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Chiamaka Francisca Igweonu
Department of Biological,
Sciences Western Illinois
University, USA

Correspondence
Chiamaka Francisca Igweonu
Department of Biological,
Sciences Western Illinois
University, USA

Understanding plant-microbe interactions using functional genomics

Chiamaka Francisca Igweonu

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Abstract

Plant-microbe interactions (PMIs) play a vital role in agriculture, influencing everything from plant health to productivity and resilience in various ecological settings. Thanks to the rise of high-resolution functional genomics, significant strides have been made in understanding the intricate molecular conversations between plants and microbes, whether they're harmful or helpful. This review offers a thorough overview of the latest advancements in PMI functional genomics, covering areas like host immune profiling, effector biology, and co-evolutionary genomic signatures. Emphasis were made on how techniques like transcriptomics, proteomics, and metabolomics have unveiled dynamic patterns of defense and symbiosis over time and space, while studies on epigenomics and small RNAs have shed light on post-transcriptional regulation and communication across different kingdoms. The increasing use of CRISPR-Cas systems was reviewed, reverse genetics, and synthetic biology to validate key regulators and create new traits. Innovations like spatial transcriptomics and single-cell omics are paving the way for precise functional mapping, allowing us to pinpoint microbe-responsive gene expression at the cellular level. At the same time, synthetic microbial communities (SynComs) and genome-guided microbiome engineering are emerging as groundbreaking methods for enhancing plant-microbe compatibility. Despite the progresses made, challenges remain, such as functional redundancy, limited mapping of genotypes to microbiomes, and issues with data integration. In response, artificial intelligence (AI) and machine learning are being harnessed to build predictive models of host-microbe networks, speeding up trait discovery and practical applications in crops. By combining insights from model systems and applying them to crop-microbe interactions, this work envisions a future where sustainable, genomically informed agriculture is propelled by a deep understanding of PMIs—from the molecular level all the way to ecosystems.

Keywords: Plant-microbe interactions, functional genomics, Crispr-cas systems, Trancsriptomics, synthetic microbial community, microbiome engineering

Introduction

Plant-microbe interactions (PMIs) encompass a wide range of ecological relationships that play a crucial role in shaping plant health, productivity, and resilience. These interactions can be beneficial, like those involving arbuscular mycorrhizal fungi, nitrogen-fixing rhizobia, and plant growth-promoting rhizobacteria (PGPR), or they can be harmful, as seen with various pathogens [1, 2]. Beneficial microbes help plants absorb nutrients, boost growth, and alleviate stress, which can lessen the need for chemical fertilizers in agriculture [3]. On the other side, pathogenic microbes can disrupt plant functions, leading to significant crop losses and destabilizing ecosystems. Gaining a deeper understanding of these complex interactions at the molecular level is essential for developing microbiome-based strategies that promote climate-smart and sustainable agriculture. In the past, research on PMIs primarily relied on traditional methods like culture-based isolation, mutagenesis, and microscopy. While these foundational techniques have their merits, they often fall short in capturing the intricate dynamics of interactions found in natural settings [4, 5]. The heavy reliance on model organisms such as Arabidopsis thaliana can limit the ecological relevance of findings, and the functional redundancy within microbial communities can obscure the relationships between genes and their functions [6, 7]. These challenges highlight the urgent need for advanced, integrative tools that can unravel the complex signaling and metabolic networks involved. Functional genomics has stepped up as a robust framework to tackle this issue. It includes techniques like transcriptomics, proteomics, metabolomics, and epigenomics, which together provide a thorough understanding of gene function and regulation across various biological contexts [8]. Transcriptomic analyses show how hosts change their gene expression during symbiosis or infection, while proteomic studies pinpoint the microbial effectors and plant resistance proteins that shape the outcomes of these interactions [9]. Metabolomics emphasizes the role of rhizosphere signals like strigolactones and flavonoids, which help recruit microbes and bolster plant defenses [2]. The recent combination of CRISPR-Cas9 with next-generation sequencing has shifted the field from merely describing phenomena to actively analyzing their functions. Gene editing in plants has allowed researchers to confirm the roles of crucial defense regulators, such as OsSWEET13 and SlJAZ2, which enhance resistance to pathogens [10, 11, 12]. By knocking out genes in *Pseudomonas fluorescens* and *Bacillus subtilis*, scientists have uncovered the mechanisms that drive rhizosphere competence and biofilm formation [13]. This review brings together these functional genomic breakthroughs and highlights new directions—like spatial transcriptomics, single-cell genomics, and synthetic microbiome engineering—serving as a guide for the future of plant-microbe research and sustainable agriculture.

2. Functional Genomics

Toolbox in Plant-Microbe Studies has truly transformed our understanding of plant-microbe interactions (PMIs). It provides a detailed framework for unraveling the intricate biological responses that occur at cellular, tissue, and ecological levels. Traditional transcriptomics, particularly bulk RNA-seq, has greatly improved our grasp of how genes respond to microbial colonization, defense mechanisms, and nutrient signaling. For example, in *Medicago truncatula*, specific genes related to nodulation, such as ENODs and nodulins, play a crucial role in forming symbiotic relationships with rhizobia [14]. In cereals, genes associated with immunity, like PRRs and WRKY transcription factors, show increased activity during attacks from pathogens [1]. However, bulk methods often miss the spatial and cellular diversity found in tissues like roots and nodules. Thankfully, the rise of high-resolution techniques—like single-cell RNA-seq (scRNA-seq), single-nucleus RNA-seq (snRNA-seq), and spatial transcriptomics—has helped fill this gap. Recent research utilizing these advanced tools has shed light on the timing and location of gene expression during PMIs. For instance, [15] found that just 30 minutes after exposure to Nod factors, the epidermal and cortical cells of M. truncatula temporarily activated defense genes, which later decreased, suggesting a finely tuned transition from immunity to symbiosis. Earlier microdissection studies [16] and newer spatial technologies like Visium and Slide-seq further emphasize the necessity of considering spatial context when examining host-microbiome interactions [17]

Beyond just transcriptomics, the use of integrative multi-omics approaches where transcriptome data connect with proteomics and metabolomics has really deepened the understanding of how things function. For instance, proteomics has revealed some key early-response proteins, like PR proteins and ROS-detoxifying enzymes, that come into play during signaling triggered by microbes [18, 19] On the metabolomics side, it has beem discovered that certain exudates, such as coumarins and benzoxazinoids, play a crucial role in shaping the rhizosphere by attracting beneficial microbes while keeping pathogens at bay [20, 21, 22]. These metabolic signals serve as important biochemical connections between plant hosts and their microbial communities. Moreover, when mycorrhizal roots through proteomics was analyzed, it was discovered that there are upregulated phosphate transporters and redox regulators that boost nutrient uptake and help plants withstand stress [23] All in all, combining spatial transcriptomics with multi-omic datasets gives us a comprehensive view of plant-microbe interactions. This powerful toolkit not only sheds light on molecular networks but also opens up exciting possibilities for creating microbiome-optimized crops that are tailored to specific environmental conditions and genetic backgrounds.

3. Applications of Functional Genomics in Plant-Pathogen Interactions: Functional genomics has significantly deepened our understanding of how plants sense and react to pathogens on a molecular level. The plant immune system employs a two-pronged defense strategy: pattern-triggered immunity (PTI), which kicks off thanks to pattern recognition receptors (PRRs) like FLS2 and EFR, and effector-triggered immunity (ETI), which is driven by nucleotide-binding leucine-rich repeat receptors (NLRs) that identify pathogen effectors [24]. Through transcriptomics and proteomics, insight have been gaineed that both PTI and ETI responses utilize similar transcription factors (like WRKYs and MYBs), although they vary in their timing and intensity [25] Innovative tools such as CRISPR-Cas9 have helped confirm the importance of certain genes, including SWEET sugar transporters in rice, where knocking them out boosts resistance to *Xanthomonas oryzae*, and FLS2, which plays a crucial role in defending against *Pseudomonas syringae* [26] Moreover, metabolomic research has highlighted how specialized metabolites like camalexin, glucosinolates, and phenylpropanoids serve as both antimicrobial agents and immune signaling regulators [27].

Pathogen effectors are secreted proteins or RNAs that target the components of plant immunity to undermine defenses, often by mimicking host enzymes or hijacking transcriptional processes. For instance, *P. syringae's* AvrPtoB degrades FLS2 [28], while TAL effectors from Xanthomonas activate SWEET genes [29]. Structural studies have shown that effectors like AvrBs3 imitate transcription factors to directly influence gene expression [30]. In response, plants deploy NLR proteins equipped with integrated domains that act as molecular traps, such as Arabidopsis' RRS1-R, which recognizes the Ralstonia effector PopP2 [31]. Genome editing of effector binding sites, like the promoters of SWEET genes, highlights the exciting potential of effector biology in enhancing crop resistance. The coevolution between hosts and pathogens has played a crucial role in shaping the architecture of resistance genes (R genes) and the diversity of effectors. NLR genes, for instance, often undergo rapid diversification, gene duplications, and positive selection, as observed in plants like Arabidopsis and rice [32]. Pathogens such as *Phytophthora infestans* have what's known as "two-speed" genomes, evolving their effectors in regions that are rich in repeats and highly adaptable [33]. The dynamics of coevolution—whether it's an arms race or trench warfare—leave behind genomic traces of balancing selection and adaptive trade-offs [34]. Additionally, epigenetic mechanisms play a role, with transposable elements located near R genes fostering diversity, while pathogens may silence their effectors to avoid detection [35]. Thanks to integrative tools like GWAS, RenSeq, and pan-genomics, we can now pursue precision breeding aimed at achieving durable, broad-spectrum resistance [36, 37].

4. Functional Genomics in Plant-Symbiont and Beneficial Microbe Interactions: Functional genomics has made remarkable strides in deepening our understanding of the mutualistic relationships between plants and microbes, especially in symbioses involving rhizobia, arbuscular mycorrhizal fungi (AMF), endophytes, and plant growth-promoting rhizobacteria (PGPRs). These beneficial partnerships are essential for enhancing plant productivity, resilience, and overall soil health. In the rhizobium-legume symbiosis, flavonoids produced by plants kickstart the expression of rhizobial nod genes through NodD regulators, leading to the production of Nod factors that are recognized by the host's LysM receptors (NFR1/5). This recognition sets off a cascade of calcium signaling and activates transcription factors like ERN1 and NSP1/2 [38, 39].

This cascade plays a crucial role in orchestrating nodulation genes like ENOD11. When it comes to low-oxygen conditions in nodules, bacteria regulate their functions through systems like FixLJ and FnrN to ensure nitrogenase works optimally. On top of that, rhizobial quorum-sensing through RhiRI boosts competitiveness and helps in forming infection threads. Thanks to CRISPR/Cas9 tools, we can now fine-tune the genetics of both hosts and rhizobia, leading to better symbiosis and stress adaptation. This highlights the intricate coevolution between plant transcriptional programs and bacterial signaling networks. Arbuscular mycorrhizal fungi, such as *Rhizophagus irregularis*, create a lipid-based nutrient exchange with the roots of their host plants. To facilitate fungal growth, plants release palmitic acid (C16:0) through enzymes like FatM, RAM2, and ABC transporters (STR/STR2), all under the regulation of RAM1 [40]. If lipid biosynthesis genes are disrupted, as seen in FatM or RAM2 mutants, it leads to issues with arbuscule formation and colonization [41]. The expression of phosphate transporters, like PT4, is closely associated with cells containing arbuscules, further emphasizing the metabolic coordination between the host and fungi. Genomic studies on ectomycorrhizal fungi, such as Laccaria bicolor, have uncovered a variety of secreted effectors (like MiSSP7) that help suppress host defenses by stabilizing JAZ6, ensuring compatibility with the fungus [42] Endophytes and plant growth-promoting rhizobacteria (PGPRs) play a significant role in modulating plant physiology by solubilizing nutrients, regulating hormones, and helping plants cope with stress. For example, Azospirillum is known for fixing nitrogen, while Bacillus amyloliquefaciens FZB42 produces auxins, solubilizes phosphate, and synthesizes antibiotics [43] These microbes can influence the hormone pathways in their host, with certain strains producing IAA, cytokinins, and ACC

Functional genomics has shed light on how certain bacteria influence defense priming. For instance, *Paenibacillus polymyxa* and *Azospirillum brasilense* kickstart the activation of both growth and defense genes in *Arabidopsis thaliana* [44]. Meanwhile, plant growth-promoting rhizobacteria (PGPRs) like *Pseudomonas fluorescens* release DAPG to ward off pathogens [45] while others produce chitinases and glucanases that are effective against Fusarium species. The ever-changing assembly of plant microbiomes is influenced by factors such as root structure, host genotype, and the composition of exudates. Interestingly, it's the convergence of functional traits, rather than just taxonomic similarities, that drives microbial selection across various crops like maize, tomato, and pea [46] For example, traits like root diameter can affect colonization by creating oxygen gradients and retaining exudates [47] while compounds such as glycerol and α-ketoglutarate are linked to microbial diversity. Metagenome-wide association studies (mGWAS) have pinpointed quantitative trait loci (QTLs) in tomatoes that are associated with microbial recruitment and nutrient cycling [48]. In rhizoplane metagenomes, functional gene enrichments related to motility, chemotaxis, and nutrient acquisition are prevalent, as observed in cucumber and wheat [49] this highlights the fact that microbial functionality plays a crucial role in successful colonization and the establishment of symbiotic relationships.

5. Advances in Single-Cell and Spatial Omics in PMI Studies: Recent breakthroughs in spatial transcriptomics and single-cell omics have truly transformed how plant-microbe interactions (PMIs) can be studied. These innovations allow researchers to pinpoint gene expression profiles with an incredible level of spatial and cellular detail. They offer a vital perspective on the cellular and subcellular diversity of host responses, providing high-resolution insights into the intricate molecular conversations between plants and their associated microbes, whether they are helpful symbionts or harmful pathogens. Spatial transcriptomics (ST) has become a game-changer by preserving tissue architecture while mapping gene expression across specific spatial regions. This approach addresses the shortcomings of bulk RNA sequencing, which tends to average out transcriptional signals across mixed tissues, obscuring the activities of specific cell types [50] With ST, researchers can pinpoint transcriptional hotspots during microbial colonization or immune responses. For example, a groundbreaking study on *Medicago truncatula* utilized spatial transcriptomics and single-nucleus RNA sequencing (snRNA-seq) to reveal distinct cell populations within root cortical layers that interact with *Rhizophagus irregularis*. This research identified arbuscule-containing cells that showed heightened expression of symbiosis-related genes like MtPT4, effectively linking spatial gene expression patterns to the exchange of nutrients in symbiosis. In a similar vein, high-resolution ST mapping in wheat roots has broadened the application of these tools to non-model crops, uncovering conserved gene expression programs across cereals and Arabidopsis, especially in epidermal and cortical tissues. Additionally, soybean nodules analyzed through integrated snRNA-seq and ST revealed transitional transcriptomic states in both infected and uninfected cells, providing insights into the distinct cellular functions during nodule development and nitrogen fixation [51].

6. Synthetic Biology and Functional Validation Approaches: Synthetic biology is shaking up the world of plant-microbe interactions (PMI) by allowing us to design, tweak, and validate microbial traits that boost plant growth, resilience, and overall health. One of the standout innovations in this field is the creation of synthetic microbial communities, or SynComs. These communities are made up of carefully selected strains that are informed by genomic data, and they work to replicate or enhance the functions of natural microbiomes, such as nutrient mobilization, phytohormone production, and pathogen suppression [52]. For instance, SynComs that include *Bacillus subtilis*, Trichoderma, and Aspergillus have been shown to significantly enhance pepper growth by secreting IAA, promoting siderophore activity, and inducing plant defenses. However, factors like environmental conditions and competition among microbes can hinder success in the field, which is why we need AI-driven designs to ensure the stability and effectiveness of these SynComs [53]. Reverse genetics, particularly through techniques like CRISPR/Cas9 and transposon mutagenesis, is essential for validating gene functions within SynComs and their host systems. By knocking out specific biosynthetic genes in *Bacillus subtilis* and *Pseudomonas fluorescens*, researchers have gained insights into how these microbes contribute to immunity and nutrient uptake [43, 53]. Moreover, engineered biosynthetic pathways have enabled microbes such as *Cupriavidus pinatubonensis* and yeast to develop inducible hormone production systems that aid in root development and help them adapt to stress [54, 55]. These synthetic strategies are paving the way for PMI research to evolve into a predictive, engineering-focused discipline, opening up exciting possibilities for sustainable and eco-friendly agriculture

7. Case Studies and Success Stories

Model systems like *Arabidopsis thaliana*, *Medicago truncatula*, and *Oryza sativa* have significantly pushed the boundaries of functional genomics in plant-microbe interactions. For instance, in Arabidopsis, studies using synthetic communities (SynComs) have shown that plant exudates, such as coumarins, can influence the microbiome's makeup, promoting beneficial Pseudomonas strains. In Medicago, researchers have used spatial transcriptomics and CRISPR to uncover how lipid biosynthesis and phosphate transporter genes play a role in arbuscular mycorrhizal symbiosis. Meanwhile, in rice, SynComs derived from intercropping systems have enhanced root architecture and nutrient absorption, even in low-input environments [56]. Translational genomics bridges these discoveries to real-world crop improvements. Techniques like single-cell genomics and genome-wide association studies (GWAS) have pinpointed microbiome-associated quantitative trait loci (QTLs) and identified beneficial taxa such as Pantoea and Pseudomonas that stick around [57]. Additionally, engineered SynComs have been employed to lessen disease severity in rice [58] Projects like the Crop Microbiome Cryobank and genomics-guided breeding are now working to fine-tune host-microbe compatibility, aiming to boost resilience and sustainability in agriculture.

8. Challenges and Knowledge Gaps

Even though great strides have been made in understanding plant-microbiome functional genomics, there are still some pretty big hurdles to overcome before this knowledge can effectively be applied in the real world. One of the main challenges is functional redundancy, where various microbes take on similar roles, which makes it tough to pinpoint specific traits to individual taxa [56]. On top of that, pleiotropy adds another layer of complexity to genetic mapping, since plant traits like root structure can affect multiple microbial functions at once. When it comes to connecting host genotypes to microbiome traits through microbiome genome-wide association studies (mGWAS), we hit some limitations due to low heritability and the polygenic nature of traits. Often, host SNPs account for less than 1% of the variation in the microbiome, and results can be muddled by environmental factors and population structures [59]. Lastly, we still face challenges with data integration and annotation. Incomplete metagenome-assembled genomes and uncharacterized genes can really throw off our ability to predict functions accurately [60] while advanced tools like Seurat and MOFA+ show promise, they demand a lot of computational power and aren't fully optimized for plant microbiome datasets yet.

9. Future Directions and Emerging Frontiers

The field of plant-microbe interactions (PMI) is advancing at a breakneck pace, thanks to breakthroughs in AI, systems biology, and synthetic genomics. Nowadays, AI and machine learning are stepping up to the plate, helping us decode complex multi-omic datasets, automate gene annotation, and even predict how phenotypes connect with microbiomes. Tools like MOFA+ and LIGER are making it easier to integrate transcriptomic and spatial data [61]. With predictive modeling frameworks such as KGHIV and MetConSIN, we can forecast microbial functions and host-microbe interactions, which is a game-changer for designing synthetic communities [62]. Synthetic biology is also paving the way for microbiome engineering through techniques like CRISPR editing, stress-inducible circuits, and seed coatings that boost resilience and nutrient efficiency [63] While challenges like functional redundancy and the limited mapping of genotypes to microbiomes still exist, AI and modeling tools are helping to close these gaps. The merging of genomics, spatial biology, and microbial design holds great promise for climate-smart agriculture, highlighting the need for interdisciplinary collaboration to create sustainable, high-yield crop systems.

Conclusion

Functional genomics has really changed the game in plant-microbe interaction (PMI) research, giving us a deeper understanding of how plants defend themselves, form symbiotic relationships, and interact with their surrounding soil environment. With tools like transcriptomics, CRISPR-Cas gene editing, and systems biology, we can now decode the intricate conversations happening between plants and microbes, which helps us better predict and influence how plants respond to threats. Research into the relationships between rhizobia and legumes, as well as arbuscular mycorrhizal fungi (AMF), has uncovered key signaling pathways that support these beneficial partnerships. Thanks to advancements in spatial transcriptomics and single-cell omics, we can analyze gene expression at the cellular level during infection and colonization. Synthetic biology is also stepping in with engineered SynComs and new biosynthetic pathways to boost crop resilience. Although we still face challenges like functional redundancy and mapping the genotype-microbiome interactions, AI models and machine learning are helping us tackle these issues. By applying what we learn from model species like Arabidopsis to important crops, we’re driving genomics-informed breeding forward. In the end, working together across disciplines is essential for creating sustainable, high-yielding crop-microbiome systems that balance molecular precision with ecological health.

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