (Daudu et al. 2017). Parallel work on eukaryotic HK evolution identified extensive domain reshuffling and functional divergence, highlighting the ancient origin and continued diversification of HK proteins across fungi, algae, and plants (Kabbara et al. 2018). At the same time, research into RLKs and related receptor families revealed a broader network of phosphorylation-based signaling mechanisms participating in stress adaptation and developmental regulation (Gandhi & Oelmüller 2023).

The convergence of developmental biology, stress physiology, and molecular signaling underscores the central role of HKs in coordinating growth responses with environmental conditions. This review synthesizes insights from biochemical, structural, evolutionary, and physiological studies to provide a comprehensive understanding of HK-mediated developmental processes in plants.

2. Structure and Evolution of Plant Histidine Kinases

Histidine kinases in plants have undergone substantial diversification, reflecting their functional complexity and the evolutionary pressures associated with terrestrial adaptation. Early work characterized plant HKs as components of two-component systems (TCS), structurally similar to their bacterial counterparts but modified to support multicellular signaling requirements (Schaller 2000). Plant HKs generally contain multiple conserved domains: an input domain that perceives extracellular or intracellular signals, a histidine kinase domain responsible for autophosphorylation, and a receiver domain that communicates with downstream phosphotransfer proteins. The evolutionary modification of these domains allowed HKs to integrate a wider range of signals, including osmotic stress, nutrient status, and hormonal cues.

Recent analyses have expanded our understanding of HK evolution considerably. A comprehensive evolutionary survey demonstrated that eukaryotic HKs have undergone repeated episodes of duplication, domain shuffling, and neofunctionalization, leading to the emergence of divergent sensor families with distinct physiological roles (Kabbara et al. 2018). This work revealed that CHASE-domain-containing HKs likely originated early in eukaryotic evolution, with subsequent lineage-specific adaptations giving rise to the major cytokinin receptors present in land plants today. Comparative studies also indicate that gene loss and functional divergence shaped the HK repertoires of flowering plants, gymnosperms, and bryophytes, contributing to differences in developmental and stress-response strategies.

Figure 1. Domain Architecture of Plant Histidine Kinases

This schematic shows the conserved modular organization of plant histidine kinases, including the extracellular CHASE domain responsible for cytokinin binding, the histidine kinase (HK) catalytic domain responsible for autophosphorylation, and the receiver domain that participates in phosphate transfer to downstream signaling proteins.

Histidine kinases are now recognized as multifunctional proteins rather than simple sensors. Their structural complexity enables integration of multiple environmental signals into the TCS phosphorelay system, influencing diverse developmental processes. A recent synthesis highlighted the wide functional spectrum of HKs, emphasizing their roles in developmental programs, stress signaling, and metabolic regulation (Hoang et al. 2021). This diversity results from both molecular evolution and biochemical specialization, allowing HKs to support plant adaptation across vastly different ecological niches.

3. Cytokinin Receptors and CHASE Domain Functionality

Cytokinin receptors form a distinct subgroup of plant HKs characterized by their extracellular CHASE domains, which mediate the perception of cytokinin molecules such as zeatin and isopentenyl adenine. Early biochemical and genetic studies revealed that cytokinin binding induces conformational changes in the CHASE domain, activating the histidine kinase activity and initiating downstream phosphorelay signaling (Heyl et al. 2012). These receptors are critical regulators of cell division, shoot organogenesis, meristem maintenance, and phyllotaxy.

A landmark study on apple tree HK receptors demonstrated that even within a single species, CHASE-containing receptors possess distinct cytokinin-binding properties, suggesting that ligand specificity and affinities have diversified to support species-specific developmental needs (Daudu et al. 2017). This work highlighted the structural variations in CHASE domains and linked them to functional specialization in shoot architecture, growth regulation, and hormone responsiveness. Similar studies in other plant species, including maize, have emphasized the importance of receptor heterogeneity in tuning cytokinin sensitivity across tissues and developmental stages.

The functional and evolutionary complexity of cytokinin receptors has been comprehensively described through integrated structural, biochemical, and phylogenetic analyses. These receptors exhibit modular organization, incorporating both sensory and kinase domains that cooperate to transduce external signals into cellular responses (Heyl et al. 2012). Their evolutionary history suggests repeated duplication and divergence events, leading to distinct receptor families that regulate overlapping but non-identical developmental processes

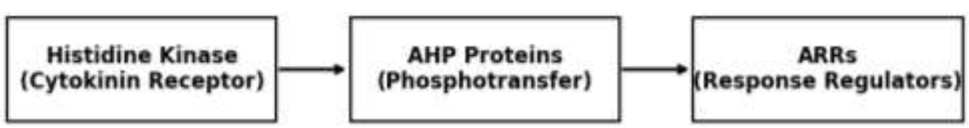

Figure 2. Simplified Cytokinin Signaling Pathway

This figure illustrates the core steps of the multistep phosphorelay involved in cytokinin signaling. Perception begins when a cytokinin molecule binds to a membrane-bound histidine kinase receptor. The receptor undergoes autophosphorylation and transfers the phosphate group to AHP (Arabidopsis Histidine Phosphotransfer) proteins, which then shuttle the signal to nuclear ARR (Arabidopsis Response

Regulator) proteins. This ultimately activates downstream gene expression regulating plant developmental processes.

Recent work also places cytokinin receptors within a broader context of plant HK diversity. The emerging picture indicates that cytokinin signaling integrates with environmental sensing pathways, enabling plants to coordinate growth with stress responses. This interplay is particularly evident in drought and salinity responses, where cytokinin receptor activity modulates developmental trade-offs between shoot growth and stress tolerance.

4. Histidine Kinases in Plant Development

Histidine kinases play crucial roles in regulating plant development, particularly through their involvement in cytokinin signaling pathways that control meristem maintenance, organogenesis, and cell differentiation. Research has demonstrated that HK-mediated phosphorelay systems govern the expression of key regulatory genes, modulating developmental decisions in response to internal hormonal cues and external stimuli (Kieber & Schaller 2018). In shoot apical meristems, for example, cytokinin receptors regulate the balance between stem cell proliferation and differentiation, ensuring sustained organ formation while maintaining structural integrity.

Histidine Kinase Type	**Primary Function**	**Representative Genes**
Cytokinin Receptors	Cytokinin perception	AHK2, AHK3, AHK4
Osmosensors	Drought/salt sensing	AHK1
Ethylene Receptors	Ethylene signal perception	ETR1, ERS1
Hybrid HKs	Integrative environmental sensing	Various species-specific HKs

Table 1. Types of Plant Histidine Kinases

Summarizes major classes of histidine kinases in plants, including cytokinin receptors, osmosensors, ethylene receptors, and hybrid HKs, along with their primary biological roles and representative genes.

A recent synthesis of HK functions highlighted their involvement in a wide range of developmental processes, including root architecture modulation, vascular differentiation, reproductive development, and seed dormancy regulation (Hoang et al. 2021). The versatility of HKs arises from their ability to integrate hormonal signals with environmental variables such as nutrient availability, osmotic conditions, and light cues. Their role in modulating developmental plasticity makes them central players in enabling plants to adjust growth patterns under fluctuating environments.

Additionally, HKs participate in cross-hormonal interactions, influencing auxin distribution, ethylene signaling, and ABA-dependent pathways. Many developmental processes depend on the fine-tuned balance between cytokinin and auxin, mediated in part by HK activity. For instance, shoot regeneration and de novo organogenesis require precise coordination of cytokinin perception and auxin gradients, and disruptions in HK signaling can impair tissue reprogramming. Moreover, HKs contribute to the timing and regulation of leaf senescence, a complex developmental process that integrates metabolic status with hormonal signaling pathways.

Studies in multiple plant species, including Arabidopsis, maize, and apple, reinforce the conclusion that HKs serve as master regulators of growth and development. Their functional diversity and centrality within signaling networks underscore their fundamental significance in plant developmental biology.

5. Histidine Kinases in Abiotic Stress Responses

Beyond developmental regulation, histidine kinases are essential mediators of abiotic stress responses. As sensors of osmotic, drought, and salinity stress, plant HKs regulate phosphorylation cascades that activate stress-adaptive genes and pathways. Multiple studies have demonstrated that TCS components modulate responses to dehydration, ionic imbalance, and temperature fluctuations by adjusting hormone biosynthesis, antioxidant pathways, and cellular osmoprotection mechanisms.

A comprehensive review of HK functions revealed their involvement in sensing environmental conditions and orchestrating signaling networks that help plants maintain homeostasis under stress (Hoang et al. 2021). Their role extends beyond simple stress sensing; HKs modulate developmental trade-offs, allowing plants to redirect resources from growth toward survival. For instance, reduced cytokinin signaling under drought conditions promotes root elongation and inhibits excessive shoot growth, helping plants maximize water uptake and minimize transpiration.

Further research on receptor-like protein kinases (RLKs) has shown that they operate in parallel with HKs to regulate responses to cold, heat, drought, and salinity (Gandhi & Oelmüller 2023). RLKs interact with HK-dependent pathways, contributing to stress-induced remodeling of cellular processes such as membrane stabilization, ROS detoxification, and cytoskeletal rearrangement. This integrated signaling framework demonstrates how plants utilize a combination of HKs and RLKs to enhance resilience against environmental challenges.

Evolutionary studies indicate that stress-responsive HKs originated early in plant evolution, with subsequent divergence enabling species-specific adaptations. Their conservation across eukaryotic lineages highlights their fundamental role in sensing and responding to environmental variables (Kabbara et al. 2018). Together, these findings underscore the importance of HKs in linking stress physiology with developmental regulation.

6. Evolutionary Diversification of Sensor Histidine Kinases

The evolutionary diversification of HKs across eukaryotes has played a foundational role in shaping their functions in plants. Comparative analyses have revealed that HKs originated from ancient signaling proteins in prokaryotes, later incorporating additional domains to support the complexities of eukaryotic tissue differentiation and multicellular communication (Kabbara et al. 2018). Over time, lineage-specific expansions produced families of HKs with specialized sensory capabilities, including cytokinin receptors, osmosensors, and photoreceptors.

Domain architecture analysis demonstrates that HK diversification involved repeated cycles of domain fusion, loss, and recombination, producing receptors with unique ligand-binding properties and signaling roles. The CHASE domain, responsible for cytokinin perception, represents a key evolutionary innovation that enabled plants to regulate growth through hormone-mediated signaling. Divergence of CHASE-domain sequences across species such as Arabidopsis, rice, and apple reflects adaptive specialization to ecological conditions and developmental constraints.

Evolutionary studies further show that the diversification of HKs correlates with the emergence of land plants, where new environmental stresses and developmental demands required more sophisticated signaling systems. Gene family expansions in angiosperms suggest strong selection for HK-mediated control of organogenesis, stress tolerance, and metabolic regulation.

7. Concluding Remarks and Future Perspectives

Histidine kinases represent one of the most versatile and evolutionarily significant signaling families in plants. Their dual roles in development and environmental responses position them as central integrators of internal and external cues. The diversity of cytokinin receptors and CHASE-domain-containing HKs across species underlies the complexity of developmental regulation, while recent advances highlight their contributions to stress adaptation, senescence, organogenesis, and meristem function.

Future research should focus on high-resolution structural analyses of HK–ligand interactions, tissue-specific receptor functions, HK-mediated crosstalk with other hormonal pathways, and the integration of omics approaches to map HK signaling networks. Understanding the evolutionary trajectories of HK diversification may reveal new insights into plant development and resilience, offering potential applications in crop improvement, stress tolerance engineering, and developmental control.

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