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## CURRENT REVIEW

# 2000-2019: Twenty Years of Highly Influential Publications in Molecular Plant Immunity

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**Molecular plant immunity is a dynamic research field that broadly addresses how plants interact with their associated organisms and defend themselves against pests and pathogens. Here, we aimed at providing readers with a snapshot of influential molecular plant immunity research by identifying and analyzing 170 highly influential publications in molecular plant immunity (hereafter called HIPPYs) published in this field between 2000 and 2019. Our analysis draws a broad analytical knowledge of influential scientific advances in the field as well as of the research community that made them. We notably show that HIPPYs are shared by a small, structured, and connected research community. The HIPPYs address coherent research questions using a handful of key model objects (i.e., organisms or molecules) and report findings and concepts that contribute to our integrated understanding of the molecular interactions between plants and their associated organisms. Our ‘HIP in’ (‘highly influential publication in’ ...) method is easily transposable to other large research areas and may help early career researchers to gain a broader knowledge of their field of interest.**

*Keywords:* *Arabidopsis thaliana*, bibliometric pipeline, microbe, plant defense, plant pathology, symbiont, Web of Science

Molecular plant immunity is a dynamic research field that studies how plants defend themselves against pathogens, with the ultimate goal to improve plant health and achieve sustainable agriculture (Michelmore et al. 2017). The field can be viewed as a subdiscipline of plant molecular biology intersecting with microbiology (and to a lesser extent entomology) and is also often referred to as molecular plant pathology, plant biotic inter-

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actions, plant-pathogen interactions, or molecular plant-microbe interactions (prominent journals or journal subsections including these terms in their name are listed in Supplementary Table S1). In the early 2000s, the field coalesced around key conceptual models that guided the coordinated investigations of the molecular basis of the interactions between plants and their associated organisms (Jones and Dangl 2006). An impressive body of knowledge has built up over the last 20 years, with discoveries and conceptual insights scattered through more than 80,000 research articles and reviews (discussed below). Gaining an expert, broad conceptual understanding of such a large research field is complex and daunting, especially for early career scientists who may not know how to select and analyze key influential publications.

The number of citations that an article receives informs on its influence among a community of active publishing researchers. As an article-based metric, it better indicates the influence of a given paper than journal-based metrics (e.g., a journal impact factor), which indicate only on the global influence of the journal (Pal and Rees 2022). Importantly, papers published in high-profile journals, by renowned authors (likely due to the so called ‘Matthew effect’), or by male authors tend to receive more citations, a phenomenon globally known as ‘citation bias’ (Dworkin et al. 2020; Urlings et al. 2021). Due to this phenomenon, a citation rate cannot be considered as an absolute measure of the quality of a paper.

This paper aims at providing readers with a snapshot of influential molecular plant immunity research. To do so, we identified and analyzed 170 highly influential (i.e., highly cited) publications in molecular plant immunity (hereafter called HIPPYs) published between 2000 and 2019 (Fig. 1A). We designed and executed our analytical pipeline to answer the four following questions. Who publish HIPPYs (e.g., which institutions, journals, countries)? What specific research topics do HIPPYs address? What specific model objects (i.e., organisms or molecules) do HIPPYs use? How are HIPPYs and their research ecosystem structured? Altogether, our study offers a comprehensive analytical overview of the most influential recent scientific advances in molecular plant immunity as well as the research community that shared them.

## A BIBLIOMETRIC PIPELINE IDENTIFIES 170 HIPPYs

To identify HIPPYs, we designed a Web of Science–based bibliometric pipeline aimed at identifying the most-cited molecular plant immunity research articles and reviews published between 2000 and 2019 (Fig. 1A; Supplementary Fig. S1). Briefly, we performed three successive searches using the keywords ‘plant immunity’, ‘plant pathogen’, and ‘plant defense’ throughout seven

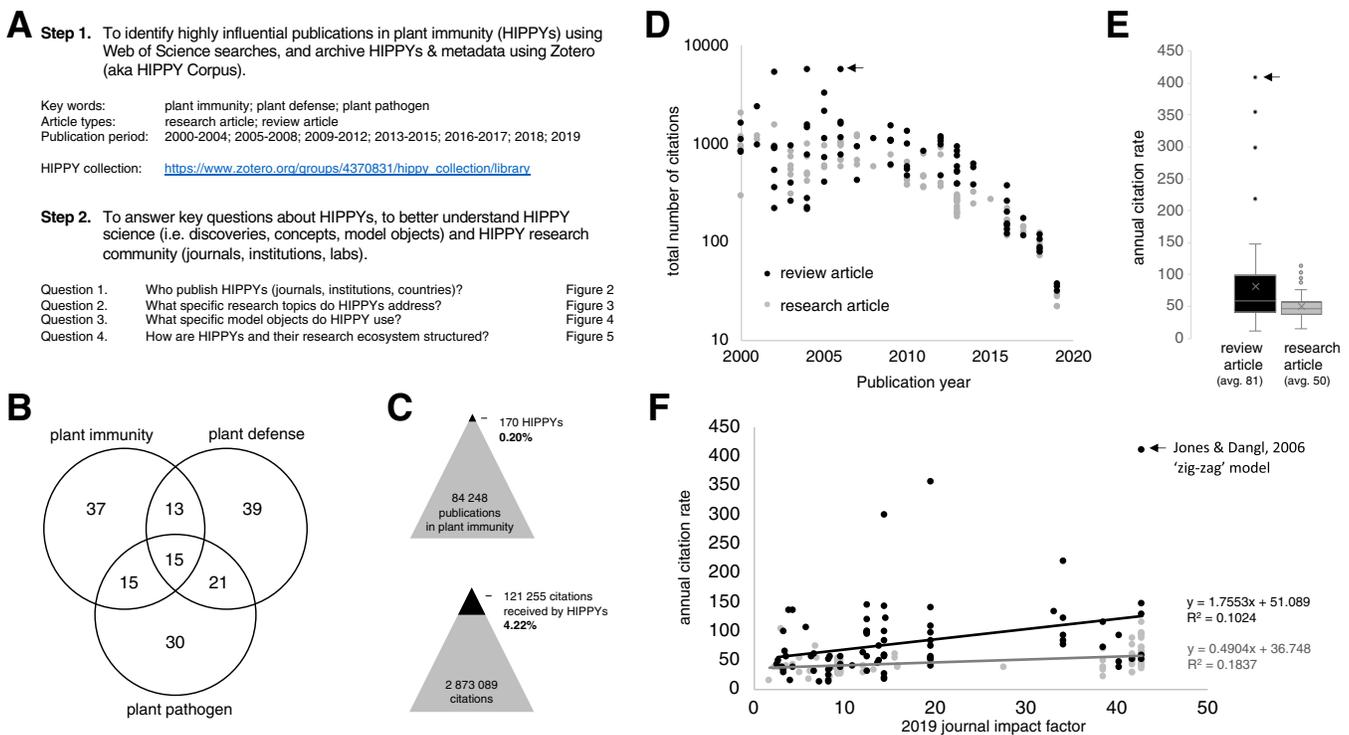
time periods (2000 to 2004, 2005 to 2009, 2010 to 2012, 2013 to 2015, 2016 to 2017, 2018, and 2019) and selected for each keyword–time period combination the most cited research articles or reviews, irrespectively of the journal (and its impact factor) in which they appeared (details are provided in Supplementary Methods S1, section A). Those searches identified, in total, 170 nonredundant HIPPYs (90 research articles and 80 review articles) (Fig. 1B). We archived the full text and metadata of the HIPPYs in a Zotero web folder (Supplementary Dataset S1); a public version of the folder (that we named ‘HIPPY collection’) containing only the publication metadata (for copyright compliance) is accessible at the web address below.

The 170 HIPPYs represent only 0.2% of all the research articles and reviews published in the field of molecular plant immunity between 2000 and 2019, but they account for 4.22% of the citations in this field over the same period (Fig. 1C). HIPPYs published in 2019 received on average  $29 \pm 6$  citations, while HIPPYs published between 2000 and 2010 received on average 1,044 citations (ranging from 217 to 5,730) (Fig. 1D). On average, HIPPYs receive 64 citations per year (i.e., annual citation rate of 64); reviews showing, on average, a higher cita-

tion rate than research articles (81 vs. 50) (Fig. 1E). The HIPPY with both the highest number of total citations (5,730) and the highest annual citation rate (409) is the Jones and Dangl [2006] review that presented the seminal ‘zig-zag model’ of the plant immune system. Interestingly, HIPPY annual citation rates do not correlate with the impact factor of the journal in which they were published (Fig. 1F). We conclude that the HIPPYs are influential publications that are likely to present recent seminal discoveries and dominant concepts in molecular plant immunity and, thus, constitute a suitable resource to build a snapshot of influential research achievement (and associated communities) in this field.

## A HANDFUL OF ACADEMIC ACTORS PUBLISH MOST OF THE HIPPYs

To apprehend the HIPPY research ecosystem, we analyzed the metadata of HIPPYs to identify the main journals, institutions, and countries that published them. In total, HIPPYs were published by 52 journals, by over 90 institutions (to which were affiliated 165 unique corresponding authors), and by



**Fig. 1.** Overview of the 170 highly influential publications in plant immunity (HIPPYs). **A**, Overview of the two-step analytical pipeline used in this study. In Step 1, we identified 170 HIPPYs by using advanced searches on the Web of Science portal using various keywords, article type, and publication period parameters (details can be found in Supplementary Methods S1, section A). We then collected and archived the PDF version and metadata of the 170 HIPPYs into a Zotero folder (available from the HIPPY collection website) according to the search output. Then, in step 2, we analyzed the HIPPY collection by answering key questions, with the aim to better understand both the scientific knowledge brought to readers by HIPPYs (i.e., the science) and the structure of the research community behind HIPPYs (i.e., the people, labs, and institutions). **B**, Venn diagram showing the overlapping contribution of the three keyword searches ('plant immunity', 'plant defense', and 'plant pathogen') to the HIPPY collection. **C**, Share of the HIPPYs within the plant immunity literature, in terms of number of publications (upper panel) and total number of citations (lower panel). HIPPYs represent approximately 0.20% of the publications in the field of plant immunity (170 HIPPYs among 84,248 publications) but account for 4.22% of the total number of citations (121,255 citations among a total of 2,873,089). The surface of the black triangles is proportional to the indicated percentage. **D**, Scatterplot displaying the number of total citations of individual research article HIPPYs (gray) or review HIPPYs (black), according to their year of publication. The total number of citation value was extracted from the Web of Science portal (accessed in June 2020). An arrow points to the HIPPY with the highest total number of citations (5,730) in 2006. **E**, Boxplot indicating the annual citation rate (i.e., average number of citations per year) of research article HIPPYs (gray) or review HIPPYs (black). The handful of boxplot outliers are indicated as dots. The number below each boxplot (as well as the cross superimposed on the boxplot) indicate the average value of annual citation rate (avg. 81 for review articles, avg. 50 for research articles). **F**, Scatterplot displaying the annual citation rate of individual HIPPYs according to the value of the 2019 impact factor of the journal in which the HIPPYs were published. Black and gray dots indicate review and research articles, respectively. Linear trendlines are indicated for each article type along with trendline equations and  $r$  squared values (black, review article; gray, research article). In C, D, and E, each dot indicates a single HIPPY, and the arrow indicates the HIPPY with the highest total number of citations and annual citation rate (i.e., the 2006 review article by Jones and Dangl that presented the zig-zag conceptual model of the plant immune system). The raw data used to build this figure are available in Supplementary Dataset S1 (columns A to H).

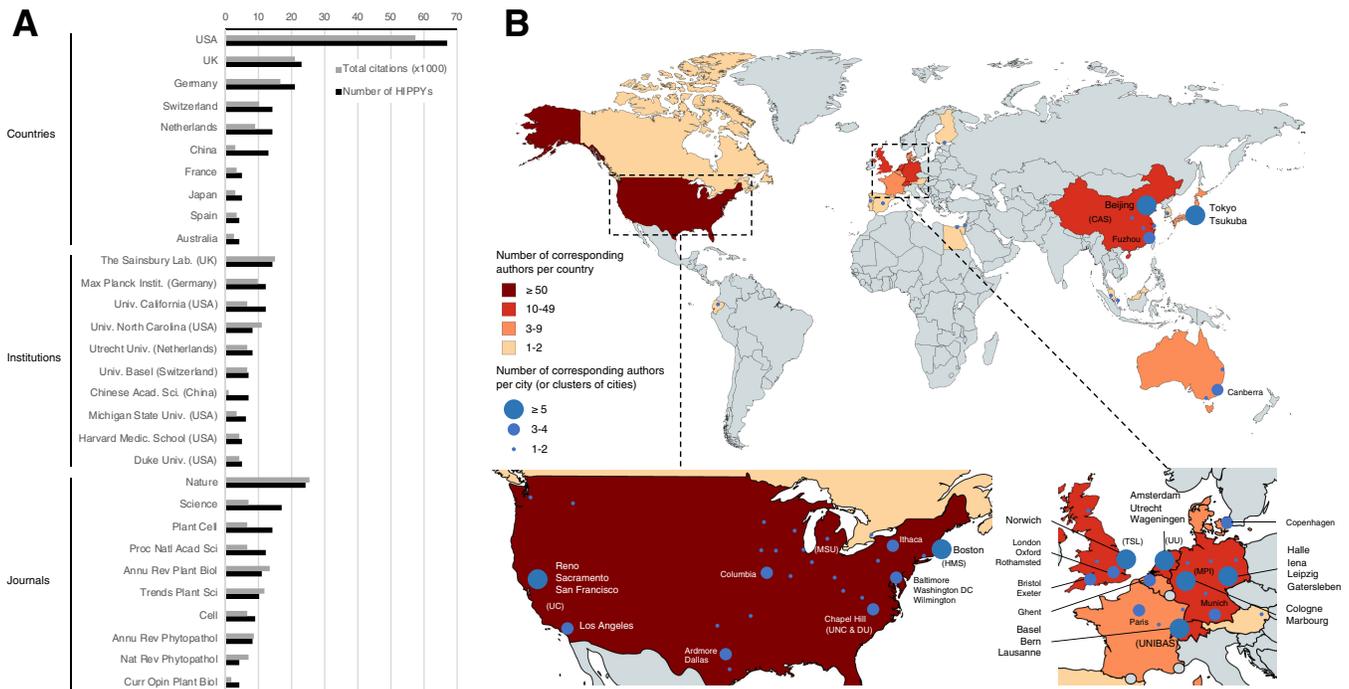
21 countries (Supplementary Dataset S1, columns I to N; Supplementary Methods S1, section B). Interestingly, a small number of those journals, institutions, and countries contributed most of the HIPPYs (Fig. 2A). Indeed, only six journals (including *Nature*, *Science*, and *Cell*) published over half of the HIPPYs, and only six countries (the United States, Germany, the United Kingdom, Switzerland, The Netherlands, and China) contributed over 80% of the HIPPYs. The ten institutions that published the most HIPPYs (accounting for >40% of the HIPPY collection) are all based in these six countries. Among those ten institutions, three published ten or more HIPPYs, The Sainsbury Laboratory (U.K.), the Max Planck Institute (Germany), and the University of California (U.S.A.).

To identify cities and larger urban areas (hereafter employment areas) from which HIPPYs originate, we mapped the laboratories of the corresponding authors of HIPPYs worldwide (Fig. 2B). This analysis identified 76 employment areas (including 26 in the United States and 23 in Europe) in which at least one HIPPY corresponding author has their laboratory. Interestingly, nine employment areas located in Europe (five), in the United States (two), in China (one), or in Japan (one) showed over five HIPPY-publishing laboratories. For instance, in Europe, such areas comprise the city of Norwich (U.K., host of The Sainsbury Laboratory and the John Innes Center) or the urban area of Amsterdam, Utrecht, and Wageningen (The Netherlands, host of the Utrecht University and the Wageningen University) (Fig. 2B). To conclude, this analysis shows that only a handful of actors publish HIPPYs, including employment areas that are likely to host a dense research ecosystem in molecular plant immunity.

Also, the fact that a significant share of the HIPPYs appears in generalist journals highlights the high visibility of molecular plant immunity as a research field.

## HIPPYs ADDRESS NINE MAIN RESEARCH QUESTIONS

To get an analytical understanding of HIPPYs, we aimed at identifying the research questions they address. To do so, we performed iterative readings of all the manuscripts combined with keyword tagging to categorize HIPPYs into topics and subtopics (Fig. 3A; Supplementary Dataset S1, columns O to R; Supplementary Methods S1, section C). This analysis grouped the 170 HIPPYs into nine main topics as follows: i) pathogen recognition (25 HIPPYs; how do plants sense pathogens?), ii) immune signaling (24 HIPPYs; how do plants signal pathogen recognition?), iii) phytohormonal modulation (33 HIPPYs; how do hormones modulate immune signaling?), iv) gene regulation (nine HIPPYs; what is the genetic program of defense, and how is it activated?), v) defense responses (21 HIPPYs; how do plants effectively fend off pathogens?), vi) pathogens and pathogenicity (20 HIPPYs; how do pathogens manipulate and colonize host plants?), vii) microbiota and symbionts (22 HIPPYs; how do plants and their associated microbes interact?), viii) general reviews (15 HIPPYs; how do we conceptually understand plant immunity as a whole?), and ix) translational research (one HIPPY; how to develop better plants for agriculture? [Fig. 3A]). We refer readers to the Supplementary Text S1 file for a comprehensive and detailed analysis of the HIPPY scientific content for



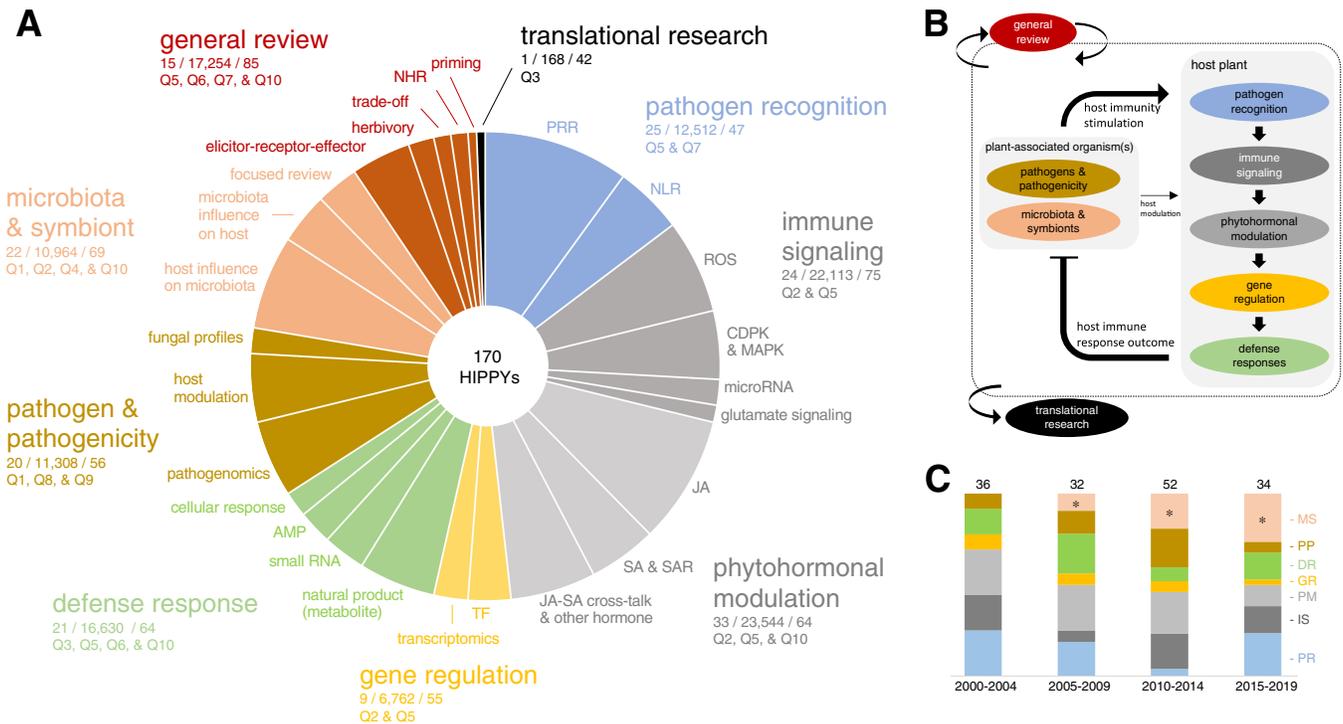
**Fig. 2.** A handful of countries, cities, institutions, and journals publish most of the highly influential publications in plant immunity (HIPPYs). **A**, Bar chart showing the ten countries, institutions, and journals that published the most HIPPYs. Countries, institutions, and journals rank from top to bottom according to the number of HIPPYs they published. For each country, institution, or journal, the number of HIPPYs and citations (in thousands) are indicated with black and gray bars, respectively. Only countries and institutions of the first-mentioned affiliation of the corresponding authors were considered for this analysis. **B**, Color-coded world map indicating the countries and cities (or cluster of cities) where HIPPY corresponding authors are primarily affiliated. The map was created MapChart (available online) and was then customized using Microsoft PowerPoint. Data were extracted directly from the publication metadata, then compiled, and were analyzed into Microsoft Excel. Noteworthy, countries with over three HIPPY corresponding author (brown, red, or orange on the map) belong to the group of countries that spend a high percentage (2.5% on average) of their gross domestic product on research and development in general (Our World in Data website). TSL = The Sainsbury Laboratory, MPI = Max Planck Institute, UC = University of California, UU = Utrecht University, UNC = University of North Carolina at Chapel Hill, UNIBAS = University of Basel, MSU = Michigan State University, DU = Duke University, HMS = Harvard Medical School, CAS = Chinese Academy of Science. The raw data used to build this figure are available in Supplementary Dataset S1 (columns I to N).

each topic, and to Box 1 for a comparative analysis between the HIPPYs research questions and the recently published Top 10 unanswered questions in molecular plant-microbe interactions (Harris et al. 2020).

Each of the nine topics comprises one to five subtopics that pertain to a more specific research question. For instance, the phytohormonal modulation topic comprises three subtopics, jasmonic acid (JA) (how does the JA signaling pathway function?), salicylic acid (SA) and systemic acquired resistance (how does the SA signaling pathway function at different spatial scales?), and JA-SA cross-talk and other hormones (how does the cross talk between different hormones affects immune signaling outcome?). We positioned these nine topics into a simplified conceptual framework of molecular plant immunity research, that considers two topics focused on plant-associated organisms (pathogens and pathogenicity as well as microbiota and

symbionts), five focused on host plants (pathogen recognition, immune signaling, phytohormonal modulation, gene regulation, and defense responses), and two overarching topics that produce general concepts (gene regulation) and innovations (translational research) (Fig. 3B).

To identify potential research trends in influential molecular plant immunity research, we analyzed the evolution of the size of the topics (in terms of number of HIPPYs) between 2000 and 2019, by periods of five years. We excluded the general reviews and translational research topics from this analysis, as they do not inform on research trends. This analysis revealed that most topics gathered HIPPYs in all time periods considered, with no clear trend of linear expansion or contraction between 2000 and 2019 (Fig. 3C). One striking exception is the topic microbiota and symbionts, which gradually expands over the four periods considered, from zero HIPPYs for the 2000 to 2004 period to



**Fig. 3.** Highly influential publications in plant immunity (HIPPYs) address nine main research topics and 27 subtopics. **A**, Pie chart displaying the nine main topics and 27 subtopics addressed by HIPPYs, color-coded as follows: pathogen recognition (PR) (light blue), immune signaling (IS) (dark gray), phytohormonal modulation (PM) (light gray), gene regulation (GR) (gold), defense response (DR) (light green), pathogen and pathogenicity (PP) (dark yellow), microbiota and symbiont (MS) (light orange), general review (dark red), and translational research (black). Subtopics are indicated as separated pie segments within each main topic. For each topic, the number of HIPPYs, the total number of citations, and the average annual citation rate are indicated (e.g., 25 / 12,512 / 47) as well as the relevant Top 10 unanswered questions in MPMI (e.g., Q1). The design of the topics and subtopics as well as the assignment of the HIPPYs to them was based on multiple and iterative expert reading and keyword association of the HIPPY collection. NLR = NOD-like receptor, PRR = pattern-recognition receptor, MAPK = mitogen-activated protein kinase, ROS = reactive oxygen species, CDPK = calcium-dependent protein kinase, SA = salicylic acid, JA = jasmonic acid, SAR = systemic acquired resistance, AMP = antimicrobial protein, NHR = nonhost resistance, TF = transcription factor. **B**, Conceptual framework of plant immunity integrating the nine main topics. The nine topics are shown as ovals, with the same naming and color code as in A. Topics are grouped according to their primary study object, the host plant (right) or the plant-associated organism (left). The five topics that pertain to the host plant are organized from top to bottom, as a simplified representation of the events that can occur sequentially during an immune response. Plant-associated organisms can be beneficial symbionts (often existing as host-associated complex communities referred to as microbiota and symbionts) or deleterious organisms (i.e., microbial pathogens or herbivorous invertebrates, labeled pathogens and pathogenicity), which both modulate host-plant structures and functions to promote colonization. Host plants (right) first recognize their associated organisms (pathogen recognition), then signal this recognition (immune signaling). This signaling, which can be modulated by phytohormones (phytohormonal modulation), results in the regulation of gene expression (i.e., alteration of the genetic program, gene regulation). In turn, this regulation triggers effective immune responses (i.e., host immune response outcome, defense responses) that limit or contain the progression or proliferation of various organisms on the host plant. Broad literature reviews (general reviews) feed on discoveries to build conceptual models that describe the above-mentioned phenomena, thus providing research communities with strong conceptual frameworks that shape research investigations. Applied research (translational research) builds on the fundamental research to innovate and develop products for agriculture. **C**, Percent stacked bar chart displaying the evolution of the relative size of each topic over time. The size of a given stack correlates with the percentage of all HIPPYs published from the indicated time period that were assigned to the topic. Color code and acronyms are the same as in A. The ‘general reviews’ and ‘translational research’ topics were not included in the analysis, because the general review topic is not informative regarding research trend evolution and the translational research topic comprises a single HIPPY. Numbers above the bars indicate the total number of HIPPYs for each time period. Asterisks indicate the microbiota and symbiont topic, which increases in size over time. The raw data used to build this figure are available in Supplementary Dataset S1 (columns O to R).

nine for the 2015 to 2019 period (i.e., 26% of the HIPPYs published over this period). A similar pattern of increase can be seen while performing a keyword search using ‘plant microbiota symbiont’ on the PubMed search engine, suggesting that the increase of HIPPYs from the microbiota and symbiont topic mirrors a general trend in the scientific literature. To conclude, this set of analyses shows that HIPPYs address fundamental research questions that pertain to various well-defined aspects of the molecular interactions between plants and their associated organisms. HIPPY topics are stable over time, indicative of a mature research field, except for the striking rise of the microbiota and symbiont topic.

## HIPPYS FOCUS ON A HANDFUL OF KEY MODEL ORGANISMS AND MOLECULES

Academic research in life sciences often relies on shared common objects that serve as models. Such objects can be molecules (e.g., FLS2, a model receptor kinase) or organisms (e.g., *Arabidopsis thaliana*, the model plant). To get a snapshot of the most-used objects in HIPPYs, we performed a word occurrence analysis of the title and abstracts of the HIPPYs combined with word cloud generation. To do so, we performed an iterative text enrichment for all words that refer to specific molecules or molecular families (e.g., ‘FLS2’ or ‘protein’), as well as words that refer to specific organisms or groups of organisms (e.g.,

*thaliana*, fungus, or symbiont [Supplementary Fig. S2; Supplementary Datasets S1, columns S and T, and S2; Supplementary Methods S1, section D]). This analysis allowed building a word cloud comprising the 200 most frequently used words referring to living or molecular objects in the titles and abstracts of HIPPYs (Fig. 4A). The largest words in the cloud highlight the prominence of key groups of plant-associated organisms (e.g., bacteria, fungi, *Pseudomonas*), model plants (e.g., *A. thaliana*, rice), nonproteinaceous molecules (e.g., jasmonate, hormones, RNA), or proteins (e.g., NPR1, FLS2). To gain a more accurate view of the molecules and organisms central to each topic, we built word clouds for each topic, except for the general review and translational research topics (Supplementary Fig. S2B). Some words, such as pathogen, occurred in all clouds, while others showed a topic-specific enrichment (e.g., jasmonate, SA, and JA, as well as kinases, MAPK, and ROS for the phytohormonal modulation and immune signaling topics, respectively).

To complement the above-described approach, we executed an expert reading of the HIPPYs to determine the key plant and plant-associated organisms emphasized (if any) by individual HIPPYs. This analysis first revealed that nearly 75% of the HIPPYs highlight at least one organism (or one group of organisms; Supplementary Dataset S1, columns U and V). On one hand, we determined that 101 HIPPYs highlighted at least one plant species or plant group (Fig. 4B). Nearly 80% of those HIPPYs highlight *A. thaliana* as a central experimental model; the remaining 20% emphasize cereals, Solanaceae, or less-studied angiosperms (i.e., flowering plants). On the other hand, we determined that 98 HIPPYs highlight at least one plant-associated species or taxonomic group (Fig. 4C). Nearly 60% of those HIPPYs highlight bacteria (alone or with an additional taxonomic group, often filamentous pathogens) and nearly 20% highlight fungi (predominantly ascomycetes); the remaining 20% emphasize herbivorous invertebrates (mostly insects), viruses, and oomycetes. The proportion of these groups remained overall stable between 2000 and 2019 (Supplementary Fig. S3), suggesting that investigations in the field rely on well-established model organisms. Finally, we built a top five list of the most prominent i) plant species, ii) plant-associated species, iii) nonproteinaceous molecules, and iv) proteins used as key objects by HIPPYs (Fig. 4D). Globally, these analyses revealed the prominence i) of *A. thaliana*, *Pseudomonas syringae*, and *Botrytis cinerea* as central model organisms, ii) of phytohormones and ROS as highly investigated small molecules, and iii) of immune receptors and signaling kinases as highly investigated protein families.

## OVER 60% OF THE HIPPYS ARE CONNECTED TO AT LEAST ONE OTHER HIPPY

We surmised that key scientific discoveries and concepts gain high visibility (and become highly influential) when they are shared, strengthened, discussed, and contextualized by series of papers (i.e. connected publications). Three examples of links that can exist between academic publications are i) back-to-back or simultaneous papers sharing a similar discovery or literature review (i.e., coinciding papers), ii) discoveries followed by other studies reinforcing them (i.e., follow-up studies), and iii) discoveries followed by reviews that contextualize them and highlight their significance for a broader audience (i.e., follow-up review). To determine the level of connectivity within the HIPPY collection (i.e., determine if HIPPYs are connected with other HIPPYs), we looked for the three types of links mentioned above (coinciding papers, follow-up studies, or follow-up review) among the HIPPY collection (Supplementary Methods S1, section E). In total, we found that 108 HIPPYs (i.e., over 63% of the

### Box 1. Highly influential publications in plant immunity (HIPPYs) and the Top 10 unanswered questions in molecular plant-microbe interactions.

In 2020, Harris and colleagues established a community-sourced list of the Top 10 fundamental questions in molecular plant-microbe interactions that will likely drive research investigations in the 2020s (Harris et al. 2020). Such questions were ranked from Q1 to Q10 based on the number of votes that they received from the attendees of the 2019 International Congress on Molecular Plant-Microbe Interactions in Glasgow, U.K. To compare this Top 10 list with the nine HIPPY topics from this study, we systematically associated the HIPPYs and the topics with at least one of the Top 10 questions to which it pertains the most (Fig. 3A; Supplementary Dataset S1 [column Z]; Supplementary Methods S1 [section G]). This analysis revealed that some Top 10 questions overlap with multiple topics (e.g., Q2, ‘How does abiotic stress, such as climate change, influence plant-microbe interactions?’), associates with four different topics), whereas others overlap with one specific topic (e.g., Q8, ‘Why do some pathogens need so many effectors when others need a few?’), associates specifically with the pathogen and pathogenicity topic). Interestingly, three of the four most popular questions (Q1, ‘How do plants engage with beneficial microorganisms while at the same time restricting pathogens?’), Q3, ‘How can we translate basic research into emerging crop plants?’), and Q4, ‘How do microbe-microbe interactions affect plant-microbe interaction?’) were nearly absent from the early HIPPYs, while they started to be regularly addressed after 2010 by HIPPYs from the emerging microbiota and symbiont and translational research topics (Fig. 3C). This illustrates well the research ambition within the 2020s to tackle molecular plant immunity in a broader context and to translate findings into real-world agricultural innovations to promote crop health (Harris et al. 2020; Michelmores et al. 2017).

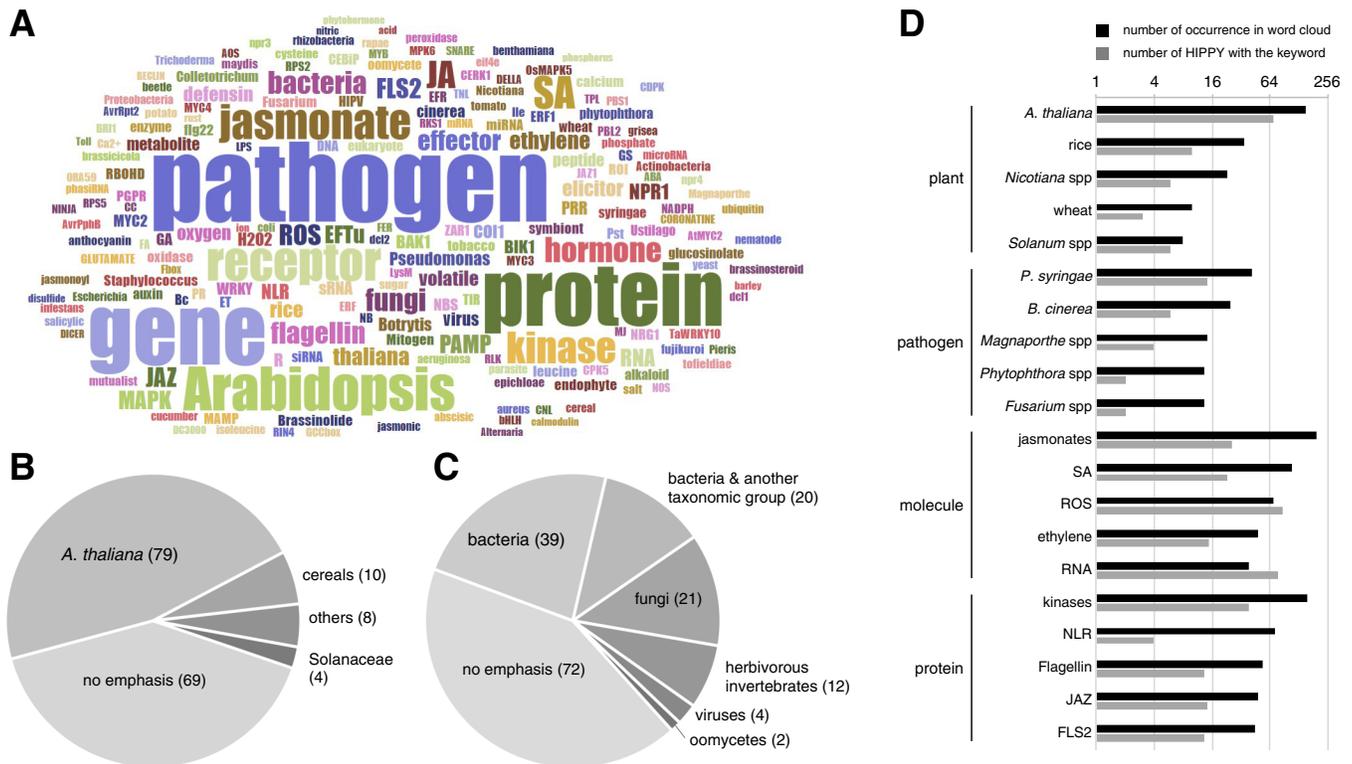
HIPPY collection) connect with at least one other HIPPY; those 108 HIPPYs form a fragmented network comprising 174 links in total (Supplementary Figs. S4A and S5; Supplementary Dataset S1, columns W to Y). The most abundant type of link was coinciding publication (49 HIPPYs), followed by follow-up review (19) and follow-up studies (16). Notably, 24 HIPPYs show multiple types of links (e.g., simultaneously coinciding papers and follow-up review). Interestingly, those highly connected papers received more citations than isolated HIPPYs (annual citation rate of 90 vs. 52 on average; the number of links positively correlating with the annual citation rate [Supplementary Fig. S6]).

We further investigated the network of connected HIPPYs for each individual topic. First, this showed that all topics contain over 40% of connected HIPPYs, indicating that all topics contain a significant share of connected HIPPYs (Supplementary Fig. S4B). Second, the majority (75%) of the links occurred between HIPPYs from the same topic (Supplementary Fig. S4C).

Interestingly, three topics (pathogen recognition, immune signaling, phytohormonal modulation) that are adjacent in our simplified framework of plant immunity show both a high proportion of connected HIPPYs (over 60%) and a high number of links (over 10) to HIPPYs from other topics, including, notably, the general review topic (Supplementary Fig. S4C). Those three highly connected topics thus appear as a hub among the HIPPYs collection. To conclude, this set of analyses revealed that more than half of the HIPPYs are connected to each other, especially within the three specific topics that address how plants recognize and modularly signal pathogen recognition.

## CROSS-CITATION ANALYSIS REVEALS HIPPY RESEARCH COMMUNITY STRUCTURATION

To evaluate the structure of the HIPPY research community, we aimed at evaluating the transfer of information between



**Fig. 4.** The highly influential publications in plant immunity (HIPPYs) focus on a limited number of model organisms and molecules. **A**, A word cloud displaying the most frequently appearing words referring to molecules (or groups of molecules) and organisms (or groups of organisms) in the title and abstract of HIPPYs. The word cloud was built using a filtered text file including the title and the abstract of all HIPPYs deprived of words that did not explicitly refer to molecules or organisms. The word cloud displays 200 words; the size of the words positively correlates with their frequency in the text file. Word colors are meaningless; they were randomly generated to assist visual word discrimination. **B**, A pie chart displaying the main plant organism (or groups of organisms) emphasized in HIPPYs. Nine HIPPYs from the *Arabidopsis thaliana* section emphasize an additional species (either a rice or a Solanaceae species). HIPPYs from the cereals section emphasize Poaceae species (rice, wheat, or maize), while HIPPYs from the Solanaceae section emphasize *Solanum* spp. (potato or tomato) or *Nicotiana* spp. HIPPYs from the other sections emphasize various angiosperm species (including barrelclover, carrot, sugarbeet, cucumber, and Fabaceae species). **C**, A pie chart displaying the main groups of plant-associated organisms emphasized in HIPPYs. Nearly half (18 of 39) of the HIPPYs from the bacteria section emphasize Pseudomonadaceae species. Nearly all (18 of 20) HIPPYs from the bacteria and another taxonomic group section emphasize filamentous pathogens (fungi or oomycetes) in addition to bacteria. More than half (13 of 21) of the HIPPYs from the fungi section emphasize ascomycetes. Three quarter (nine of 12) of the herbivorous invertebrates section emphasize insects. **D**, A bar chart displaying the five most emphasized plant species (plant), plant-associated species (pathogen), nonproteinaceous molecules (molecule), and protein or protein families (protein). The black bar indicates the total number of occurrences of various relevant keywords in the word cloud depicted in A (e.g., the words ‘*Arabidopsis*’ and ‘*thaliana*’ for the category ‘*A. thaliana*’). The gray bar indicates the number of HIPPYs identified using a keyword search in Zotero (i.e., essentially the number of HIPPYs that include the keyword in their title, abstract, or keyword sections). Items within each category are sorted top to bottom from the highest to the lowest black bar values. Specific additional keywords were considered for the following categories: *Pseudomonas syringae* (‘pst’ and ‘DC3000’), *Magnaporthe oryzae* (‘grisea’), jasmonates (‘JA’, ‘jasmonoyl’, ‘JA-Ile’, and ‘jasmonic’), SA (salicylic acid) (‘salicylate’), ROS (reactive oxygen species) (‘ROI’ and ‘H<sub>2</sub>O<sub>2</sub>’), and kinases (‘MAPK’, ‘mitogen’, ‘MPK’, and ‘CDPK’), NLR (NOD-like receptor) (‘NB-LRR’, ‘NBS-LRR’, ‘CNL’, and ‘R’ for ‘Resistance’, if used in a meaningful context), and flagellin (‘flg22’). In B and C, the number of HIPPYs is indicated between parentheses; HIPPYs from the no emphasis sections do not highlight a specific organism or group of organisms. JAZ = jasmonate zim; FLS2 = flagellin sensing 2. Word clouds that specifically pertain to individual topics are shown in Supplementary Fig. S2, which accompanies this figure along with Supplementary Fig. S3. The raw data are available in Supplementary Datasets S1 (columns S to V) and S2.

topics by using cross-citation patterns as a proxy. To this end, we implemented a recently described method for cross-citation analyses (Petre 2020), which calculates a citation score that reflects how often a given group of review articles cite a given group of authors (Supplementary Methods S1, section F). Here, we considered the 80 HIPPYs that are review articles and their matching 78 corresponding authors, grouped according to their topic (Supplementary Fig. S4D; Supplementary Dataset S3). Globally, this analysis revealed high citation scores within topics (i.e., intra-topic citation, average citation score of 1.15, ranging from 0.37 to 2.58). Notably, the three highly connected topics pathogen recognition, immune signaling, and phytohormonal modulation showed the highest citation scores, suggesting a strong flow of information within these topics and, thus, a robust community structure. At the opposite, citation scores between topics (i.e., inter-topic citation) were lower (average citation score of 0.20, ranging from 0 to 0.82), with seven and nine category intersections showing null or near-null ( $<0.01$ ) values (Supplementary Fig. S4D). Interestingly, a handful of inter-topic intersections showed high citation scores, notably within the three highly connected topics pathogen recognition, immune signaling, and phytohormonal modulation, indicative of significant information flow between some topics and, thus, of a structuration of the research communities that transcends the topics defined in the present article. Altogether, this analysis suggests that the HIPPY community coalesces into well-structured topics or groups of topics in which conceptual flow occurs along with a globally low though existing flow of information between less connected topics.

## CONCLUSION AND OUTLOOK

The present study has shown that the last two decades of influential molecular plant immunity research has developed as a well-established and well-structured community. The findings and concepts shared by that community—via HIPPYs that addressed a diversity of coherent topics—collectively addressed central questions about the molecular interplay that occurs between plants and their associated organisms and that determines the outcome of their interaction. As an outlook for the next twenty years, we believe that the main challenge of the field as a whole will be to translate the wealth of knowledge we gained into innovations to achieve sustainable agriculture and global food security (Dangl et al. 2013; Michelmore et al. 2017). Considering the increasing importance of influential researches focused on plant microbiota and symbionts, the research community may undertake such challenge via integrated approaches aimed at bioengineering agrosystems in which the plant immune system not only keeps pathogens at bay but rather maintains a microbial homeostasis beneficial for plant health (Hacquard et al. 2017).

As a concluding note, we encourage readers who wish to broaden their understanding of a given research field to implement our HIP in method to their research area of interest by using Supplementary Dataset S1 as a working template (Louet et al. 2021). Among other things, such studies may help academics to apprehend and compare the structure of the research communities in which they work, which would better inform their strategic decisions, both research- and career-wise. Noteworthy, we encourage readers who want to develop a deeper expertise of a given field to complement the use of the HIP in method with

a further exploration of the literature (i.e., an exploration that goes beyond the highly cited papers), in order to access a more diverse literature and to diversify the knowledge and conceptual frameworks to which they are exposed. Such task can be done by using filters while performing bibliographic searches (e.g., to exclude or to select publications dealing with specific objects or originating from specific institutions).

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## AUTHOR-RECOMMENDED INTERNET RESOURCES

Zotero HIPPY collection files:

[https://www.zotero.org/groups/4370831/hippy\\_collection/library](https://www.zotero.org/groups/4370831/hippy_collection/library)

MapChart website: <https://www.mapchart.net/>

Our World in Data website: <https://ourworldindata.org/grapher/research-and-development-expenditure-of-gdp>

PubMed search engine: <https://pubmed.ncbi.nlm.nih.gov>

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