Plant Immune System: Understanding Pathogen Recognition and Defense Mechanisms

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ABSTRACT
Plants deploy advanced defense mechanisms through their immune systems for detecting pathogenic threats which protects them from death while sustaining performance. A dual defense system operates in plants under two main mechanisms labeled Pattern-Triggered Immunity (PTI) and Effector-Triggered Immunity (ETI). Broad-spectrum resistance begins through Pattern Recognition Receptors (PRRs) detection of Microbe-Associated Molecular Patterns (MAMPs) which constitutes PTI as the initial defense line. ETI provides a more elaborate form of defense by having Nucleotide-binding Leucine-rich Repeat (NLR) proteins inside cells recognize pathogen effectors which leads to amplified immune responses resulting in localized cell death.

The immune responses function through three series of molecular signaling cascades that consist of Mitogen-Activated Protein Kinase (MAPK) pathways and calcium signaling together with reactive oxygen species (ROS) production. The defense mechanisms receive hormone regulation from substances like salicylic acid (SA) and jasmonic acid (JA) which optimize immune responses. Pathogens have developed multiple counterstrategies including effector-mediated suppression of host immunity to continue their constant evolutionary struggle with plants.

Plant immunity research benefits from new discoveries that show PRR structures along with synthetic immune receptors development and CRISPR-based techniques to make plants more disease resistant. The complex defensive approaches of plants require thorough analysis for developing pathogen-resistant crops which protect food availability and support sustainable farming systems in the midst of shifting infective-threats.

Keywords: Plant immunity, Pathogen recognition, Pattern-triggered immunity, Effector-triggered immunity, Plant defense mechanisms

Introduction

Importance of Plant Immunity

It is known that plants are surrounded by various potential pathogens throughout their life, which can be in the form of bacteria, fungi, viruses, and nematodes that are potentially dangerous to plants.[1,2] Mobile immune/getaway cells are absent in plants, and therefore, plants have adapted complex defense mechanisms to combat these persistent bio challenges at molecular, cellular, and systemic levels.[3,4] Knowledge of plant immunity is necessary for the protection of the individual plant but also for current global food security problems, losses in crop yields, and ecosystem stability (Figure 1).[1–3]

It should be noted that plant immunity is not only important to save the life of each plant but also means much more. In the world, crop diseases have been proved to cause considerable yield losses ranging between 20-40% potential agricultural production per annum.[5,6] This knowledge, so it appears, is not only important for basic plant biology but for solving food security issues, development of sustainable agriculture practices, and stability of the world's ecosystems.[7,8]

Recent research highlights the integration of plant immune responses with other stress signals, such as abiotic stress, to optimize survival.[43] Plants must constantly balance growth and defense, and their ability to modulate immune responses based on environmental cues is a growing area of study.[50]

Introduction to Pathogen Recognition and Defense System

Plant immune systems employ a sophisticated, multi-layered defense strategy characterized by two primary response mechanisms:

Pattern-Triggered Immunity (PTI)

- Requires the identification of conserved microbial molecular patterns
- Presents first-tier, general, overall-action platforms
- Triggers high signal of cellular protection mechanisms[2] of potential pathogens, including bacteria, fungi, viruses, and nematodes, which pose significant threats to plant survival and productivity[1,2]

Unlike animals with mobile immune cells, plants have evolved intricate defense mechanisms that operate at molecular, cellular, and systemic levels to protect against these persistent biological challenges.[3,4]

There are certain advancements in existing studies that advance knowledge regarding PTI. Recently, new, more specialized pattern-recognition receptors (PRRs), such as FLS3, which recognizes bacterial flagellin variants, were identified, proving that PRRs can be highly diverse and plastic.[4,6,9–11] Many receptor complexes and cryo-electron microscopy (cryo-EM) FLS2-BAK1 receptor interactions that show conformational changes important for functional signaling have been studied.[11]

The significance of plant immunity extends far beyond individual plant survival. Globally, crop diseases result in substantial yield losses, estimated at approximately 20–40% of potential agricultural production annually.[5,6] Understanding plant immune systems is therefore critical not only for fundamental biological research but also for addressing global

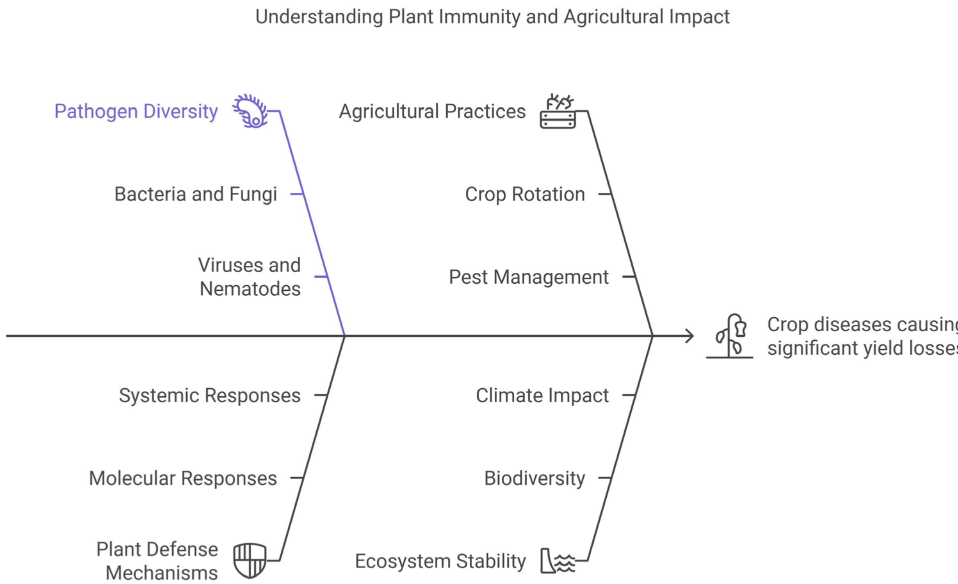

Fig 1 | Plant immunity

food security challenges, sustainable agriculture, and ecosystem resilience.[7,8]

Overview of Pathogen Recognition and Defense Mechanisms

Plant immune systems employ a sophisticated, multi-layered defense strategy characterized by two primary response mechanisms:

1. PTI

- Involves recognition of conserved microbial molecular patterns
- Provides broad-spectrum, initial defense responses
- Activates rapid cellular defense mechanisms[12,13]

2. Effector-Triggered Immunity (ETI)

Includes specific resistance (R) genes and identifies effector proteins that are specific to a given pathogen

- Triggers more severe targeted immune actions[14,15]
- PRs include PRRs,
- Receptor-like kinase (RLK)–interlocked signaling hierarchies
- Hormonal regulation systems:[16–18]
- Recognition of pathogen- or microbe-associated molecular patterns (MAMPs)
- Detection of endogenous ligands or danger signals, which include damage-associated molecular patterns (DAMPs).
- Functional reprogramming
- Synthesis of antimicrobial compounds.[19–21] of potential pathogens, including bacteria, fungi, viruses, and nematodes, which pose significant threats to their survival and productivity[1,2]

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ETI, by intracellular NLR proteins, is bidirectional and continues to be the subject of many research studies. The identification of 'auxiliary' NLRs that actually enhance signal propagation clarifies the complex layers of immune signal transduction pathways. Furthermore, synthetic biology techniques have designed synthetic NLRs to recognize other previously unknown pathogen effectors.[8,12,13]

Overview of Pathogen Recognition and Defense Mechanisms

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1. PTI

- Involves the recognition of conserved microbial molecular patterns
- Provides broad-spectrum, initial defense responses
- Activates rapid cellular defense mechanisms[12,13]

2. ETI

- Involves specific resistance (R) genes
- Recognizes pathogen-specific effector proteins
- Triggers more intense, localized immune responses[14,15]

These mechanisms rely on complex molecular recognition systems, primarily:

- PRRs
- RLKs

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- Sophisticated signaling networks
- Hormonal regulation systems[16–18]

Key molecular components include:
- Detection of MAMPs
- Recognition of DAMPs
- Rapid signal transduction
- Transcriptional reprogramming
- Production of antimicrobial compounds[19–21]

Historical Context of Plant Immunity Research: Early Conceptualizations of Plant Defense

The knowledge of plant defense mechanisms has significantly changed over the last couple of decades. Previous research indicated that plants are organisms that cannot organize complex defense reactions.[1,2] Initial investigations of plants were mainly centered on the phenomenological appearance of disease and plant reaction, coupled with little knowledge about defects at the molecular level.[3,4]

Pioneering Discoveries: The Pre-Molecular Era Classical Phytopathology Observations

It was toward the end of the nineteenth and at the beginning of the twentieth century that various scholars started to note that plants had the capability to stand for pathogens.

- 0 levels of susceptibility of plants to diseases
- Resistant population density
- Variable reactions of the plant to attacks by pathogens began to recognize that plants possessed inherent mechanisms to resist pathogens.[5,6]

Key early observations included:
- Variation in disease resistance among plant varieties
- Localized resistance responses
- Differential plant responses to pathogen attacks[5,6]

Breakthrough: The Jones and Dangl Paradigm (2006)

The paper by Jones and Dangl[7] can be considered as the starting point in the study of plant immunity.

- Conserved microbial pattern recognition
- Initial response represents a pivotal moment in plant immunity research

Published in *Nature*, this work fundamentally reshaped understanding of plant immune mechanisms by introducing the concept of a two-tiered immune system:

1. PAMP-triggered immunity (PTI)
   - First line of defense
   - Recognition of conserved microbial patterns
   - Broad-spectrum initial response

2. ETI
   - More specific, gene-for-gene resistance
   - Recognition of pathogen-specific effector proteins
   - More intense, localized immune response

Key conceptual contributions include:
- Challenged previous linear models of plant-pathogen interactions
- Introduced molecular perspective to plant defense
- Highlighted the dynamic nature of plant immune responses[7,8]

Molecular Revolution in Plant Immunity: Development of Key Conceptual Frameworks

1. PRRs stands for PRRs.
   - They were described as critical molecular sensor
   - Ability to detect MAMPs
   - Possess highly developed abilities in molecular recognition.[12,13]
   - Discovered as specific genes responsible for resistance to pathogens, a diverse pattern of human genetic responses to immunity.
   - Demonstrated aspects for a potential partial resistance breeding[14,15]

2. Resistance (R) genes
   - Discovered as specific genetic determinants of pathogen resistance
   - Revealed complex genetic basis of immune responses
   - Showed potential for targeted resistance breeding[14,15]

Evolutionary Perspective on Immunity Development

The methodologies that were excised in this study include genomic and proteomic methods. Systems biology approaches and the evolutionary significance of plant immune systems:[18,19]

Key evolutionary insights include:
- Plant immunity as a dynamic, adaptive system
- Continuous coevolution with pathogenic organisms
- Molecular arms race between plants and pathogens
- Convergent evolution of defense mechanisms[16,17]

Technological Advances Driving Understanding

Several technological breakthroughs have accelerated plant immunity research:

1. Molecular biology techniques
   - Gene sequencing
   - Transgenic technologies
   - Advanced microscopy

2. Genomic and proteomic approaches
   - Whole genome analyses
   - Protein interaction mapping
   - Systems biology approaches[18,19]

Paradigm Shift: From Passive to Active Defense

- From being considered a passive organism
- Designated as sophisticated responsive systems
- Can communicate with complex molecules
- Have complex defense mechanisms.[20,21] Current plant immune system research now distinguishes:
- Multilayered defense
- Microbial defense

Table 1 | Comparative table for PTI and ETI

Characteristic	PTI	ETI
Recognition Mechanism	Detection of conserved microbial patterns (PAMPs)	Detection of specific pathogen effector proteins by R proteins
Response Intensity	Initial, broad-spectrum defense	More intense, localized immune response
Molecular Components	Pattern-recognition receptors (PRRs), BAK1 co-receptor	Nucleotide-binding leucine-rich repeat (NLR) proteins
Typical Outcome	Rapid cellular defense activation	Hypersensitive response (HR), programmed cell death

- Systemic acquired resistance (SAR)
- Molecular communication networks
- Adaptive immune-like responses[22,23]
- Ecological significance of plant defense systems

A Continuing Journey of Discovery

To understand the historical scientific journey in plant immunity research, we present it as an incredible example. Our understanding of disease resistance has progressed from early observations to the modern era of molecular insight and what we know of the complexity of plant defense mechanisms.

Key milestones are as follows:

- Late 19th century: Initial resistance observations during disease
- Mid-20th century: Resistance genetic basis identified
- 2006: Jones and Dangl's two-tiered immunity model
- Current era: Molecular- and systems-level understanding

Types of Plant Immunity (Table 1)

PAMP-Triggered Immunity (PTI):

The recognition of PAMP by PRRs located on the plant cell surface is the major step of PTI. This elicits a defense response series, callose deposition, and some defense-related genes.[2]

PRRs' Role

FLS2 and EFR are examples PRRs that can detect PAMP flagellin and elongation factor Tu (EF-Tu), respectively. Functional activation of PRRs, which leads to immune signaling via mitogen-activated protein kinase (MAPK) cascades, requires co-receptors like BAK1.[4]

Key Studies PAMP-Triggered Immunity (PTI)

Key Studies A number of landmark studies have made important contributions to the understanding of PAMP-triggered immunity (PTI) as it relates to plant-pathogen-recognition receptors. In these studies, molecular bases for PRR activation, signal transduction, and downstream immune responses have been uncovered.

Study 1: FLS2 (Gómez-Gómez & Boller, 2000)

Flagellin-perception *Arabidopsis thaliana* revolutionizes PTI research with the discovery of flagellin receptor FLS2. Specificity of the FLS2 LRR-RLK for a conserved 22-amino-acid epitope of bacterial flagellin, termed flg22,[8] was also demonstrated.

Arabidopsis plants that lacked functioning FLS2 genes were unable to recognize flagellin and were, therefore, more susceptible to bacterial infection, as shown by their experiments. In this study we have confirmed that FLS2 functions as a PRR capable of initiating immune responses by responding to microbial features.

Study 2: The FLS2-BAK1 Complex (Chinchilla et al., 2007)

It discovered how FLS2 works with another RLK, BAK1 (BRI1 associated kinase 1). Secondly, they showed that upon recognizing flagellin, FLS2 forms a heterodimeric complex with BAK1 and that phosphorylation events triggered by that complex initiate immune signaling.[7]

Earlier, mutant plants deficient in BAK1 exhibited a weaker immune response, indicating the critical role of BAK1 as a co-receptor. It established the concept of the formation of receptor complexes in plant immunity and paralleled our understanding of immune receptor complexes in animals.

Study 3: EFR (Zipfel et al. (2014)), recognizing EF-Tu

When botanists set out to discover PRRs, they found another PRR, EFR, which recognizes a conserved peptide of the bacterial protein elongation factor Tu. Like FLS, EFR activates immune responses to EF-Tu-derived peptides.

The study also showed that EFR-mediated immunity improves the resistance of plants to numerous bacteria pathogens, suggesting the importance of PRR diversification for broad-spectrum immunity.[6,4,24]

Study 4: Boller and Felix (2009) Molecular Mechanisms of PRR Activation

PTI mechanisms were reviewed in detail, and a comprehensive summary of molecular events initiated by PRR activation was provided. They then listed key defense responses, such as calcium ion influx, reactive oxygen species (ROS) production, and MAPK cascade activation, which appear important to their work.[2]

They also emphasized that PRRs have been conserved during evolution among as distant as possible plant species and cited these as important for innate immune responses.

Study 5: Smakowska-Luzan et al. Structural Insights into PRR Activation (2018)

However, recent structural biology advancements have revealed atomic-level details of PRR complexes. They solved the 3D structure of a number of LRR RLKs, including FLS2, and showed how receptor activation hinges upon conformational changes in ligand binding.[7]

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Based on this structural understanding, we have engineered synthetic PRRs with improved sensitivity and broader recognition capability.

Study 6: PTI and ETI Crosstalk (Thomma et al., 2011)
Neither PTI nor ETI are cut-and-dry immune pathways, and the sharing of overlapping components between immune pathways was proposed.[25] According to their findings, the immune signaling process is dynamic and can also synergistically activate in the presence of simultaneous triggering of both PRR and R protein pathways.

These key studies contributed to our current understanding of how PTI is initiated through receptor activation and signal transduction, as well as downstream immune responses. In addition, the work has also guided translational research involving genetic engineering and breeding programs to increase disease resistance in crops.

ETI Mechanisms and Significance

When pathogen effectors are delivered into plant cells, ETI is initiated through sensing by intracellular R proteins. In contrast with PTI, ETI typically results in a stronger and prolonged response, often involving HR, a form of programmed cell death that limits the spread of the pathogen.[12]

R Protein-Effector Interaction

R proteins detect pathogen effectors by direct or indirect interactions and include primarily nucleotide-binding leucine-rich repeat (NLR) proteins. Downstream signaling components are activated and generate strong defense responses.[3]

Molecular Recognition Mechanism: Detailed Analysis of PRRs

Microbial signature detection critically relies on PRRs. PRRs involved in bacterial pathogen recognition include well-characterized PRRs, FLS2, and EFR. They depend on conserved leucine-rich repeat (LRR) domains for PAMP detection.[4]

Signaling Pathways Activated by Pathogen Detection

Upon PAMP detection, PRRs activate several signaling pathways, including:

- MAPK Cascades: MAPK activation causes phosphorylation of transcription factors that control the development of the immune genes.
- Calcium Signaling: Calcium influx triggers immune responses by calcium-dependent protein kinases (CDPKs).
- ROS Production: Cell wall strengthening and pathogen inhibition require a burst of ROS.[7]

Recent studies suggest that redox signaling plays an essential role in plant defense, regulating cellular responses to both biotic and abiotic stress.[46] Additionally, structural studies have identified specificity mechanisms in PRR activation, further refining our understanding of immune perception.[47]

Role of Co-receptors (BAK1)

BAK1 can act as a co-receptor for several PRRs that signal by PAMP recognition, amplifying immune signaling. In addition to its role in PTI and regulation of cell death during pathogen attack,[7] it functions as a ubiquitin E3 ligase for target degradation.[12]

Defense Signaling Pathways

External pathogen and internal hormonal cues intersect to modulate effective immune responses in plant defense signaling pathways, which include protein phosphorylation, hormone signaling, transcriptional reprogramming, and secondary metabolite production.

Enhanced Signaling Networks and Crosstalk

Plant defense signaling entails communication between different molecules for hormones, including salicylic acid (SA), jasmonic acid (JA), and ethylene (ET). Recent developments in transcriptomics have shed more light on how plants modulate these pathways depending on the pathogen's lifestyle. For example, the antagonism between SA-JA guarantees the best adaptation to biotrophic and necrotrophic pathogens.[14,15] Calcium signaling and ROS production are still pivotal elements of early immune responses, and the latest research is devoted to the function of CDPKs in transcriptional rewiring.[16–18]

Plant Immunity and the Regulation of Hormones (Table 2)

Plant hormones play central roles in regulating immune responses against various pathogens:

SA: SAR against biotrophic pathogens is mediated SA. It encourages pathogenesis-related (PR) gene transcript and produces long-lasting immunity.[26] SA accumulation triggers the imitative immune regulator non-expressor of PR genes 1 (NPR1) for activation of defense gene expression.

JA: JA is primarily developed against necrotrophic pathogens and herbivorous insects. MYC2 and the downstream genes that encode defense-related

Table 2 | Plant hormones in immune response

Hormone	Primary Function	Target Pathogens	Key Molecular Interactions
SA	SAR	Biotrophic pathogens	Activates NPR1, induces pathogenesis-related genes
JA	Defense against necrotrophic pathogens	Necrotrophic pathogens, herbivores	Activates MYC2, induces defense protein genes
ET	Synergistic defense	Necrotrophic pathogens	Works with JA, strengthens cell walls, activates defense genes

proteins, like defensins and proteinase inhibitors, participate in understanding JA signaling.[15]

ET: Just as ET combats necrotrophic pathogens synergistically with JA, we show that JA also protects plants synergistically from necrotrophic pathogens in both guard and infected cells. Cell wall strengthening, ROS production, and activation of genes for defense responses are influenced by ET signaling.[6]

These hormones talk with each other to keep the immune response in balance. For example, SA-JA antagonism enables the tuning of immune responses toward invading pathogen lifestyles.[27]

Signal Transduction Mechanisms (Table 3)

Signal transduction in plant immunity involves several interconnected molecular pathways triggered by PAMP recognition and effector detection:

MAPK Cascades: PRRs stimulated MAPKs that relay signals to the nucleus for the phosphorylation of transcription factors, such as WRKYs, which then control the expression of defense-related genes. PTI responses are central to the functions of MAPK modules such as MPK3, MPK4, and MPK6.[28]

Calcium-Dependent Signaling: Sharp rises in cytosolic calcium levels result from pathogen detection, which stimulates calcium-binding proteins, including calmodulins and CDPKs. They induce the expression of defense-related genes[29] and modulate immune responses.

ROS Burst: ROS are generated in the infection site by an oxidative burst, strengthen the cell walls, and induce programmed cell death in infected tissues. They are mediated by NADPH oxidases, such as RBOHD.[6]

Transcriptional Reprogramming: Finally, immune signaling pathways regulate the expression of hundreds of genes important for antimicrobial production, hormone biosynthesis, and cell wall modification.[30]

Ubiquitination and Protein Degradation: Protein degradation of pathogen-triggered signaling also involves a component of the ubiquitin-proteasome system. It provides a way to remove negative immune regulators and sustain defense responses.[31]

Pathogen Interactions

Pathogens that interact with plants include bacteria, fungi, viruses, and oomycetes. Various plants employ distinct methods to resist similar pathogens, while pathogens, in turn, have unique strategies to overcome plant defenses (Table 4).

Bacterial Pathogens

Bacterial pathogens like *Pseudomonas syringae*, the *Xanthomonas* species, and *Agrobacterium tumefaciens* use sophisticated strategies to suppress plant immunity:

Type III Secretion System (T3SS)

Among several bacterial pathogens, T3SS is used by many bacteria to deliver effector directly into the plant cell cytoplasm. The effectors turn on host proteins connected to immune signaling, blocking defense responses. For example, the plant defense suppressor *Pseudomonas syringae* effector AvrRpt2 cleaves and suppresses RIN4, a plant defense regulator.[13,32]

Effector-Mediated Suppression

HopAB2 effectors are able to prevent PRR-mediated signaling by targeting MAPK cascade proteins. Also, the photosynthesis-related protein interference by the cysteine protease HopN1 weakens the host's metabolic defense.[33]

Host Manipulation

Host hormone pathways are also modulated by bacteria, which favor infection. Transcription activator-like effectors (TALEs) that promote disease development are produced by the *Xanthomonas* species, for example.[34]

Table 3 | Signal transduction mechanisms

Pathway	Molecular Components	Activation Trigger	Immune Response Outcome
MAPK Cascades	MPK3, MPK4, MPK6	PRR stimulation	Phosphorylation of defense-related transcription factors
Calcium Signaling	Calmodulins, CDPKs	Cytosolic calcium influx	Expression of defense-related genes
ROS Burst	NADPH oxidases (RBOHD)	Pathogen detection	Cell wall strengthening, programmed cell death
Transcriptional Reprogramming	Multiple defense genes	Immune signaling pathways	Antimicrobial production, hormone biosynthesis

Table 4 | Pathogen interaction strategies table

Pathogen Type	Key Strategies	Examples	Mechanism of Action
Bacterial Pathogens	T3SS	Pseudomonas syringae (AvrRpt2 effector)	Directly inject effectors to suppress plant immune responses
	Effector-Mediated Suppression	HopAB2, HopN1	Target MAPK cascades, interfere with photosynthesis
	Host Hormone Manipulation	Xanthomonas spp. TALEs	Promote disease development
Fungal Pathogens	Enzymatic Degradation	Fusarium oxysporum	Use cell-wall-degrading enzymes to penetrate plant tissues
	Toxin Production	Fumonisins, Trichothecenes	Damage plant metabolism, suppress immune responses
	Effector Delivery	Haustoria structures	Suppress immune receptor activation

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Fungal Pathogens

Fungal pathogens such as *Botrytis cinerea*, *Magnaporthe oryzae*, and the *Fusarium* species deploy various strategies to invade and colonize plant tissues.

Enzymatic Degradation

In response to fungal pathogens, plant cells are breached by cell-wall-degrading enzymes, most commonly cellulases, xylanases, and pectinases. As one example, *Fusarium oxysporum* produces pectinases to penetrate tissue.[35]

Toxin Production

Fungi also create some toxins, fumonisins, and trichothecenes, which damage plant metabolism and suppress the plant's immune responses. These toxins commonly impair hormone pathways or induce oxidative stress, leading to cell death and successful colonization.[18]

Effector Delivery

Fungi, too, labor toward the delivery of effectors into plant cells with the use of specialized structures called haustoria, similar to bacteria. They affect host immunity by suppressing the activation of immune receptors and, thereby, inhibiting signaling components.[12]

Mechanisms for the Advanced Defense

Far beyond conventional immune signaling, plants have evolved numerous defense mechanisms using specialized processes, including advanced molecular processes, such as small RNA (sRNA) regulation, protein processing, and cutting-edge biotechnological applications.

sRNAs and their Roles in Immune Response Regulation

sRNAs play important roles in the regulation of plant immune responses using post-transcriptional gene silencing. By cleaving or translationally inhibiting target mRNAs, they tune immune-related gene expression.

Two key types of sRNAs involved in plant immunity are:

MicroRNAs: Specifically, the target mRNAs in which they regulate the immune gene expression. miR393: suppresses growth and enhances resistance to bacterial pathogens by targeting auxin receptor genes and is an example.[23]

Small Interfering RNAs: They are released in response to pathogenic attacks and help to maintain immunity by 'directing' the degradation of pathogen-derived RNAs.

They can also use sRNA-like molecules to turn off host immunity, resulting in an RNA-level arms race.[23] This demonstrates the intricacy of transcriptional and post-transcriptional control of plant defense as the regulation of immunity through sRNAs.

CRISPR Technology in Plant Immunity Research

One of the potentially most important applications of CRISPR-Cas9 genome editing is the study and development of plant immunity. This precision lets researchers select out only disease resistance genes that should be mutated for better function or select only genes that confer susceptibility to disease (Figure 2).

Key Applications in Plant Immunity

Knockout of Susceptibility Genes: According to Raffaele, CRISPR has been used to knock out MLO genes in wheat and barley, giving rise to resistance to powdery mildew.

Gene Editing for R-Gene Stacking: Stacking of multiple R-genes into crop genomes can produce durable resistance to evolving pathogens.

Development of Synthetic Immune Receptors: As with any custom-made and -engineered instrument, these can be engineered to recognize novel pathogen signatures, allowing for expansion of immune recognition capabilities.[8]

CRISPR's versatility represents exciting future prospects for the development of crop-breeding programs for the improvement of crop resilience in changing environmental conditions.

Plant Immunity: Evolutionary Perspectives

The coevolution of immune systems has been driven by plant pathogens; plant immune receptors have coevolved in nucleotide sequence across millions of years, and the structure and diversity of these receptors have been shaped by plant-pathogen interactions.

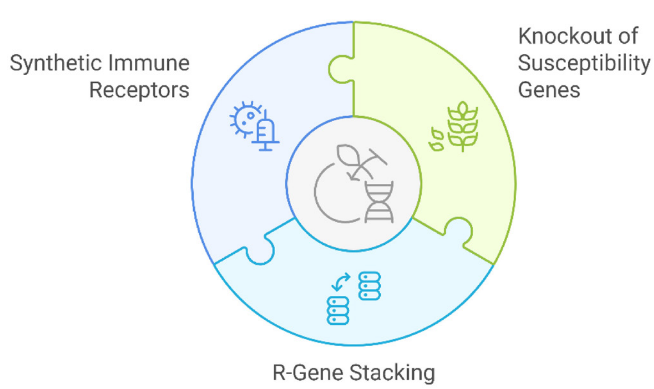

Fig 2 | Enhancing plant immunity with CRISPR

Plant Pathogens and Plants Coevolving

That evolutionary arms race between plants and pathogens has been a continuous cycle of adaptation. As a result, pathogens encode effectors to counteract plant defenses,[17] while plants have evolved new resistance proteins (R proteins) to detect these effectors.[17] The term "zigzag model" is given to this dynamic interplay.

Examples include:

Pathogen Adaptation: By surviving recognition by plant R proteins, *Pseudomonas syringae* evolves into a new effector.

Plant Adaptation: Rust pathogens of wheat and barley evolve, and their detection on hosts is coordinated using diverse R-gene families.[36]

Evolution of Immune Receptors

Finally, the plant genome has extensive gene duplications of immune receptor gene families, most notably nucleotide-binding leucine-rich repeat (NLR) proteins. For instance, the diversity we observe is due to pathogen-driven evolution via selective pressure.[19]

Evolutionary hot spots where immune genes recombine frequently were studied and have been found to increase receptor diversity. The Lr34 gene in wheat confers broad-spectrum resistance to various pathogens.[22]

Evolutionary Perspectives

The now termed as 'zigzag model' is still one of the most important conceptual models of the plant-pathogen coevolution. In the last five years, genome-wide analysis of R-genes and PRRs has depicted the differentiation and dispersion of R-genes and PRRs in the plant species surviving pathogenic changes.[33,34,37] There are also known 'hot spots' of the immune receptor gene, for example, the Lr34 gene in wheat that provides broad-spectrum resistance (Figure 3).[38]

Future Directions in Research

Advances in molecular biology, bioinformatic and agricultural biotechnological tools have burgeoned the development in plant immunity research. Improved disease resistance procedure can be implemented using emerging technologies.

High-throughput genomic approaches have expanded our understanding of plant immune receptors, enabling the identification of novel resistance genes.[40] Additionally, recent advances in machine learning and computational biology are enhancing our ability to predict and engineer plant immune responses.[41]

Future Directions

New tools are expected to provide more light on the ability of plants to resist diseases. Single-cell RNA-seq and proteomics are being used to reveal the tissue-specificity of the immune response, and machine learning is being used to fast-track the computation of new R-genes.[8,39] Future research directions, such as using synthetic biology and designing custom PRRs, have the ability to develop multiple pathogen-resistant crop varieties.[24,25]

Technologies and Methods

High-Throughput Genomics: Using whole genome sequencing, immune-related genes can be identified across various plant species. This has, in turn, expedited the finding of novel resistance genes and PRRs.[40]
Single-Cell Transcriptomics: The analysis of immune responses at the single-cell level reveals cell-specific defense strategies that can be used to map immune signaling in different tissues.[7]

Structural Biology: Some atomic level resolution of PRR-receptor complexes has been obtained using cryo-EM to further receptor engineering efforts.[7]
Machine Learning and Bioinformatics: New R-genes and effectors are predicted by advanced computational tools, which then guide experimental studies of immune signaling.[41]

Genetic Engineering for Enhanced Resistance

The application of CRISPR-Cas9 and synthetic biology techniques holds immense potential for developing disease-resistant crops:

Gene Stacking: For durability against rapidly evolving pathogens, it is the stacking of several R-genes. Synthetic PRRs: Receptors can be designed to custom-insert into crops to detect pathogens that were previously undetected.[8]

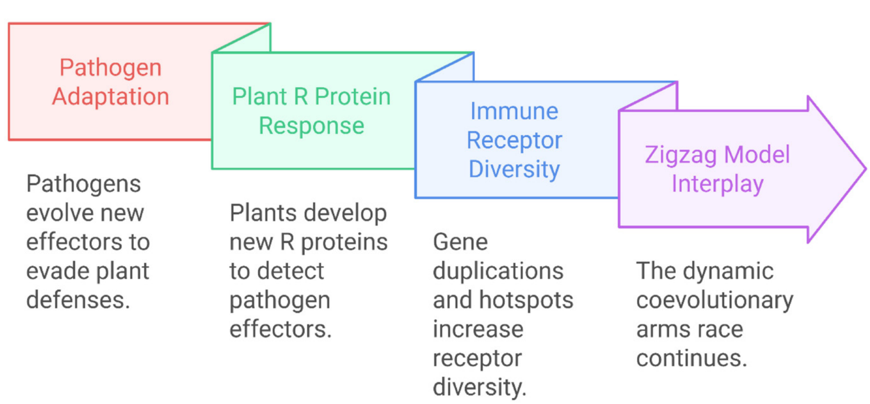

Fig 3 | Plant-pathogen coevolution sequence

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RNA Interference (RNAi): Targeted disease resistance is provided by silencing genes essential for pathogen survival.

The techniques could help bring about 'immunity-enhanced' crops, which require fewer chemically sprayed pesticides.

Cutting-Edge Biotechnological Applications: CRISPR-Cas9 in Plant Immunity

Efficient gene editing systems such as CRISPR-Cas9 have highly transformed plant immunity studies. These have uses in knocking out susceptibility (S) genes and achieving a pyramid of multiple resistance (R) genes for permanent resistance. Indeed, CRISPR has been utilized to create resistance to powdery mildew in wheat by modifying MLO genes.[19–21]

RNAi

RNAi has been identified as a promising method of pathogen pathogens for their virulence proteins. Endogenous sRNAs have been employed to suppress plant defense genes, while plants employ pathogen-derived sRNAs to counter these aggressive attacks, resulting in an RNA arms race.[22,23]

Conclusion

One of the most complex yet elegant biological defense networks is the plant immune system: struck by a pathogen (xenobiotic) attack, it must balance between pathogen resistance and maintaining growth balance. The PTI and ETI system is a two-layer defense system whose response is to the recognition of PAMPs or specific pathogen effectors. In addition, plant immunity is further advanced by such molecular mechanisms as sRNA regulation, posttranslational modification, and gene editing technologies.

Current research in plant immunity holds great promise for the sustainability of global agriculture, where agriculture can be realized to combat climate change and emerging pathogens. To gain future progress in crop improvement, it will be critical to integrate evolutionary insights, state-of-the-art gene-editing technologies, and large-scale genomic studies.

Like many biological systems, the plant immune system is highly schematic: the defense is developed against pathogens, but it implies growth and reproduction. New findings in molecular biology, biotechnology, and evolutionary genomics have, however, revolutionized the understanding of this complex system. When applied in sustainable agriculture, all these insights will go a long way in solving issues facing the world today, like climate change and food insecurity.

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