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# 2000-2019: twenty years of highly influential publications in plant immunity

Benjamin PETRE\*, Clémentine LOUET, Julie LINTZ, Sébastien DUPLESSIS

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## Abstract

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 snap-shot of top-tiers molecular plant immunity research, by identifying and analyzing the 170 most highly-cited publications (aka Highly-Influential Publications in Plant Immunity; hereafter HIPPYs) published in this field between 2000 and 2019. Our analysis draws a broad analytical knowledge of the most influential scientific advances in the field, as well as 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 collectively shape our integrated understanding on the molecular interactions between plants and their associated organisms. Our 'HIP 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

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

## Introduction

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 sub-discipline of plant molecular biology intersecting with microbiology (and to a lesser extend entomology), and is also often referred to as molecular plant pathology, plant biotic interactions, plant-pathogen interactions, or molecular plant-microbe interactions (prominent journals or journal subsections including these terms in their name; [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 over 80,000 research articles and reviews (see below). Gaining an expert, broad conceptual understanding of such a large research field is complex and daunting, especially for early-

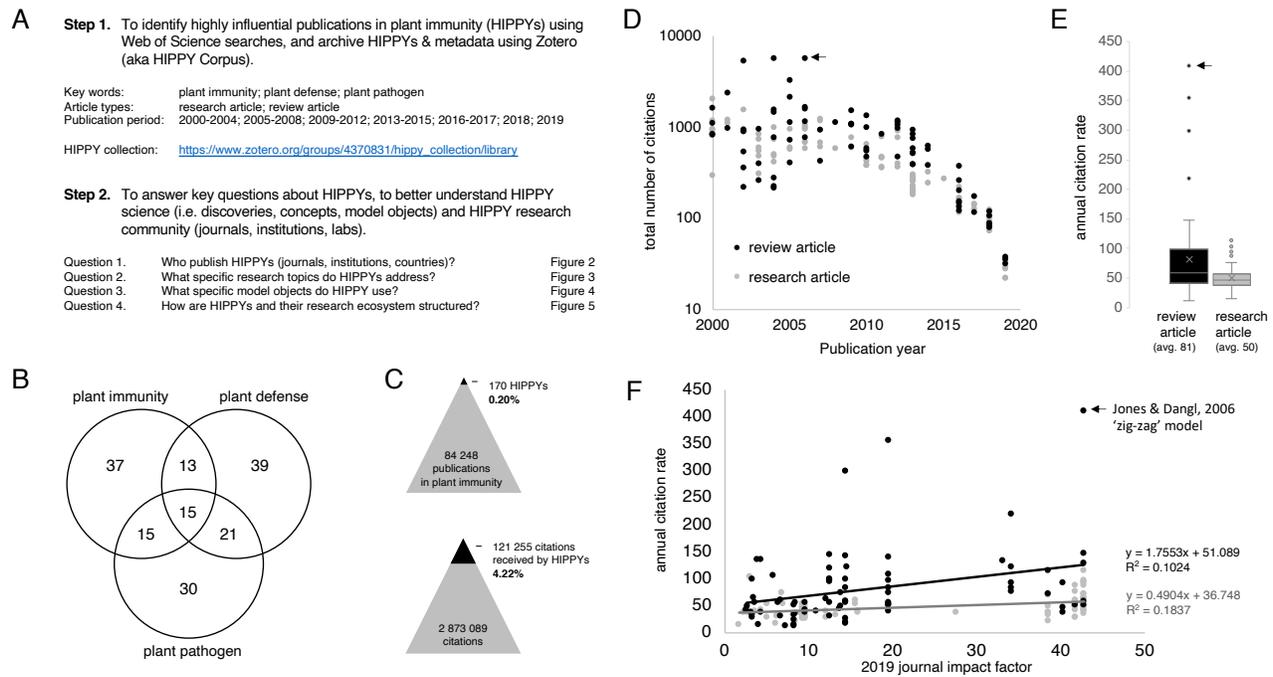
career scientists who may not know how to select and analyze key influential publications.

This paper aims at providing readers with a snap-shop of top-tiers molecular plant immunity research. To do so, we identified and analyzed 170 Highly-Influential (*i.e.* highly-cited) Publications in Plant Immunity (hereafter 'HIPPYs') published between 2000 and 2019 ([Figure 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 HIPPY 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 highly influential publications in plant immunity (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 (Figure 1A; Figure S1; Supplementary Methods - section A). We performed three successive searches using the key words 'plant

immunity', 'plant pathogen', and 'plant defense' that identified in total 170 HIPPYs (90 research articles and 80 review articles; Figure 1B). We archived the full text and metadata of the HIPPYs in a Zotero web folder (Dataset 1); a public version of the folder (named 'HIPPY collection') containing only the publication metadata (for copyright compliance) is accessible at the following Web address: [https://www.zotero.org/groups/4370831/hippy\\_collection/library](https://www.zotero.org/groups/4370831/hippy_collection/library).



**Figure 1. Overview of the 170 highly-influential publications in plant immunity (HIPPYs).**

(A) Overview of the two-step analytical pipeline used in this study. Firstly (Step 1), we identified 170 HIPPYs by using advanced searches on the Web of Science portal using various key words, article type, and publication period parameters (see Supplementary Methods - section A for details). We then collected and archived the pdf version and metadata of the 170 HIPPYs into a Zotero folder (aka HIPPY Collection) according to the search output; the public version of the Zotero folder (that includes only the metadata for copyright compliance) can be accessed by following the Web link '[https://www.zotero.org/groups/4370831/hippy\\_collection/library](https://www.zotero.org/groups/4370831/hippy_collection/library)'. Secondly (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, the labs, the institutions, ...). (B) Venn diagram showing the overlapping contribution of the three keyword searches ('plant immunity', 'plant pathogen', and 'plant defense') 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 approx. 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 (grey) 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). (E) Box plot indicating the annual citation rate (i.e. average number of citations per year) of research article HIPPYs (grey) 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. (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 grey dots indicate review and research articles, respectively. Linear trendlines are indicated for each article type along with trendlines equations and r-squared values (black: review article; grey: 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 [Figure S1](#) accompanies this figure; the raw data used to build this figure are available in the [Dataset 1](#) (columns A to H).

The 170 HIPPYs represent only 0.2% of all the research articles and reviews published in the field of plant immunity between 2000 and 2019, but they account for 4.22% of the citations in this field over the same period ([Figure 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 5730; [Figure 1D](#)). On average, HIPPYs receive 64 citations per year (*i.e.* annual citation rate of 64); reviews showing on average a higher citation rate than research articles (81 vs. 50; [Figure 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 (Jones and Dangl, 2006). Interestingly, HIPPY annual citation rates do not correlate with the impact factor of the journal in which they were published ([Figure 1F](#)). We conclude that the HIPPYs are influential publications that are likely to present recent seminal discoveries and dominant concepts in plant immunity, and thus constitute a suitable resource to build a snapshot of top-tiers 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 HIPPYs metadata 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 21 countries ([Dataset 1](#) - columns I to N; [Supplementary Methods](#) - section B). Interestingly, a small number of those journals, institutions, and countries contributed most of the HIPPYs ([Figure 2A](#)). Indeed, only six journals (including Nature, Science, and Cell) published over half of the HIPPYs, and only six countries (USA, Germany, UK, Switzerland, 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 (TSL, UK), the Max Planck Institute (MPI, Germany), and the University of California (UC, USA).

Considering that academic careers are highly competitive and fragmented by short-term contracts, early-career researchers may want to strategically target cities or larger urban areas (hereafter employment areas) with multiple and high-quality job opportunities (*i.e.* supportive institutions and influential laboratories in their field). To identify such employment areas for the field of plant immunity, we mapped the laboratories of the corresponding authors of HIPPYs worldwide ([Figure 2B](#)). This analysis identified 76 employment areas (including 26 in the USA and 23 in Europe) in which at least one HIPPY corresponding author has their laboratory. Interestingly, nine employment areas located in Europe (5), in the USA (2), in China (1), or in Japan (1) showed over five HIPPY-publishing laboratories (aka 'HIPPY cities'). For instance, in Europe such areas comprise the city of Norwich (UK, 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; [Figure 2B](#)). To conclude, this analysis shows that only a handful of actors publish HIPPYs, including employment areas that are likely to host a competitive and favorable research ecosystem. 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**

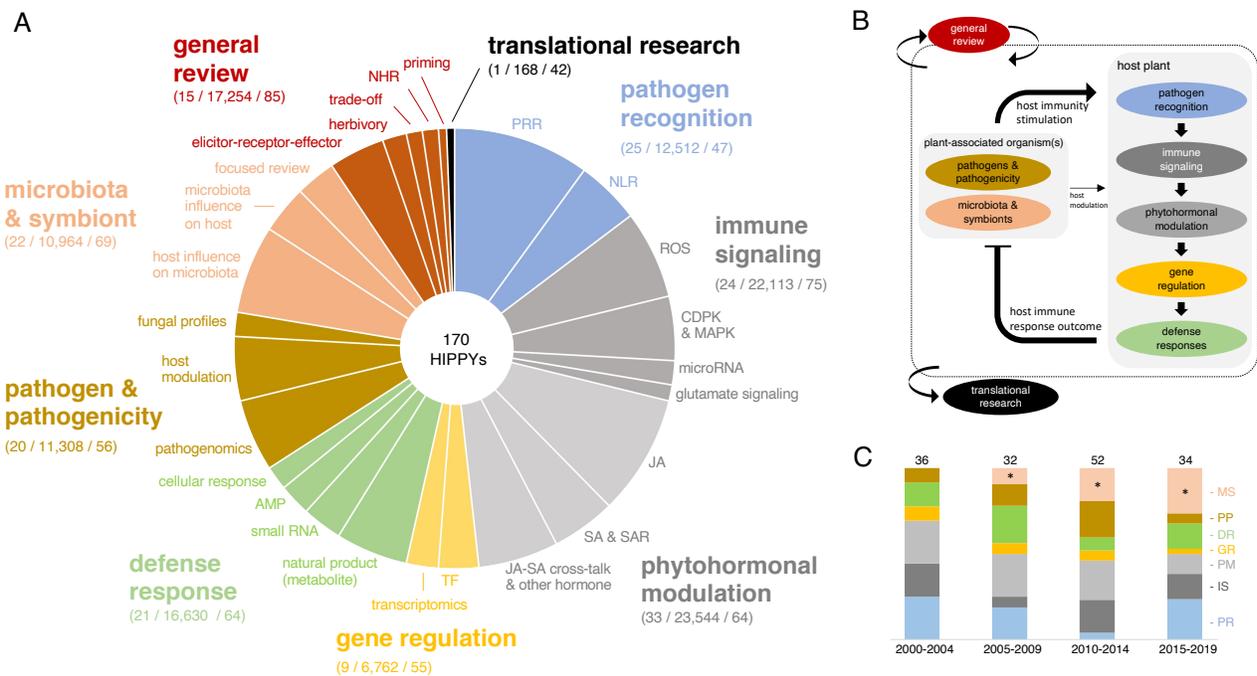
To get an analytical understanding of HIPPYs, we aimed at identifying the research questions they address. To do so, we performed iterative readings of all the manuscripts combined with key words tagging to categorize HIPPYs into topics and subtopics ([Figure 3A](#); [Dataset 1](#) - columns O to R; [Supplementary Methods](#) - section C). This analysis grouped the 170 HIPPYs into nine main topics, as follows: 1) 'Pathogen Recognition' (PR, 25 HIPPYs; *how do plants sense pathogens?*),



*immune signaling outcome?*). We positioned these nine topics into a simplified conceptual framework of plant immunity research, that considers two research topics focused on plant-associated organisms (PP & MS), five focused on host plants (PR, IS, PM, GR, and DR), and two overarching topics that produce general concepts (GR) and innovations (TR) (Figure 3B; see figure legend for details).

To identify potential research trends in influential 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 topics 'general reviews' and 'translational research' from this analysis, as they do not inform on research trends. This analysis revealed that most topics gather HIPPYs in all time period considered, with no clear trend of linear expansion or contraction between 2000 and 2019

(Figure 3C). One striking exception is the topic 'microbiota and symbionts', which gradually expands over the four periods considered, from zero HIPPY for the 2000-2004 period to nine for the 2015-2019 period (*i.e.* 26% of the HIPPYs published over this period). A similar pattern of increase can be seen while performing a key word search 'plant microbiota symbiont' on the PubMed search engine (<https://pubmed.ncbi.nlm.nih.gov/>), 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



**Figure 3. HIPPYs address nine main research topics and 27 sub-topics.**

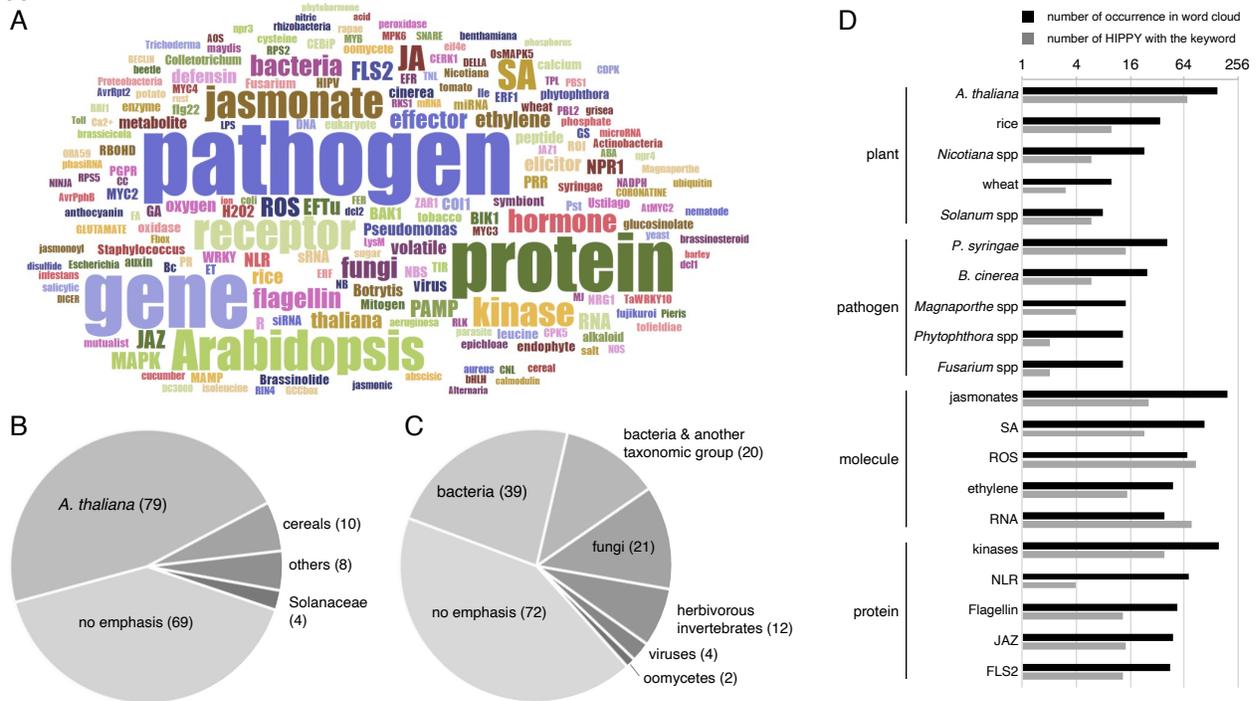
(A) Pie chart displaying the 9 main topics and 27 subtopics addressed by HIPPYs. The nine main topics are color-coded as follows: pathogen recognition (light blue), immune signaling (dark grey), phytohormonal modulation (light grey), gene regulation (gold), defense response (light green), pathogen & pathogenicity (dark yellow), microbiota & symbiont (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'). The design of the topics and subtopics, as well as the assignment of the HIPPYs to those, was based on multiple and iterative expert reading and key word association of the HIPPY collection. (B) Conceptual framework of plant immunity integrating the nine main topics depicted in (A). 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-hand side) or the plant-associated organism (left-hand side). 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 symbiont (often existing as host-associated complex communities referred to as microbiota; microbiota & symbionts; MS) or deleterious organisms (i.e. microbial pathogens or herbivorous invertebrates; pathogens and pathogenicity; PP), which both modulate host plant structures and functions to promote colonization. Host plants (right-hand side) first recognize their associated organisms (pathogen recognition; PR), then signal this recognition (immune signaling; IS). This signaling, which can be modulated by phytohormones (phytohormonal modulation; PM), results in the regulation of gene expression (i.e. alteration of the genetic programme; gene regulation; GR). In turn, this regulation triggers effective immune responses (i.e. host immune response outcome; defense responses; DR) 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 framework 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 topics 'general reviews' and 'translational research' 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 & symbiont topic, which increases in size over time. 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: non-host resistance; TF: transcription factor. The raw data used to build this figure are available in the [Dataset 1](#) - columns O to R)

### 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 snap-shot 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'; [Figure S2](#); [Dataset 1](#) - columns S & T; [Dataset 2](#); [Supplementary Methods](#) - 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 ([Figure 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), non-proteinaceous 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, excepted for the topic general review and translational research ([Figure 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 '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 near 75% of the HIPPYs highlight at least one organism (or one group of organisms; [Dataset 1](#) - columns U & V). On one hand, we determined that 101 HIPPYs highlighted at least one plant species or plant group ([Figure 4B](#)). Near 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 another hand, we determined that 98 HIPPYs highlight at least one plant-associated species or taxonomic group ([Figure 4C](#)). Near 60% of those HIPPYs highlight bacteria (alone or with an additional taxonomic group, often filamentous pathogens) and near 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 ([Figure 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) non-proteinaceous molecules, and iv) proteins used as key objects by HIPPYs ([Figure 4D](#); see figure legend for details). 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.



**Figure 4. HIPPYs focus on a limited number of model organisms and molecules.**

(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 from 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) Pie chart displaying the main plant organism (or groups of organisms) emphasized in HIPPYs. Nine HIPPYs from the *A. thaliana* section emphasize an additional species (either 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) Pie chart displaying the main groups of plant-associated organisms emphasized in HIPPYs. Near half (18 out of 39) of the HIPPYs from the bacteria section emphasize Pseudomonadaceae species. Near all (18 out of 20) HIPPYs from the bacteria & another taxonomic group section emphasize filamentous pathogens (fungi or oomycetes) in addition to bacteria. More than half (13 out of 21) of the HIPPYs from the fungi section emphasize ascomycetes. Three quarter (9 out of 12) of the 'herbivorous invertebrates' section emphasize insects. (D) Bar chart displaying the five most emphasized plant species (plant), plant-associated species (pathogen), non-proteinaceous 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 grey 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 key words were considered for the following categories: *P. syringae* ('pst' and 'DC3000'), *M. oryzae* ('grisea'), jasmonates ('JA', 'jasmonoyl', 'JA-Ile', and 'jasmonic'), salicylic acid ('SA' and 'salicylate'), ROS ('ROI' and 'H<sub>2</sub>O<sub>2</sub>'), and kinases ('MAPK', 'mitogen', 'MPK', and 'CDPK'), NLR ('NB-LRR', 'NBS-LRR', 'CNL', 'TNL', 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. *P. syringae*: *Pseudomonas syringae*; *B. cinerea*: *Botrytis cinerea*; SA: salicylic acid; ROS: reactive oxygen species; NLR: NOD-like receptor; JAZ: jasmonate zim; FLS2: flagellin sensing 2. Word clouds that specifically pertain to individual topics are shown in Figure S2. The Figure S2 and the Figure S3 accompany this figure; the raw data used to build this figure are available in the Dataset 1 (columns S to V) and in the Dataset 2.

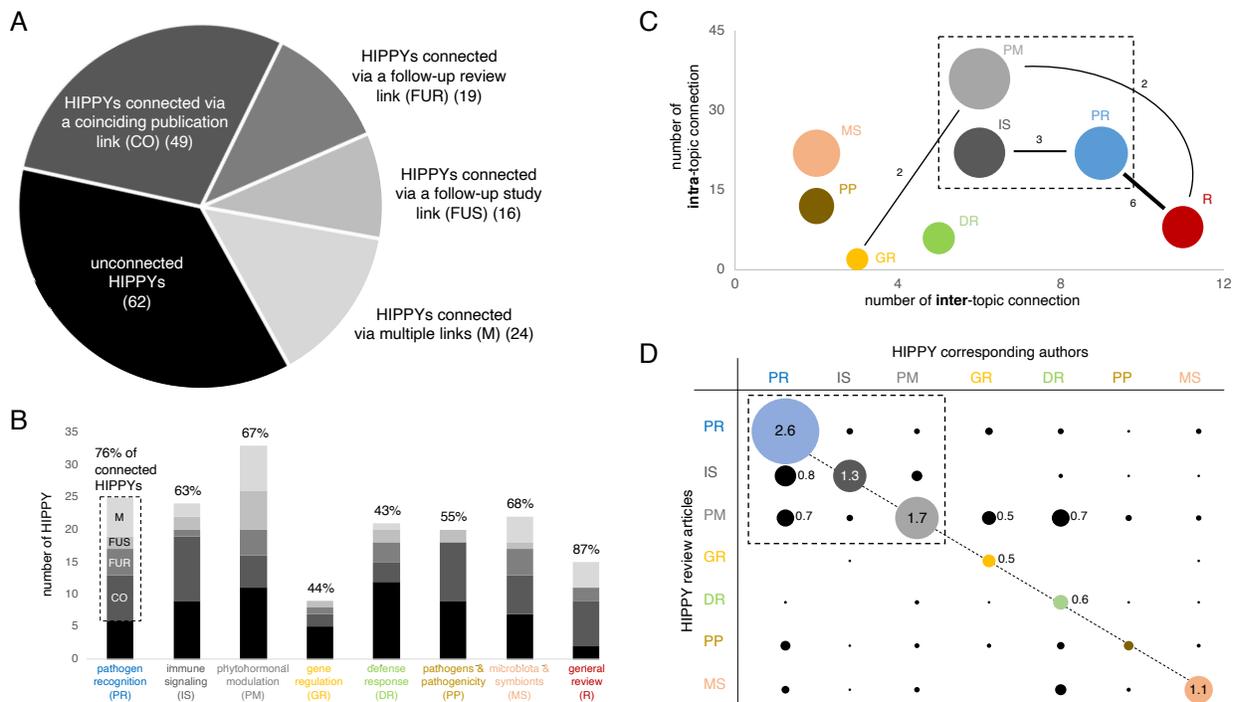
### Over 60% of the HIPPYs are connected to at least another HIPPY

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; CO), ii) discoveries followed by other studies reinforcing them (*i.e.* follow-up studies; FUS), and iii) discoveries followed by reviews that contextualize them and highlight their significance for a broader audience (*i.e.* follow-up review; FUR). To determine the level of connectivity with the HIPPHY collection (*i.e.* determine if HIPPHYs are connected with other HIPPHYs), we looked for the three types of links above mentioned (CO, FUS, or FUR) among the HIPPHY collection ([Supplementary Methods](#) - section E). In total, we found that 108 HIPPHYs (*i.e.*

over 63% of the HIPPHY collection) are connected to at least another HIPPHY; those 108 HIPPHYs form a fragmented network comprising 174 links in total ([Figure 5A](#); [Figure S4](#); [Dataset 1](#) - columns W to Y). The most abundant type of link was 'coinciding publication' (CO; 49 HIPPHYs), followed by 'follow-up review' (FUR, 19) and 'follow-up study' (FUS, 16). Notably, 24 HIPPHYs show multiple types of links (M; *e.g.* simultaneously CO and FUR). Interestingly, those 'highly-connected' HIPPHYs received more citation than isolated HIPPHYs (annual citation rate of 90 vs 52 on average; the number of links positively correlating with the annual citation rate; [Figure S5](#)).



**Figure 5. HIPPHYs and their research community are strongly connected.**

(A) The upper panel shows a pie chart that displays the various types of links that connect HIPPHYs. The coincidental (CO) type of link connects two or more HIPPHYs of the same article type that report similar findings or concepts. The follow-up study (FUS) type of link connects two research articles co-signed by an overlapping set of authors and that sequentially report coherent findings. The follow-up review (FUR) type of link connects two HIPPHYs co-signed by an overlapping set of authors and that pertain to a coherent body of knowledge. The multiple (M) type of link pertains to multi-connected HIPPHYs. The gap between connected HIPPHYs could not exceed 4 years. (B) Stacked bar chart displaying the relative proportion of connected HIPPHYs for each topic. The percentage of connected HIPPHYs is indicated on the top of the bar for each topic. (C) Bubble chart displaying the links between topics. The size of the bubbles positively correlates with the total number of links for each topic. The position of the bubble on the chart informs on the number of links that occur between HIPPHYs from the same topic (intra-topic link; Y-axis) or informs on the number of links that occurs between a HIPPHY from the topic and HIPPHYs from other topics (inter-topic link; X-axis). (D) Bubble table chart displaying cross-citation scores within the HIPPHY collection. The diameter of the bubble correlates with a citation score that indicates the average number of citations per author per article for a given intersection (see [Supplementary Methods](#) - section F for details); no bubble indicates a citation score of zero (*e.g.* no bubble at the intersection of the 'x-axis defense response' and 'y-axis immune signaling' indicates that no corresponding author from the immune signaling topic was directly referred to in the review articles assigned to the defense response topic). Bubbles that indicate the intra-topic citation scores are positioned along a dotted line. Bubbles that indicate inter-topic citation score are in black. Citation score values superior to 0.5 are indicated (rounded to one digit after the decimal point).

HIPPYs from the topics general review and translational research were not considered for the analyses shown in this figure. A visual layout of the data shown in items (A-C) is shown in [Figure S4](#). The [Figure S4](#), the [Figure S5](#), and the [Table S2](#) accompany this figure; the raw data used to build this figure are available in the [Dataset 1](#) (columns W to Y) and in the [Dataset 3](#).

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We further investigated the network of connected HIPPYs for each individual topic. Firstly, this showed that all topics contain over 40% of connected HIPPYs, indicating that all topics contain a significant share of connected HIPPYs ([Figure 5B](#)). Secondly, the majority (75%) of the links occurred between HIPPYs from the same topic ([Figure 5C](#)). 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 ([Figure 5C](#)). 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 plant recognize & signal modularly 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 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](#) - section F). Here, we considered the 80 HIPPYs that are review articles and their matching 78 corresponding authors, grouped according to their topic ([Figure 5D](#); [Dataset 3](#)). 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 ([Figure 5D](#)). 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 transcend the topics defined in the present article. Altogether, this analysis suggests that the HIPPY community coalesces into well-structured topics or groups of topics, where conceptual flow occurs, along with a globally low though existing flow of information between less connected topics.

### **Outlook**

The present study has shown that the last two decades of top-tiers 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 shaped our integrated understanding on 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 will be to translate the wealth of knowledge we gained into innovations to achieve sustainable agriculture and global food security. 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 the 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' ('Highly-Influential Publication in' ...) method to their research area of interest, by using [Dataset 1](#) as a working template.

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## Authors Contribution

BP conceived and designed the study, wrote the manuscript, and acquired data; BP, CL, and JL performed data analysis and interpretation; BP, CL, JL, and SD critically revised and edited the manuscript.

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## Conflict of interest statement

The authors declare that there is no conflict of interest

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## References

Agler, M.T., Ruhe, J., Kroll, S., Morhenn, C., Kim, S.-T., Weigel, D., and Kemen, E.M. (2016). Microbial Hub Taxa Link Host and Abiotic Factors

to Plant Microbiome Variation. *PLOS Biol.* *14*, e1002352.

Amselem, J., Cuomo, C.A., van Kan, J.A.L., Viaud, M., Benito, E.P., Couloux, A., Coutinho, P.M., de Vries, R.P., Dyer, P.S., Fillinger, S., et al. (2011). Genomic Analysis of the Necrotrophic Fungal Pathogens *Sclerotinia sclerotiorum* and *Botrytis cinerea*. *PLOS Genet.* *7*, e1002230.

Apel, K., and Hirt, H. (2004). Reactive oxygen species: Metabolism, oxidative stress, and signal transduction. *Annu. Rev. Plant Biol.* *55*, 373–399.

Asai, T., Tena, G., Plotnikova, J., Willmann, M.R., Chiu, W.-L., Gomez-Gomez, L., Boller, T., Ausubel, F.M., and Sheen, J. (2002). MAP kinase signalling cascade in Arabidopsis innate immunity. *Nature* *415*, 977–983.

Axtell, M., and Staskawicz, B. (2003). Initiation of RPS2-specified disease resistance in Arabidopsis is coupled to the AvrRpt2-directed elimination of RIN4. *Cell* *112*, 369–377.

Bari, R., and Jones, J.D.G. (2009). Role of plant hormones in plant defence responses. *Plant Mol. Biol.* *69*, 473–488.

Baxter, A., Mittler, R., and Suzuki, N. (2014). ROS as key players in plant stress signalling. *J. Exp. Bot.* *65*, 1229–1240.

Berendsen, R.L., Pieterse, C.M.J., and Bakker, P.A.H.M. (2012). The rhizosphere microbiome and plant health. *Trends Plant Sci.* *17*, 478–486.

Berendsen, R.L., Vismans, G., Yu, K., Song, Y., de Jonge, R., Burgman, W.P., Burmolle, M., Herschend, J., Bakker, P.A.H.M., and Pieterse, C.M.J. (2018). Disease-induced assemblage of a plant-beneficial bacterial consortium. *ISME J.* *12*, 1496–1507.

Bodenhause, N., Horton, M.W., and Bergelson, J. (2013). Bacterial Communities Associated with the Leaves and the Roots of *Arabidopsis thaliana*. *PLOS ONE* *8*, e56329.

Boller, T., and Felix, G. (2009). A Renaissance of Elicitors: Perception of Microbe-Associated Molecular Patterns and Danger Signals by Pattern-Recognition Receptors. *Annu. Rev. Plant Biol.* *60*, 379–406.

- Borges, A., Ferreira, C., Saavedra, M.J., and Simoes, M. (2013). Antibacterial Activity and Mode of Action of Ferulic and Gallic Acids Against Pathogenic Bacteria. *Microb. Drug Resist.* *19*, 256–265.
- Boudsocq, M., Willmann, M.R., McCormack, M., Lee, H., Shan, L., He, P., Bush, J., Cheng, S.-H., and Sheen, J. (2010). Differential innate immune signalling via Ca<sup>2+</sup> sensor protein kinases. *Nature* *464*, 418–422.
- Brogden, K.A. (2005). Antimicrobial peptides: pore formers or metabolic inhibitors in bacteria? *Nat. Rev. Microbiol.* *3*, 238–250.
- Bulgarelli, D., Rott, M., Schlaeppli, K., Ver Loren van Themaat, E., Ahmadinejad, N., Assenza, F., Rauf, P., Huettel, B., Reinhardt, R., Schmelzer, E., et al. (2012). Revealing structure and assembly cues for *Arabidopsis* root-inhabiting bacterial microbiota. *Nature* *488*, 91–95.
- Bulgarelli, D., Schlaeppli, K., Spaepen, S., van Themaat, E.V.L., and Schulze-Lefert, P. (2013). Structure and Functions of the Bacterial Microbiota of Plants. *Annu. Rev. Plant Biol.* *64*, 807–838.
- Cai, Q., Qiao, L., Wang, M., He, B., Lin, F.-M., Palmquist, J., Huang, S.-D., and Jin, H. (2018). Plants send small RNAs in extracellular vesicles to fungal pathogen to silence virulence genes. *Science* *360*, 1126–1129.
- Campos, M.L., Yoshida, Y., Major, I.T., Ferreira, D. de O., Weraduwege, S.M., Froehlich, J.E., Johnson, B.F., Kramer, D.M., Jander, G., Sharkey, T.D., et al. (2016). Rewiring of jasmonate and phytochrome B signalling uncouples plant growth-defense tradeoffs. *Nat. Commun.* *7*, 12570.
- Castel, B., Ngou, P.-M., Cevik, V., Redkar, A., Kim, D.-S., Yang, Y., Ding, P., and Jones, J.D.G. (2019). Diverse NLR immune receptors activate defence via the RPW8-NLR NRG1. *New Phytol.* *222*, 966–980.
- Castrillo, G., Teixeira, P.J.P.L., Paredes, S.H., Law, T.F., de Lorenzo, L., Feltcher, M.E., Finkel, O.M., Breakfield, N.W., Mieczkowski, P., Jones, C.D., et al. (2017). Root microbiota drive direct integration of phosphate stress and immunity. *Nature* *543*, 513–518.
- Chandrasekaran, J., Brumin, M., Wolf, D., Leibman, D., Klap, C., Pearlsman, M., Sherman, A., Arazi, T., and Gal-On, A. (2016). Development of broad virus resistance in non-transgenic cucumber using CRISPR/Cas9 technology. *Mol. Plant Pathol.* *17*, 1140–1153.
- Chen, L.-Q., Hou, B.-H., Lalonde, S., Takanaga, H., Hartung, M.L., Qu, X.-Q., Guo, W.-J., Kim, J.-G., Underwood, W., Chaudhuri, B., et al. (2010). Sugar transporters for intercellular exchange and nutrition of pathogens. *Nature* *468*, 527–532.
- Chinchilla, D., Zipfel, C., Robatzek, S., Kemmerling, B., Nuernberger, T., Jones, J.D.G., Felix, G., and Boller, T. (2007). A flagellin-induced complex of the receptor FLS2 and BAK1 initiates plant defence. *Nature* *448*, 497–501.
- Chini, A., Fonseca, S., Fernandez, G., Adie, B., Chico, J.M., Lorenzo, O., Garcia-Casado, G., Lopez-Vidriero, I., Lozano, F.M., Ponce, M.R., et al. (2007). The JAZ family of repressors is the missing link in jasmonate signalling. *Nature* *448*, 666–673.
- Chisholm, S.T., Coaker, G., Day, B., and Staskawicz, B.J. (2006). Host-Microbe Interactions: Shaping the Evolution of the Plant Immune Response. *Cell* *124*, 803–814.
- Chung, S.H., Rosa, C., Scully, E.D., Peiffer, M., Tooker, J.F., Hoover, K., Luthe, D.S., and Felton, G.W. (2013). Herbivore exploits orally secreted bacteria to suppress plant defenses. *Proc. Natl. Acad. Sci. U. S. A.* *110*, 15728–15733.
- Clay, N.K., Adio, A.M., Denoux, C., Jander, G., and Ausubel, F.M. (2009). Glucosinolate Metabolites Required for an *Arabidopsis* Innate Immune Response. *Science* *323*, 95–101.
- Collins, N.C., Thordal-Christensen, H., Lipka, V., Bau, S., Kombrink, E., Qiu, J.-L., Hüchelhoven, R., Stein, M., Freialdenhoven, A., Somerville, S.C., et al. (2003). SNARE-protein-mediated disease resistance at the plant cell wall. *Nature* *425*, 973–977.
- Conrath, U., Beckers, G.J.M., Flors, V., García-Agustín, P., Jakab, G., Mauch, F., Newman, M.-A., Pieterse, C.M.J., Poinssot, B., Pozo, M.J., et al. (2006). Priming: Getting Ready for Battle. *Mol. Plant. Microbe Interact.* *19*, 1062–1071.

- Couto, D., and Zipfel, C. (2016). Regulation of pattern recognition receptor signalling in plants. *Nat. Rev. Immunol.* *16*, 537–552.
- Dangl, J.L., and Jones, J.D.G. (2001). Plant pathogens and integrated defence responses to infection. *Nature* *411*, 826–833.
- Dat, J., Vandenabeele, S., Vranova, E., Van Montagu, M., Inze, D., and Van Breusegem, F. (2000). Dual action of the active oxygen species during plant stress responses. *Cell. Mol. LIFE Sci.* *57*, 779–795.
- De Vos, M., Van Oosten, V., Van Poecke, R., Van Pelt, J., Pozo, M., Mueller, M., Buchala, A., Mettraux, J., Van Loon, L., Dicke, M., et al. (2005). Signal signature and transcriptome changes of *Arabidopsis* during pathogen and insect attack. *Mol. Plant Microbe Interact.* *18*, 923–937.
- Dean, R., Van Kan, J.A.L., Pretorius, Z.A., Hammond-Kosack, K.E., Di Pietro, A., Spanu, P.D., Rudd, J.J., Dickman, M., Kahmann, R., Ellis, J., et al. (2012). The Top 10 fungal pathogens in molecular plant pathology: Top 10 fungal pathogens. *Mol. Plant Pathol.* *13*, 414–430.
- Dean, R.A., Talbot, N.J., Ebbole, D.J., Farman, M.L., Mitchell, T.K., Orbach, M.J., Thon, M., Kulkarni, R., Xu, J.-R., Pan, H., et al. (2005). The genome sequence of the rice blast fungus *Magnaporthe grisea*. *Nature* *434*, 980–986.
- Dicke, M., and Baldwin, I.T. (2010). The evolutionary context for herbivore-induced plant volatiles: beyond the 'cry for help'. *Trends Plant Sci.* *15*, 167–175.
- Ding, S.-W. (2010). RNA-based antiviral immunity. *Nat. Rev. Immunol.* *10*, 632–644.
- Ding, S.-W., and Voinnet, O. (2007). Antiviral Immunity Directed by Small RNAs. *Cell* *130*, 413–426.
- Dixon, R.A. (2001). Natural products and plant disease resistance. *Nature* *411*, 843–847.
- Dodds, P.N., and Rathjen, J.P. (2010). Plant immunity: towards an integrated view of plant–pathogen interactions. *Nat. Rev. Genet.* *11*, 539–548.
- Dorman, H., and Deans, S. (2000). Antimicrobial agents from plants: antibacterial activity of plant volatile oils. *J. Appl. Microbiol.* *88*, 308–316.
- Dubiella, U., Seybold, H., Durian, G., Komander, E., Lassig, R., Witte, C.-P., Schulze, W.X., and Romeis, T. (2013). Calcium-dependent protein kinase/NADPH oxidase activation circuit is required for rapid defense signal propagation. *Proc. Natl. Acad. Sci. U. S. A.* *110*, 8744–8749.
- Dudareva, N., Klempien, A., Muhlemann, J.K., and Kaplan, I. (2013). Biosynthesis, function and metabolic engineering of plant volatile organic compounds. *New Phytol.* *198*, 16–32.
- Durrant, W.E., and Dong, X. (2004). Systemic Acquired Resistance. *Annu. Rev. Phytopathol.* *42*, 185–209.
- Eulgem, T., Rushton, P.J., Robatzek, S., and Somssich, I.E. (2000). The WRKY superfamily of plant transcription factors. *Trends Plant Sci.* *5*, 199–206.
- Fernandez-Calvo, P., Chini, A., Fernandez-Barbero, G., Chico, J.-M., Gimenez-Ibanez, S., Geerinck, J., Eeckhout, D., Schweizer, F., Godoy, M., Manuel Franco-Zorrilla, J., et al. (2011). The *Arabidopsis* bHLH Transcription Factors MYC3 and MYC4 Are Targets of JAZ Repressors and Act Additively with MYC2 in the Activation of Jasmonate Responses. *Plant Cell* *23*, 701–715.
- Feussner, I., and Wasternack, C. (2002). The lipoxygenase pathway. *Annu. Rev. Plant Biol.* *53*, 275–297.
- Fisher, M.C., Henk, Daniel.A., Briggs, C.J., Brownstein, J.S., Madoff, L.C., McCraw, S.L., and Gurr, S.J. (2012). Emerging fungal threats to animal, plant and ecosystem health. *Nature* *484*, 186–194.
- Fitzpatrick, C.R., Copeland, J., Wang, P.W., Guttman, D.S., Kotanen, P.M., and Johnson, M.T.J. (2018). Assembly and ecological function of the root microbiome across angiosperm plant species. *Proc. Natl. Acad. Sci. U. S. A.* *115*, 1157–1165.
- Fu, Z.Q., and Dong, X. (2013). Systemic Acquired Resistance: Turning Local Infection into Global Defense. *Annu. Rev. Plant Biol.* *64*, 839–863.

- Fu, Z.Q., Yan, S., Saleh, A., Wang, W., Ruble, J., Oka, N., Mohan, R., Spoel, S.H., Tada, Y., Zheng, N., et al. (2012). NPR3 and NPR4 are receptors for the immune signal salicylic acid in plants. *Nature* *486*, 228–232.
- Glazebrook, J. (2005). Contrasting Mechanisms of Defense Against Biotrophic and Necrotrophic Pathogens. *Annu. Rev. Phytopathol.* *43*, 205–227.
- Gomez-Gomez, L., and Boller, T. (2000). FLS2: An LRR receptor-like kinase involved in the perception of the bacterial elicitor flagellin in Arabidopsis. *Mol. Cell* *5*, 1003–1011.
- Gómez-Gómez, L., and Boller, T. (2002). Flagellin perception: a paradigm for innate immunity. *Trends Plant Sci.* *7*, 251–256.
- Guo, Z., Li, Y., and Ding, S.-W. (2019). Small RNA-based antimicrobial immunity. *Nat. Rev. Immunol.* *19*, 31–44.
- Haas, D., and Defago, G. (2005). Biological control of soil-borne pathogens by fluorescent pseudomonads. *Nat. Rev. Microbiol.* *3*, 307–319.
- Haas, B.J., Kamoun, S., Zody, M.C., Jiang, R.H.Y., Handsaker, R.E., Cano, L.M., Grabherr, M., Kodira, C.D., Raffaele, S., Torto-Alalibo, T., et al. (2009). Genome sequence and analysis of the Irish potato famine pathogen *Phytophthora infestans*. *Nature* *461*, 393–398.
- Hacker, J., and Kaper, J.B. (2000). Pathogenicity islands and the evolution of microbes. *Annu. Rev. Microbiol.* *54*, 641–679.
- Hacquard, S., Spaepen, S., Garrido-Oter, R., and Schulze-Lefert, P. (2017). Interplay Between Innate Immunity and the Plant Microbiota. *Annu. Rev. Phytopathol.* *55*, 565–589.
- Halkier, B.A., and Gershenzon, J. (2006). Biology and biochemistry of glucosinolates. *Annu. Rev. Plant Biol.* *57*, 303–333.
- Hammond-Kosack, K.E., and Parker, J.E. (2003). Deciphering plant–pathogen communication: fresh perspectives for molecular resistance breeding. *Curr. Opin. Biotechnol.* *14*, 177–193.
- Hao, Y., Wang, T., Wang, K., Wang, X., Fu, Y., Huang, L., and Kang, Z. (2016). Transcriptome Analysis Provides Insights into the Mechanisms Underlying Wheat Plant Resistance to Stripe Rust at the Adult Plant Stage. *PLOS ONE* *11*, e0150717.
- Harman, G.E., Howell, C.R., Viterbo, A., Chet, I., and Lorito, M. (2004). *Trichoderma* species - Opportunistic, avirulent plant symbionts. *Nat. Rev. Microbiol.* *2*, 43–56.
- He, S., Nomura, K., and Whittam, T. (2004). Type III protein secretion mechanism in mammalian and plant pathogens. *Biochim. Biophys. Acta* *1694*, 181–206.
- Heese, A., Hann, D.R., Gimenez-Ibanez, S., Jones, A.M.E., He, K., Li, J., Schroeder, J.I., Peck, S.C., and Rathjen, J.P. (2007). The receptor-like kinase SERK3/BAK1 is a central regulator of innate immunity in plants. *Proc. Natl. Acad. Sci. U. S. A.* *104*, 12217–12222.
- Hiruma, K., Gerlach, N., Sacristán, S., Nakano, R.T., Hacquard, S., Kracher, B., Neumann, U., Ramírez, D., Bucher, M., O’Connell, R.J., et al. (2016). Root Endophyte *Colletotrichum tofieldiae* Confers Plant Fitness Benefits that Are Phosphate Status Dependent. *Cell* *165*, 464–474.
- Howe, G.A., and Jander, G. (2008). Plant immunity to insect herbivores. *Annu. Rev. Plant Biol.* *59*, 41–66.
- Howe, G.A., Major, I.T., and Koo, A.J. (2018). Modularity in Jasmonate Signaling for Multistress Resilience. *Annu. Rev. Plant Biol.* *69*, 387–415.
- Hu, L., Robert, C.A.M., Cadot, S., Zhang, X., Ye, M., Li, B., Manzo, D., Chervet, N., Steinger, T., van der Heijden, M.G.A., et al. (2018). Root exudate metabolites drive plant-soil feedbacks on growth and defense by shaping the rhizosphere microbiota. *Nat. Commun.* *9*, 2738.
- Hu, Y., Jiang, L., Wang, F., and Yu, D. (2013). Jasmonate Regulates the INDUCER OF CBF EXPRESSION-C-REPEAT BINDING FACTOR/DRE BINDING FACTOR1 Cascade and Freezing Tolerance in Arabidopsis. *Plant Cell* *25*, 2907–2924.
- Huot, B., Yao, J., Montgomery, B.L., and He, S.Y. (2014). Growth–Defense Tradeoffs in Plants: A Balancing Act to Optimize Fitness. *Mol. Plant* *7*, 1267–1287.

- Jiang, Y., Wang, W., Xie, Q., Liu, N., Liu, L., Wang, D., Zhang, X., Yang, C., Chen, X., Tang, D., et al. (2017). Plants transfer lipids to sustain colonization by mutualistic mycorrhizal and parasitic fungi. *Science* 356, 1172–1175.
- Jones, D., and Takemoto, D. (2004). Plant innate immunity - direct and indirect recognition of general and specific pathogen-associated molecules. *Curr. Opin. Immunol.* 16, 48–62.
- Jones, J.D.G., and Dangl, J.L. (2006). The plant immune system. *Nature* 444, 323–329.
- Jones, J.D.G., Vance, R.E., and Dangl, J.L. (2016). Intracellular innate immune surveillance devices in plants and animals. *Science* 354, aaf6395.
- Kadota, Y., Sklenar, J., Derbyshire, P., Stransfeld, L., Asai, S., Ntoukakis, V., Jones, J.D.G., Shirasu, K., Menke, F., Jones, A., et al. (2014). Direct Regulation of the NADPH Oxidase RBOHD by the PRR-Associated Kinase BIK1 during Plant Immunity. *Mol. Cell* 54, 43–55.
- Kaemper, J., Kahmann, R., Boelker, M., Ma, L.-J., Brefort, T., Saville, B.J., Banuett, F., Kronstad, J.W., Gold, S.E., Mueller, O., et al. (2006). Insights from the genome of the biotrophic fungal plant pathogen *Ustilago maydis*. *Nature* 444, 97–101.
- Kaku, H., Nishizawa, Y., Ishii-Minami, N., Akimoto-Tomiyama, C., Dohmae, N., Takio, K., Minami, E., and Shibuya, N. (2006). Plant cells recognize chitin fragments for defense signaling through a plasma membrane receptor. *Proc. Natl. Acad. Sci. U. S. A.* 103, 11086–11091.
- Kessler, A., and Baldwin, I.T. (2002). Plant responses to insect herbivory: The emerging molecular analysis. *Annu. Rev. Plant Biol.* 53, 299–328.
- Kourelis, J., and van der Hoorn, R.A.L. (2018). Defended to the Nines: 25 Years of Resistance Gene Cloning Identifies Nine Mechanisms for R Protein Function. *Plant Cell* 30, 285–299.
- Kovtun, Y., Chiu, W., Tena, G., and Sheen, J. (2000). Functional analysis of oxidative stress-activated mitogen-activated protein kinase cascade in plants. *Proc. Natl. Acad. Sci. U. S. A.* 97, 2940–2945.
- Kunkel, B.N., and Brooks, D.M. (2002). Cross talk between signaling pathways in pathogen defense. *Curr. Opin. Plant Biol.* 5, 325–331.
- Kunze, G., Zipfel, C., Robatzek, S., Niehaus, K., Boller, T., and Felix, G. (2004). The N terminus of bacterial elongation factor Tu elicits innate immunity in Arabidopsis plants. *Plant Cell* 16, 3496–3507.
- Lebeis, S.L., Paredes, S.H., Lundberg, D.S., Breakfield, N., Gehring, J., McDonald, M., Malfatti, S., Glavina del Rio, T., Jones, C.D., Tringe, S.G., et al. (2015). Salicylic acid modulates colonization of the root microbiome by specific bacterial taxa. *Science* 349, 860–864.
- Li, L., Li, M., Yu, L., Zhou, Z., Liang, X., Liu, Z., Cai, G., Gao, L., Zhang, X., Wang, Y., et al. (2014). The FLS2-Associated Kinase BIK1 Directly Phosphorylates the NADPH Oxidase RbohD to Control Plant Immunity. *Cell Host Microbe* 15, 329–338.
- Liu, Y., and Zhang, S. (2004). Phosphorylation of 1-aminocyclopropane-1-carboxylic acid synthase by MPK6, a stress-responsive mitogen-activated protein kinase, induces ethylene biosynthesis in Arabidopsis. *Plant Cell* 16, 3386–3399.
- Liu, Y., Schiff, M., Czymmek, K., Talloczy, Z., Levine, B., and Dinesh-Kumar, S. (2005). Autophagy regulates programmed cell death during the plant innate immune response. *Cell* 121, 567–577.
- Loake, G., and Grant, M. (2007). Salicylic acid in plant defence—the players and protagonists. *Curr. Opin. Plant Biol.* 10, 466–472.
- van Loon, L.C., Rep, M., and Pieterse, C.M.J. (2006). Significance of inducible defense-related proteins in infected plants. *Annu. Rev. Phytopathol.* 44, 135–162.
- Lorenzo, O., Piqueras, R., Sanchez-Serrano, J., and Solano, R. (2003). ETHYLENE RESPONSE FACTOR1 integrates signals from ethylene and jasmonate pathways in plant defense. *Plant Cell* 15, 165–178.
- Lorenzo, O., Chico, J., Sanchez-Serrano, J., and Solano, R. (2004). Jasmonate-insensitive1 encodes a MYC transcription factor essential to discriminate

- between different jasmonate-regulated defense responses in *Arabidopsis*. *Plant Cell* *16*, 1938–1950.
- Lu, D., Wu, S., Gao, X., Zhang, Y., Shan, L., and He, P. (2010). A receptor-like cytoplasmic kinase, BIK1, associates with a flagellin receptor complex to initiate plant innate immunity. *Proc. Natl. Acad. Sci. U. S. A.* *107*, 496–501.
- Lundberg, D.S., Lebeis, S.L., Paredes, S.H., Yourstone, S., Gehring, J., Malfatti, S., Tremblay, J., Engelbrekton, A., Kunin, V., Rio, T.G. del, et al. (2012). Defining the core *Arabidopsis thaliana* root microbiome. *Nature* *488*, 86–90.
- Melotto, M., Underwood, W., Koczan, J., Nomura, K., and He, S.Y. (2006). Plant stomata function in innate immunity against bacterial invasion. *Cell* *126*, 969–980.
- Mendes, R., Kruijt, M., de Bruijn, I., Dekkers, E., van der Voort, M., Schneider, J.H.M., Piceno, Y.M., DeSantis, T.Z., Andersen, G.L., Bakker, P.A.H.M., et al. (2011). Deciphering the Rhizosphere Microbiome for Disease-Suppressive Bacteria. *Science* *332*, 1097–1100.
- Mendes, R., Garbeva, P., and Raaijmakers, J.M. (2013). The rhizosphere microbiome: significance of plant beneficial, plant pathogenic, and human pathogenic microorganisms. *FEMS Microbiol. Rev.* *37*, 634–663.
- Meng, X., and Zhang, S. (2013). MAPK Cascades in Plant Disease Resistance Signaling. In *ANNUAL REVIEW OF PHYTOPATHOLOGY, VOL 51*, VanAlfen, NK, ed. pp. 245–266.
- Meyers, B.C., Kozik, A., Griego, A., Kuang, H., and Michelmore, R.W. (2003). Genome-Wide Analysis of NBS-LRR-Encoding Genes in *Arabidopsis*. *Plant Cell* *15*, 809–834.
- Michelmore, R., Coaker, G., Bart, R., Beattie, G., Bent, A., Bruce, T., Cameron, D., Dangl, J., Dinesh-Kumar, S., Edwards, R., et al. (2017). Foundational and Translational Research Opportunities to Improve Plant Health. *Mol. Plant. Microbe Interact.* *30*, 515–516.
- Mittler, R. (2002). Oxidative stress, antioxidants and stress tolerance. *Trends Plant Sci.* *7*, 405–410.
- Miya, A., Albert, P., Shinya, T., Desaki, Y., Ichimura, K., Shirasu, K., Narusaka, Y., Kawakami, N., Kaku, H., and Shibuya, N. (2007). CERK1, a LysM receptor kinase, is essential for chitin elicitor signaling in *Arabidopsis*. *Proc. Natl. Acad. Sci. U. S. A.* *104*, 19613–19618.
- Mou, Z., Fan, W., and Dong, X. (2003). Inducers of Plant Systemic Acquired Resistance Regulate NPR1 Function through Redox Changes. *Cell* *113*, 935–944.
- Mousavi, S.A.R., Chauvin, A., Pascaud, F., Kellenberger, S., and Farmer, E.E. (2013). GLUTAMATE RECEPTOR-LIKE genes mediate leaf-to-leaf wound signalling. *Nature* *500*, 422–426.
- Mukhtar, M.S., Carvunis, A.-R., Dreze, M., Epple, P., Steinbrenner, J., Moore, J., Tasan, M., Galli, M., Hao, T., Nishimura, M.T., et al. (2011). Independently Evolved Virulence Effectors Converge onto Hubs in a Plant Immune System Network. *Science* *333*, 596–601.
- Mysore, K., and Ryu, C. (2004). Nonhost resistance: how much do we know? *Trends Plant Sci.* *9*, 97–104.
- Nakagami, H., Pitzschke, A., and Hirt, H. (2005). Emerging MAP kinase pathways in plant stress signalling. *Trends Plant Sci.* *10*, 339–346.
- Nakano, T., Suzuki, K., Fujimura, T., and Shinshi, H. (2006). Genome-wide analysis of the ERF gene family in *Arabidopsis* and rice. *Plant Physiol.* *140*, 411–432.
- Nakashita, H., Yasuda, M., Nitta, T., Asami, T., Fujioka, S., Arai, Y., Sekimata, K., Takatsuto, S., Yamaguchi, I., and Yoshida, S. (2003). Brassinosteroid functions in a broad range of disease resistance in tobacco and rice. *Plant J.* *33*, 887–898.
- Navarro, L., Dunoyer, P., Jay, F., Arnold, B., Dharmasiri, N., Estelle, M., Voinnet, O., and Jones, J.D.G. (2006). A Plant miRNA Contributes to Antibacterial Resistance by Repressing Auxin Signaling. *Science* *312*, 436–439.
- Noctor, G., Reichheld, J.-P., and Foyer, C.H. (2018). ROS-related redox regulation and signaling in plants. *Semin. Cell Dev. Biol.* *80*, 3–12.

- Nurnberger, T., and Brunner, F. (2002). Innate immunity in plants and animals: emerging parallels between the recognition of general elicitors and pathogen-associated molecular patterns. *Curr. Opin. Plant Biol.* *5*, 318–324.
- Nurnberger, T., Brunner, F., Kemmerling, B., and Piater, L. (2004). Innate immunity in plants and animals: striking similarities and obvious differences. *Immunol. Rev.* *198*, 249–266.
- Oldroyd, G.E.D. (2013). Speak, friend and enter: signalling systems that promote beneficial symbiotic associations in plants. *Nat. Rev. Microbiol.* *11*, 252–263.
- Pan, Q., Wendel, J., and Fluhr, R. (2000). Divergent evolution of plant NBS-LRR resistance gene homologues in dicot and cereal genomes. *J. Mol. Evol.* *50*, 203–213.
- Parisi, K., Shafee, T.M.A., Quimbar, P., van der Weerden, N.L., Bleackley, M.R., and Anderson, M.A. (2019). The evolution, function and mechanisms of action for plant defensins. *Semin. Cell Dev. Biol.* *88*, 107–118.
- Pauwels, L., Barbero, G.F., Geerinck, J., Tilleman, S., Grunewald, W., Pérez, A.C., Chico, J.M., Bossche, R.V., Sewell, J., Gil, E., et al. (2010). NINJA connects the co-repressor TOPLESS to jasmonate signalling. *Nature* *464*, 788–791.
- Perez-Jaramillo, J.E., Mendes, R., and Raaijmakers, J.M. (2016). Impact of plant domestication on rhizosphere microbiome assembly and functions. *Plant Mol. Biol.* *90*, 635–644.
- Petre, B. (2020). Toward the Discovery of Host-Defense Peptides in Plants. *Front. Immunol.* *11*, 1825.
- Philippot, L., Raaijmakers, J.M., Lemanceau, P., and van der Putten, W.H. (2013). Going back to the roots: the microbial ecology of the rhizosphere. *Nat. Rev. Microbiol.* *11*, 789–799.
- Pieterse, C.M.J., Leon-Reyes, A., Van der Ent, S., and Van Wees, S.C.M. (2009). Networking by small-molecule hormones in plant immunity. *Nat. Chem. Biol.* *5*, 308–316.
- Pieterse, C.M.J., Van der Does, D., Zamioudis, C., Leon-Reyes, A., and Van Wees, S.C.M. (2012). Hormonal Modulation of Plant Immunity. *Annu. Rev. Cell Dev. Biol.* *28*, 489–521.
- Pieterse, C.M.J., Zamioudis, C., Berendsen, R.L., Weller, D.M., Van Wees, S.C.M., and Bakker, P.A.H.M. (2014). Induced Systemic Resistance by Beneficial Microbes. *Annu. Rev. Phytopathol.* *52*, 347–375.
- Qi, T., Song, S., Ren, Q., Wu, D., Huang, H., Chen, Y., Fan, M., Peng, W., Ren, C., and Xie, D. (2011). The Jasmonate-ZIM-Domain Proteins Interact with the WD-Repeat/bHLH/MYB Complexes to Regulate Jasmonate-Mediated Anthocyanin Accumulation and Trichome Initiation in *Arabidopsis thaliana*. *Plant Cell* *23*, 1795–1814.
- Reymond, P., Weber, H., Damond, M., and Farmer, E. (2000). Differential gene expression in response to mechanical wounding and insect feeding in *Arabidopsis*. *Plant Cell* *12*, 707–719.
- Robert-Seilaniantz, A., Grant, M., and Jones, J.D.G. (2011). Hormone Crosstalk in Plant Disease and Defense: More Than Just JASMONATE-SALICYLATE Antagonism. *Annu. Rev. Phytopathol.* *49*, 317–343.
- Rodriguez, M.C.S., Petersen, M., and Mundy, J. (2010). Mitogen-Activated Protein Kinase Signaling in Plants. *Annu. Rev. Plant Biol.* *61*, 621–649.
- Rushton, P.J., Somssich, I.E., Ringler, P., and Shen, Q.J. (2010). WRKY transcription factors. *Trends Plant Sci.* *15*, 247–258.
- Schardl, C.L., Young, C.A., Hesse, U., Amyotte, S.G., Andreeva, K., Calie, P.J., Fleetwood, D.J., Haws, D.C., Moore, N., Oeser, B., et al. (2013). Plant-Symbiotic Fungi as Chemical Engineers: Multi-Genome Analysis of the Clavicipitaceae Reveals Dynamics of Alkaloid Loci. *PLOS Genet.* *9*, e1003323.
- Schenk, P.M., Kazan, K., Wilson, I., Anderson, J.P., Richmond, T., Somerville, S.C., and Manners, J.M. (2000). Coordinated plant defense responses in *Arabidopsis* revealed by microarray analysis. *Proc. Natl. Acad. Sci. U. S. A.* *97*, 11655–11660.
- Schulz, B., and Boyle, C. (2005). The endophytic continuum. *Mycol. Res.* *109*, 661–686.

- Schweizer, F., Fernandez-Calvo, P., Zander, M., Diez-Diaz, M., Fonseca, S., Glauser, G., Lewsey, M.G., Ecker, J.R., Solano, R., and Reymond, P. (2013). Arabidopsis Basic Helix-Loop-Helix Transcription Factors MYC2, MYC3, and MYC4 Regulate Glucosinolate Biosynthesis, Insect Performance, and Feeding Behavior. *Plant Cell* 25, 3117–3132.
- Sewelam, N., Kazan, K., and Schenk, P.M. (2016). Global Plant Stress Signaling: Reactive Oxygen Species at the Cross-Road. *Front. Plant Sci.* 7, 187.
- Sheard, L.B., Tan, X., Mao, H., Withers, J., Ben-Nissan, G., Hinds, T.R., Kobayashi, Y., Hsu, F.-F., Sharon, M., Browse, J., et al. (2010). Jasmonate perception by inositol-phosphate-potentiated COI1-JAZ co-receptor. *Nature* 468, 400–405.
- Smirnoff, N., and Arnaud, D. (2019). Hydrogen peroxide metabolism and functions in plants. *New Phytol.* 1197–1214.
- Stegmann, M., Monaghan, J., Smakowska-Luzan, E., Rovenich, H., Lehner, A., Holton, N., Belkhadir, Y., and Zipfel, C. (2017). The receptor kinase FER is a RALF-regulated scaffold controlling plant immune signaling. *Science* 355, 287–289.
- Sun, Y., Li, L., Macho, A.P., Han, Z., Hu, Z., Zipfel, C., Zhou, J.-M., and Chai, J. (2013). Structural Basis for flg22-Induced Activation of the Arabidopsis FLS2-BAK1 Immune Complex. *Science* 342, 624–628.
- Sunkar, R., Li, Y.-F., and Jagadeeswaran, G. (2012). Functions of microRNAs in plant stress responses. *Trends Plant Sci.* 17, 196–203.
- Tada, Y., Spoel, S.H., Pajerowska-Mukhtar, K., Mou, Z., Song, J., Wang, C., Zuo, J., and Dong, X. (2008). Plant Immunity Requires Conformational Changes of NPR1 via S-Nitrosylation and Thioredoxins. *Science* 321, 952–956.
- Tang, D., Wang, G., and Zhou, J.-M. (2017). Receptor Kinases in Plant-Pathogen Interactions: More Than Pattern Recognition. *Plant Cell* 29, 618–637.
- Thines, B., Katsir, L., Melotto, M., Niu, Y., Mandaokar, A., Liu, G., Nomura, K., He, S.Y., Howe, G.A., and Browse, J. (2007). JAZ repressor proteins are targets of the SCFCO11 complex during jasmonate signalling. *Nature* 448, 661–665.
- Thomma, B., Cammue, B., and Thevissen, K. (2002). Plant defensins. *Planta* 216, 193–202.
- Thordal-Christensen, H. (2003). Fresh insights into processes of nonhost resistance. *Curr. Opin. Plant Biol.* 6, 351–357.
- Torres, M., Dangl, J., and Jones, J. (2002). Arabidopsis gp91(phox) homologues AtrbohD and AtrbohF are required for accumulation of reactive oxygen intermediates in the plant defense response. *Proc. Natl. Acad. Sci. U. S. A.* 99, 517–522.
- Toruno, T.Y., Stergiopoulos, I., and Coaker, G. (2016). Plant-Pathogen Effectors: Cellular Probes Interfering with Plant Defenses in Spatial and Temporal Manners. *Annu. Rev. Phytopathol.* 54, 419–441.
- Toyota, M., Spencer, D., Sawai-Toyota, S., Jiaqi, W., Zhang, T., Koo, A.J., Howe, G.A., and Gilroy, S. (2018). Glutamate triggers long-distance, calcium-based plant defense signaling. *Science* 361, 1112–1115.
- Turlings, T.C.J., and Erb, M. (2018). Tritrophic Interactions Mediated by Herbivore-Induced Plant Volatiles: Mechanisms, Ecological Relevance, and Application Potential. *Annu. Rev. Entomol.* 63, 433–452.
- Tyler, B.M., Tripathy, S., Zhang, X., Dehal, P., Jiang, R.H.Y., Aerts, A., Arredondo, F.D., Baxter, L., Bensasson, D., Beynon, J.L., et al. (2006). *Phytophthora* genome sequences uncover evolutionary origins and mechanisms of pathogenesis. *Science* 313, 1261–1266.
- Van der Does, D., Leon-Reyes, A., Koornneef, A., Van Verk, M.C., Rodenburg, N., Pauwels, L., Goossens, A., Korbes, A.P., Memelink, J., Ritsema, T., et al. (2013). Salicylic Acid Suppresses Jasmonic Acid Signaling Downstream of SCFCO11-JAZ by Targeting GCC Promoter Motifs via Transcription Factor ORA59. *Plant Cell* 25, 744–761.
- Vejan, P., Abdullah, R., Khadiran, T., Ismail, S., and Boyce, A.N. (2016). Role of Plant Growth Promoting Rhizobacteria in Agricultural Sustainability-A Review. *MOLECULES* 21.

- Verma, V., Ravindran, P., and Kumar, P.P. (2016). Plant hormone-mediated regulation of stress responses. *BMC Plant Biol.* *16*, 86.
- Vlot, A.C., Dempsey, D.A., and Klessig, D.F. (2009). Salicylic Acid, a Multifaceted Hormone to Combat Disease. *Annu. Rev. Phytopathol.* *47*, 177–206.
- Walling, L.L. (2000). The myriad plant responses to herbivores. *J. Plant Growth Regul.* *19*, 195–216.
- Wang, C., Deng, P., Chen, L., Wang, X., Ma, H., Hu, W., Yao, N., Feng, Y., Chai, R., Yang, G., et al. (2013). A Wheat WRKY Transcription Factor TaWRKY10 Confers Tolerance to Multiple Abiotic Stresses in Transgenic Tobacco. *PLOS ONE* *8*, e65120.
- Wang, J., Wang, J., Hu, M., Wu, S., Qi, J., Wang, G., Han, Z., Qi, Y., Gao, N., Wang, H.-W., et al. (2019a). Ligand-triggered allosteric ADP release primes a plant NLR complex. *Science* *364*, eaav5868.
- Wang, J., Hu, M., Wang, J., Qi, J., Han, Z., Wang, G., Qi, Y., Wang, H.-W., Zhou, J.-M., and Chai, J. (2019b). Reconstitution and structure of a plant NLR resistosome conferring immunity. *Science* *364*, eaav5870.
- Wang, M., Weiberg, A., Lin, F.-M., Thomma, B.P.H.J., Huang, H.-D., and Jin, H. (2016). Bidirectional cross-kingdom RNAi and fungal uptake of external RNAs confer plant protection. *Nat. Plants* *2*, 16151.
- Wasternack, C., and Hause, B. (2013). Jasmonates: biosynthesis, perception, signal transduction and action in plant stress response, growth and development. An update to the 2007 review in *Annals of Botany*. *Ann. Bot.* *111*, 1021–1058.
- Waszczak, C., Carmody, M., and Kangasjarvi, J. (2018). Reactive Oxygen Species in Plant Signaling. *Annu. Rev. Plant Biol.* *69*, 209–236.
- Weiberg, A., Wang, M., Lin, F.-M., Zhao, H., Zhang, Z., Kaloshian, I., Huang, H.-D., and Jin, H. (2013). Fungal Small RNAs Suppress Plant Immunity by Hijacking Host RNA Interference Pathways. *Science* *342*, 118–123.
- Wiemann, P., Sieber, C.M.K., Von Bargen, K.W., Studt, L., Niehaus, E.-M., Espino, J.J., Huss, K., Michielse, C.B., Albermann, S., Wagner, D., et al. (2013). Deciphering the Cryptic Genome: Genome-wide Analyses of the Rice Pathogen *Fusarium fujikuroi* Reveal Complex Regulation of Secondary Metabolism and Novel Metabolites. *PLOS Pathog.* *9*, e1003475.
- Wildermuth, M., Dewdney, J., Wu, G., and Ausubel, F. (2001). Isochorismate synthase is required to synthesize salicylic acid for plant defence. *Nature* *414*, 562–565.
- Xiong, L., and Yang, Y. (2003). Disease resistance and abiotic stress tolerance in rice are inversely modulated by an abscisic acid-inducible mitogen-activated protein kinase. *Plant Cell* *15*, 745–759.
- Yang, D.-L., Yao, J., Mei, C.-S., Tong, X.-H., Zeng, L.-J., Li, Q., Xiao, L.-T., Sun, T., Li, J., Deng, X.-W., et al. (2012). Plant hormone jasmonate prioritizes defense over growth by interfering with gibberellin signaling cascade. *Proc. Natl. Acad. Sci. U. S. A.* *109*, 1192–1200.
- Yang, J., Kloepper, J.W., and Ryu, C.-M. (2009). Rhizosphere bacteria help plants tolerate abiotic stress. *Trends Plant Sci.* *14*, 1–4.
- You, M., Yue, Z., He, W., Yang, X., Yang, G., Xie, M., Zhan, D., Baxter, S.W., Vasseur, L., Gurr, G.M., et al. (2013). A heterozygous moth genome provides insights into herbivory and detoxification. *Nat. Genet.* *45*, 220–225.
- Zeidler, D., Zähringer, U., Gerber, I., Dubery, I., Hartung, T., Bors, W., Hutzler, P., and Durner, J. (2004). Innate immunity in *Arabidopsis thaliana*: lipopolysaccharides activate nitric oxide synthase (NOS) and induce defense genes. *Proc. Natl. Acad. Sci. U. S. A.* *101*, 15811–15816.
- Zhai, J., Jeong, D.-H., De Paoli, E., Park, S., Rosen, B.D., Li, Y., Gonzalez, A.J., Yan, Z., Kitto, S.L., Grusak, M.A., et al. (2011). MicroRNAs as master regulators of the plant NB-LRR defense gene family via the production of phased, trans-acting siRNAs. *Genes Dev.* *25*, 2540–2553.
- Zhang, J., Li, W., Xiang, T., Liu, Z., Laluk, K., Ding, X., Zou, Y., Gao, M., Zhang, X., Chen, S., et al. (2010). Receptor-like Cytoplasmic Kinases Integrate Signaling from Multiple Plant Immune

Receptors and Are Targeted by a *Pseudomonas syringae* Effector. *Cell Host Microbe* 7, 290–301.

Zhou, W., Lozano-Torres, J.L., Blilou, I., Zhang, X., Zhai, Q., Smant, G., Li, C., and Scheres, B. (2019). A Jasmonate Signaling Network Activates Root Stem Cells and Promotes Regeneration. *Cell* 177, 942–956.

Zipfel, C., and Oldroyd, G.E.D. (2017). Plant signalling in symbiosis and immunity. *Nature* 543, 328–336.

Zipfel, C., Robatzek, S., Navarro, L., Oakeley, E.J., Jones, J.D.G., Felix, G., and Boller, T. (2004). Bacterial disease resistance in *Arabidopsis* through flagellin perception. *Nature* 428, 764–767.

Zipfel, C., Kunze, G., Chinchilla, D., Caniard, A., Jones, J.D.G., Boller, T., and Felix, G. (2006). Perception of the Bacterial PAMP EF-Tu by the Receptor EFR Restricts *Agrobacterium*-Mediated Transformation. *Cell* 125, 749–760.

SUPPLEMENTARY MATERIAL

Figure S1

key word	article type	time period	nb. of publications selected	total nb. of publications selected for each key word & article type pair	total nb. of publications selected	total nb. of non-redundant publications selected
plant immunity	research article	2000-2004	10	40	240	170 HIPPYS
		2005-2009	10			
		2010-2012	6			
		2013-2015	6			
		2016-2017	4			
		2018-2019	2			
plant pathogen	review	[as above]	40	40	240	170 HIPPYS
	research article	[as above]	40			
plant defense	research article	[as above]	40	40	240	170 HIPPYS
	review	[as above]	40			

Figure S1. Schematic overview of the pipeline that identified the 170 HIPPYS.

This Supplementary Figure accompanies [Figure 1](#).

Figure S2

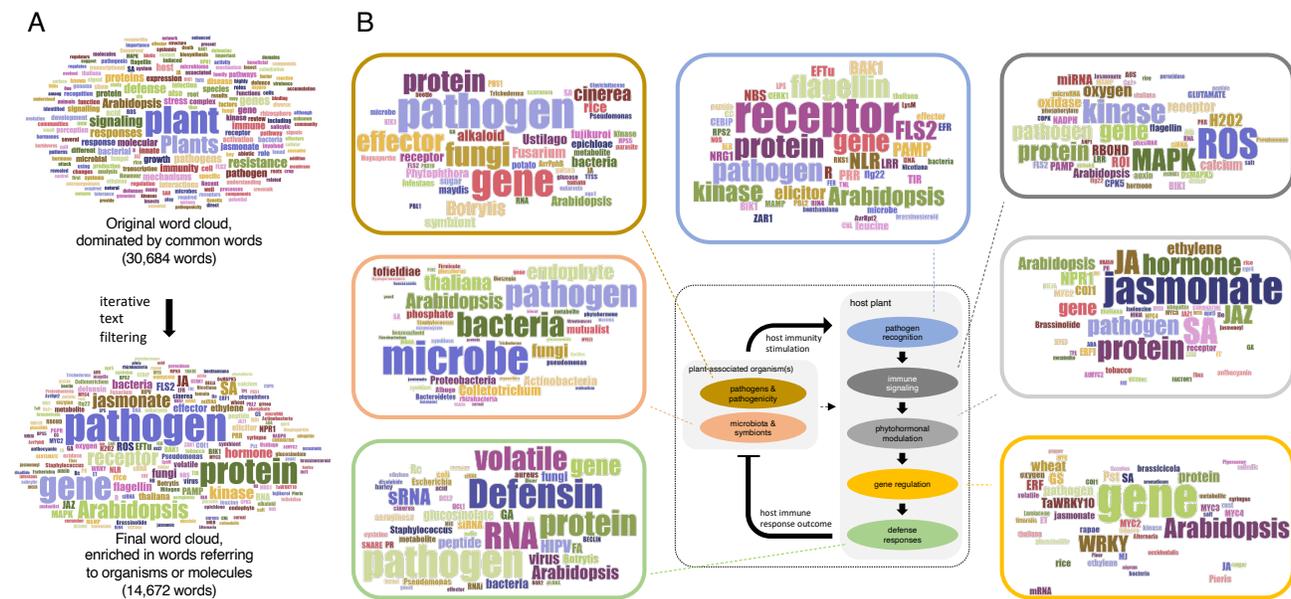
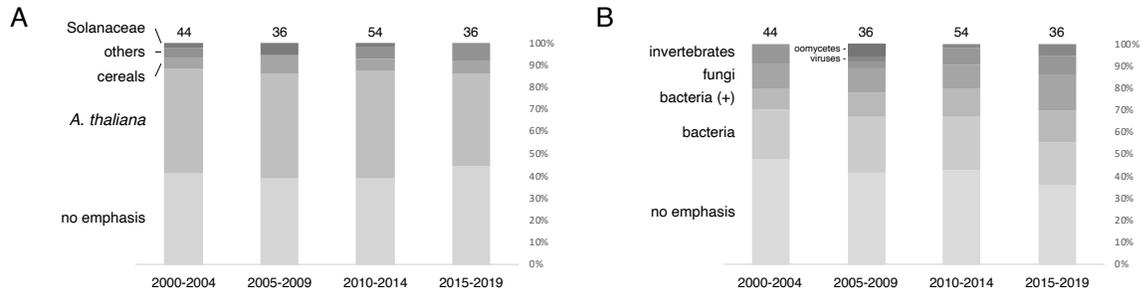


Figure S2. Topics focus on key organisms or molecules

(A) Word cloud built before (upper panel) and after (lower panel) the word filtering process of HIPPYS title and abstract. (B) The central panel shows the simplified conceptual framework of plant immunity shown in [Figure 3B](#), surrounded by seven different word clouds that correspond to the seven topics (the topics 'general review' and 'translational research' were not considered in this analysis). Each surrounding word cloud is lined with the same color code as in [Figure 3](#). Each word cloud comprises 50 words, and was built using a subset of the [Dataset 2](#) that pertains to it (*i.e.* the words extracted from the title and abstracts of the HIPPYS of the topic). This Supplementary Figure accompanies [Figure 4](#). The raw data used to build this Supplementary Figure are available in the [Dataset 1](#) (columns S to V).

**Figure S3**



**Figure S3. HIPPYs investigated well-established model organisms between 2000 and 2019.**

(A) Percent stacked bar charts showing the evolution of the relative proportion of the plant (or groups of plants) investigated by HIPPYs between 2000 and 2019. (B) Percent stacked bar charts showing the evolution of the relative proportion of taxonomic groups of plant-associated species investigated by HIPPYs between 2000 and 2019. For (A) and (B), the numbers above the bars indicate the total number of HIPPYs for each time period. Color code and names are the same as in Figure 4 (see Figure 4 legend for details). This Supplementary Figure accompanies Figure 4. The raw data used to build this Supplementary Figure are available in the Dataset 1 (columns S to V).

Figure S4

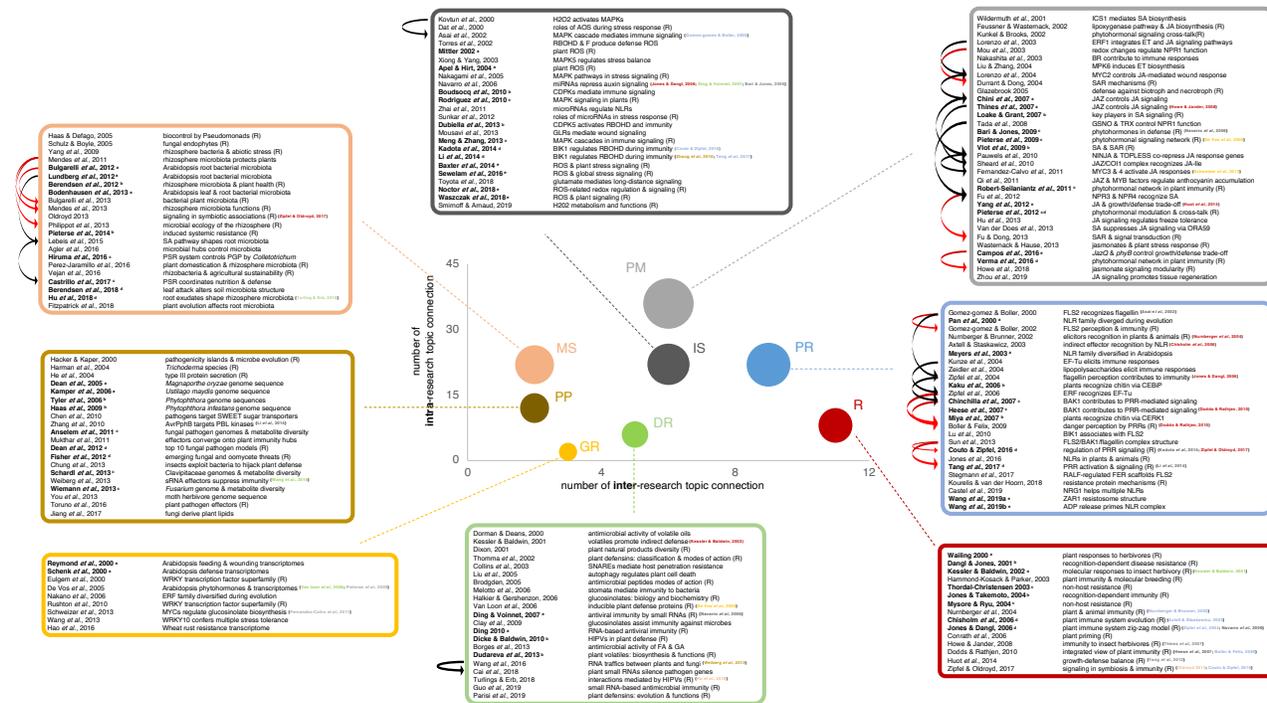
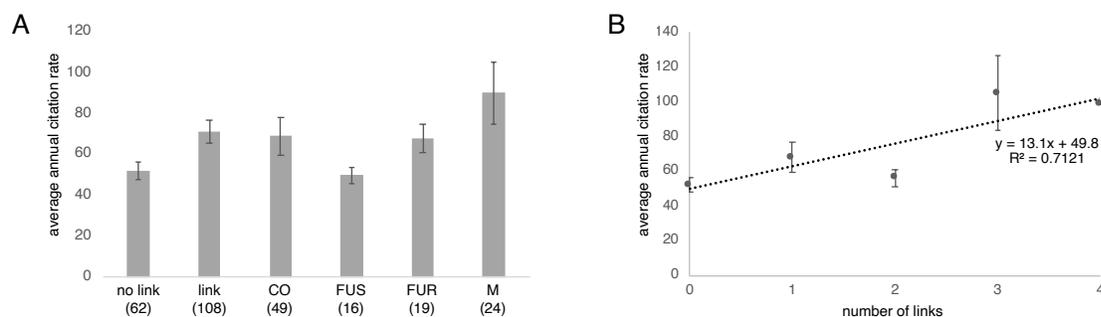


Figure S4. A total of 108 HIPPYs are connected to at least another HIPPY.

The center of the figure shows the bubble chart shown in Figure 5C (see figure legend for details). For each topic, all the HIPPYs that compose the topic are indicated in a corresponding text box lined using the same color code as the bubble chart. Each HIPPY is referred according to the 'name / year' nomenclature, and is accompanied by a short statement that summarizes its content (e.g. Wildermuth *et al.*, 2001; ICS1 mediates SA biosynthesis). Links connecting HIPPYs from different topics are indicated as a reference appearing in superscript after the content statement; the color of the superscript text indicates the topic of the connected HIPPY. Links connecting HIPPYs from the same topic are indicated as black arrows (follow-up study 'FUS' type of link) or red arrows (follow-up review 'FUR' type of link) on the left-hand side of the text boxes, or as bold references with matching superscript letters (coinciding publications 'CO' types of links). FLS2: flagellin sensing 2; NLR: NOD-like receptor; RPS2: resistance to *Pseudomonas syringae* protein 2; AvrRpt2: avirulence protein Rpt2; EF-Tu: elongation factor Tu; CEBip: chitin elicitor-binding protein; ERF: EF-Tu receptor; BAK1: brassinosteroid insensitive 1-associated receptor kinase 1; PRR: pattern-recognition receptor; CERK1: chitin elicitor receptor kinase 1; BIK1: *Botrytis*-induced kinase 1; RAFL: rapid alkalization factor; FER: Feronia; NRG1: N requirement gene 1; ZARI: hopz-activated resistance 1; ADP: adenosine diphosphate; H2O2: hydrogen peroxide; MAPK: mitogen-activated protein kinase; RBOH: respiratory burst oxidase homolog; ROS: reactive oxygen species; CDPK: calcium-dependent protein kinase; GLR: glutamate receptor-like; ICS1: isochlorismate synthase 1; SA: salicylic acid; ERF1: ethylene response factor 1; ET: ethylene; JA: jasmonic acid; NPR1: non-expressor of pathogenesis-related protein 1; BR: brassinosteroid; JAZ: jasmonate zim; GSNO: S-nitrosoglutathione; TRX: thioredoxin; NINJA: novel interactor of JAZ; COI1: coronatine insensitive 1; ORA59: octadecanoid-responsive Arabidopsis AP2/ERF domain protein 59; phyB: phytochrome B; PBL: PBS1-like; PSR: phosphate starvation response; PGP: plant growth promotion; FA: ferulic acid; GA: gallic acid; miRNA: micro RNA; SAR: systemic acquired resistance; AMP: antimicrobial protein. This Supplementary Figure accompanies Figure 5. The raw data used to build this figure are available in the Dataset 1 (columns W to Y).

**Figure S5**



**Supplementary Figure S5. Connected HIPPYs receive more citations.**

(A) Bar chart displaying the average annual citation rate for various groups of connected or not connected HIPPYs. No link: group of 62 HIPPYs that show no connection with another HIPPY; link: group of 108 HIPPYs that are connected to at least another HIPPYs (includes the groups CO, FUS, FUR, and M); CO: group of 49 HIPPYs connected via a 'coinciding publication' type of link; FUS: group of 16 HIPPYs connected via a 'follow-up study' type of link; FUR: group of 19 HIPPYs connected via a 'follow-up review' type of link; M: group of 24 HIPPYs connected via multiple types of links (e.g. FUS and FUR). Error bars: standard error. (B) Scatterplot displaying the average annual citation rate of HIPPYs according to their number of links to another HIPPY (i.e. zero, one, two, three, or four). The dotted line indicates the linear regression; the equation and  $R^2$  are indicated on the graph. Error bar: standard error. This Supplementary Figure accompanies [Figure 5](#). The raw data used to build this Supplementary Figure are available in the [Dataset 1](#) (columns W to Y).

**Table S1. Influential journals that pertain to molecular plant immunity research and associated key words.**

Google Scholar category	Journal	h5-index	number of HIPPYs	relevant section or theme	relevant key words
Plant pathology	Annual Review of Phytopathology	46	8	-	phytopathology
Plant pathology	Phytopathology	43	-	-	phytopathology
Plant pathology	Molecular Plant Pathology	42	2	-	molecular; pathology
Plant pathology	Crop protection	42	-	-	crop; protection
Plant pathology	Molecular Plant-Microbe Interactions	38	2	-	molecular; microbe; interaction
Plant pathology	Plant Disease	36	-	-	pathology

Plant pathology	Plant Pathology	35	-	-	pathology
Plant pathology	European Journal of Plant Pathology	28	-	-	pathology
Plant pathology	The Plant Pathology Journal	33	-	-	pathology
Plant pathology	Physiological and Molecular Plant Pathology	27	-	-	molecular; pathology
Botany	Frontiers in Plant Science	108	1	Plant Pathogen Interactions	pathogen; interaction
Botany	New Phytologist	102	3	Interaction	interaction
Botany	Plant Physiology	85	1	-	
Botany	Journal of Experimental Botany	84	1	Plant-Environment interactions	environment; interaction
Botany	Trends in Plant Sciences	81	10	-	
Botany	Nature plants	79	1	Plant-microbe interactions; disease resistance	microbe; interaction; disease; resistance
Botany	The Plant Cell	79	14	-	
Botany	The Plant Journal	75	1	-	
Botany	Molecular Plant	72	1	Plant-microbe interaction	microbe; interaction
Botany	Current Opinion in Plant Biology	65	4	Biotic interactions	biotic; interaction
Life sciences	Nature	376	24	-	
Life sciences	Science	356	17	-	

Life sciences	Nature communications	273	2	-	
Life sciences	Cell	269	9	-	
Life sciences	Proceedings of the National Academy of Sciences	228	12	-	
Life sciences	Nucleic Acid Research	219	-	-	
Life sciences	Nature Genetics	180	1	-	
Life sciences	Scientific Reports	178	-	-	
Life sciences	PLOS ONE	175	3	-	
Life sciences	Nature Biotechnology	154	-	-	
Microbiology	Frontiers in Microbiology	117	-	Microbe and Virus Interactions with Plants	microbe; virus; interaction
Microbiology	Nature Reviews Microbiology	115	5	-	
Microbiology	The ISME Journal	101	1	-	
Microbiology	mBio	85	-	-	
Microbiology	Antimicrobial Agents and Chemotherapy	83	-	-	
Microbiology	Trends in Microbiology	75	-	-	
Microbiology	Applied Microbiology and Biotechnology	75	-	-	

Microbiology	Journal of Clinical Microbiology	72	-	-	
Microbiology	Environmental Microbiology	71	-	-	
Microbiology	Clinical Microbiology Reviews	70	-	-	

**Table S2. Cross-citation analysis values.**

Topic	Defense response	Gene regulation	Immune signaling	Microbiota & Symbiosis	Pathogen & Pathogenicity	Pathogen recognition	Hormonal modulation
Defense response	0.58	0.08	0.00	0.04	0.05	0.10	0.17
Gene regulation	0.00	0.50	0.09	0.09	0.00	0.00	0.00
Immune signaling	0.17	0.00	1.27	0.01	0.07	0.82	0.41
Microbiota & Symbiosis	0.43	0.00	0.02	1.08	0.16	0.30	0.21
Pathogen & Pathogenicity	0.29	0.17	0.03	0.15	0.37	0.38	0.19
Pathogen recognition	0.23	0.29	0.25	0.21	0.11	2.58	0.22
Hormonal modulation	0.68	0.54	0.25	0.20	0.24	0.67	1.66

Supplementary Table S2 accompanies [Figure 5](#); the raw data used to calculate the values are available in the [Dataset 3](#).

**Dataset 1. Raw dataset including the 170 HIPPYs and main meta data.**

**Dataset 2. Filtered text file of the 170 HIPPYs titles and abstract.**

**Dataset 3. Cross-citation pattern analysis matrix.**

## SUPPLEMENTARY TEXT 1

We grouped HIPPYs into nine main topics ([Figure 3A](#)). The supplementary text below presents a comprehensive analysis of the 170 HIPPYs in the context of their topics and subtopics. We refer readers to the main text and the figure captions to access the fully-spelled acronyms used below, to the [Dataset 1](#) to access raw data information, and to the Zotero web folder 'HIPPY Collection' [https://www.zotero.org/groups/4370831/hippy\\_collection/library](https://www.zotero.org/groups/4370831/hippy_collection/library) to access HIPPY metadata.

### **Pathogen recognition (PR) - how do plants sense pathogens?**

The topic 'pathogen recognition' comprises 25 publications that collectively gathered over 12k citations, and is organized in two subtopics: 'PRR' (17) and 'NLR' (8). This topic comprises 7 reviews and 18 research articles. The seven reviews pertain to the diversity, regulation, and function of NLRs (Jones et al., 2016; Kourelis and van der Hoorn, 2018) or PRRs (Boller and Felix, 2009; Couto and Zipfel, 2016; Gómez-Gómez and Boller, 2002; Nurnberger and Brunner, 2002; Tang et al., 2017). On another hand, the 18 research articles pertain to the subtopics 'PRR' (12) and 'NLR' (6). The six articles focused on NLRs reported on their phylogenetic diversity (Meyers et al., 2003; Pan et al., 2000), on the mechanism of effector indirect recognition (Axtell and Staskawicz, 2003), on the key role of helper NLRs (Castel et al., 2019), or on the structural arrangements and activation mechanisms (Wang et al., 2019a, 2019b). The 12 papers focused on PRRs reported the identification of the chitin receptors CEBip (Kaku et al., 2006) and CERK1 (Miya et al., 2007), the discovery of the bacterial elongation factor Tu (Ef-tu) as an elicitor of plant immunity (Kunze et al., 2004) and then the identification of EF-tu receptor EFR (Zipfel et al., 2006), the identification of the FLS2 locus responsible for Flagellin detection and its importance in plant immunity (Gomez-Gomez and Boller, 2000; Zipfel et al., 2004), the identification of the FLS2 co-receptor BAK1 (Chinchilla et al., 2007), and the structural arrangement of the FLS2-BAK1-flg22 complex (Sun et al., 2013). Three publications focused on the mechanisms of signaling or regulation of PRR-triggered immunity mediated by BAK1, BIK1, of FER (Heese et al., 2007; Lu et al., 2010; Stegmann et al., 2017).

Finally, one article reported the perception of lipopolysaccharides by plants (Zeidler et al., 2004).

### **Immune signaling (IS) - how do plants signal pathogen recognition?**

The topic 'immune signaling' comprises 24 publications that collectively gathered over 22k citations, and is organized in four subtopics: ROS (11), kinases (8), micro-RNAs (3), and glutamate distal signaling (2). This topic comprises 12 reviews and 12 research articles. The 12 reviews pertain to general ROS stress signaling (Apel and Hirt, 2004; Baxter et al., 2014; Dat et al., 2000; Mittler, 2002; Noctor et al., 2018; Sewelam et al., 2016; Smirnov and Arnaud, 2019; Waszczak et al., 2018), MAPK cascades in plant immunity (Meng and Zhang, 2013; Nakagami et al., 2005; Rodriguez et al., 2010), or micro-RNA functions in stress signaling (Sunkar et al., 2012). On another hand, the 12 research articles pertain to the subtopics 'kinases' (5), 'ROS' (3), 'glutamate distal signaling' (2), or 'micro-RNAs' (2). Five articles focused on kinases and reported that CDPKs (Boudsocq et al., 2010; Dubiella et al., 2013) and MAPKs (Asai et al., 2002) mediate immune signaling, that H<sub>2</sub>O<sub>2</sub> activates MAPK (Kovtun et al., 2000), or that rice MAPK5 balances abiotic/biotic stress signaling (Xiong and Yang, 2003). Three papers reported that RBOHD and RBOHF mediate ROS accumulation during defense responses (Torres et al., 2002) or that BIK1 regulates RBOHD (Kadota et al., 2014; Li et al., 2014). Two papers showed that GRLs (Mousavi et al., 2013) and glutamate (Toyota et al., 2018) trigger long-distance immune signaling. Finally, two papers reported that micro-RNAs negatively control NLR expression (Zhai et al., 2011) or auxin signaling (Navarro et al., 2006).

### **Phytohormonal modulation (PM) - how do hormones modulate immune signaling?**

The topic 'phytohormonal modulation' comprises 33 publications that collectively gathered over 23k citations, and is organized in three subtopics: 'JA' (15), 'SA & SAR' (8), and 'JA-SA cross-talk, other hormones' (10). This topic comprises 14 reviews and 19 research articles. The 14 reviews pertain to the biosynthesis and function of jasmonates & JA (Feussner and Wasternack, 2002; Howe et al., 2018; Wasternack and Hause, 2013), the biosynthesis and function of SA and particularly its role in SAR (Durrant and Dong, 2004; Fu and Dong, 2013;

Loake and Grant, 2007; Vlot et al., 2009), as well as the cross-talk between hormones and especially between JA & SA (Bari and Jones, 2009; Glazebrook, 2005; Kunkel and Brooks, 2002; Pieterse et al., 2009, 2012; Robert-Seilaniantz et al., 2011; Verma et al., 2016). On another hand, the 19 research articles pertain to the subtopics 'JA' (9), 'SA & SAR' (4) and 'JA-SA cross-talk, other hormones' (3). Seven publications identified and characterized key molecular players in the JA signaling pathways : JAZ as the master regulator of the JA pathway by back-to-back publications (Chini et al., 2007; Thines et al., 2007), JAZ co-repressors TOPLESS/TPR (Pauwels et al., 2010), JAZ co-receptor complex with COI for jasmonate recognition (Sheard et al., 2010), and MYC & ERF1 transcription factors (Fernandez-Calvo et al., 2011; Lorenzo et al., 2003, 2004). Five other papers reported the broader role of JA in defense/growth trade-off (Campos et al., 2016; Yang et al., 2012), freezing tolerance (Hu et al., 2013), cell regeneration (Zhou et al., 2019), and anthocyanin accumulation (Qi et al., 2011). Four articles reported on the mechanism of SA biosynthesis (Wildermuth et al., 2001), NPR1 activation via redox and conformational changes (Mou et al., 2003; Tada et al., 2008), and NPR1 regulation via its degradation (Fu et al., 2012). Finally, three papers reported findings that pertain to the molecular regulation of the JA-SA antagonism (Van der Does et al., 2013), the biosynthesis of ET via MAPK6 (Liu and Zhang, 2004), and the role of brassinosteroid in immunity (Nakashita et al., 2003).

### **Gene regulation (GR) - what is the genetic program of defense, and how is it activated?**

The topic 'gene regulation' comprises nine publications that collectively gathered over 6k citations, and is organized in three subtopics: two subtopics: 'TF' (5), and 'transcriptomics' (4). This topic comprises two reviews and seven research articles. The two reviews pertain to the WRKY family of transcription factors (Eulgem et al., 2000; Rushton et al., 2010). On another hand, the seven research articles pertain to the subtopics 'TF' (3) and 'transcriptomics' (4). Three papers focused on transcription factors, and reported on the diversity of ERFs in Arabidopsis and rice (Nakano et al., 2006), on the role of MYCs against herbivores (Schweizer et al., 2013), and on the role of WRKYs during abiotic stress (Wang et al., 2013). Three

papers described multiple defense genetic programs of *A. thaliana* using microarrays analyses (De Vos et al., 2005; Reymond et al., 2000; Schenk et al., 2000), and one described the defense genetic program of wheat against a rust pathogen (Hao et al., 2016).

### **Defense responses (DR) - how do plants effectively fend off pathogens?**

The topic 'defense responses' comprises 21 publications that collectively gathered over 16k citations, and is organized in four subtopics: 'natural products' (9), 'small RNA' (5), 'AMPs' (4), and 'cellular responses' (3). This topic comprises 12 reviews and 9 research articles. A first set of four reviews addressed the diversity and functions of eukaryotic AMPs (Brogden, 2005), plant AMPs (van Loon et al., 2006), and plant defensins (Parisi et al., 2019; Thomma et al., 2002). A second set of five reviews focused on antimicrobial natural products (Dixon, 2001; Halkier and Gershenzon, 2006) and plant volatiles (Dicke and Baldwin, 2010; Dudareva et al., 2013; Turlings and Erb, 2018). Finally, a third set of three review addressed small-RNA based immunity against viruses (Ding, 2010; Ding and Voinnet, 2007) or bacteria (Guo et al., 2019). On another hand, the nine research articles pertain to the subtopics 'natural products' (4), 'cellular responses' (3), and 'small RNAs' (2). Those papers reported on the antimicrobial activity - or role in plant immunity - of specific compounds (Borges et al., 2013; Clay et al., 2009; Dorman and Deans, 2000; Kessler and Baldwin, 2002), on specific cellular responses that restrict the penetration or spread of pathogens (Collins et al., 2003; Liu et al., 2005; Melotto et al., 2006), or on cross-kingdom RNA interference (Cai et al., 2018; Wang et al., 2016).

### **Pathogens & pathogenicity (PP) - how do pathogens manipulate and colonize host plants?**

The topic 'pathogens & pathogenicity' comprises 20 publications that collectively gathered over 11k citations, and is organized in three subtopics: 'pathogen genomics' (9), 'host modulation' (8), and 'fungal pathogen' (3). This topic comprises 6 reviews and 14 research articles. A set of three reviews focused on specific groups of fungal species, discussed as plant symbionts (Harman et al., 2004), model pathogens in molecular plant

pathology (Dean et al., 2012) or emerging pathogens (Fisher et al., 2012). The three other reviews dealt with the function (He et al., 2004; Toruno et al., 2016) or genomic organization (Hacker and Kaper, 2000) of pathogenicity determinants. On another hand, the 14 research articles pertain to the subtopics 'pathogenomics' (8) and 'host modulation' (6). The eight papers from the pathogenomics subtopic reported the deciphering of the genome sequences of ascomycete fungi (Amselem et al., 2011; Dean et al., 2005; Schardl et al., 2013; Wiemann et al., 2013), of the basidiomycete fungus *Ustilago maydis* (Kaemper et al., 2006), of *Phytophthora* (oomycetes) species (Haas et al., 2009; Tyler et al., 2006), or of a herbivorous moth (You et al., 2013). Three papers reported on pathogen effector proteins that target hub within the plant immune system (Mukhtar et al., 2011; Zhang et al., 2010) or modulate host sugar transporter expression (Chen et al., 2010). Two papers showed that insects suppress plant defenses by exploiting bacteria (Chung et al., 2013), whereas fungi do so by using small RNAs (Weiberg et al., 2013). Finally, one paper reported that fungi recruit plant fatty acid biosynthesis program for host colonization (Jiang et al., 2017).

### **Microbiota & symbionts (MM) - how do plants and their associated microbes interact?**

The topic 'microbiota & symbionts' comprises 22 publications that collectively gathered over 10k citations, and is organized in three subtopics: 'host influence on microbiota' (11), 'microbiota influence on host' (6), and 'focused reviews' (5). This topic comprises 11 reviews and 11 research articles. The 11 reviews address broad microbiota & symbiont-related topics (Bulgarelli et al., 2013; Mendes et al., 2013; Oldroyd, 2013; Philippot et al., 2013; Schulz and Boyle, 2005), the rhizosphere microbiome (Berendsen et al., 2012; Perez-Jaramillo et al., 2016), or the influence and use of microbiota and beneficial microbes to protect host plants (Haas and Defago, 2005; Pieterse et al., 2014; Vejan et al., 2016; Yang et al., 2009). On another hand, the 11 research articles pertain to the subtopics 'host influence on microbiota' (9) and 'microbiota influence on host' (2). Those papers describe how the microbiota protects plants (Mendes et al., 2011), the composition of the bacterial microbiome of *A. thaliana* (Bodenhausen et al., 2013; Bulgarelli et al., 2012; Lundberg et al., 2012), and how host

molecules, host physiological status, and host diversity influence and shape root microbiota (Aglar et al., 2016; Berendsen et al., 2018; Castrillo et al., 2017; Fitzpatrick et al., 2018; Hiruma et al., 2016; Hu et al., 2018; Lebeis et al., 2015).

### **General reviews (GR) - how do we conceptually understand plant immunity as a whole?**

The topic 'general reviews' comprises 15 publications (all reviews) that collectively gathered over 17k citations, and is organized in five subtopics: 'elicitor-receptor-effector' (7), 'immunity vs. herbivore' (3), 'non-host resistance' (2), 'trade-offs' (2), and 'priming' (1). Seven papers addressed the molecular interplay between pathogen elicitors and effectors on one side and plant immune receptors on the other side, and simultaneously proposed conceptual models focused on the plant immune system (Chisholm et al., 2006; Dangl and Jones, 2001; Dodds and Rathjen, 2010; Jones and Dangl, 2006), comparative analyses with the animal immune system (Jones and Takemoto, 2004; Nurnberger et al., 2004), or perspectives for molecular resistance breeding (Hammond-Kosack and Parker, 2003). Three papers addressed the signaling pathways triggered by herbivores as well as the roles of plant volatile compounds (Howe and Jander, 2008; Kessler and Baldwin, 2002; Walling, 2000). Finally, five papers discussed the phenomenon of non-host resistance (Mysore and Ryu, 2004; Thordal-Christensen, 2003), the balance between defense and growth (Huot et al., 2014) or between the accommodation of symbionts and the defense against pathogens (Zipfel and Oldroyd, 2017), or the induction of resistance (aka priming) (Conrath et al., 2006).

### **Translational research (TR) - how to leverage academic knowledge to improve agriculture?**

This topic comprises a single research article that gathered >150 citations, and that reports the development of virus-resistant cucumber using the CRISPR/Cas9 technology (Chandrasekaran et al., 2016).

## **SUPPLEMENTARY METHODS**

### **A. Identification of the 170 highly-influential publications in plant immunity (HIPPYs)**

We identified and retrieved HIPPYs by using a seven-step pipeline that relied on the Web of Science website and the Zotero software. We first performed a publication search using the 'basic search' tool ('Topic' parameter, key words 'plant immunity') on the Web of Science website (step 1). We then selected 'article' in the 'document type' section (to select only research articles), and defined seven periods based on publication years (2000-2004; 2005-2009; 2010-2012; 2013-2015; 2016-2017; 2018; 2019) using the 'publication years' section (step 2). As a note, we used time periods (7) rather than individual years (20) to accelerate the whole pipeline of data acquisition; we also designed the size of the periods to ensure the identification of highly-cited articles throughout all the twenty years considered in this analysis. For each of these seven periods, we proceeded as follow. We sorted the research output (*i.e.* the list of publications) according to the number of times they were cited, using the 'time cited: highest to lowest' tool (step 3). We then selected the most cited publications in the list, considering two publications per years comprised in the period (*e.g.* we selected 10 publications for the period 2000-2004, but only 2 publications for the period 2019; step 4). While doing so, we systematically examined the title and abstract of the publication, to manually disregard those that did not pertain to plant immunity. Doing so excluded approximately 50 papers, that pertained to the biomedical field (*e.g.* papers not addressing plants or plant-associated organisms), to strict plant biology (*e.g.* genome analyses, cell signaling & development), or to non-molecular plant immunity (*e.g.* ecology, modeling, epidemiology). We then gathered the publication selection using the 'Marked List' tool and exported all the metadata of the publications (*e.g.* title, abstract, author list, journal, ...) using the 'export to EndNote Desktop' tool of the 'Marked list' section (step 5). We imported the metadata into Zotero, into a folder with an explicit name that informs about the search criteria used (*e.g.* 'plant immunity-article-2000-2004'; step 6). Finally, for each publication we retrieved the main text and supplementary files using either the 'Find available PDFs' tool implemented in Zotero or other search engines and databases (step 7).

We identified review articles HIPPYs by repeating the same seven-step procedure detailed above, but with selecting 'review' instead of 'article' during step 2 (to select only review articles). To further complete the initial collection of 80 publications (40

research articles and 40 reviews - see above), we repeated the full pipeline described above; first using the key words 'plant pathogen', and then using the key words 'plant defense' during step 1. After these two additional searches, we retained the novel publications (90) and disregarded the redundant ones (70; *i.e.* publications that were already identified using previous searches with different key words). Thus, in total, we identified and collected 170 publications (90 research articles & 80 review articles; referred to as HIPPYs in the present article). We archived the publication metadata in a public Zotero web folder named 'HIPPY Collection, according to the search criteria used to identify them ([https://www.zotero.org/groups/4370831/hippy\\_collection/library](https://www.zotero.org/groups/4370831/hippy_collection/library)) as well as in the [Dataset 1](#).

## **B. Identification of the countries, institutions, journals, and cities that published HIPPYs**

To identify the countries, institutions, journals, and cities that published the HIPPYs, we compiled specific publication metadata, such as journal, corresponding author(s), and for each corresponding author, their first mentioned affiliation (*i.e.* institution of the corresponding authors), and the city and country where the institution is based ([Dataset 1](#) - columns I to N). We considered all the indicated corresponding authors (for HIPPYs with multiple corresponding authors) or all the authors (in the rare cases when we could not identify an explicit corresponding author). We defined city clusters as a group of cities close enough to each other to constitute a single employment and living area. For each country, institution, and journal, we calculated the total number of publications and citations. The world map was created using the mapchart.net website (<https://mapchart.net/>), and then customized using Microsoft PowerPoint.

## **C. Categorization of publications into topics and subtopics**

To group HIPPYs according to the research topic they pertain to, we performed an iterative analytical reading of the publications. Throughout this process, we tagged the HIPPYs with key words, and refined these key words iteratively, and then used these key words to group the HIPPYs into topics and subtopics ([Dataset 1](#) - columns O to R). A

handful of HIPPYs could have been assigned to more than one topic; such HIPPYs are indicated in [Dataset 1](#) (column Q). We created a new subfolder named 'TOPICS' in the Zotero web folder, which archives the HIPPYs according to their topic and subtopic. To evaluate the temporal distribution of the HIPPYs within each topic, we quantified their number in four five-year periods: 2000-2004, 2005-2009, 2010-2014, and 2015-2019.

#### **D. Data analysis, charts generation, and building of word clouds**

We built and analyzed matrix datasets using Microsoft Excel. We built and modified text files using BBEdit or Notepad++. We built pie charts and bar charts using Microsoft Excel, then exported them into Microsoft PowerPoint for figure preparation. We generated word clouds using the online Jason Davies Word Cloud Generator (<https://www.jasondavies.com/wordcloud/>), with the following parameters: Archimedean spiral, horizontal orientation (0° to 0°), n scale, and 200 words (50 words for the topic-specific word clouds). We imported title and abstract text from Zotero metadata into a Microsoft Excel spreadsheet ([Dataset 1](#) - columns S & T), and then imported the text into a text file. We filtered the text files using the 'find' and 'replace all' tools implemented in Text Wrangler. We first replaced punctuation elements by spaces, replaced plurals by singulars (e.g. replace 'pathogens' by 'pathogen'), and then used an iterative process (>25 iterations) of 'find & replace' targeted at common words followed by word cloud generation until we obtained a word cloud containing only words referring to specific organisms & molecules (or groups of organisms and molecules). That whole process allowed to removed almost half of the words in total, moving from 30,684 words in the unfiltered text file (i.e. all the words from the HIPPY titles and abstracts) to 14,672 words in the filtered text file ([Dataset 2](#)). Final word clouds were exported as images and stored in PowerPoint slides. We quantified the most frequent words using the search tool in Text Wrangler, and archived the obtained values in an Excel spreadsheet.

#### **E. HIPPY connectivity analysis**

We analyzed how HIPPYs connect to each other by expert reading of the articles and their metadata, combined with HIPPY expert association ([Dataset](#)

[1](#) - columns W to Y). We considered that HIPPYs can connect via three types of links. Firstly, coincidental publication (CO) type of link connects two or more HIPPYs of the same article type that report similar findings or concepts (e.g. concomitant reviews on similar topics, back-to-back papers, competing research articles reporting similar findings). For instance, two 'CO' HIPPYs reported the discovery of BAK1 as a PRR co-receptor (Chinchilla et al., 2007; Heese et al., 2007). Secondly, the follow-up study (FUS) type of link connects two research articles co-signed by an overlapping set of authors and that sequentially report coherent findings. For instance, a pair of HIPPYs reported EF-Tu as a PAMP and then later the identification of its receptor (Kunze et al., 2004; Zipfel et al., 2006). Thirdly, the follow-up review (FUR) type of link connects two HIPPYs (at least one research article and a post-published review) co-signed by an overlapping set of authors and that pertain to a coherent body of knowledge. For instance, a pair of HIPPYs identified NPR3 & NPR4 as SA receptors and later contextualized this finding in a review (Fu et al., 2012; Fu and Dong, 2013). Finally, the multiple (M) type of link pertains to multi-connected HIPPYs (i.e. HIPPYs being connected to other HIPPYs via at least two different types of links). For each HIPPY, we noted the type of link (if any), the number of links to other HIPPYs, and whether the connected HIPPYs belonged to the same topic or not. We arbitrarily set up the maximal gap between connected HIPPYs to four years (i.e. two connected HIPPYs cannot show a gap superior to four years between their publication years).

#### **F. Cross-citation pattern analysis**

To perform a cross-citation pattern analysis, we followed a pipeline previously described (Petre, 2020). Briefly, we first considered the 80 HIPPY that are review articles and the matching 78 corresponding authors (hereafter influential authors). We then build a matrix of review articles (80 lines) x corresponding authors (78 columns), arranged according to their topic ([Dataset 3](#)). The topics 'translational research' and general review were not considered for this analysis. In the matrix, the number at each intersection indicates the number of times the name of a given author appears in the reference section of a given review article (i.e. a proxy for the number of times the author is cited by the review article). We obtained these numbers

by screening articles with the key word search tool in Zotero, and by manually inspecting the reference section of each article with a positive hit in the key word search. Self-citations were reported in the matrix between brackets, and were not further considered. We calculated a citation score for each of the 49 topic intersections (i.e. 7 x 7) by calculating the average of the values displayed in the corresponding matrix area divided by the total number of single intersections in the area. These 49 values were used to build a bubble table chart, in which the values correlate with the diameter of the bubbles, so that the diameter of the bubbles positively correlates with citation scores.