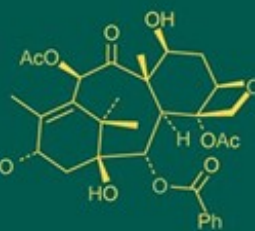
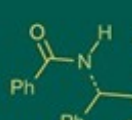


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Emerging late blight threat in potato in North Gujarat: integrative multi-omics technologies for molecular mechanisms and precision management

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ABSTRACT

Late blight, caused by *Phytophthora infestans*, remains the most destructive disease of potato, threatening sustainable production and food security. The rapid evolution and genetic diversity of the pathogen frequently overcome host resistance and reduce the effectiveness of conventional disease management strategies. Recent advances in multi-omics technologies, including genomics, transcriptomics, proteomics, metabolomics and epigenomics, have significantly improved our understanding of potato late blight, *P. infestans* interactions by identifying resistance genes, pathogen effectors, defense pathways and molecular biomarkers associated with durable resistance. The integration of multi-omics with bioinformatics, artificial intelligence, genome editing and precision agriculture is accelerating resistance breeding, early disease diagnosis and predictive disease management. The review critically examines recent advances, current limitations, and future prospects of multi-omics approaches in understanding host-pathogen interactions and improving resistance breeding. Integrative multi-omics approaches hold considerable promise for developing durable resistance and improving sustainable late blight management.

Keywords: Artificial intelligent, Emerging plant diseases, Multi-omics, *Phytophthora infestans*, Potato

Introduction

Potato (*Solanum tuberosum* L.) is the world's third most important food crop after rice and wheat and plays a crucial role in global food security, nutrition and agricultural economies. However, potato productivity is severely constrained by numerous biotic stresses, among which late blight, caused by *Phytophthora infestans* (Mont.) de Bary, remains the most devastating disease. Late blight is historically renowned as the causal agent of the Irish Potato Famine (1845-1852), one of the most catastrophic plant disease epidemics that resulted in widespread famine, economic collapse and human migration (Bourke, 1964; Savary *et al.*, 2017) [1, 2]. The pathogen, believed to have originated in Central Mexico or South America, has since spread to virtually all potato-growing regions worldwide (Fry *et al.*, 2015) [3]. Despite more than a century of intensive research and substantial improvements in disease management, late blight continues to threaten sustainable potato production owing to the remarkable adaptability and evolutionary potential of the pathogen.

The economic impact of late blight remains enormous, with annual global losses, including yield reduction and disease management costs, estimated at several billion US dollars. In developing countries, where potato serves as both a staple food and an important cash crop, epidemics frequently result in yield losses exceeding 60%, particularly under resource-limited farming systems with restricted access to effective fungicides and resistant cultivars (Copeland *et al.*, 1993; Andersson *et al.*, 2015) [5, 4]. Consequently, late blight represents a major challenge to food security, farmer livelihoods and sustainable agricultural production.

Under cool, humid conditions (10-23 °C, relative humidity above 90%), *P. infestans* produces abundant sporangia that are readily dispersed by wind and rain splash, resulting in explosive epidemics capable of destroying entire potato fields within a few days (Aylor, 2003; Gevens *et al.*, 2013; Nowicki *et al.*, 2012) [6, 7, 8]. The pathogen's extraordinary genetic diversity and continuous evolution through mutation, recombination and migration enable it to overcome host resistance and reduce fungicide sensitivity, substantially complicating disease management.

Conventional management strategies, including fungicide application, resistant cultivars, cultural practices and integrated disease management, often fail to provide durable protection because of rapid pathogen evolution and growing environmental concerns over intensive fungicide use. Climate change is further expected to intensify outbreaks and expand the pathogen's geographical range, underscoring the need for a deeper understanding of host-pathogen molecular interactions.

Recent advances in omics technologies have revolutionized plant pathology by enabling comprehensive investigation of biological systems at multiple molecular levels. Genomics, transcriptomics, proteomics, metabolomics, epigenomics and phenomics have collectively enhanced our understanding of the molecular mechanisms governing potato *P. infestans* interactions (Paluchowska *et al.*, 2022) [9]. These technologies facilitate the identification of resistance (*R*) genes, pathogen effectors, virulence determinants, defense-responsive genes, regulatory networks, proteins, metabolites and molecular biomarkers associated with disease resistance and pathogenicity (Kieu *et al.*, 2021) [10]. Moreover, the rapid advancement of next-generation sequencing (NGS), single-cell sequencing, high-throughput phenotyping, bioinformatics, machine learning, artificial intelligence (AI) and systems biology has greatly accelerated multi-omics data integration, enabling holistic characterization of host–pathogen interactions with unprecedented precision.

Although numerous studies have employed individual omics platforms, limited efforts have integrated multi-layered datasets to elucidate the dynamic regulatory networks governing potato *P. infestans* interactions. This lack of integrative analyses hinders the identification of robust molecular targets for durable resistance breeding. Integrative multi-omics approaches provide an unprecedented opportunity to bridge genotype-to-phenotype relationships, decipher complex molecular networks, identify robust biomarkers and accelerate the development of durable late blight-resistant potato cultivars. Such approaches are expected to support precision breeding, climate-resilient agriculture and sustainable disease management under changing environmental conditions.

This review comprehensively summarizes recent advances in genomics, transcriptomics, proteomics, metabolomics, epigenomics and phenomics in understanding potato *P. infestans* interactions. Furthermore, it highlights emerging applications of systems biology,

artificial intelligence, bioinformatics and integrated multi-omics for improving disease resistance, accelerating breeding programs and developing sustainable strategies for long-term management of potato late blight.

Genomics approaches in late blight

Genomics has revolutionized the understanding of potato late blight by providing comprehensive insights into the genome architecture, pathogenicity mechanisms, evolutionary dynamics and host resistance associated with *P. infestans*. The availability of high-quality reference genomes, coupled with advances in next-generation sequencing (NGS), long-read sequencing, molecular markers and functional genomics, has enabled detailed characterization of both the pathogen and its host. These technologies have facilitated the identification of genomic regions controlling disease resistance, virulence determinants, effector repertoires and molecular pathways involved in host–pathogen interactions, thereby accelerating the development of durable resistance breeding strategies and precision disease management approaches (Haas *et al.*, 2009; Vleeshouwers *et al.*, 2011) [11, 12].

One of the most significant contributions of genomics has been the discovery and characterization of potato late blight resistance (*R*) genes and their corresponding avirulence (*Avr*) genes in *P. infestans*. Genome-wide analyses have greatly improved our understanding of the molecular basis of gene-for-gene interactions and the evolutionary arms race between host resistance and pathogen virulence. The integration of genomic information into potato improvement programs has facilitated marker-assisted selection (MAS), genomic selection (GS), quantitative trait locus (QTL) mapping, gene pyramiding and genome editing technologies such as CRISPR/Cas systems, thereby accelerating the development of potato cultivars with broad-spectrum and durable resistance to late blight (Paluchowska *et al.*, 2022) [9].

Table 1. Major Late Blight Resistance (*R*) Genes Identified Through Genomic Approaches

R Gene	Donor Species	Chromosome	Resistance Spectrum	Reference
<i>R₁</i>	<i>S. demissum</i>	V	Race-specific	Vleeshouwers <i>et al.</i> , 2011
<i>R_{3a}</i> / <i>R_{3b}</i>	<i>S. demissum</i>	XI	Race-specific	Vleeshouwers <i>et al.</i> , 2011
<i>RB</i> / <i>R_{pi-blb1}</i>	<i>S. bulbocastanum</i>	VIII	Broad-spectrum	Paluchowska <i>et al.</i> , 2022
<i>R_{pi-blb2}</i>	<i>S. bulbocastanum</i>	VI	Broad-spectrum	Vleeshouwers <i>et al.</i> , 2011
<i>R_{pi-vnt1}</i>	<i>S. venturii</i>	IX	Broad-spectrum	Paluchowska <i>et al.</i> , 2022
<i>R_{pi-amr1}</i> / <i>R_{pi-amr3}</i>	<i>S. americanum</i>	IV / XI	Broad-spectrum	Witek <i>et al.</i> , 2021; Kourelis <i>et al.</i> , 2023
<i>R_{pi-sto1}</i>	<i>S. stoloniferum</i>	IX	Race-specific	Paluchowska <i>et al.</i> , 2022

The pathogenic success of *P. infestans* is largely attributed to its extensive repertoire of secreted effector proteins, particularly the RxLR and Crinkler (CRN) families, which manipulate host cellular processes and suppress immune responses to promote successful infection and colonization. Functional genomics integrated with transcriptomic analyses has enabled the identification of numerous genes involved in pathogen development, sporulation, host specificity, signal transduction, stress adaptation and infection biology, providing valuable insights into the molecular determinants of pathogenicity (Mazumdar *et al.*, 2021; Juma *et al.*, 2025) [14, 13].

Comparative genomics and population genomics have further enhanced understanding of the genetic diversity, population structure, migration history and evolutionary dynamics of *P. infestans* worldwide. Genome-wide analyses have revealed extensive genetic variation arising from mutation, sexual recombination, copy number varia-

tion and transposable element activity, contributing to the rapid emergence of highly aggressive pathogen lineages capable of overcoming multiple host resistance genes and exhibiting reduced sensitivity to fungicides (Fry *et al.*, 2015) [3]. Consequently, genomic surveillance has become an essential component of integrated disease management by enabling continuous monitoring of pathogen evolution, virulence profiles and the emergence of novel strains, thereby supporting resistance breeding, epidemiological forecasting and evidence-based disease management strategies.

Overall, genomics provides the foundation for deciphering the complex molecular interactions between potato and *P. infestans*. The integration of genomic resources with transcriptomics, proteomics, metabolomics, phenomics, artificial intelligence and systems biology is expected to further accelerate the identification of broad-spectrum

resistance mechanisms and facilitate the development of climate-resilient potato cultivars for sustainable late blight management.

Whole genome sequencing

Whole-genome sequencing (WGS) has significantly advanced our understanding of the genetic architecture, pathogenicity, adaptation and evolutionary dynamics of *P. infestans*. Genome-wide analyses have revealed a highly dynamic genome characterized by extensive structural variation, transposable element expansion, copy number variation and rapidly evolving effector gene families, which collectively contribute to the pathogen's remarkable adaptability, virulence and ability to overcome host resistance under diverse environmental conditions. These genomic features underpin the rapid evolution of new pathogen lineages and highlight the complex molecular mechanisms driving host–pathogen co-evolution.

Parallel advances in potato genomics have greatly accelerated the discovery of genomic regions associated with late blight resistance in both cultivated germplasm and wild *Solanum* species. High-quality reference genomes, long-read sequencing technologies, pan-genome analyses, haplotype-resolved genome assemblies, genome-wide association studies (GWAS) and quantitative trait locus (QTL) mapping have substantially improved the identification, fine mapping and functional characterization of resistance-associated loci and candidate genes. Potato pan-genomics has expanded the genetic landscape beyond a single reference genome by capturing structural variation and rare resistance alleles present in diverse cultivated and wild *Solanum* species. (Tang *et al.*, 2022) [15]. Genomic information serves as the foundation for integrating transcriptomic, proteomic, metabolomic, and phenomic datasets, enabling identification of functional resistance pathways rather than relying solely on sequence-based predictions. The integration of these genomic resources with comparative genomics and functional validation approaches provides valuable insights into the genetic basis of durable resistance and offers powerful tools for genomics-assisted breeding, marker development, genomic selection, and genome editing aimed at developing climate-resilient potato cultivars with broad-spectrum resistance to late blight.

CRISPR and genome editing

Genome editing technologies, particularly the CRISPR/Cas system, have emerged as powerful tools for improving potato resistance to late blight through precise modification of susceptibility (*S*) genes, resistance-associated genes, transcription factors and immune signaling pathways. Recent studies have demonstrated that editing susceptibility-related genes such as StDMR6-1 can enhance potato resistance against *P. infestans* by modulating host immune responses. Unlike conventional transgenic approaches, CRISPR/Cas enables targeted and efficient genome modification with minimal unintended genomic changes, thereby facilitating the development of disease-resistant potato cultivars while preserving desirable agronomic traits. The integration of CRISPR/Cas technology with genomics, transcriptomics, pan-genomics, high-throughput phenotyping and artificial intelligence (AI)-assisted breeding is facilitating precision crop improvement by accelerating the identification, validation and deployment of durable resistance genes (Chen *et al.*, 2019; Jansing *et al.*, 2019) [16, 17].

Recent advances in multiplex CRISPR genome editing have further expanded its application by enabling the simultaneous modification of multiple genes involved in host immunity, disease resistance and abiotic stress adaptation, thereby enhancing breeding efficiency and broad-spectrum resistance (Zhang *et al.*, 2018; Manghwar *et al.*, 2019) [19, 18]. In addition, emerging genome-editing platforms, including base editing and prime editing, offer opportunities for introducing precise nucleotide substitutions without generating double-stranded DNA breaks, thereby increasing editing accuracy and reducing undesirable mutations. These next-generation technologies hold considerable promise for functional genomics and the development of climate-resilient potato cultivars with durable resistance to *P. infestans*. Recent studies have demonstrated that editing susceptibility-related genes such as StDMR6-1 can enhance potato resistance against *P. infestans* by modulating host immune responses.

Despite these advances, several challenges continue to limit the widespread application of CRISPR/Cas-based breeding in potato, including low transformation and regeneration efficiency, genotype-dependent editing responses, potential off-target effects, polyploid genome complexity, regulatory uncertainty and public acceptance of genome-edited crops (Razzaq *et al.*, 2019) [20]. Continued improvements in genome-editing platforms, delivery systems, transformation protocols and regulatory frameworks are expected to facilitate the broader adoption of CRISPR-assisted breeding for sustainable management of potato late blight.

Transcriptomics in potato–late blight interaction

Transcriptomics has emerged as a powerful approach for deciphering the complex molecular interactions between potato and *P. infestans* by providing comprehensive insights into gene expression dynamics during pathogen infection. Advances in high-throughput transcriptome profiling technologies, including RNA sequencing (RNA-seq), dual RNA-seq, long-read transcript sequencing, single-cell RNA sequencing (scRNA-seq) and spatial transcriptomics, have enabled detailed characterization of host and pathogen transcriptional responses across different stages of disease development. These approaches have revealed extensive transcriptional reprogramming associated with pathogen recognition, immune activation, cellular signaling and defense regulation, thereby improving our understanding of the molecular basis of late blight resistance (Ah-Fong *et al.*, 2017) [21].

Genome-wide transcriptome analyses have identified numerous differentially expressed genes (DEGs) involved in pathogen perception, pattern-triggered immunity (PTI), effector-triggered immunity (ETI), reactive oxygen species (ROS) production, calcium-mediated signaling, mitogen-activated protein kinase (MAPK) cascades and phytohormone-regulated defense pathways mediated by salicylic acid (SA), jasmonic acid (JA), ethylene (ET), and abscisic acid (ABA) (Wang *et al.*, 2023) [22]. Transcriptomic studies have also demonstrated dynamic regulation of several transcription factor families, including WRKY, MYB, NAC, bZIP, AP2/ERF and bHLH, which regulate downstream defense responses through modulation of immune signaling networks, biosynthesis of antimicrobial compounds and stress-responsive gene expression (Chen *et al.*, 2019) [16].

Table 2. Major Defense Pathways Identified by Transcriptomics

Defense Pathway / Process	Key Components	Hormone(s)	Reference
Pattern-triggered immunity (PTI)	Pattern-recognition receptors (PRRs), MAPK cascade	—	Ah-Fong <i>et al.</i> , 2017
Effector-triggered immunity (ETI)	NLR resistance proteins, hypersensitive response	—	Wang <i>et al.</i> , 2023
Reactive oxygen species (ROS) burst	NADPH oxidases, antioxidant enzymes	—	Ah-Fong <i>et al.</i> , 2017
Ca ²⁺ -mediated signaling	Calcium sensors, calcium-dependent protein kinases	—	Wang <i>et al.</i> , 2023

(continued on next page)

Defense Pathway / Process	Key Components	Hormone(s)	Reference
Systemic acquired resistance (SAR)	PR gene induction, WRKY/NAC transcription factors	Salicylic acid (SA)	Chen <i>et al.</i> , 2019
Induced systemic resistance / wound response	Defensins, proteinase inhibitors	Jasmonic acid (JA), Ethylene (ET)	Chen <i>et al.</i> , 2019
Stress and senescence modulation	ABA-responsive transcription factors	Absciscic acid (ABA)	Wang <i>et al.</i> , 2023

Dual RNA-seq has enabled simultaneous profiling of gene expression changes in both potato and *P. infestans*, providing unprecedented insights into the molecular dialogue underlying host–pathogen interactions. These investigations have identified coordinated expression of pathogen effector genes, host resistance genes, defense-related proteins, secondary metabolite biosynthetic pathways, cell wall reinforcement mechanisms and programmed cell death regulators that collectively influence disease progression and resistance outcomes (Ah-Fong *et al.*, 2017) [21]. Furthermore, comparative transcriptomic analyses of resistant and susceptible potato genotypes have revealed key regulatory networks and candidate genes associated with durable late blight resistance, offering valuable targets for functional validation and crop improvement.

The integration of transcriptomics with genomics, proteomics, metabolomics, epigenomics, phenomics and advanced bioinformatics has substantially enhanced systems-level understanding of potato *P. infestans* interactions. Combined with machine learning and artificial intelligence-driven analytical approaches, multi-omics transcriptome data are facilitating identification of regulatory hubs, molecular biomarkers and predictive regulatory networks that support precision breeding, functional genomics and the development of climate-resilient potato cultivars with durable resistance to late blight.

Proteomics approaches in potato–late blight interaction

Proteomics has emerged as a powerful approach for investigating the molecular mechanisms underlying potato–*Phytophthora infestans* interactions by providing direct insights into the proteins that regulate host defense, pathogen virulence and disease progression. Unlike genomics and transcriptomics, which assess genetic potential and gene expression, proteomics characterizes the functional protein complement of cells, thereby offering a more accurate representation of the biological processes occurring during host–pathogen interactions. Recent advances in high-resolution mass spectrometry, including liquid chromatography–tandem mass spectrometry (LC–MS/MS), tandem mass tag (TMT)-based quantitative proteomics, isobaric tags for relative and absolute quantification (iTRAQ), label-free quantitative proteomics, phosphor proteomics and targeted proteomic approaches, have enabled comprehensive identification and quantification of proteins, post-translational modifications (PTMs) and protein–protein interactions associated with late blight resistance and susceptibility. Recent proteomics-informed studies have further advanced structure-guided engineering of resistance, including NLR immune receptor–nanobody fusions that confer novel disease resistance (Kourelis *et al.*, 2023) [23], refined understanding of *P. infestans* effector biology and host targets (Yang *et al.*, 2023) [24], and comprehensive reappraisal of the genetic and proteomic basis of late blight resistance in potato (Tarabain *et al.*, 2025) [25].

Proteomic investigations have identified numerous defense-related proteins involved in pathogen recognition, reactive oxygen species (ROS) metabolism, antioxidant defense, pathogenesis-related (PR) proteins, heat shock proteins (HSPs), chitinases, β -1,3-glucanases, protease inhibitors, and enzymes involved in phenylpropanoid and lignin biosynthesis. In addition, quantitative proteomic analyses have revealed temporal changes in protein abundance associated with phytohormone signaling, energy metabolism, photosynthesis, cell wall remodeling, vesicle trafficking and immune signaling during different stages of *P. infestans* infection. Characterization of pathogen-secreted proteins, including effector-associated proteins and enzymes involved

in host tissue colonization, has improved understanding of the molecular determinants of pathogenicity and disease development.

Recent developments in phosphor proteomics, secretomics, interactomics and structural proteomics have provided new insights into protein phosphorylation, extracellular protein secretion, protein interaction networks and signaling pathways that coordinate host immune responses. When integrated with genomics, transcriptomics, metabolomics and advanced bioinformatics, proteomics enables systems-level characterization of regulatory networks governing potato *P. infestans* interactions. Such multi-omics integration facilitates the discovery of protein biomarkers, candidate resistance factors and molecular targets for precision breeding, functional validation and the development of durable, climate-resilient potato cultivars with enhanced resistance to late blight.

Protein profiling

Comparative proteomic analyses have revealed extensive alterations in protein abundance and regulatory networks associated with potato responses to *P. infestans* infection. Resistant potato genotypes generally exhibit enhanced accumulation of proteins involved in pathogen recognition, immune signaling, reactive oxygen species (ROS) scavenging, antioxidant defense, pathogenesis-related (PR) proteins, heat shock proteins (HSPs) and enzymes associated with phenylpropanoid metabolism and cell wall reinforcement compared with susceptible cultivars (Xiao *et al.*, 2019) [26]. These coordinated proteomic changes contribute to rapid activation of host defense mechanisms, restriction of pathogen colonization and improved resistance to late blight.

Quantitative proteomic platforms, including tandem mass tag (TMT)-based proteomics and label-free liquid chromatography–tandem mass spectrometry (LCMS/MS), have substantially improved the identification and quantification of resistance-associated proteins, post-translational modifications and signaling networks involved in host immunity. Furthermore, comparative analyses of resistant and susceptible potato genotypes have identified key protein biomarkers and regulatory pathways related to phytohormone signaling, redox homeostasis, energy metabolism, stress adaptation and defense activation. These findings provide promising molecular targets for functional validation, biomarker-assisted selection and precision breeding aimed at developing potato cultivars with durable resistance to *P. infestans*.

Secretome analysis

The secretome comprises the complete repertoire of extracellular proteins secreted by both the host and the pathogen that mediate host–pathogen communication during infection. In *P. infestans*, the secretome includes effector proteins (RxLR and Crinkler (CRN) effectors), elicitors, necrosis-inducing proteins, cell wall-degrading enzymes (CWDEs) such as pectinases, cellulases, xylanases, cutinases and glycosyl hydrolases, as well as proteases and protease inhibitors that facilitate host colonization, suppress immune responses and promote disease development. Conversely, potato secretes a diverse array of defense-related proteins into the apoplast, including pathogenesis-related (PR) proteins such as PR-1, β -1,3-glucanases (PR-2), chitinases (PR-3), thaumatin-like proteins (PR-5), peroxidases, defensins, lipid transfer proteins and protease inhibitors, which collectively inhibit pathogen growth, strengthen cell wall integrity and activate immune signaling. In addition, extracellular antioxidant enzymes, including superoxide dismutase (SOD), catalase (CAT), ascorbate peroxidase (APX), glutathione peroxidase (GPX) and enzymes involved in the phenylpropanoid pathway such as phenylalanine ammonia-lyase (PAL) and polyphenol oxidase (PPO) play critical roles in maintain

ing redox homeostasis, lignification and the production of antimicrobial compounds during late blight infection.

Secretome analyses have demonstrated that apoplastic interactions, effector recognition, extracellular immune signaling and defense protein accumulation are key determinants of disease resistance and susceptibility. Consequently, secretomics has emerged as an indispensable approach for identifying pathogen virulence factors, extracellular protein biomarkers and host immune targets, thereby providing valuable insights into the molecular mechanisms governing plant immunity, pathogen infection strategies and the development of durable resistance against potato late blight (Kamoun, 2006; Wang *et al.*, 2018; Seidl *et al.*, 2022) [27, 28, 29]. Despite significant advances, secretome analysis remains technically challenging due to the low abundance of extracellular proteins, contamination from intracellular proteins, dynamic protein secretion, and limited annotation of pathogen-secreted effectors. Improved protein enrichment strategies and high-resolution mass spectrometry are expected to overcome these limitations.

Table 3. Defense-Related Proteins Identified in Potato–*P. infestans* Interactions

Protein / Enzyme Class	Example(s)	Functional Role
Pathogenesis-related proteins	PR-1, PR-2 (β -1,3-glucanase), PR-3 (chitinase), PR-5 (thaumatin-like), PR-9 (peroxidase)	Direct antimicrobial action, cell-wall degradation of pathogen
Antioxidant enzymes	SOD, CAT, APX, GST	ROS detoxification and redox homeostasis
Phenylpropanoid-pathway enzymes	PAL, PPO, CAD	Lignification, phytoalexin and antimicrobial compound biosynthesis
Heat shock proteins	HSP ₇₀ , HSP ₉₀	Protein folding/stability under infection-associated stress
Protease inhibitors and defensins	Kunitz-type protease inhibitors, plant defensins	Inhibition of pathogen-secreted proteases and membrane disruption

Pathogen virulence proteins

Proteomic studies have significantly advanced the understanding of *P. infestans* virulence by identifying key pathogenicity determinants, including RXLR effectors, Crinkler (CRN) proteins, necrosis- and ethylene-inducing peptide 1-like proteins (NLPs), elicitors and cell wall-degrading enzymes involved in host tissue colonization. Functional characterization of these proteins has demonstrated their roles in suppressing host immunity, manipulating host metabolism, facilitating nutrient acquisition and promoting pathogen growth and disease development. Furthermore, characterization of effector–host target interactions continues to provide critical insights into the molecular basis of pathogenicity and development of durable resistance in potato (Kamoun, 2006; Seidl *et al.*, 2022; Yang *et al.*, 2023) [27, 29, 24].

Metabolomics in potato–*P. infestans* interaction

Unlike genomics and transcriptomics, metabolomics captures the terminal products of cellular processes, thereby providing the closest representation of the physiological state of the plant during pathogen infection. Metabolomics provides a comprehensive assessment of biochemical changes occurring during potato *P. infestans* interactions by profiling low-molecular-weight metabolites that directly reflect cellular responses to pathogen infection. Recent advances in Gas Chromatography Mass Spectrometry (GC-MS), Liquid Chromatography Mass Spectrometry (LC-MS) and nuclear magnetic resonance (NMR) spectroscopy have facilitated the identification of metabolites associated with plant defense, pathogen adaptation and disease resistance. Integration of metabolomics with transcriptomics and proteomics has substantially improved understanding of the metabolic networks involved in potato immunity (Fernie *et al.*, 2009; Fiehn, 2022) [32, 33].

Defense-related proteins

Proteomic investigations have identified numerous defense-associated proteins that play crucial roles in potato resistance against *P. infestans*, including pathogenesis-related (PR) proteins such as PR-1, β -1,3-glucanases (PR-2), chitinases (PR-3), thaumatin-like proteins (PR-5), peroxidases (PR-9), protease inhibitors, defensins, heat shock proteins (HSPs), superoxide dismutases (SOD), catalases (CAT), ascorbate peroxidases (APX), glutathione S-transferases (GST) and enzymes involved in the phenylpropanoid biosynthetic pathway, including phenylalanine ammonia-lyase (PAL), polyphenol oxidase (PPO) and cinnamyl alcohol dehydrogenase (CAD). Increased abundance of these proteins and enzymes is consistently associated with enhanced resistance through rapid pathogen perception, reinforcement of cell wall architecture by lignification and callose deposition, detoxification of reactive oxygen species (ROS), maintenance of cellular redox homeostasis, biosynthesis of antimicrobial secondary metabolites and phytoalexins, inhibition of pathogen growth and activation of local as well as systemic immune responses, including systemic acquired resistance (SAR) (Ali *et al.*, 2018; Balotf *et al.*, 2022) [30, 31].

Secondary metabolites and phytoalexins

Metabolomic analyses have demonstrated increased accumulation of phenolic compounds, flavonoids, steroidal glycoalkaloids and sesquiterpenoid phytoalexins following *P. infestans* infection. Metabolites such as chlorogenic acid, caffeic acid, α -solanine, α -chaconine, rishitin and phytuberin contribute to antimicrobial activity, reinforcement of plant cell walls and inhibition of pathogen growth and colonization. Resistant potato genotypes generally exhibit stronger induction of phenylpropanoid metabolism than susceptible cultivars (Stobiecki *et al.*, 2003; Lattanzio *et al.*, 2006; Ahuja *et al.*, 2012) [35, 36, 34].

Antioxidant Defense and Stress Metabolites

Infection by *P. infestans* induces oxidative stress, resulting in the accumulation of antioxidant metabolites including ascorbate, glutathione, carotenoids, tocopherols, flavonoids, proline and polyamines. These metabolites play essential roles in reactive oxygen species (ROS) detoxification, osmotic regulation and defense signaling during pathogen attack (Foyer and Noctor, 2005; Gill and Tuteja, 2010; Mittler, 2002).

Metabolic Reprogramming

Global metabolomic analyses have revealed extensive reprogramming of carbohydrate, amino acid, lipid and phenylpropanoid metabolism during potato *P. infestans* interactions. Resistant cultivars exhibit rapid accumulation of defense related metabolites and activation of secondary metabolic pathways, whereas susceptible cultivars undergo metabolic changes that favor pathogen colonization (Ahuja *et al.*, 2012).

Metabolomics-Based Biomarkers

Advances in metabolomics have accelerated the identification of metabolic biomarkers for disease diagnosis, resistance

screening and crop improvement. Steroidal glycoalkaloids, phenolic acids, flavonoids and phytoalexins have been proposed as promising metabolic biomarkers for evaluating resistance to late blight and supporting metabolomics-assisted breeding strategies (Fernie and Schauer, 2009). The limitation of the metabolomics and Challenges and Future Perspectives in Metabolomics

Emerging omics technologies

Recent advances beyond conventional omics have substantially expanded our understanding of potato *P. infestans* interactions by revealing additional layers of molecular regulation that govern host immunity and pathogen adaptation. Emerging technologies, including epigenomics, small RNAomics, phenomics, ionomics, single-cell omics and spatial omics, provide high-resolution insights into gene regulation, cellular heterogeneity, nutrient homeostasis and dynamic host–pathogen interactions that cannot be fully resolved using conventional bulk omics approaches (Van den Broeck *et al.*, 2021) [37]. These complementary platforms enable high-resolution characterization of cell type-specific responses, epigenetic modifications, non-coding RNA-mediated regulation and mineral nutrient dynamics during infection, thereby improving our understanding of the complex molecular networks underlying late blight resistance. Furthermore, integration of these next-generation omics technologies with genomics, transcriptomics, proteomics, metabolomics, advanced bioinformatics and artificial intelligence (AI)-based analytical frameworks is facilitating systems-level analyses, accelerating biomarker discovery and supporting precision breeding for the development of climate-resilient potato cultivars with durable resistance to *P. infestans*.

Epigenomics

Epigenetic mechanisms, including DNA methylation, histone modification and chromatin remodeling, regulate plant defense gene expression during pathogen infection. Epigenetic regulation contributes to immune priming, stress memory and enhanced disease resistance, representing a promising avenue for crop improvement (Hewezi *et al.*, 2016; Kumar *et al.*, 2021) [38, 39].

Small RNA and miRNA

Small RNAs (sRNAs) and microRNAs (miRNAs) play crucial roles in post-transcriptional regulation of plant immunity. Members of the potato miR482 family regulate nucleotide-binding leucine-rich repeat (NLR) resistance genes involved in defense against *P. infestans*. RNA interference-based approaches, including host-induced gene silencing (HIGS), have emerged as promising strategies for sustainable management of late blight (Shivaprasad *et al.*, 2012; Weiberg *et al.*, 2014) [40, 41].

Phenomics and ionomics

High-throughput phenotyping now integrates a range of complementary imaging modalities that together enable rapid, non-destructive disease assessment and resistance screening. RGB imaging provides high-resolution visible-spectrum records of lesion development and canopy architecture; chlorophyll fluorescence imaging detects early photosynthetic impairment before visible symptoms appear, allowing pre-symptomatic identification of susceptible versus resistant genotypes; thermal imaging captures pathogen-induced changes in stomatal conductance and leaf temperature associated with the hypersensitive response; hyperspectral imaging resolves fine spectral signatures linked to biochemical and physiological changes during infection, supporting disease severity indices and genotype discrimination; 3D imaging reconstructs canopy structure and biomass loss caused by disease progression; and automated greenhouse and field phenotyping platforms combine these sensors with robotics and UAV or ground-based rovers to screen large breeding populations continuously and objectively. Coupled with machine learning-based image analysis,

these platforms accelerate high-throughput resistance screening, reduce reliance on subjective visual scoring, and enable genomic and phenomic selection to be integrated for faster development of late blight-resistant potato cultivars. Likewise, ionomics has revealed important roles of calcium, silicon, zinc and potassium in modulating plant immunity and stress tolerance (Baxter, 2015) [42]. One important emerging technology is pangenomics. Although mentioned earlier, it should also appear here because it is increasingly regarded as a next-generation omics resource.

Single-cell omics

Single-cell transcriptomics and spatial omics technologies enable investigation of cell-specific responses during infection. These approaches facilitate identification of rare immune-responsive cell populations and spatial defense gradients, providing a new dimension to understanding plant immunity (Rich-Griffin *et al.*, 2020) [43].

Multi-omics integration and systems biology

The integration of genomics, transcriptomics, proteomics, metabolomics and phenomics has transformed plant pathology research by enabling systems-level analysis of host-pathogen interactions. Systems biology combines omics datasets with computational modeling to understand biological processes as interconnected networks. Gene co-expression analysis, protein interaction networks and metabolic pathway reconstruction have revealed key regulatory hubs controlling potato immunity and pathogen virulence (Kitano, 2002) [44].

Artificial intelligence (AI) and machine learning (ML) are increasingly integrated with multi-omics data for biomarker discovery, genomic prediction, disease forecasting and resistance breeding. Deep learning algorithms have demonstrated high accuracy in predicting disease outbreaks and identifying candidate resistance genes.

Bioinformatics tools and databases

Bioinformatics forms the foundation for modern omics-based research by enabling storage, analysis and interpretation of large-scale biological datasets. Public repositories such as NCBI GenBank, Ensembl Plants, UniProt, Sol Genomics Network (SGN) and EuPathDB provide extensive genomic and transcriptomic resources for potato and *P. infestans* research (Fernandez-Pozo *et al.*, 2015; Batley *et al.*, 2016) [46, 45].

Functional annotation tools including Blast2GO, InterProScan, eggNOG Mapper and Gene Ontology (GO) enrichment analyses facilitate characterization of candidate genes and biological pathways (Conesa *et al.*, 2016) [47]. Pathway databases such as KEGG, Reactome and MetaCyc support metabolic reconstruction and defense pathway analysis (Kanehisa *et al.*, 2023) [48].

Network visualization tools including Cytoscape, STRING and BioGRID have become essential for analyzing host-pathogen interaction networks and identifying key regulatory proteins associated with resistance responses (Szklarczyk *et al.*, 2023) [49].

Applications in precision disease management

Integration of omics technologies with AI, remote sensing, molecular diagnostics and digital agriculture has enabled precision management of potato late blight. These approaches improve disease monitoring, forecasting and decision-making while reducing fungicide dependence and environmental impacts.

Resistant cultivar development

Genomics-assisted breeding, genomic selection, GWAS and genome editing technologies have accelerated the development of resistant cultivars carrying broad-spectrum resistance genes such as *R_{pi-amr1}*, *R_{pi-vnt1}* and *R_{pi-blb1}* (Witek *et al.*, 2021; Kourelis *et al.*, 2023) [50, 23].

Molecular diagnostics

Advanced diagnostic technologies including qPCR, LAMP, nanopore sequencing and CRISPR-based platforms provide rapid and sensitive detection of *P. infestans* and fungicide-resistant strains (Broughton *et al.*, 2020) [51].

Early disease detection and precision agriculture

Hyperspectral imaging, thermal cameras, UAV surveillance, IoT-based sensors and AI-assisted image analysis enable early disease detection before the appearance of visible disease symptoms. Precision agriculture platforms facilitate targeted fungicide application and real-time disease monitoring.

Smart surveillance systems

Genomic surveillance combined with climate analytics and GIS mapping enables continuous monitoring of pathogen populations and disease outbreaks, supporting proactive disease management strategies (Cooke *et al.*, 2012) [52].

Conclusion

Late blight caused by *Phytophthora infestans* remains one of the most devastating diseases threatening global potato production. Recent advances in genomics, transcriptomics, proteomics, metabolomics, epigenomics, phenomics and single-cell omics have significantly enhanced our understanding of host-pathogen interactions and the molecular basis of disease resistance. The integration of multi-omics with bioinformatics, artificial intelligence, genome editing, and precision agriculture is accelerating the discovery of resistance genes, molecular biomarkers, and predictive disease management and precision breeding strategies. However, challenges such as multi-omics data integration, high implementation costs and climate-driven pathogen evolution continue to hinder large-scale application. Future research should focus on combining multi-omics, systems biology and AI-driven analytics to develop climate-resilient potato cultivars with durable late blight resistance. Such integrative approaches will play a pivotal role in achieving sustainable potato production, reducing fungicide dependence, and strengthening global food security. The convergence of multi-omics technologies, artificial intelligence, and precision agriculture is expected to redefine late blight research, enabling the transition from reactive disease management to predictive, data-driven, and sustainable crop protection.

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